The role of fetal magnetic resonance imaging in the diagnosis and management of congenital anomalies of the fetal body

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Thesis submitted in fulfilment of the requirements
for the degree of Doctor of Philosophy

April 2025

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Division of Clinical Medicine
School of Medicine and Population Health

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I. Acknowledgements

First and foremost, I would like to thank my supervisor Dr Elspeth Whitby, without whom this research would not have been possible. I will be eternally grateful for her guidance, experience and support throughout the entire process. I would also like to thank Professor Kate Reed and Dr Ashok Raghavan for their expertise and collaboration on individual chapters of this thesis.

To all the radiography staff within the MRI department at Sheffield Teaching Hospitals, and my colleagues at the University of Sheffield. I would like to thank you for making me feel so welcome and supported.

To the families who consented for their information and images to be used in this research, especially those who took part in the interviews, I cannot thank you enough. Your stories provided valuable insights into the patient journey following the diagnosis of a fetal anomaly and I have great respect for your incredible strength and courage.

There are many healthcare professionals who took time out from their busy schedules to provide their expertise and individual views, both in the gradings and qualitative interviews, for which I am very grateful.

Finally, to my family. Thank you for all the love and help along the way. To my husband Jonathan, I cannot express enough gratitude for your encouragement, kindness and unwavering support over the past three years.

II. Abstract

Objectives - This thesis studies fetal magnetic resonance imaging as a diagnostic tool in addition to ultrasound in congenital anomalies of the fetal body.
The aims were to assess the overall diagnostic accuracy, examine its role in diagnosis and prognostication of specific anomalies and assess patient experience during fetal MRI and professional opinions on its utility.

Methods - Retrospective and prospective recruitment of patients referred for a fetal MRI due to concerns of a fetal body anomaly on ultrasound. Ultrasound and MRI findings were correlated with pregnancy outcome and final diagnosis made by imaging, surgery or postmortem. Expert panel reviews were conducted to assess the value of the MRI information.
We studied the role of fetal MRI in prognostication of congenital diaphragmatic hernia and in diagnosis of tracheo-oesophageal fistula/oesophageal atresia. A case series of neck masses assessed the role of fetal MRI in diagnosis and prediction of postnatal airway compromise.
A qualitative study was undertaken with patients and healthcare professionals to gain insight into the patient experience and the utility of the MRI information for clinical practice.

Results - The diagnostic accuracy study included 242 cases and found fetal MRI has an improved diagnostic accuracy over ultrasound alone of 24.6%.
The qualitative study found patient themes including the misconceptions of antenatal screening, perceptions of MRI and interaction with the MRI image. Professional themes comprised the role of reassurance, how MRI informs clinical practice and multidisciplinary collaboration.

Conclusions - Fetal MRI improves the accuracy of the diagnosis of congenital anomalies of the fetal body when used in addition to ultrasound. It also provides additional information for certain anomalies which can be used for prognostication and management planning.
Fetal MRI is an acceptable investigation for parents and the findings are used by a variety of healthcare professionals with increasing reliance.

III. Abbreviations

AP - Antero-Posterior
BMI - Body Mass Index
BPS - Broncho-Pulmonary Sequestration
CAKUT - Congenital Anomalies of the Kidney and Urinary Tract
CC - Cranio-Caudal
CDH - Congenital Diaphragmatic Hernia
CHAOS - Congenital High Airway Obstruction Syndrome
CHARGE syndrome - Coloboma of the eye, Heart defects, Atresia choanae, Restricted growth, Genital defects, Ear anomalies
CNS - Central Nervous System
CPAM - Congenital Pulmonary Airway Malformation
CT scan - Computed Tomography scan
DWI - Diffusion Weighted Imaging
ECMO - Extracorporeal Membrane Oxygenation
EXIT - Ex Utero Intrapartum Treatment
FETO - Fetoscopic Endoluminal Tracheal Occlusion
FIESTA - Fast Imaging Employing Steady-state Acquisition
FMU - Fetal Medicine Unit
GI - Gastrointestinal
GU - Genito-Urinary
HASTE - Half-Fourier Acquisition Single-shot Turbo spin-Echo
HLH - Haemophagocytic Lympho-Histiocytosis
IRAS - Integrated Research Application System
ISSVA - International Society for the Study of Vascular Anomalies
iuMRI - in utero Magnetic Resonance Imaging
LHR - Lung-to-Head Ratio
MCDK - Multicystic Dysplastic Kidney
MDT - Multidisciplinary Team
ML - Medio-Lateral
MRI - Magnetic Resonance Imaging
MSK - Musculoskeletal
NHS - National Health Service
NPV - Negative Predictive Value
O/E TLV - Observed-to-Expected Total Lung Volume
PPHN - Persistent Pulmonary Hypertension of the Newborn

PPV - Positive Predictive Value

PRISMA - Preferred Reporting Items for Systematic Reviews and Meta-Analyses

PROSPERO - International Prospective Register of Systematic Reviews

PUJO - Pelvi-Ureteric Junction Obstruction

PUV - Posterior Urethral Values

ROC curve - Receiver Operating Characteristic curve

SSFSE - Single Shot Fast Spin Echo

TOF/OA - Tracheo-Oesophageal Fistula/Oesophageal Atresia

TOP - Termination of Pregnancy

USS - Ultrasound Scan

VACTERL association - Vertebral defects, Anorectal anomalies, Cardiac defects, Tracheo-oesophageal fistula/oesophageal atresia, Renal abnormalities, Limb abnormalities

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Chapter 1 – Introduction to fetal magnetic resonance imaging

This chapter provides an introduction and overview of fetal magnetic resonance imaging, detailing its history and development over time, safety considerations, the advantages and disadvantages in comparison with ultrasound and its current use in clinical practice within the United Kingdom. The second part of this chapter explores the aims and objectives of this research.

Author contributions

This chapter was planned, researched and written by me prior to a final review by Dr Elspeth Whitby.

1.1 Introduction to fetal magnetic resonance imaging

The history of fetal magnetic resonance imaging

The assessment of the fetus during pregnancy in order to diagnose congenital anomalies, monitor growth and ensure wellbeing, has routinely been undertaken with ultrasound since the late 1950s. However, antenatal ultrasound scanning (USS) has some limitations such as a small field of view and operator dependence. As a result of this, fetal magnetic resonance imaging (MRI) has developed as an additional imaging technique. Fetal MRI has been shown to be safe in pregnancy, does not involve radiation and provides detailed images of the anatomical structure of the fetus [1]. In recent years it has become a widely utilised adjunct to ultrasound in pregnancy for the assessment of fetal congenital anomalies [1].

The first report of magnetic resonance imaging being used in pregnancy for fetal assessment was in 1983 [2]. It showed good visualisation of the fetus was possible from 16-18 weeks gestation, with more structural detail seen than with ultrasound. There were issues however, mainly with artefact caused by fetal movement affecting the image quality. These issues were overcome in 1999 when ultrafast MRI sequences were developed, with good quality images generated from over 20 weeks gestation [3].

The safety of fetal magnetic resonance imaging

Fetal MRI is performed in the second or third trimester of pregnancy. This is primarily because before 16 weeks gestation fetal structures are very small and highly affected by movement artefact. In addition, any potential teratogenic effects of MRI have not been confirmed in early pregnancy meaning fetal MRI is best performed after organogenesis which is completed at around 16 weeks [4]. Several studies have shown MRI to be safe during pregnancy however there have been some animal studies which raised the possibility of teratogenicity in early pregnancy [5]. However, as fetal MRI is currently used in the UK as a secondary imaging tool following fetal anatomy ultrasound scan at 18-20 weeks gestation, these concerns are negated.

Current practice within the UK involves MRI in pregnancy without the need for any maternal medication or sedation. Intravenous contrast media is not used as it has been shown to cross the placenta and its safety during pregnancy remains uncertain [6]. A significant concern regarding the introduction of ultrafast imaging sequences has been the noise levels produced by the MRI scanner and the potential impact on fetal hearing. However, there have

been several studies which have shown the uterus provides protection to the fetus against noise, meaning the risk of sensorineural hearing loss in infancy is no higher following fetal MRI than for the general population [7].

Advantages and disadvantages of fetal MRI and ultrasound

At present, antenatal ultrasound remains the gold standard for visualisation of the fetus and diagnosis of congenital structural anomalies. It has several advantages over MRI as it is widely available, cost-effective and non-invasive. The superior image resolution of fetal MRI means it overcomes some of the limitations of ultrasound as discussed below, however, there are some drawbacks including cost and limited availability due to the specialised nature of fetal MRI. A comparison of the advantages and disadvantages of antenatal ultrasound and fetal MRI is shown in table 1.1.

Antenatal ultrasound	**Fetal magnetic resonance imaging**
Real-time, non-invasive imaging	No radiation, superior tissue resolution
Cost-effective	Expensive, time-consuming, claustrophobia
Widely available	Limited availability
Operator dependent	Relatively operator independent
Small field of view	Larger field of view
Poor imaging quality in maternal obesity & oligohydramnios	More detailed fetal anatomy independent of fetal position or maternal obesity
Risk of artefact due to reverberation from maternal bowel gas	Poor visualisation before 16 weeks, poor visualisation of bone, artefact cause by fetal motion

Table 1.1. Comparison of antenatal ultrasound and fetal MRI advantages and limitations

Indications for fetal magnetic resonance imaging

Fetal MRI is used to complement antenatal ultrasound when further information is required for diagnosis of a structural anomaly. Even in the hands of practitioners who are highly experienced in performing antenatal ultrasounds, the presence of maternal obesity, oligohydramnios and difficult fetal position can affect the diagnostic accuracy [8]. Fetal MRI however, has a larger field of view meaning it can provide more detailed information irrespective of fetal position and maternal factors. Unlike in adult medicine where

computerised tomography (CT) scans may be used, the ionising radiation makes CT unsuitable in pregnancy meaning fetal MRI has become the second line imaging modality of choice.

The main indications for referral for fetal MRI are for confirmation or clarification of congenital anomalies or findings seen on ultrasound, in detection or exclusion of associated anomalies and in cases where the ultrasound is normal but there is family history of certain disorders [1]. Fetal MRI is also frequently used for examination of the placenta if there are concerns regarding placenta previa or an abnormally adherent placenta which may affect plans for mode of delivery.

There has been increasing use of fetal MRI both within the UK and worldwide over the last few years as the subspeciality of fetal medicine has been expanding. Fetal MRI can provide important diagnostic and prognostic information used in perinatal counselling and aid with planning for delivery and postnatal management. The more recent developments in the world of fetal surgery, such as in utero surgery for myelomeningocoele and fetoscopic endoluminal tracheal occlusion (FETO) for congenital diaphragmatic hernia, have further increased the use of fetal MRI as it provides accurate depiction of anatomical structures prior to intervention. Advancements in genetic testing and the development of fetal whole genome sequencing also mean fetal MRI findings are frequently used to provide a detailed phenotype to inform genetic counselling [9].

Congenital anomalies commonly seen on fetal MRI

Common reasons for fetal MRI due to anomalies of the fetal body seen on ultrasound include anomalies of the chest, abdomen and genito-urinary tract. Limb anomalies and lymphovascular anomalies are also frequently referred for fetal MRI for further evaluation.

Genito-urinary malformations make up a large proportion of fetal MRI scans for non-central nervous system (CNS) anomalies. Hydronephrosis caused by pelvi-ureteric junction obstruction, vesicoureteric reflux, megaureter and posterior urethral valves is commonly seen. In addition, renal anomalies such as multicystic dysplastic kidney (MCDK), renal agenesis, horseshoe and pelvic kidneys are also frequently assessed. In cases of renal anomalies, the diffusion weighted imaging (DWI) function of MRI is useful in assessing the function of the kidneys which provides prognostic information used in perinatal counselling.

Examples of thoracic anomalies commonly include congenital diaphragmatic hernia (CDH),

congenital pulmonary airway malformation (CPAM), broncho-pulmonary sequestration (BPS) and lung agenesis. In these cases, fetal MRI also plays an important role in calculation of lung volumes to provide prognostic information in addition to clarifying the diagnosis.

Fetal MRI is commonly used to aid prognostication in cases of congenital diaphragmatic hernia (CDH), a topic which is discussed extensively in this thesis. CDH prognostication is determined by a number of factors including the degree of pulmonary hypoplasia which can be measured using ultrasound and MRI. Ultrasound is used to generate the lung to head ratio (LHR) i.e. the ratio of the lung contralateral to the diaphragmatic defect to the fetal head circumference. A large systematic review [10] concluded that a LHR ≥ 0.6 had the greatest odds ratio for survival but that at a threshold of LHR ≥1.0 there was also a strong survival advantage compared to LHR <1.0. The finding of liver in the fetal chest is also considered a poor prognostic feature. MRI is used to determine the degree of pulmonary hypoplasia by measurement of the total fetal lung volume as a percentage of what would be expected, either for the gestational age or in comparison to the total fetal body volume. Use of gestation as the determinant of expected lung volume is most commonly used in clinical practice as measuring total body volume on MRI can be time consuming. However, no significant differences have been observed in predictive accuracy between either method [11]. Initial studies assessing percentage total fetal lung volume and prognosis suggested using <25% observed-to-expected lung volume as a cut-off for poor prognosis [12], however survival in CDH is improving and more recent work suggests these estimates may be overly pessimistic [13]. The use of observed-to-expected total fetal lung volume from MRI has been shown to have a better predictive value than lung to head ratio from ultrasound alone in left-sided CDH, therefore it is recommended that fetal MRI is included in the diagnostic process [14].

Abdominal wall defects such as gastroschisis and omphalocoele are often referred for evaluation with fetal MRI following diagnosis on antenatal ultrasound. Other anomalies such as duplication cysts and atresias such as duodenal atresia and oesophageal atresia are frequently referred for fetal MRI to characterise them further. Examples of lymphovascular anomalies in which MRI is useful include lymphatic malformations, especially those arising from the neck where there are concerns regarding airway compression.

The focus of this research is on congenital anomalies of the fetal body not relating to the central nervous system. Therefore, anomalies of the brain and spine will not be discussed as they are considered a separate entity with a wide array of ongoing research.

Current use of fetal magnetic resonance imaging

Every fetus with a suspected congenital anomaly has a multidisciplinary team (MDT) approach to their management. Each patient will have an assessment at the fetal medicine unit in a tertiary centre. It is common practice for the ultrasound scan to be repeated at the tertiary centre, if referred from elsewhere, as part of assessment on the fetal medicine unit (FMU) prior to referral for fetal MRI. The subsequent timing of the MRI scan is therefore largely influenced by when the anomaly is first seen on ultrasound, with this most commonly occurring at 18-20 weeks as part of the fetal anatomy ultrasound scan. Referral for fetal MRI is usually made shortly after as scan timing will be influenced by legislation regarding termination of pregnancy and protocols for fetal intervention, for example in utero surgery for myelomeningocoele is performed at 26 weeks.

Fetal MRI is performed later in pregnancy in cases of late diagnosis or when the congenital anomaly warrants a repeat MRI to allow for postnatal management planning and assessment shortly before delivery is required. For example, in cases such as lymphatic malformation of the neck to determine the degree of airway compression.

Fetal MRI is considered a quaternary investigation within the UK. Gold standard practice is for the reporting radiologist to be present throughout the scan to allow dynamic changes to the MRI protocol to be made if new pathology is seen or there is movement artefact, for example [15].

During the MRI scan the mother is laid supine or in the left lateral position depending on which is most comfortable and is given ear protection. At our local centre the fetal MRI scans are performed using a 1.5 Tesla MRI scanner. 3 Tesla scanners are used in some centres worldwide; but research has shown that although the higher strength magnet provides more detail to structures, artefact in cases of polyhydramnios and maternal obesity is more problematic [16].

MRI in pregnancy is performed during free breathing with respiratory gating to reduce artefact from movement during maternal respiration. Standard protocols for the imaging sequence include a localiser sequence, T2-weighted imaging in the coronal, sagittal and axial planes to evaluate fetal anatomical structures and T1-weighted imaging to visualise hyperintense tissues such as meconium in the bowel. T2 single shot fast spin echo (SSFE) is used to reduce artefact caused by fetal motion. Diffusion weighted imaging is then used to

assess perfusion and therefore function of structures such as the brain, kidneys and placenta. In certain circumstances other sequences may be used for assessment of specific anomalies such as dynamic visualisation of fetal swallowing using the cine mode in cases of suspected oesophageal atresia.

In our centre, immediately following the MRI scan, the pregnant woman is seen by the reporting radiologist, MRI findings are discussed and images are shown. The MRI report is then generated and sent back to the FMU where it will be discussed within the MDT and perinatal counselling by the necessary teams i.e. obstetricians, neonatologists and paediatric surgeons will take place.

Our centre is a teaching hospital in the North of England offering both fetal and placental MRI scans to pregnant women. It serves a local area of over half a million people and also receives referrals from centres across Yorkshire and a few other centres in Derbyshire and the North West. Approximately ten in utero MRI scans are performed each week with around one third of these being undertaken to look for structural abnormalities of the fetal body; with the rest being anomalies of the central nervous system or placenta. The reporting consultant radiologist has over 25 years experience of fetal MRI and provides a reporting service for fetal MRIs performed in the North East of England, Cambridge and some areas of London in addition to those performed at our centre. Given this breadth of experience and patient numbers, our centre was felt to be an appropriate place to conduct this research.

1.2 Research aims

This research hypothesises that fetal MRI improves diagnostic accuracy of congenital anomalies of the fetal body and aids with decision making for clinicians and parents. This hypothesis will be explored through several aims as detailed below.

Aims of this research:

1. To determine the degree to which fetal MRI improves diagnostic accuracy of fetal body anomalies when used in addition to antenatal ultrasound.
2. To examine in which conditions MRI is most useful in diagnosis, prognosis and management planning. This is in order to aid efficient service delivery.
3. To evaluate to what extent the MRI findings help with counselling for parents and their own decision making, in order to improve understanding of the patient's experience of the fetal MRI pathway.
4. To determine how the added information from fetal MRI aids with and/or alters management of the pregnancy and planning for delivery, and how useful it is considered to be by clinicians.

Chapter 2 – The diagnostic accuracy of fetal magnetic resonance imaging

Context of the research

This chapter explores the current evidence for the use of fetal MRI as an additional diagnostic tool alongside antenatal ultrasound in the form of a systematic review with meta-analysis concerning the diagnostic accuracy of fetal MRI in congenital anomalies of the fetal body. The subsequent subchapters then detail the primary research we have undertaken concerning the diagnostic accuracy of fetal MRI in a patient cohort and work with medical professionals concerning how useful the information provided by fetal MRI is in clinical practice and its impact on clinical decision making.

This chapter comprises three manuscripts, the first of which is published. The published manuscript has been reproduced in line with journal permissions.

Author contributions

2.1 - The value of fetal magnetic resonance imaging in diagnosis of congenital anomalies of the fetal body: A systematic review and meta-analysis

Wilson, L., Whitby, E.H. The value of fetal magnetic resonance imaging in diagnosis of congenital anomalies of the fetal body: a systematic review and meta-analysis. *BMC Med Imaging* 24, 111 (2024). https://doi.org/10.1186/s12880-024-01286-5

The planning of this research was undertaken by both me and Dr Elspeth Whitby. I undertook the searches for relevant papers and the selection of papers for inclusion was undertaken by both me and Dr Elspeth Whitby. I completed the data extraction and analysis with some statistical support from Dr Jean Russell. The overall write-up was completed by me prior to the final review by Dr Elspeth Whitby. I submitted the research for publication and undertook the necessary revisions following peer review, under the advice of Dr Elspeth Whitby.

2.2 - The diagnostic accuracy of fetal magnetic resonance imaging in congenital anomalies of the fetal body

The planning of this research was undertaken by both me and Dr Elspeth Whitby. I recruited and consented patients alongside Dr Whitby as part of the prospective recruitment phase. I

undertook the data collection with some assistance from Dr Whitby in contacting external hospitals. I then completed the data analysis and final write-up prior to the final review by Dr Elspeth Whitby.

2.3 - Fetal MRI for congenital anomalies of the fetal body: How useful is it in clinical practice?

The planning of this research was undertaken by both me and Dr Elspeth Whitby. This work involved sessions with five medical professionals (Dr Emma Ferriman, Dr Victoria Stern, Dr Vincent Kirkbride, Dr Tamanna Williams and Dr Christopher Vas) who graded the utility of the information provided by fetal MRI. These grading sessions were undertaken by me and Dr Elspeth Whitby, with the gradings recorded and field notes of the discussions taken. I completed the data analysis and write-up prior to the final review by Dr Elspeth Whitby.

2.1 The value of fetal magnetic resonance imaging in diagnosis of congenital anomalies of the fetal body: A systematic review and meta-analysis

Abstract

Introduction - The aim of this study was to undertake a systematic review to assess the accuracy of fetal MRI in diagnosis of non-CNS congenital anomalies of the fetal body in comparison with antenatal ultrasound when correlated to postnatal diagnosis.
Methods - Searches were conducted from electronic databases, key journals and reference lists for eligible papers. Inclusion criteria was original research studies comparing the diagnostic results of antenatal ultrasound, fetal MRI and final postnatal diagnosis via imaging, surgery or post-mortem testing. Studies of CNS anomalies were excluded. Studies were assessed for risk of bias by two reviewers working independently and data was then extracted by a single reviewer.
Results - 12 studies were included with a total of 361 eligible patients who underwent USS and MRI and had a postnatal diagnosis. USS alone had a diagnostic accuracy of 60.6% whereas MRI had an improved diagnostic accuracy of 86.4%. The overall Log_nOR was 0.86 (CI 0.202-1.519 and p-value <0.01).
Conclusion - Fetal MRI makes a significant contribution to accurate diagnosis of congenital abnormalities of the fetal body; especially in genito-urinary anomalies. More research is needed to improve the evidence base for the role of fetal MRI in diagnosis of congenital anomalies in other body systems

Introduction

Congenital anomalies not affecting the central nervous system (CNS) occur in approximately 206 per 10,000 UK births [17]. While ultrasound scanning (USS) is recognised as the gold standard for diagnosis of congenital anomalies there is increasing evidence for magnetic resonance imaging (MRI) [18]. Fetal MRI is safe in pregnancy and overcomes some limitations of ultrasound such as poor visualisation of the fetus where there is high maternal body mass index (BMI), in oligohydramnios or atypical fetal position [18].

Significant research has been undertaken concerning the diagnostic accuracy of fetal MRI in anomalies of the fetal brain [19,20]. There has also been extensive research concerning fetal MRI in prognostication of anomalies such as congenital diaphragmatic hernia [21]. However, systematic review evidence for the role of MRI in diagnosis of abnormalities of the fetal body is lacking and there is no consensus on its role in antenatal counselling and decision

making.

Methods

The aim of this study was to assess whether fetal MRI diagnoses congenital body anomalies more accurately than ultrasound alone and to determine how frequently fetal MRI gives additional information which affects management.

The protocol was developed using guidelines from the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) [22]. It has been registered with the International Prospective Register of Systematic Reviews (PROSPERO no. CRD42022379721).

Eligibility criteria

The eligibility criteria consisted of primary research of congenital anomalies of the fetal body comparing antenatal ultrasound and fetal MRI findings with postnatal diagnosis. A key requirement was for studies to comment on the diagnostic accuracy of both the fetal ultrasound and MRI separately in comparison with the postnatal findings made by imaging, surgery or post-mortem examination.

Studies of the CNS and studies of imaging in prognostication were excluded. Studies published prior to 2000 were excluded because few centres were using fetal MRI clinically at this time and data prior to this time may have been biased by technological limitations. Case reports and narrative reviews were excluded. Any study with three or fewer patients was excluded as these were considered as case reports. Studies involving research of cardiac fetal MRI were also excluded as this was considered to be a separate entity [23], as cardiac fetal MRI is predominantly performed as research and very few centres offer cardiac fetal MRI as a clinical service.

Studies not reported in English and where translation was unavailable were also excluded. For studies where only abstracts were available the authors were contacted directly to request the full paper; studies were excluded where the full paper was not available.

Search Strategy

A search of electronic databases was undertaken using the search strategy illustrated in

appendix 6.1. Databases searched were Medline (via Ovid 1966-present), Embase (via Ovid 1980-present) and Web of Science (1900-present) [24]. Relevant journals were also searched and references from key papers were examined. The searches were conducted in December 2022.

Studies were assessed for inclusion by two reviewers working independently and any disagreements were resolved by consensus. A PRISMA flow chart was completed detailing the selection process as shown in figure 2.1.

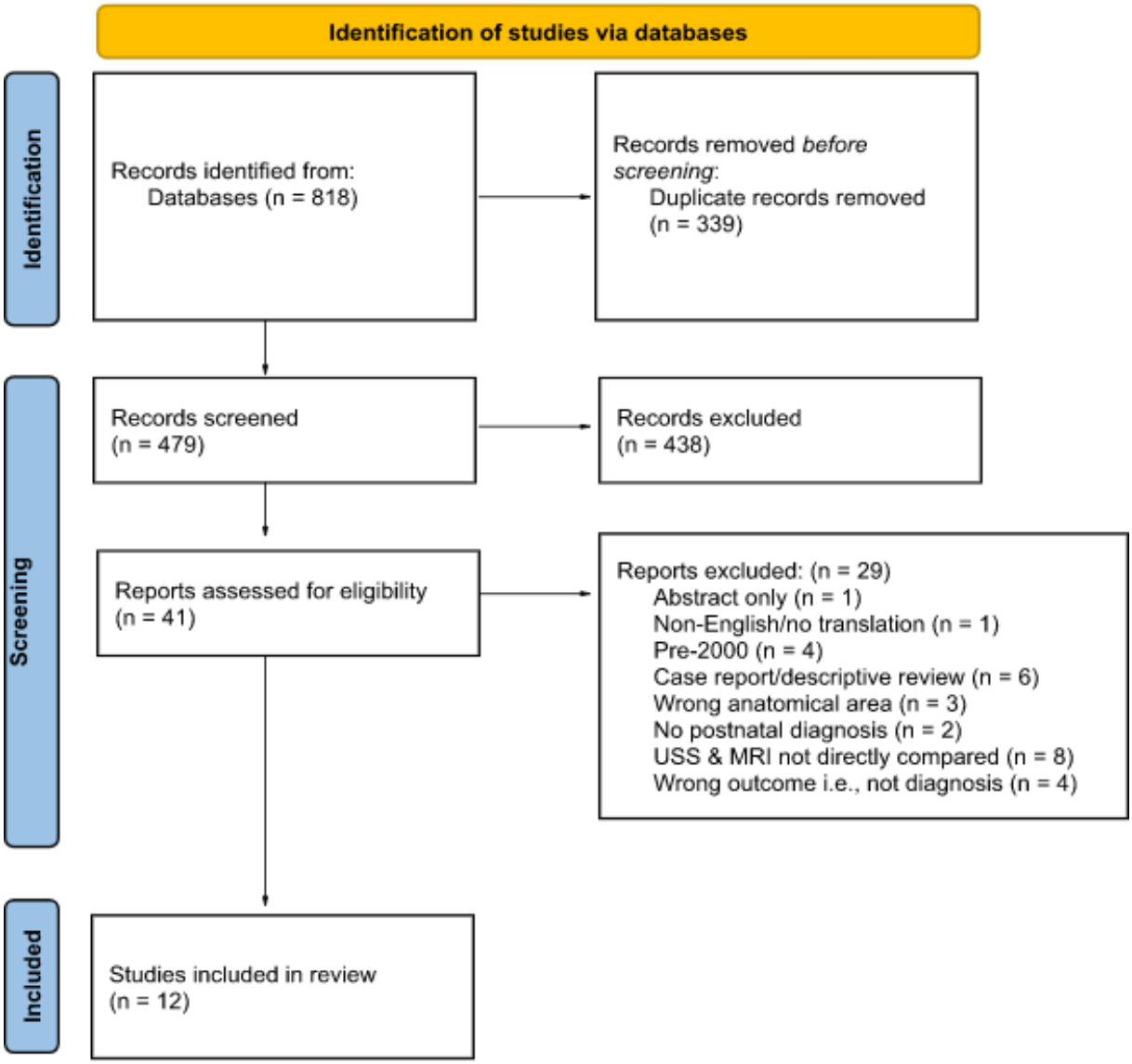

Figure 2.1. PRISMA flow chart of study selection

Risk of bias assessment

Included studies were assessed for methodological quality using a risk of bias assessment (QUADAS 2 tool) [25]. Risk of bias was assessed by two reviewers working independently and any disagreements were resolved by discussion and consensus. Risk of bias was assessed in the four domains: patient selection, index test, reference standard and flow and timing. Applicability was assessed in terms of patient selection, index test and reference standard. The bias of the index test was considered high in studies where MRI was performed following an inconclusive ultrasound diagnosis. Index test applicability was considered low risk of bias provided ultrasounds performed in other centres were repeated at the tertiary centre prior to MRI and the tertiary ultrasounds were used for the analysis. This was in order to minimise bias caused by variation in sonographer expertise. The use of clinical assessment in reporting of outcome as a reference standard was considered low risk in assessment of bias. This was because although some variability will be introduced this was felt to reflect clinical practice. A time lapse of greater than two weeks between ultrasound and MRI was considered to introduce a high risk of bias; in studies where timings were not specified the risk of bias was deemed unclear.

Data extraction

Data from the studies was extracted by a single reviewer using a pre-specified data collection tool (appendix 6.2). Data collected included key study characteristics, the individual diagnostic accuracy of antenatal ultrasound and fetal MRI in comparison with the postnatal diagnosis and how frequently there was agreement or disagreement between the two modalities. For studies which assessed both CNS and non-CNS abnormalities data collection focused on the body anomalies only.

Sensitivity and specificity of the imaging techniques could not be assessed as included studies involved patients referred for fetal MRI scan following an abnormality detected on ultrasound, meaning there were no control groups. Diagnostic accuracy was determined by the total number of true positive and true negative results in comparison to the total number of tests i.e. how frequently the ultrasound and MRI diagnosis was in alignment with the final postnatal diagnosis. The relative Log_nOR for the paired MRI and USS diagnostic accuracies were calculated using McNemar's odds ratio with a 0.5 correction for zero cells. The Log_nORs were combined using a random effects model. A funnel plot for assessment of publication bias was also undertaken.

Results

The searches retrieved 818 studies which were reduced to 479 studies once duplicates were removed. Abstract screening reduced the number of studies to 41 studies which were assessed for eligibility. Following assessment, twelve studies were included in the final analysis. Details of the reasons for exclusion can be found in figure 2.1. PRISMA flow chart. All included studies compared the diagnosis made on ultrasound with a fetal MRI which was performed after the ultrasound anomaly had been detected. This process reflects clinical practice and allows assessment of whether the MRI provided additional information which altered the management of the pregnancy.

Study characteristics

The twelve included studies and their characteristics are listed in table 2.1. The studies were published between 2003 and 2021, with the majority (n=9) being published after 2009. Three studies [26–28] were prospective and the remainder [29–37] were retrospective. Two studies [28,30] specified consecutive patient recruitment whereas the remaining studies [26,27,29,31–37] did not specify the recruitment process.

Seven studies [26–29,31,33,34] investigated renal or urinary tract anomalies. Two studies [30,32] looked at anomalies of the fetal chest, another two studies [32,36] focused on abdominal anomalies, one study [35] examined vascular anomalies and one [37] was investigating fetal genital anomalies. None of the included studies involved neck masses, although these were not specifically excluded.

The median gestation at the time of ultrasound was 28.5 weeks as given in two studies [27,37]. The gestational age at the time of fetal MRI was stated in four studies [27,29,30,37] which had a combined median gestation of 29 weeks.

The twelve included studies looked at a total of 757 patients. 361 patients (47.7%) were included in this review as 300 did not undergo fetal MRI, five were lost to follow-up, 82 had CNS anomalies and nine had no post-natal diagnosis for comparison. Of the 300 patients who did not undergo MRI, 296 came from one study of urinary tract anomalies [34] in which there were a total of 342 patients but only 46 were referred for fetal MRI. The other four patients who did not undergo fetal MRI were in a study of lung malformations [30]. The reasons for including these patients in the study and not referring these patients for MRI was not clear.

Author & Year	Title	Country	Population	Study selection	Retrospective (R) or Prospective (P)	No. patients	No. patients included in review
Abdelazim 2010	Complementary roles of prenatal sonography and magnetic resonance imaging in diagnosis of fetal renal anomalies	Egypt	Renal anomalies	Unclear	P	20	18
Alamo 2010	Fetal MRI as complement to US in the diagnosis and characterization of anomalies of the genito-urinary tract	Switzerland	Genito-Urinary tract anomalies	Unclear	R	15	15
Alamo 2013	Comparison of foetal US and MRI in the characterisation of congenital lung anomalies	Switzerland	Congenital lung malformation	Consecutive	R	30	26
Barseghyan 2008	Complementary Roles of Sonography and MRI in assessment of fetal urinary tract anomalies	USA	Renal anomalies	Unclear	R	39	39
Behairy 2015	Diagnostic value of fetal MRI in evaluating fetal urinary anomalies	Egypt	Urinary tract anomalies	Unclear	P	30	30
Breysem 2003	The value of fast MR imaging as an adjunct to ultrasound in prenatal diagnosis	Belgium	Brain, neck/chest and abdominal anomalies	Unclear	R	40	14

Table 2.1. Included studies and their characteristics (part a)

Crivelli 2021	Contribution of magnetic resonance imaging to the prenatal diagnosis of common congenital vascular anomalies	Switzerland & France	Vascular malformations	Unclear	R	24	24
Gupta 2010	The role of magnetic resonance imaging in fetal renal anomalies	India	Renal anomalies	Consecutive	P	86	27
Hugele 2015	Does prenatal MRI enhance fetal diagnosis of intra-abdominal cysts?	France	Abdominal cysts	Unclear	R	56	49
Ji 2018	Magnetic resonance imaging for evaluation of foetal multicystic dysplastic kidney	China	Multicystic dysplastic kidneys	Unclear	R	55	53
Kajbafzadeh 2007	Comparison of magnetic resonance urography with ultrasound studies in detection of fetal urogenital anomalies	Iran	Genito-Urinary tract anomalies	Unclear	R	342	46
Millischer 2017	Fetal MRI compared with ultrasound for the diagnosis of obstructive genital malformations	France	Genital malformations	Unclear	R	20	20

Table 2.1. Included studies and their characteristics (part b)

Methodological quality

The methodological quality of included studies was assessed using the QUADAS-2 tool [25] and results are summarised in figure 2.2. The risk of bias in patient selection was considered low risk in all studies as studies with unsuitable patients had been excluded.

	PATIENT SELECTION	INDEX TEST	REFERENCE STANDARD	FLOW AND TIMING
Abdelazim 2010	Low	Low	Low	Unclear
Alamo 2010	Low	High	Low	Low
Alamo 2013	Low	Low	Low	Low
Barseghyan 2008	Low	Low	Low	Unclear
Behairy 2015	Low	Low	Low	Low
Breysem 2003	Low	Low	Low	Unclear
Crivelli 2021	Low	Low	Low	Unclear
Gupta 2010	Low	Low	Low	Unclear
Hugele 2015	Low	Low	Low	Low
Ji 2018	Low	Low	Low	Low
Kajbafzadeh 2008	Low	High	Low	Unclear
Millischer 2017	Low	High	Low	High

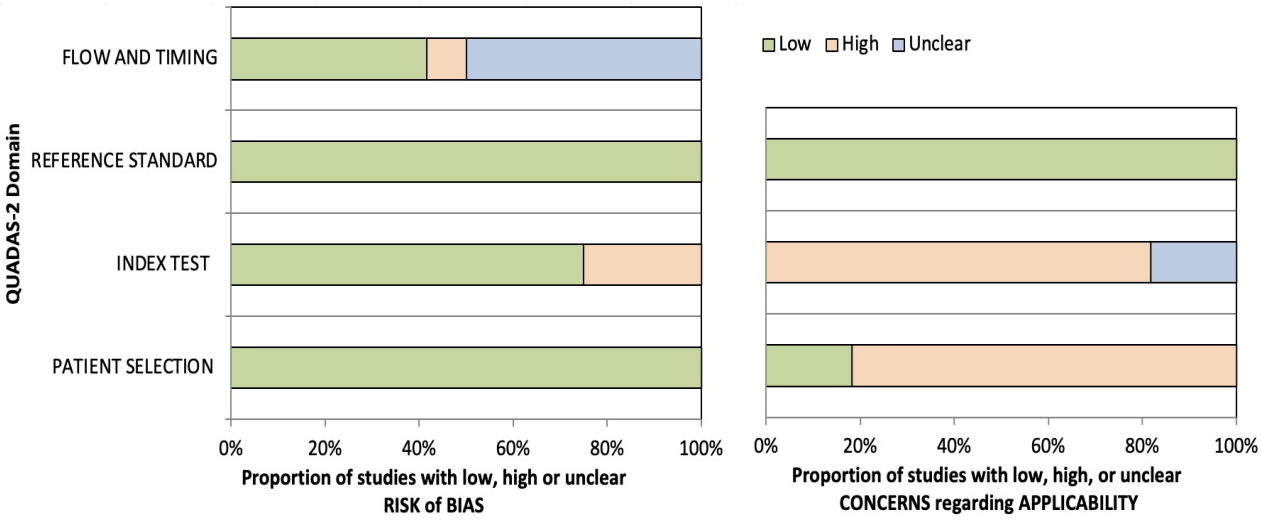

Figure 2.2. Risk of bias and assessment of applicability using QUADAS-2 tool

Risk of bias concerning the index test was high in 3/12 studies [29,34,37] where MRI scans were performed due to inconclusive ultrasound results and was low risk in the remaining

nine studies [26–28,30–33,35,36]. Risk of bias introduced by the reference standard was low risk in all studies as ultrasounds were repeated by the tertiary centres performing the MRIs and the diagnoses made from these ultrasounds were used in the analysis. The risk of bias relating to flow and timing was determined by the time between ultrasound and MRI scan; this was low risk in 5/12 [27,29–31,36], unclear in 6/12 [26,28,32–35] where scan timings were not given and high risk in 1/12 [37] where there was more than two weeks between ultrasound and MRI scan.

Diagnostic accuracy of USS and MRI

The diagnostic accuracy across all twelve studies combined when imaging diagnosis was compared with postnatal diagnosis was 60.6% (219/361) for antenatal ultrasound and 86.4% (312/361) for fetal MRI. All studies showed an improvement in diagnostic accuracy following fetal MRI scan and despite heterogeneity the overall Log_nOR when studies were combined was 0.86 (95% confidence interval 0.202-1.519 and p-value <0.01). The forest plot of the Log_nOR for each study and overall is shown in figure 2.3.

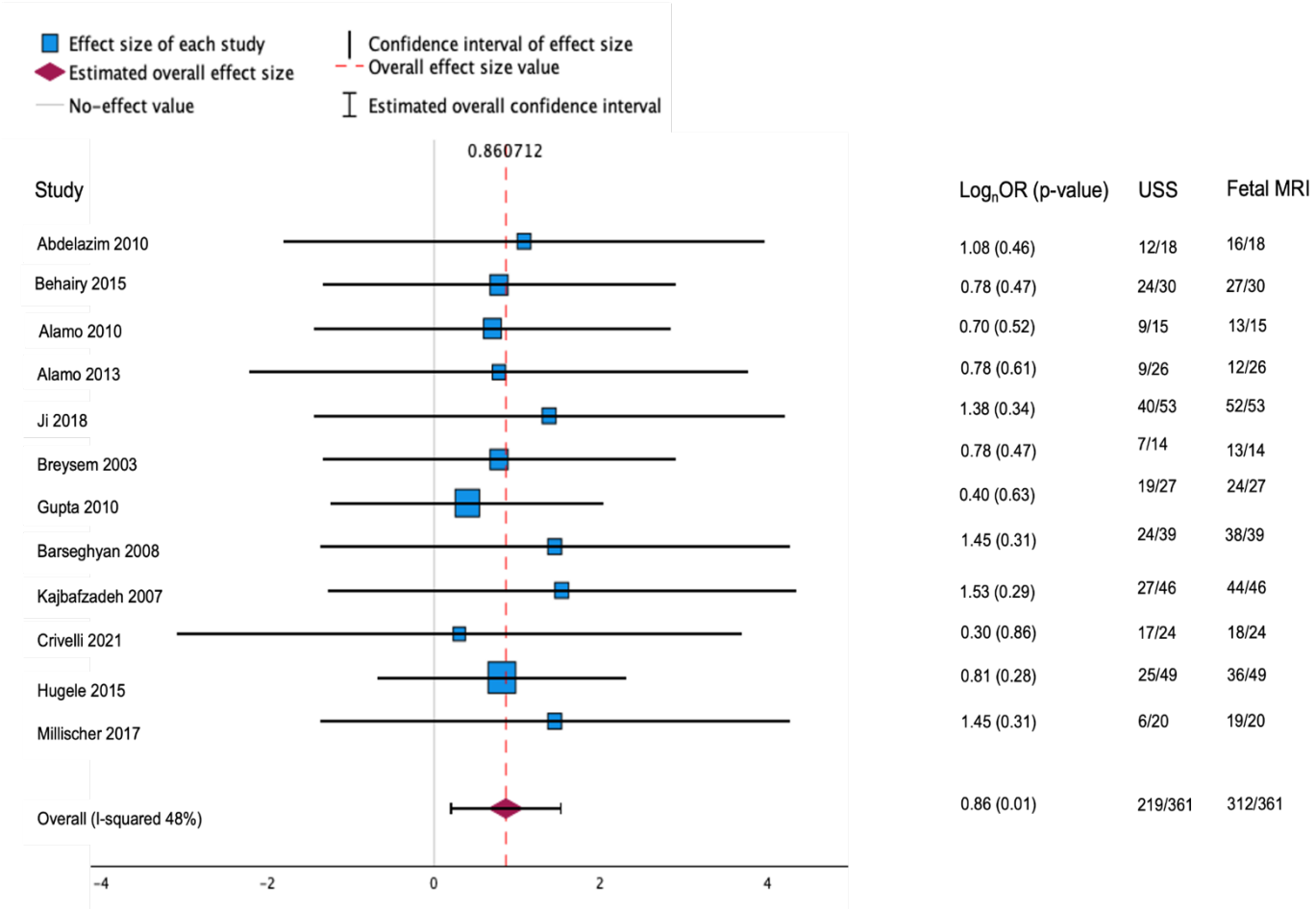

Figure 2.3. Forest plot of Log_nOR for individual studies and overall. Note weights are from random effects analysis

The I^2 for the results of the forest plot is 0.48 indicating modest heterogeneity between studies, however as the figure is less than 0.5 it was deemed reasonable to combine them [38]. A funnel plot was generated for assessment of publication bias which showed reasonable symmetry meaning it is less likely any bias or heterogeneity within the meta-analysis is significantly affecting the results. This is detailed in figure 2.4.

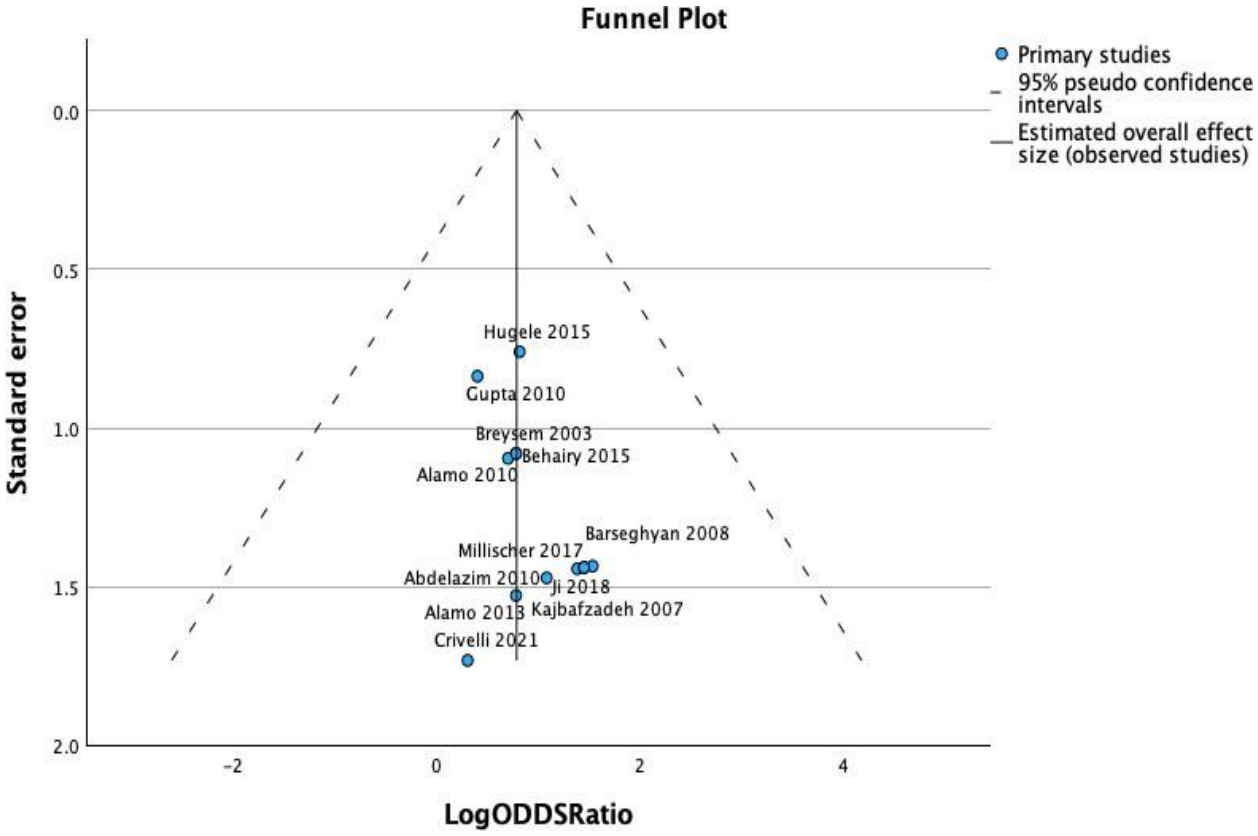

Figure 2.4. Funnel plot of Log_nOR and standard error for individual studies

The seven studies investigating renal and urinary tract abnormalities [26–29,31,33,34] reported a combined accuracy of 68% (155/228) for ultrasound and 94% (214/228) for MRI. The two studies of chest anomalies [30,32] found the diagnostic accuracy to be 40% (12/30) and 53% (16/30) for ultrasound and MRI respectively. The abdominal studies [32,36] reported the diagnostic accuracy as 49% (29/59) for ultrasound and 76% (45/59) for MRI. The study looking at detection of vascular anomalies [35] found similar results between ultrasound and MRI in terms of diagnostic accuracy; the ultrasound diagnosis was correct in 71% (17/24) and MRI was correct in 75% (18/24). When this study split their results into detection of lymphatic malformations and haemangiomas separately, they concluded the same rates of diagnostic accuracy for haemangiomas, which were poorly described by both imaging modalities, as 25% (1/4) and a marginally improved rate with MRI diagnosis of lymphatic malformations (ultrasound 16/20 correct and MRI 17/20 correct). The study of

obstructive genital malformations [37] had a relatively small sample size of 20 patients but showed a significant difference in diagnostic accuracy between ultrasound (30% or 6/20) and MRI (95% or 19/20). This was predominantly due to the ability of MRI to correctly exclude cloacal abnormalities.

Agreement between USS and MRI

Antenatal ultrasound and fetal MRI were in agreement with each other and the final postnatal diagnosis in 59% (213/361) of cases. In 6.4% (23/361) the ultrasound and MRI were in agreement but gave an incorrect diagnosis compared with the final outcome. This discordance was most pronounced in the studies assessing chest lesions [30,32] where ultrasound and MRI agreed but were wrong in 40% of cases (12/30). This was primarily in complex lung lesions where both imaging modalities gave non-specific findings.

Change in diagnosis following MRI

The MRI diagnosis correctly changed the ultrasound diagnosis i.e. the MRI was in concordance with the postnatal outcome diagnosis, but ultrasound was incorrect in 28% of cases (101/361). This was most notable in the abdominal studies [32,36] in which MRI correctly changed the diagnosis in 30.5% (18/59) and in the renal/urinary tract studies [26–29,31,33,34] in which 28% (64/228) of the ultrasound diagnoses were correctly changed by MRI.

In 1.7% of fetuses (6/361) the MRI scan incorrectly changed the diagnosis given by the ultrasound. This was again noted in the abdominal studies [32,36] and urinary tract studies [26–29,31,33,34] in which the MRI gave an incorrect diagnosis, but the initial ultrasound report was in agreement with the postnatal diagnosis.

Additional information provided by MRI and change in management

The MRI scans gave additional diagnostic information in 26.8% of fetuses (93/347) as reported by eleven of the twelve studies; this information was not clearly given in one study [32]. Seven studies [26–30,33,37] commented on the number of cases where the additional information provided by the fetal MRI changed the management of the pregnancy. They found antenatal management was influenced by the MRI report in 14.9% of cases (26/175) as illustrated in figure 2.5. This was most significant in the study of obstructive genital malformations [37] in which management was changed in 14/20 cases (70%). The change in management consisted of termination of pregnancy (n=8), continuation of pregnancy (n=13), plans for immediate delivery and postnatal management/surgery (n=4) and a change in body system anomaly diagnosed (n=1).

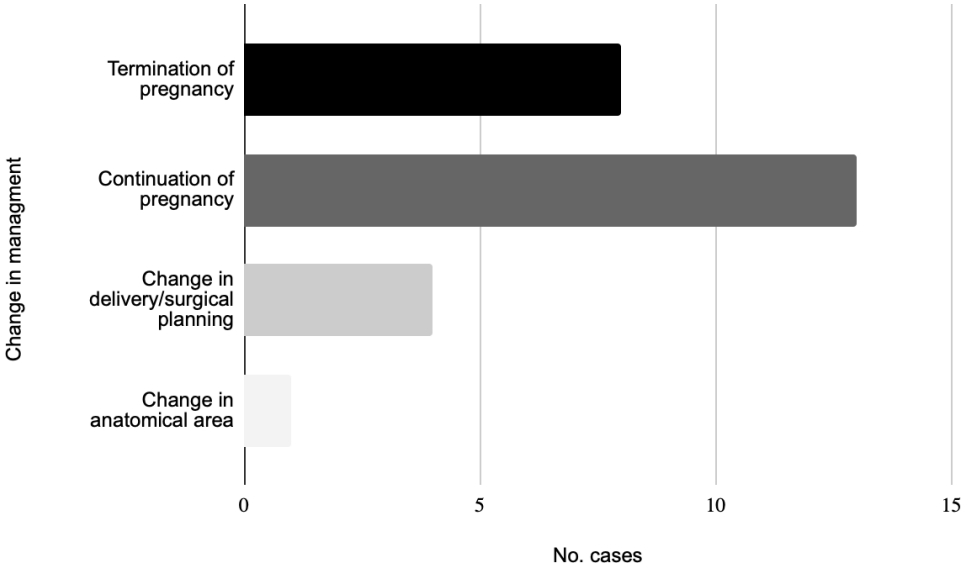

Figure 2.5. Cases with change in management following fetal MRI scan (n = 26)

All studies except two [32,33] commented on the anomaly or diagnosis in which the addition of MRI was felt to have the most benefit. MRI was concluded to be the most useful in detection and severity of bilateral renal disease in three studies [26,27,31], in detection of fetal pelvic anomalies [29], in cases where oligohydramnios affected ultrasound scan accuracy [28] and in exclusion of cloacal anomalies [37].

Discussion

This review has demonstrated an increase in diagnostic accuracy of 25.8% in congenital anomalies of the fetal body with the use of fetal MRI compared with antenatal ultrasound alone in relation to the final postnatal diagnosis. Despite focusing on congenital anomalies of different areas of the fetal body each study reported an overall increase in diagnostic accuracy with fetal MRI and the combined Log_nOR was 0.86 (CI 0.202-1.519 and p value <0.01). Additional information was provided by the MRI in 26.8% and management was changed in 14.9%. There were a small number of cases in which the MRI incorrectly changed the diagnosis and was discordant with the postnatal diagnosis (1.7%).

This data highlights the importance of the use of fetal MRI as an adjunct to clinical expertise and the views of families when making decisions regarding the management of a pregnancy. This is shown most prominently in the seven studies which reported an overall change in management in 14.9% of cases based on the results of the MRI. These changes in management led to continuation of pregnancy in 50% of the 26 cases discussed and 30% of

families opting for termination of pregnancy following the change in diagnosis. The additional information provided allowed precise planning of delivery and postnatal management in 15%.

Previous research has shown that image quality in fetal MRI is less affected by high maternal BMI, atypical fetal position and oligohydramnios than in antenatal ultrasound [18]. While it is clear there is some impact by these factors, there is a role for fetal MRI in diagnosis of renal disorders especially in cases of oligohydramnios. This is supported by three of the studies concluding that fetal MRI was most useful in detection and assessment of severity in bilateral renal disease. Other studies that did not meet the criteria for inclusion in this paper have reported similar improvement in diagnostic accuracy for renal anomalies in both unilateral and bilateral pathologies [39].

The overall scope of the review is limited predominantly by sample size as only twelve studies met the eligibility criteria and the total number of patients included was 361. Whilst there is a reasonable amount of evidence concerning renal and genito-urinary problems (seven studies with 228 patients) some of the other conditions were only represented by a single study each. Furthermore, congenital lung malformations were only represented by two studies which seems discordant with clinical data as thoracic anomalies account for 5-18% of all congenital anomalies [40].This may be due to the plethora of studies assessing various aspects of fetal MRI in cases of congenital diaphragmatic hernia but none looking at diagnostic accuracy. Studies that did not fit the criteria for inclusion suggest a range of diagnostic accuracy, however fetal MRI has been shown to be superior to ultrasound in most of these [41,42]. Others have shown how lung lesions change over time making prediction of the histological type difficult [43], leading to many centres providing a description of the lesion at a certain point in time and not a diagnosis. The time period covered by these studies has seen significant evolution of both the quality of MRI scans and the ability of radiologists to interpret them. These improvements may limit study quality; however, ultrasound image quality has also improved over this time.

These results have significant implications for future research to consolidate the evidence concerning improved diagnostic accuracy of fetal MRI. Improved diagnostic accuracy enables antenatal counselling to be tailored to each individual patient and will provide support for both parents and clinicians when making difficult decisions regarding the pregnancy. The additional information provided by fetal MRI could also aid in planning of delivery and the management of the neonate after birth.

The evidence provided by future larger studies could have an important role in the development of consensus both within the UK and internationally on the role that MRI should play in the diagnosis of congenital anomalies of the fetal body. Development of standardised protocols of how feto-maternal medicine units use MRI to aid diagnosis, parental counselling and antenatal management decisions will ensure this process is evidence based.

Conclusion

In conclusion, this systematic review summarises the current evidence on the diagnostic accuracy of fetal MRI in diagnosis of non-CNS congenital anomalies compared with antenatal ultrasound alone. It shows an improvement in correct diagnosis up to 25.8% when MRI is used in addition to ultrasound with Log_nOR of 0.86. Antenatal ultrasound remains the gold standard in diagnosis of congenital anomalies of the fetal body, however fetal MRI can be used as an adjunct to provide further diagnostic information which may impact management.

However, the review is limited by the sample size of the studies with only single studies conducted for certain anatomical areas. Further research is needed to supplement these findings.

2.2 The diagnostic accuracy of fetal magnetic resonance imaging in congenital anomalies of the fetal body

Abstract

Introduction - Current evidence suggests fetal MRI has improved diagnostic accuracy when used in addition to antenatal ultrasound for diagnosis of congenital anomalies of the fetal body. However, robust study evidence is lacking.
Methods - Combined retrospective and prospective study of all patients referred for fetal MRI at our centre due to a suspected anomaly of the fetal body from December 2020 to September 2023. Ultrasound and MRI diagnoses were compared with the final diagnosis made by imaging, surgery or postmortem.
Results - 242 cases were included in the final analysis. Fetal MRI had improved diagnostic accuracy over ultrasound alone by 24.6% ($p<0.001$).
Conclusion - Fetal MRI has improved diagnostic accuracy over ultrasound alone making it an important adjunct in the diagnosis of congenital anomalies of the fetal body.

Introduction

The current evidence for the diagnostic accuracy of fetal magnetic resonance imaging (MRI) in the literature and summarised in our systematic review [44] shows MRI to be a useful adjunct to ultrasound in cases of anomalies of the fetal body. This has already been studied in depth for congenital central nervous system (CNS) anomalies [19], however large studies of non-CNS anomalies are less prevalent. Improved diagnostic certainty has a significant impact not only in clinical practice but also for the families involved [45]. Therefore, more evidence is needed to support the use of fetal MRI in addition to ultrasound in certain cases. It is also important to refine the role of fetal MRI, ensuring appropriate use of resources within a healthcare system.

General non-structural anomalies

There are several non-structural anomalies of the fetal body or risk factors that might prompt a referral for a fetal MRI scan. The most common non-structural reasons for fetal MRI referral are patients with too little amniotic fluid (oligohydramnios) or too much amniotic fluid (polyhydramnios). In patients with oligohydramnios, visualisation of the fetus can be more difficult with ultrasound [18] therefore MRI is used as second line imaging to ensure normal structure and to rule out potential causes such as bilateral renal agenesis. Fetal MRI is used

in cases of polyhydramnios to rule out structural causes for excess amniotic fluid such as obstructions of the fetal gastrointestinal tract including oesophageal atresia and duodenal atresia. MRI imaging of oligohydramnios and polyhydramnios is shown in figure 2.6.

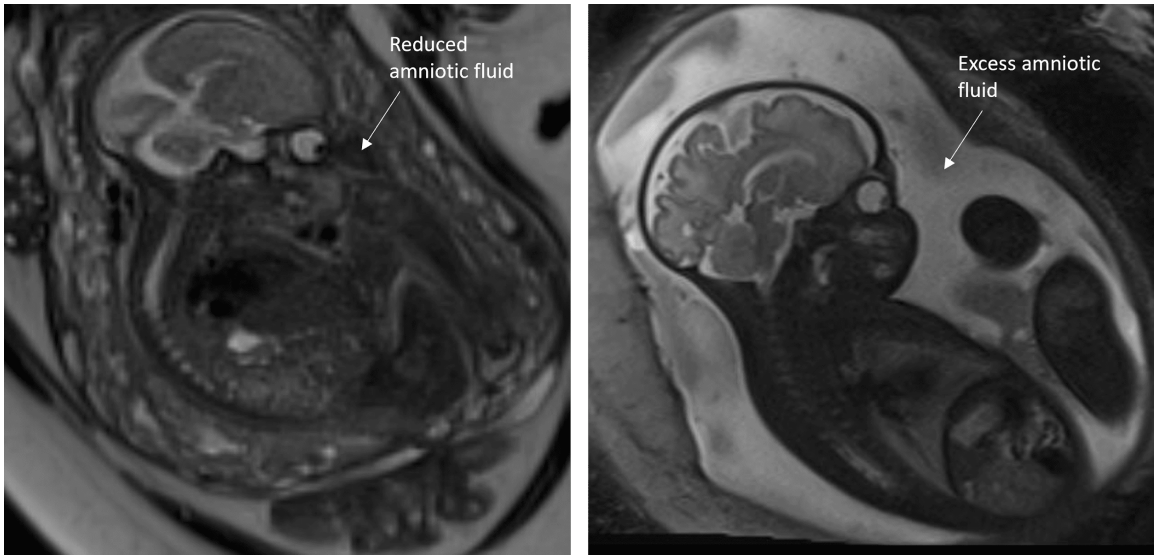

Figure 2.6. T2 HASTE Sagittal MRI image of oligohydramnios in 22+5 week fetus (left) and T2 HASTE Sagittal MRI image of polyhydramnios in 34+0 fetus (right)

Fetal MRI may also be used in cases where there has been exposure to a certain teratogen, such as cytomegalovirus or parvovirus, to examine the fetus in more detail for signs of congenital infection. Less frequently fetal MRI may also be used for patients with significant family history of complex genetic conditions to look for known phenotypic manifestations or for families with previous children with structural anomalies.

Thoracic anomalies

The most common anomalies of the chest and lungs seen on fetal MRI are congenital lung malformations which account for up to 18% of all congenital anomalies [46], the most prevalent of which are congenital pulmonary airway malformations (CPAMs). CPAMs are characterised by overgrowth of terminal bronchioles leading to a cystic malformation usually affecting one lobe of the lung, as shown in figure 2.7. Large CPAMs can cause respiratory distress at birth, recurrent lower respiratory tract infections in childhood [47] and may have malignant potential later in life [48] therefore antenatal diagnosis allows appropriate management at birth and surgical resection in childhood.

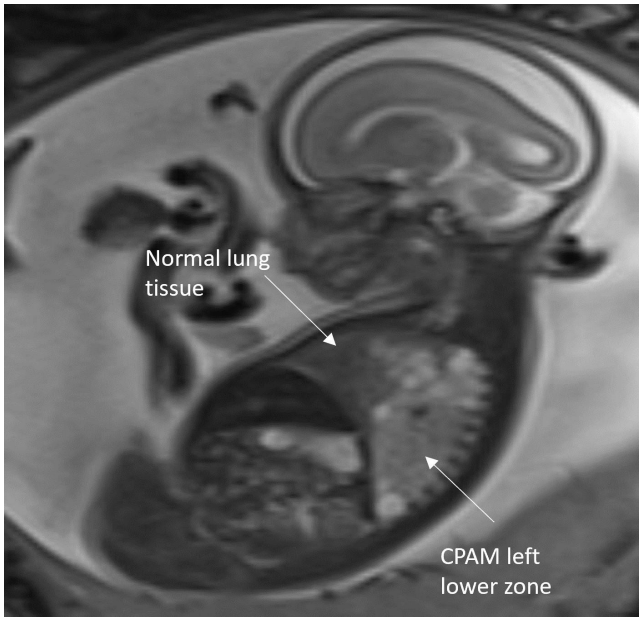

Figure 2.7. T2 HASTE STIR Sagittal MRI image of left lower zone CPAM in 22+4 week fetus

Congenital diaphragmatic hernia (CDH), where there is a defect in the diaphragm allowing herniation of the abdominal contents into the thoracic cavity interrupting lung expansion, is also a frequent indication for fetal MRI. This is because prognostication in CDH is often based on lung volume measurements undertaken using fetal MRI [49] as shown in figure 2.8. Fetal MRI can also be useful in refining the diagnosis of CDH, especially where the majority of the herniated contents is the liver, as liver and lung texture can appear similar on ultrasound meaning the only ultrasound findings may be mediastinal shift. Fetal MRI may also be used in cases of diaphragmatic eventration, where the diaphragm is abnormally elevated as shown in figure 2.9, to ensure there is no defect.

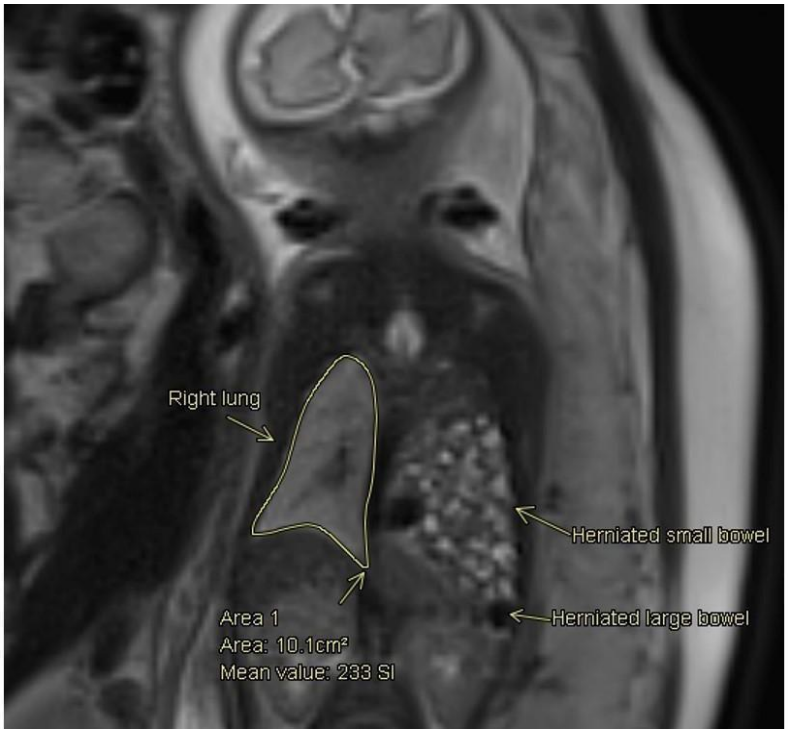

Figure 2.8. T2 Coronal MRI image of left-sided CDH with measurement of right lung volume in 32 week fetus

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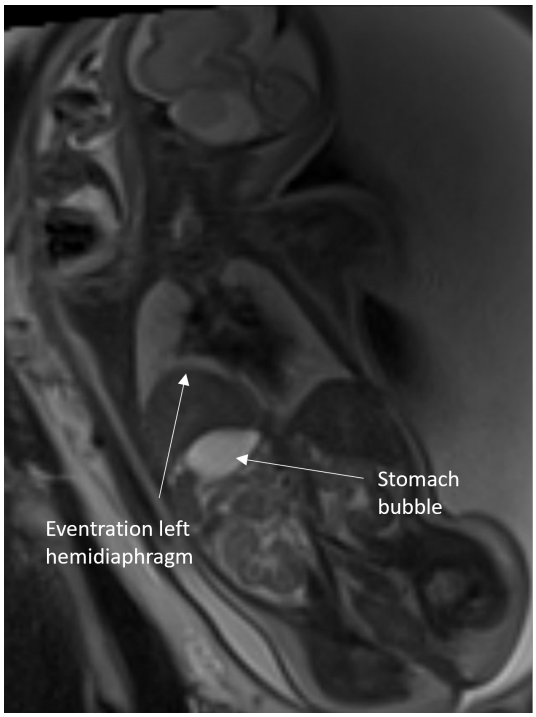

Figure 2.9. T2 HASTE Coronal MRI image of eventration of left hemidiaphragm in 35 week fetus

Other common referrals for fetal MRI include pleural effusions, as shown in figure 2.10, and lung hypoplasia either of the whole lung, as shown in figure 2.11, or lobar agenesis.

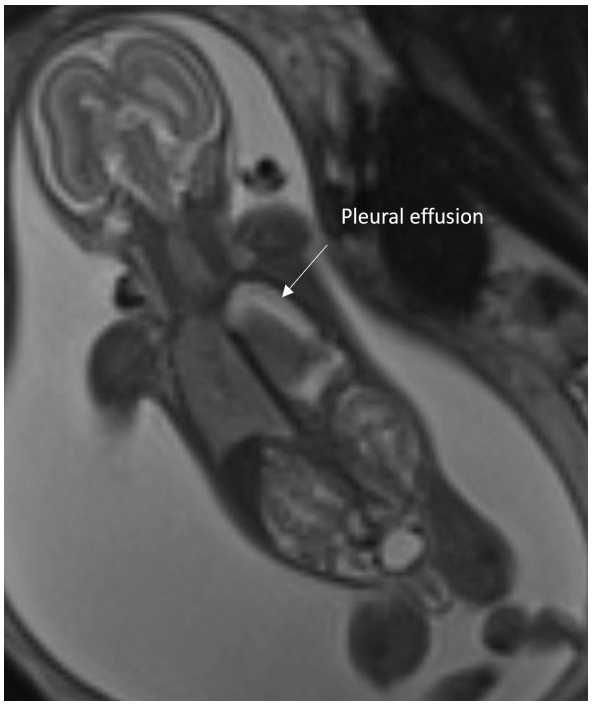

Figure 2.10. T2 HASTE Coronal MRI image of pleural effusion in 20+4 week fetus

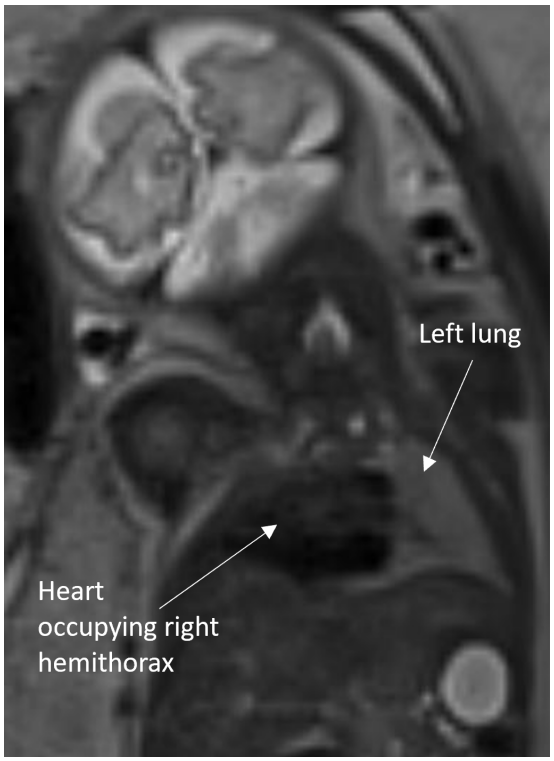

Figure 2.11. T2 HASTE Coronal MRI image of right lung agenesis in 32 week fetus

Abdominal and gastrointestinal anomalies

Fetal MRI may be used in cases of abdominal wall defects to provide a more detailed diagnosis. For example, in cases of gastroschisis where the abdominal contents are herniated through a defect usually on the right side of the umbilical cord and in cases of exomphalos where the herniated contents are covered by a membrane. Fetal MRI imaging of gastroschisis is shown in figure 2.12. The detailed information from fetal MRI can be used to help predict prognosis in gastroschisis [50] and look for associated anomalies seen with exomphalos [51].

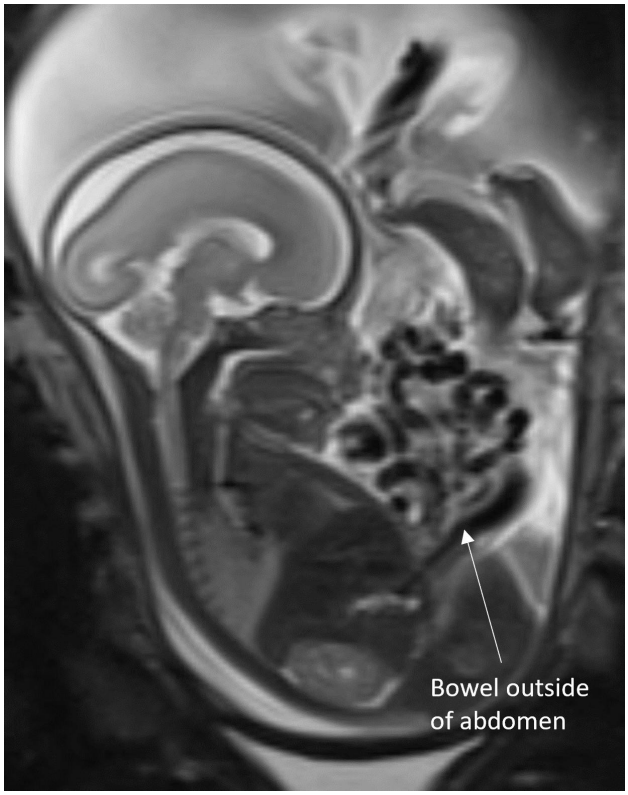

Figure 2.12. T2 HASTE STIR Sagittal MRI image of gastroschisis in 25 week fetus

In cases of suspected tracheo-oesophageal fistula, with or without oesophageal atresia, fetal MRI may be used to try and confirm the diagnosis. It is commonly suspected on ultrasound when the stomach bubble appears absent or small, and if there is the presence of oesophageal dilatation due to obstructed swallowing which may be seen on MRI [52], as shown in figure 2.13.

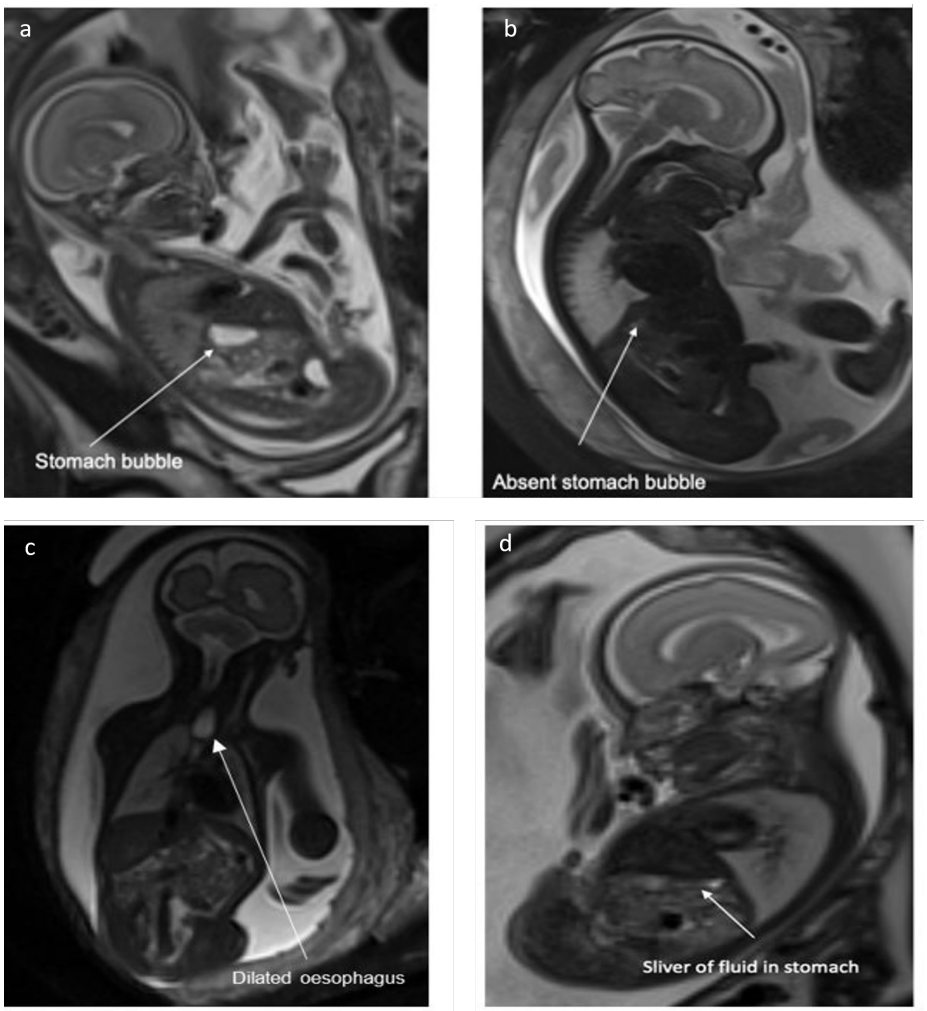

Figure 2.13.

a) Sagittal T2 SSFSE MRI image of a normal stomach bubble in 22 week fetus
b) Sagittal T2 SSFSE MRI image of an absent stomach bubble in a 30 week fetus
c) Coronal T2 SSFSE MRI image of a dilated oesophagus in 30 week fetus
d) Sagittal T2 SSFSE MRI image of 25 week fetus with a sliver of fluid visible in the stomach

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Other types of gastrointestinal tract atresia, such as suspected duodenal atresia, are also commonly referred for fetal MRI for confirmation of diagnosis, as seen in figure 2.14 where the ‘double bubble’ sign is seen as a result of dilatation of the proximal duodenum and stomach. Fetal MRI is also frequently used to refine the diagnosis in cases of abdominal cyst by determining the likely origin of the cyst such as ovarian cysts, as shown in figure 2.15.

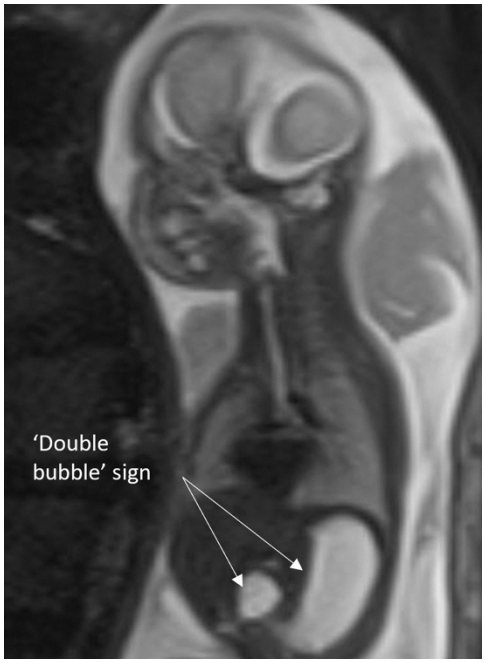


Figure 2.14. T2 HASTE STIR Coronal MRI image of duodenal atresia in 24+1 week fetus

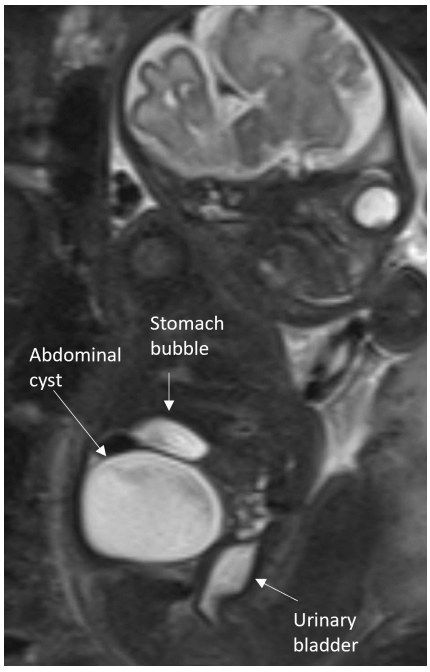


Figure 2.15. T2 HASTE STIR Coronal MRI image of abdominal cyst in 32+2 week fetus

Congenital anomalies of the kidney and urinary tract

Fetal MRI is used extensively for congenital anomalies of the kidney and urinary tract (CAKUT) to refine and confirm a diagnosis. Common examples include multicystic dysplastic kidneys (MCDK), as shown in figure 2.16, renal agenesis and cases of genitourinary (GU)

tract obstruction such as pelvi-ureteric junction obstruction (PUJO) and posterior urethral valves (PUV), shown in figure 2.17. The additional value of MRI is the use of diffusion weighted imaging (DWI) to assess for presence of renal function, which can be useful when confirming bilateral renal agenesis as confidence is key in these cases owing to the poor prognosis.

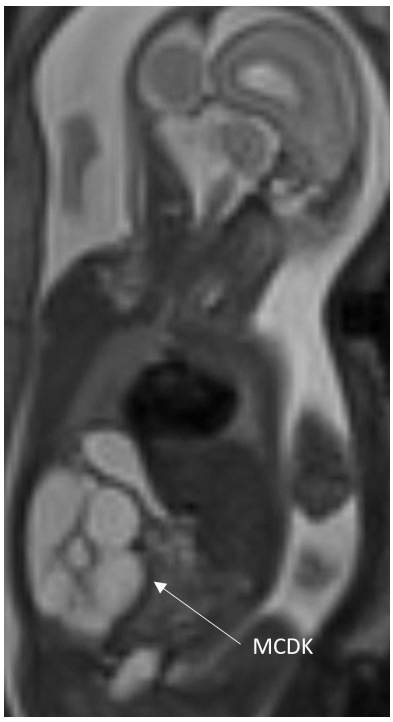


Figure 2.16. T2 HASTE Coronal MRI image of left MCDK in 22+3 week fetus

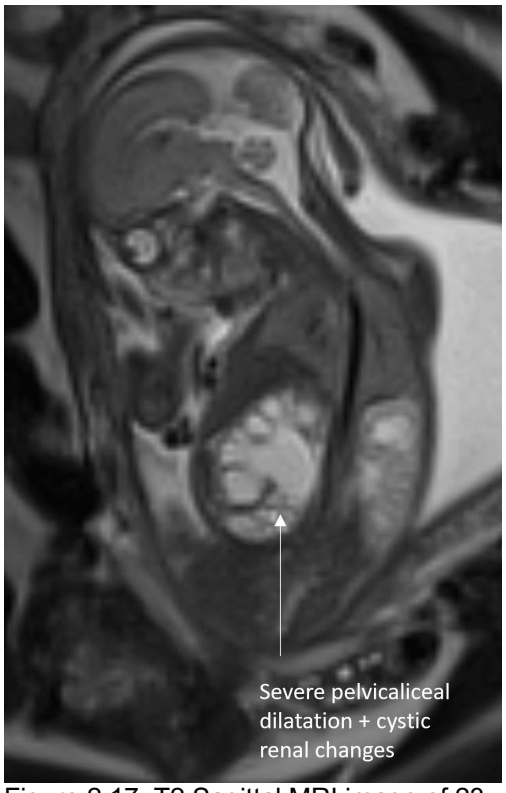


Figure 2.17. T2 Sagittal MRI image of 23 week fetus with posterior urethral valves

Musculoskeletal anomalies

Common musculoskeletal referrals for fetal MRI include talipes, a deformity of the foot position, limb defects such as an absent hand or forearm and suspected skeletal dysplasia. Figures 2.18 and 2.19 show fetal MRI imaging of fetuses with talipes and an absent hand respectively. In these cases, MRI is frequently used to differentiate between isolated and more complex anomalies, which informs prognostication [53].

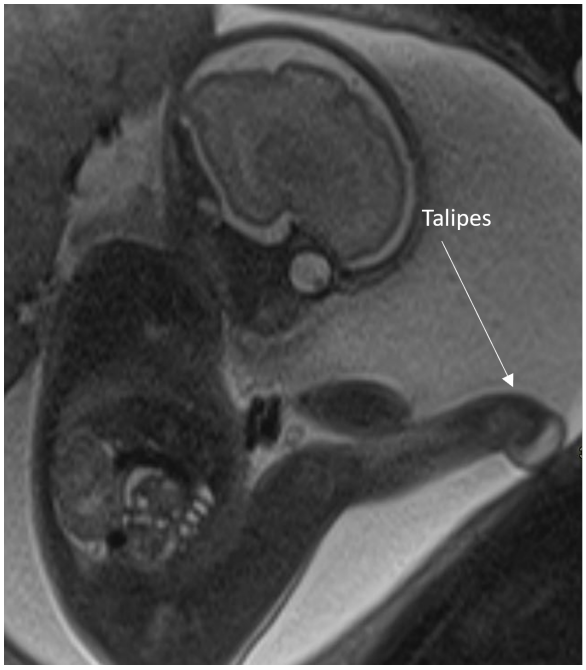


Figure 2.18. T2 HASTE STIR Sagittal MRI image of talipes in 29+6 week fetus

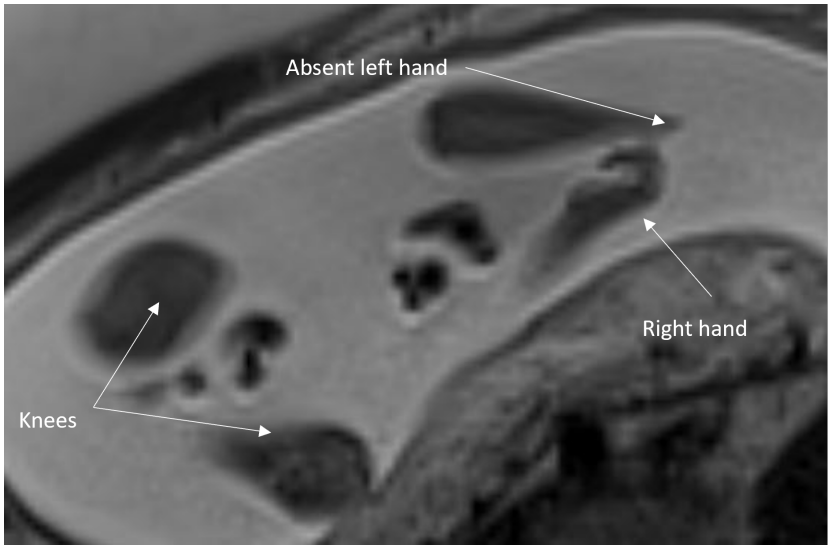


Figure 2.19. T2 HASTE Coronal MRI image of 22+1 week fetus with absent left hand

Lymphovascular anomalies

Congenital lymphatic malformations are frequently referred for fetal MRI to enable more detailed characterisation of the malformation and the extent of the lesion. More specifically in lymphatic malformations of the neck, as shown in figure 2.20, fetal MRI has an additional role of assessing airway patency which will inform management at birth.

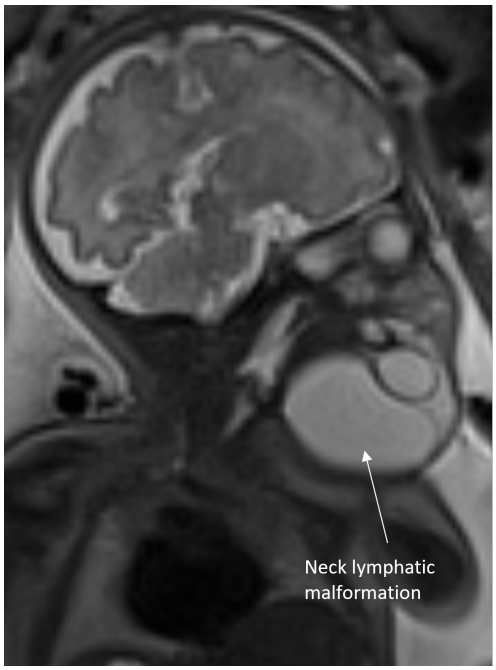


Figure 2.20. T2 HASTE Coronal MRI image of 25 week fetus with anterior neck lymphatic malformation

Head and neck anomalies

Finally, fetal MRI may be used to provide more detail in cases of suspected cleft lip and/or palate as shown in figure 2.21 and in cases of micrognathia shown in figure 2.22. In such cases, fetal MRI can confirm the diagnosis and also assess for presence of other associated congenital anomalies.

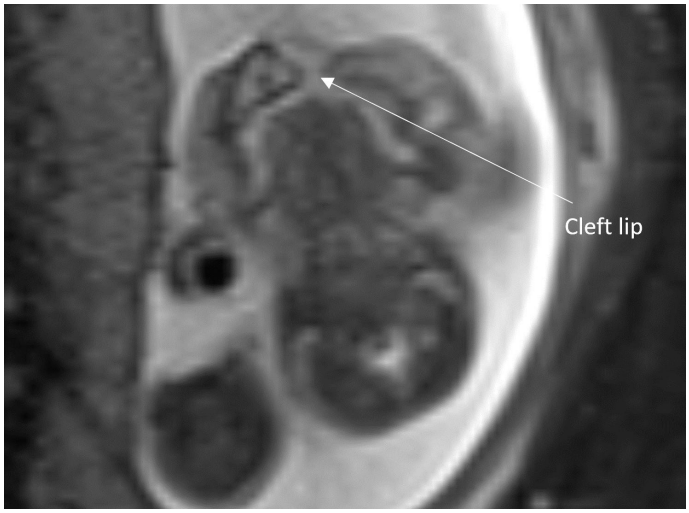


Figure 2.21. T2 Axial MRI image of cleft lip in 21 week fetus

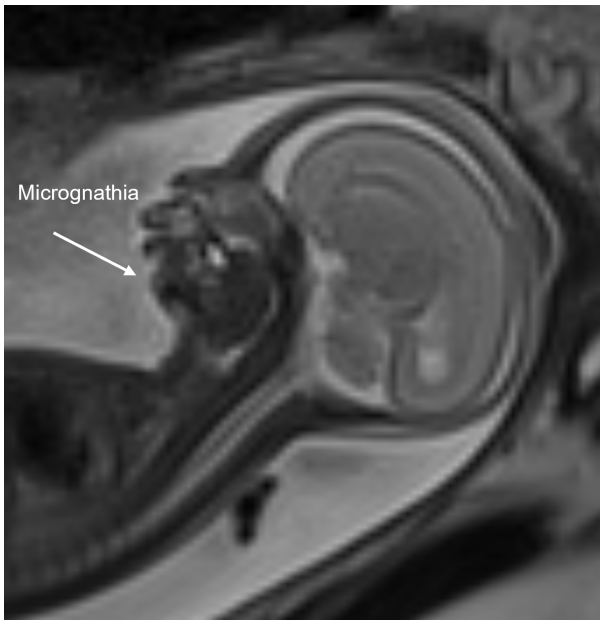


Figure 2.22. T2 HASTE Sagittal MRI image of micrognathia in a 25 week fetus

Aims

The aim of this research was to assess the diagnostic accuracy of fetal MRI for congenital anomalies of the fetal body using postnatal diagnosis made by imaging, surgery or post-mortem examination as the reference standard.

Methods

Ethical approval for this study was provided by the Health Research Authority (IRAS project ID 222053 and REC reference 17/EE/0162). This study was a combined retrospective and

prospective review of all patients referred to our centre for fetal MRI between 1st December 2020 and 30th September 2023. The patient data collected from this time period has not been previously studied. Data collection was undertaken from September 2022 to March 2024 to allow time for the outcomes of all the pregnancies and the final diagnosis to be available at the point of analysis.

The inclusion criteria were patients referred for a fetal MRI as part of their National Health Service (NHS) care within the United Kingdom due to a suspected abnormality of the fetal body, or presence of risk factors for such anomalies. These patients were under the care of a Fetal Medicine Unit and had undergone ultrasound at the tertiary centre prior to their MRI. Patients with suspected anomalies of the fetal brain, spinal cord or placenta were excluded. A sample size calculation was not performed for this study as the aim was to include the maximum number of patients who underwent fetal MRI during the study period. A power calculation was not possible for this cohort owing to the heterogeneity of pathology being studied.

Data collection

Data was collected from the maternal medical notes concerning the suspected diagnosis from the antenatal ultrasound, the reason for referral for fetal MRI, the fetal MRI report and the outcome of the pregnancy including termination of pregnancy, miscarriage, stillbirth or live birth. In cases of live birth, the neonatal notes were also reviewed to determine the final diagnosis and outcome for the baby. The MRI scans were undertaken using a 1.5 Tesla Siemens Avanto scanner (Erlangen, Germany) and images reviewed using the Agfa Healthcare (Mortsel, Belgium) Enterprise Imaging platform. The images were reported by a consultant radiologist with over 25 years of experience in fetal MRI and reviewed with a second consultant radiologist with significant paediatric and fetal radiology experience prior to the reports being finalised. The final diagnosis was made from postnatal imaging or surgical findings. In cases of termination of pregnancy (TOP), miscarriage, stillbirth or neonatal death the diagnosis from the post-mortem examination was obtained where available.

Data analysis

The patients were analysed in groups relating to the anatomical area of concern or system involved i.e. thoracic, abdominal, genito-urinary tract, head and neck, musculoskeletal and lymphovascular systems. A miscellaneous category was used to analyse fetuses referred for

MRI without a structural anomaly seen on ultrasound. This was where a fetal medicine unit referral and subsequent fetal MRI was undertaken in cases with risk factors for congenital anomalies such as family history or teratogen exposure. For fetuses referred for MRI with multiple anomalies of more than one system the diagnostic accuracy assessment was done individually for each body system. The final diagnosis made by postnatal imaging, surgery or postmortem examination was used as the outcome reference diagnosis, the ultrasound and MRI diagnoses were compared with this in order to assess diagnostic accuracy. Diagnostic accuracy was defined as the number of correct diagnoses (true positives and true negatives) in comparison with the total number of tests. McNemar's test was used to determine if the difference in diagnostic accuracy between the two imaging modalities was statistically significant. The positive predictive value (PPV) and negative predictive value (NPV) were used in parts when summarising diagnostic accuracy. Sensitivity and specificity were not deemed appropriate global measures as the rates of true negatives and false negatives were unknown for ultrasound meaning such results would have been flawed.

The utility of the information provided by the fetal MRI in clinical practice was then graded by obstetric and neonatal consultants; this work is presented in the subsequent chapter.

Results – Overall diagnostic accuracy

Patient characteristics

A total of 937 MRI scans were performed during the time period 1st December 2020 to 30th September 2023. 626 of these scans were excluded from the analysis as they were MRIs for CNS anomalies (n=420), placental anomalies (n=171) or they were repeat scans of fetuses with body anomalies (n=35). There were a total of 311 fetal MRI scans performed either due to suspected structural anomaly seen on ultrasound (n=292) or a risk factor for a structural anomaly (n=19). The 19 patients with only a risk factor for a structural anomaly were reviewed, however, these cases were not included in the diagnostic accuracy analysis as there was no structural anomaly seen on ultrasound for comparison. This is summarised in figure 2.23.

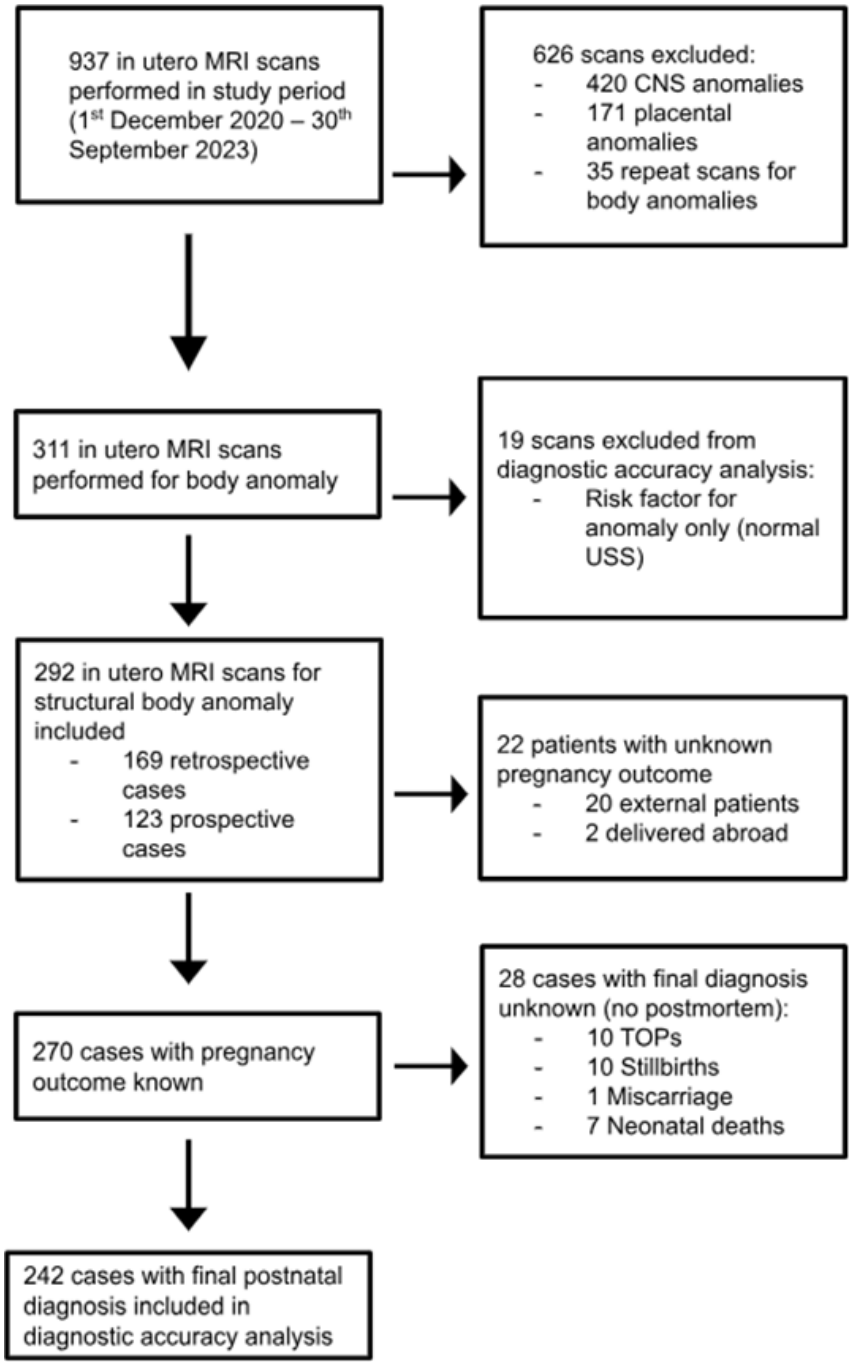


Figure 2.23. Process of case selection and final numbers included

292 patients were included in the analysis, 169 of these were retrospectively analysed as their scans were performed before September 2022 with the other 123 patients analysed prospectively during the study period. 70 patients were referred from a total of ten external sites, the remaining 222 patients were referred for fetal MRI from our centre. There were 281 singleton pregnancies and eleven twin pregnancies.

The mean gestational age at the time of MRI was 26.7 weeks with a range of 13-39 weeks

as shown in figure 2.24. As expected, there is a peak in MRIs performed at 21-23 weeks reflecting referral following the ultrasound anatomy scan which is undertaken at around 20 weeks. The time between referral for MRI and the scan being performed was 0-25 days with a mean of 7.9 days.

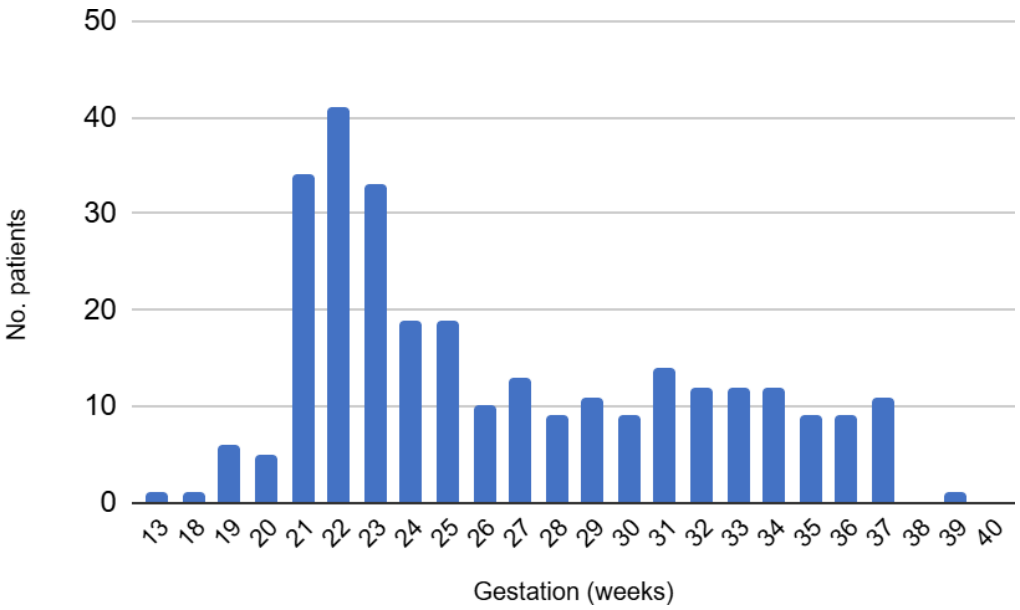


Figure 2.24. Gestation at time of fetal MRI

Data regarding the outcome of the pregnancy was available for 270 of the 292 patients. A final postnatal diagnosis, made by imaging, surgery or postmortem examination, was available in 242 patients. For the 22 patients with no pregnancy outcome, 16 were delivered in external centres who did not respond to our requests for information, four delivered in external centres but the centre was unable to obtain this information from their system and two delivered abroad. The pregnancy outcomes where available are summarised in table 2.2.

Pregnancy Outcome	**No. patients (n=270)**
Termination of pregnancy	22
Miscarriage (<24 weeks)	2
Stillbirth (>24 weeks)	12
Live birth	234
Live birth outcomes:	**No. patients (n=234)**
Alive & well	202
Neonatal death	22
Death after neonatal period	10

Table 2.2. Pregnancy outcomes

There were 28 patients in whom the pregnancy outcome was known but a final diagnosis could not be made. This was due to a postmortem examination not being performed following termination of pregnancy (n=10), miscarriage (n=1), stillbirth (n=10) and early neonatal death following planned palliative delivery (n=7).

There were 242 patients with pregnancy outcome and final diagnosis known used in the analysis of diagnostic accuracy. There were a total of 248 diagnoses as some patients had multiple anomalies. The anatomical systems of the anomalies were thoracic (n=51), abdominal and gastrointestinal (GI) tract (n=79), genito-urinary and renal tract (n=69), musculoskeletal (n=25), head and neck (n=15) and lymphovascular (n=9). The proportion of the different body systems the anomalies related to is shown in figure 2.25.

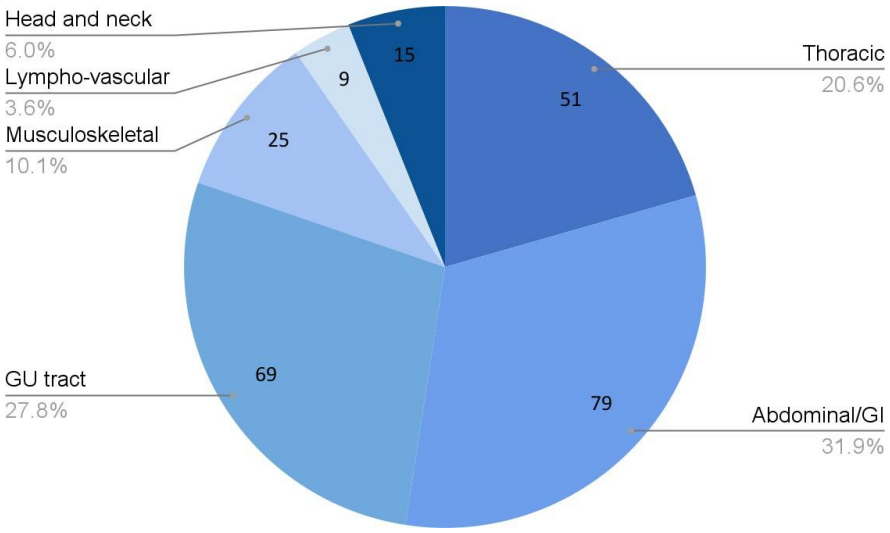


Figure 2.25. The body systems of the anomalies included in the study (n=248)

Overall diagnostic accuracy

The ultrasound diagnosis was correct in 149/248 cases (60.1%) and the MRI diagnosis was correct in 210/248 cases (84.7%). McNemar's test was used to determine that the improved diagnostic accuracy with the addition of MRI of 24.6% was statistically significant as $p<0.001$. This was further confirmed with a Cochrane's Q test which also showed $p<0.001$. The negative predictive value for MRI was 93.6% as 44/47 cases reported to be normal by MRI did not have any structural anomalies diagnosed after birth.

Results – Thoracic anomalies

There were 59 cases with suspicion of a thoracic anomaly who underwent fetal MRI during the study period. This included 60 fetuses as one case was of conjoined twins. The mean gestational age at the time of MRI was 24.6 weeks with a range of 13-37 weeks. The mean time between ultrasound and MRI was 6.2 days. The pregnancy outcome was available in 58 cases as one was from an external site who were unable to provide further information. A postnatal diagnosis was made in 51 cases as there were three terminations of pregnancy, two stillbirths and two neonatal deaths following palliative delivery all of whom did not undergo postmortem examination. There were three cases of twin pregnancy but only one where both twins had a structural anomaly. Overall, there were seven terminations of pregnancy, two stillbirths and 49 live births. Of the live births there were seven neonatal deaths, of which three were following a planned palliative delivery, and three further deaths outside the neonatal period.

Following the MRI twelve different diagnoses were made, including normal findings. The MRI diagnoses (n=59) are summarised below in table 2.3. The most common MRI diagnoses were congenital pulmonary airway malformation (CPAM, n=17), congenital diaphragmatic hernia (CDH, n=12), pleural effusion (n=6), of which four were bilateral, and lung aplasia (n=4) of which two were lobar and two were complete right lung aplasia. The cases with a normal MRI (n=6) included ultrasound suspicions of congenital diaphragmatic hernia, a chest wall mass, sternal calcification, a cyst behind the heart, an accessory rib and left-sided cardiac deviation.

MRI diagnosis	**No. cases (n=59)**
Cystic pulmonary airway malformation	17
Congenital diaphragmatic hernia	12
Pleural effusion - Bilateral - Unilateral	6 - 4 - 2
Lung aplasia - Entire single lung - Lobar	4 - 2 - 2
Diaphragmatic eventration	3
Lobar emphysema	3
Bronchogenic cyst	2
Lung hypoplasia (globally small lungs)	2
Pentalogy of Cantrell	2
Conjoined twins (shared heart)	1
Pericardial effusion (isolated)	1
Normal findings	6

Table 2.3. Diagnosis made by fetal MRI in thoracic anomaly group

The final diagnoses made by imaging, surgery or postmortem examination are shown in Table 2.4. There were seven cases with no abnormality detected at birth, five of these had a normal MRI scan and two had pleural effusions which had resolved by the time of birth. The most common diagnoses were again CPAM (n=16) and CDH (n=8). All cases of CPAM were

live born and these patients were all alive and well at the time of data analysis. Seven of the eight CDH cases were live born, with one undergoing termination of pregnancy. There were unfortunately two neonatal deaths with CDH, but the remaining five patients have undergone successful surgical repair. In this cohort there were three patients diagnosed with a previously unknown cardiac abnormality after delivery, but as fetal body MRI is not used in our centre to detect cardiac anomalies; this has not been considered a missed diagnosis during the analysis.

Postnatal diagnosis	**No. cases (n=51)**
Cystic pulmonary airway malformation	16
Congenital diaphragmatic hernia	8
Lung aplasia	4
Cardiac anomaly	3
Bronchogenic cyst	3
Diaphragmatic eventration	2
Lung hypoplasia	2
Pentalogy of Cantrell	2
Pleural effusion	2
Foregut duplication cyst in chest	1
Lobar emphysema	1
No abnormality	7

Table 2.4. Final thoracic anomaly diagnosis made by postnatal imaging, surgery or postmortem

Diagnostic accuracy for thoracic anomalies

The diagnostic accuracy for diagnosis of thoracic anomalies was 66.7% (34/51) for ultrasound and 88.2% (45/51) for MRI. Therefore, with the addition of fetal MRI there was an improvement in diagnostic accuracy of 21.5% which was statistically significant with $p<0.001$ using McNemar's test. The negative predictive value for MRI was 100%. There were 6/51 cases where the MRI information did not align with the postnatal diagnosis. There were two pleural effusions which were not present at birth, a missed CDH which had been reported as diaphragmatic elevation in a patient with comorbid gastroschisis and two cases of lobar emphysema on MRI which were diagnosed as CPAM after birth. There was also one

suspected CPAM who had a normal chest x-ray after birth although they did not have a computed tomography (CT) scan, as is the gold standard in CPAM diagnosis, as they unfortunately died in the neonatal period and did not undergo postmortem examination.

In CDH the positive predictive value of MRI was 100% but there was one missed case as discussed above. In cases of CPAM the PPV for MRI was 87.5% owing to the cases discussed above and a case which was diagnosed as a foregut duplication cyst after birth. There were two cases of Pentalogy of Cantrell which is a complex condition with poor prognosis comprising a collection of five midline defects of the heart, pericardium, diaphragm, sternum and abdominal wall [54].

Results – Abdominal and gastrointestinal tract anomalies

There were 98 cases referred for fetal MRI due to a suspected anomaly of the abdomen or gastrointestinal tract. The mean gestational age at the point of MRI scan was 27.1 weeks with a range of 18-39 weeks. The mean time between ultrasound and MRI was eight days. Data regarding the outcome of the pregnancy was available for 87 cases, as eleven cases were referred from external centres which were unable to provide outcome data. In this cohort there were six terminations of pregnancy, four stillbirths and 77 live births. In the group of 77 live births there were seven deaths in the neonatal period, of which one was a planned palliative delivery, and four deaths outside the neonatal period. The remaining 66 patients were alive and well at the time of data collection.

A total of 79 patients had a final diagnosis made by imaging, surgery or postmortem examination. This is because eleven external cases had no outcome data and there were three terminations, four stillbirths and one neonatal death who did not undergo postmortem examination.

There were a total of 101 diagnoses made from the fetal MRI as three patients were given more than one diagnosis. The most common MRI diagnoses were suspected tracheo-oesophageal fistula/oesophageal atresia (TOF/OA, n=18), abdominal wall defects (n=16) such as gastroschisis and exomphalos and intra-abdominal cysts (n=19). The intra-abdominal cysts were split in specific diagnosis, ovarian cysts were included in this cohort as they are frequently referred for MRI as non-specific intra-abdominal cysts. The details of all the MRI diagnoses are shown in table 2.5. There was one case of normal gastrointestinal tract findings, but a diagnosis of suspected neuromuscular condition made following MRI, this was a case referred for MRI due to a small stomach on ultrasound to rule out TOF/OA,

but the MRI was highly suggestive of amyoplasia.

MRI diagnosis	**No. cases (n=101)**
TOF/OA	18
Abdominal wall defects - Gastroschisis - Exomphalos - Pentalogy of Cantrell - Umbilical cord hernia	16 - 8 - 4 - 2 - 2
Ovarian cyst	9
Abdominal cyst	7
Duodenal atresia	6
Ascites	5
Liver cyst	3
Small/compressed bowel	3
Anal atresia (dilated rectum)	2
Delayed stomach emptying	1
Dilated bowel loops	1
Hepatosplenomegaly	1
Heterotaxy	1
Large/dilated stomach	1
Non-GI diagnosis (amyoplasia)	1
Prominent mucosal fold of stomach	1
Normal MRI findings	25

Table 2.5. Diagnosis made by fetal MRI in abdominal/GI tract anomaly group

The final diagnosis made by imaging, surgery or postmortem is shown in table 2.6 (n=79). The most common anomalies at birth were the abdominal wall defects, with gastroschisis being the most common (n=8). All cases of gastroschisis were liveborn with one death in the neonatal period. There were 30 patients with no anomaly detected at birth. Ten of these patients had TOF/OA suspected on their antenatal imaging as discussed below, two had

abdominal cysts on MRI which had resolved on subsequent ultrasound scans prior to birth and the remaining 18 had a normal MRI report. Seven patients had coexisting anomalies of other body systems at birth, four were known cardiac defects, there was one cloacal anomaly, one neuromuscular disorder and one case of CHARGE syndrome (Coloboma of the eye, Heart defects, Atresia choanae, Restricted growth, Genital defects, Ear anomalies).

Postnatal diagnosis	**No. cases (n=79)**
Abdominal wall defects - Gastroschisis - Exomphalos - Pentalogy of Cantrell - Umbilical cord hernia	1 5 - 8 - 4 - 2 - 1
Abdominal cyst	5
Duodenal atresia	4
Ovarian cyst	4
TOF/OA	4
Ascites	3
Adrenal haemorrhage	1
Congenital haemophagocytic lymphohistiocytosis (HLH)	1
Extrapulmonary sequestration	1
Imperforate anus & cloacal anomaly	1
Liver calcification	1
Pyloric web	1
Stomach polyp	1
No GI tract/abdominal anomaly - No anomaly - Anomaly of other system	3 7 - 30 - 7

Table 2.6. Final abdominal/GI tract anomaly diagnosis made by postnatal imaging, surgery or postmortem

Diagnostic accuracy for abdominal and gastrointestinal tract anomalies

The diagnosis made by ultrasound was correct in 41/79 cases (51.9%) and the diagnosis made by MRI was correct in 61/79 (77.2%). Therefore, MRI had an improved diagnostic accuracy over ultrasound of 25.3% which was statistically significant with $p<0.001$ using McNemar's test. The negative predictive value of MRI was 95.2% as there was one case reported as normal on MRI which had liver calcification on a postnatal ultrasound. This case was initially referred for MRI due to a diaphragmatic lesion seen on ultrasound.

There were 18 cases (22.8%) where the MRI diagnosis was not the same as the postnatal diagnosis. Ten of these cases were suspected TOF/OA which is discussed in detail in the professional gradings and in the subchapter concerning diagnosis of TOF/OA. One of the incorrect cases suspected to be anal atresia due to a dilated sigmoid colon on MRI was diagnosed with a cloacal anomaly including an imperforate anus after birth. Another misdiagnosed case was a patient with urethral obstruction with massive cystic dilatation of the left kidney seen on postmortem examination which was diagnosed as an abdominal cyst on ultrasound and a cyst with ascites on MRI. There were two cases of an abdominal cyst which was no longer present at birth which were not considered to be an incorrect diagnosis by the initial USS and MRI as this is a known process and the resolution was observed on subsequent ultrasound imaging prior to delivery.

The PPV for MRI in cases of gastroschisis was 100%, ultrasound also had 100% PPV. MRI had 100% PPV for exomphalos compared with 60% for ultrasound. As previously discussed in the thoracic anomalies section, one of these cases included a suspected isolated exomphalos on ultrasound which had Pentalogy of Cantrell diagnosed on MRI and at birth. For the cases of duodenal atresia MRI had 100% PPV. Ultrasound had 80% PPV for duodenal atresia as one of the suspected cases had an intrapulmonary sequestration diagnosed both on MRI and at birth.

Results – Congenital anomalies of the kidney and urinary tract

There were 91 cases of suspected congenital anomalies of the kidney and urinary tract (CAKUT) who underwent fetal MRI. The mean gestational age at the time of MRI was 25.5 weeks with a range of 19-37 weeks. The mean time between ultrasound and MRI was 7.9 days with a range of 0-24 days. 82 cases had outcome data available as seven cases were from external sites and two patients are thought to have delivered abroad. The outcomes for these patients included termination of pregnancy in eight, one miscarriage, five stillbirths and

68 live births from which there were eight neonatal deaths and two deaths after the neonatal period.

A postnatal diagnosis was made in 69 cases which have been used to assess diagnostic accuracy. The final diagnosis was missing for 22 patients because nine did not have outcome data and because postmortem examination was not performed in the case that miscarried, three of the terminations, all five stillbirths and four of the neonatal deaths.

There were 93 diagnoses made following fetal MRI as 91 cases were imaged but two cases had two separate anomalies diagnosed. A breakdown of the conditions diagnosed is shown in table 2.7 below. The most common diagnoses were multicystic dysplastic kidney (MCDK, n=18) of which the majority were unilateral (n=15) and renal agenesis (n=17) from which nine were unilateral and eight were bilateral. There were two cases referred for MRI due to suspected CAKUT which were diagnosed with anomalies of different body systems following the MRI. One of these was a suspected absent kidney which on MRI was seen to be a CDH with the kidney visualised in the thorax. The other was a diagnosis of a suspected complex genetic problem as multiple anomalies were seen on MRI which had been referred as a possible horseshoe kidney on ultrasound.

MRI diagnosis	No. cases (n=93)
Multicystic dysplastic kidney (MCDK) - Unilateral - Bilateral	18 - 15 - 3
Renal agenesis - Unilateral - Bilateral	17 - 9 - 8
Duplex kidney	7
Cloacal anomaly	6
Pelvic kidney	6
Pelvi-ureteric junction obstruction (PUJO)	6
Posterior urethral valves (PUV)	4
Renal hypoplasia	4
Horseshoe kidney	3
Bright kidneys	2
Hydroureter	1
Urinoma	1
Urogenital sinus	1
Suprarenal cyst	1
Crossed fused ectopia	1
Anomaly of other body system	2
No anomaly detected	13

Table 2.7. Diagnosis made by fetal MRI in CAKUT group

The final diagnosis made by imaging, surgery or postmortem examination is shown in Table 2.8. The most common diagnoses were again MCDK (n=16) and renal agenesis (n=13). All cases of unilateral MCDK are alive and well but the three bilateral cases unfortunately died in the neonatal period. There were eight patients with unilateral renal agenesis who were all live born; five of the eight patients are alive and well. There were five cases of bilateral renal agenesis with outcome data, three underwent termination of pregnancy and the other two died shortly after birth as palliative management at delivery was planned.

Postnatal diagnosis	No. cases (n=69)
Multicystic dysplastic kidney - Unilateral - Bilateral	16 - 13 - 3
Renal agenesis - Unilateral - Bilateral	13 - 8 - 5
Pelvic kidney	5
Duplex kidney	4
Posterior urethral valves (PUV)	4
Pelvi-ureteric junction obstruction (PUJO)	3
Bright kidneys	2
Horseshoe kidney	2
Genetic condition	2 (Pallister Killian syndrome & Fraser syndrome)
Caecoureterocoele	1
Cloacal anomaly	1
Enlarged kidney	1
Kidneys crossed but not fused	1
Renal hypoplasia	1
Suprarenal cyst	1
VACTERL (with hydronephrosis only)	1
No genitourinary tract anomaly - No anomaly - CDH with kidney in thorax	11 - 10 - 1

Table 2.8. Final CAKUT diagnosis made by postnatal imaging, surgery or postmortem

Diagnostic accuracy for CAKUT

The diagnostic accuracy was 65.2% for ultrasound (45/69 correct) and 89.9% for MRI (62/69 correct). Therefore, fetal MRI had an improved diagnostic accuracy over ultrasound of 24.7%

which was statistically significant with $p<0.001$ using McNemar's test. The negative predictive value of MRI was 83.3% as one case reported to be normal on MRI had bilateral dysplastic kidneys at birth with a genetic mutation. There was also a case of unilateral hydronephrosis noted at birth as part of VACTERL where the associated limb defects had been noted on MRI, but the kidneys were reported as normal. The MRI diagnosis did not align with the final diagnosis in 7/69 (10.1%) of cases.

In cases of multicystic dysplastic kidney, ultrasound and MRI both had a similar positive predictive value of 93.8% for ultrasound and 93.3% for MRI. The positive predictive value in cases of unilateral renal agenesis was 100% for MRI but 54.5% for ultrasound. The diagnostic accuracy of ultrasound in cases of bilateral renal agenesis was improved for ultrasound with a positive predictive value of 60%, but still lower than MRI which had 100% accuracy.

Results – Musculoskeletal anomalies

There were 29 cases either referred for fetal MRI due to suspected musculoskeletal (MSK) anomaly or with a suspected MSK anomaly seen on the fetal MRI. The mean gestational age at the time of MRI was 25.7 weeks with a range of 19-33 weeks. The average length of time between ultrasound and MRI was 8.1 days (range 0-20 days). Outcome data was available in 27 out of the 29 cases as one patient is thought to have delivered abroad and the other delivered at an external site who were unable to provide the information. A final postnatal diagnosis was available in 25 cases as two had no known outcome, and there was one termination of pregnancy and one neonatal death both of whom did not undergo a postmortem examination.

In this cohort there were four terminations of pregnancy, one miscarriage, one stillbirth and 21 live births of whom two died in the neonatal period and a further three died in infancy. The primary diagnosis made by MRI is shown in table 2.9, 31 diagnoses were made as two patients had two separate MSK anomalies. The most common anomalies were short long bones (n=6), forearm anomalies (n=6) and talipes (n=5).

MRI diagnosis	No. cases (n=31)
Short long bones	6
Forearm anomaly - Absent forearm - Absent hand - Complex deformity - Forearm short and flexed	6 - 3 - 1 - 1 - 1
Talipes - Bilateral - Unilateral	5 - 3 - 2
Caudal regression	2
Hemivertebra	2
Muscular disorder - Amyoplasia - Myopathy	2 - 1 - 1
Bilateral pedal oedema	1
Hyper-extended neck	1
Postural limb deformity	1
Sirenomelia	1
Normal MRI findings	4

Table 2.9. MRI diagnosis in MSK anomaly group

The diagnoses made after delivery are shown in table 2.10. The most common anomalies seen postnatally were talipes (n=5) and forearm anomalies (n=4). There were seven cases with no musculoskeletal anomaly at birth. All of these had been referred for an MRI due to suspected short long bones on ultrasound, four had a normal MRI and the other three had an MRI suggestive of short long bones as well. There were three cases of genetic anomaly including Jeune syndrome causing skeletal dysplasia, Pallister Killian syndrome and a Nemeline myopathy.

Final diagnosis	No. cases (n=25)
Talipes	5
Forearm anomaly - Absent forearm - Absent hand - Complex deformity	4 - 2 - 1 - 1
Scoliosis	2
Amyoplasia	1
Bilateral pedal oedema	1
Jeune syndrome (skeletal dysplasia)	1
Nemeline myopathy	1
Pallister Killian syndrome	1
Sirenomelia	1
VACTERL	1
No MSK anomaly	7

Table 2.10. Final MSK anomaly diagnosis made by postnatal imaging, surgery or postmortem

Diagnostic accuracy for musculoskeletal anomalies

The MRI diagnosis was correct in 20/25 cases (80%), whereas the ultrasound diagnosis was correct in 16/25 cases (64%). When using McNemar's test to determine if this increase in diagnostic accuracy of 16% with the addition of MRI was statistically significant, the p value was 0.125 meaning this result was not statistically significant for this group in isolation. The negative predictive value of MRI was 100%. The MRI diagnosis was incorrect in five cases, three of these were suspected short long bones which were normal at birth. The other two cases of incorrect MRI both had scoliosis after birth but hemivertebrae and a hyper-extended neck seen on MRI. The diagnostic accuracy for talipes was 100% for both ultrasound and MRI.

Results – lymphovascular anomalies

There were nine cases referred for or with fetal MRI suggestive of lymphovascular anomaly. The mean gestation at the point of fetal MRI was 29.9 weeks with a range of 23-35 weeks.

The mean time between ultrasound and MRI was 5.3 days with a range of 1-12 days. The data regarding the outcome of the pregnancy and the overall diagnosis made by postnatal imaging, surgery or postmortem examination was available for all nine patients. There were eight live births all of whom are alive and well and one termination of pregnancy for which a postmortem examination was undertaken.

MRI diagnosis	**No. cases (n=9)**
Lymphatic malformation - Abdominal wall - Neck - Arm - Chest wall - Widespread	8 - 3 - 2 - 1 - 1 - 1
Teratoma (neck)	1

Table 2.11. MRI diagnosis for lymphovascular anomaly group

The primary diagnoses made by MRI are shown in table 2.11 and the final postnatal diagnoses are shown in table 2.12. The majority of cases were of lymphatic malformation (n=8).

Final diagnosis	**No. cases (n=9)**
Lymphatic malformation	8
Teratoma	1

Table 2.12. Final lymphovascular anomaly diagnosis made by postnatal imaging, surgery or postmortem

Diagnostic accuracy for lymphovascular anomalies

The diagnostic accuracy for MRI was 100% in these cases. The ultrasound diagnosis was correct in 77.8% as in two cases it was unable to refine the diagnosis. This improvement in diagnostic accuracy of 22.8% was not statistically significant as p=0.157 using Cochrane's Q test owing to small sample numbers.

The role of fetal MRI in providing additional detail in lymphovascular anomalies is discussed further in the gradings chapter and in the pictorial case series of neck masses.

Results – Head and neck anomalies

There were 16 cases of suspected anomaly of the head and neck who underwent fetal MRI. Cases of lymphovascular anomaly were analysed and discussed in the previous section. The mean gestational age at the time of MRI was 27.4 weeks (range 19-34 weeks) and the mean time between ultrasound and MRI was 6.1 days (range 0-15 days). The outcome of the pregnancy was available for 15 of the 16 patients as one was from an external centre which did not respond to the request for information. A final diagnosis from imaging, surgery or postmortem examination was available for all 15 patients with a known pregnancy outcome. In this group there were two terminations of pregnancy and 13 live births of which there were two neonatal deaths and one further death in childhood.

The primary diagnoses made from fetal MRI are shown in table 2.13. There were 17 diagnoses for 16 patients as one patient had a suspected cleft lip and micrognathia. There were five cases where no anomaly was detected on MRI. They had been referred due to ultrasound suspicion of a small nose, choanal atresia, a neck cyst and two cases of cleft lip and palate.

MRI diagnosis	**No. cases (n=17)**
Cleft - Lip & palate - Palate only	3 - 2 - 1
Micrognathia	4
Complex craniofacial anomaly (suspected genetic condition)	1
Cryptophthalmos (suspected Fraser syndrome)	1
Enlarged thyroid	1
Low set ears	1
Small oral cavity	1
No anomaly detected	5

Table 2.13. MRI diagnosis in head and neck anomaly group

The final diagnosis made by imaging, surgery or postmortem examination for these patients

is shown in table 2.14. All five cases with no anomaly at birth had a normal MRI report. There were a significant number of genetic conditions in this cohort (26.7%), one of whom underwent termination of pregnancy and the other three died after birth.

Final diagnosis	**No. cases (n=15)**
Cleft - Palate only - Lip and palate	4 - 3 - 1
Micrognathia - Pierre Robin sequence	2 - 1
Genetic condition - CHARGE syndrome - Fraser syndrome - Noonan's syndrome - Pallister Killian syndrome	4 - 1 - 1 - 1 - 1
No anomaly	5

Table 2.14. Final head and neck anomaly diagnosis made by postnatal imaging, surgery or postmortem

Diagnostic accuracy for head and neck anomalies

The diagnosis suspected on ultrasound was in agreement with the final diagnosis in 6/15 cases (40%) and the MRI diagnosis was in agreement with the final diagnosis in 13/15 cases (86.7%). This improved diagnostic accuracy of 46.7% with MRI was statistically significant as p=0.016 using McNemar's test. The negative predictive value for MRI was 100% as all five MRIs reported as normal had no anomalies diagnosed after birth. The two cases in which the MRI diagnosis was not correct had been diagnosed as micrognathia only but also had a cleft palate at birth. In terms of cleft palate diagnosis, fetal MRI had a positive predictive value of 100% as both suspected cases with outcome data were confirmed at birth.

Results – Non-structural anomalies

There were 19 patients referred for fetal MRI due to non-structural anomalies; these cases were not included in the diagnostic accuracy analysis but were discussed by the group of professionals undertaking the utility gradings in the subsequent chapter. The reasons for

referral for MRI are listed in table 2.15.

Reason for MRI referral	No. cases (n=19)
Oligohydramnios only	7
Polyhydramnios only	4
Cytomegalovirus exposure	2
No fetal movements seen	2
Small for gestational age	2
Family history of spinal muscular atrophy	1
Family history of vesicoureteric reflux	1

Table 2.15. Reason for referral for MRI in non-structural anomaly group

Discussion

Antenatal ultrasound remains the gold standard for diagnosis of anomalies of the fetal body in the UK. Previous studies, however, have shown an increase in diagnostic accuracy with the addition of fetal MRI. The majority of studies have been focused on the antenatal diagnosis of central nervous system anomalies in isolation [19] or have studied both CNS and body malformations but with comparatively small numbers of non-CNS anomalies [42]. The current evidence for the role of fetal MRI in antenatal diagnosis of anomalies of the fetal body was summarised and analysed in a systematic review and meta-analysis which we have previously undertaken [44]. This work found ultrasound to have a diagnostic accuracy of 60.6% which improved to 86.4% with the addition of fetal MRI. This systematic review was limited by sample size, with only 12 studies with a total of 361 patients meeting the inclusion criteria and a large proportion of these studies (7/12) were focused on congenital anomalies of the kidney and urinary tract (CAKUT). Each individual study had patient numbers ranging from 14-53. Our study included 242 patients with a known pregnancy outcome and final diagnosis. Another factor limiting the systematic review was the time period over which the included studies were conducted (2003-2021) as the technology and use of fetal MRI has changed substantially over this period. This research therefore aimed to add to this knowledge base with more patient data conducted over a more recent time period with consistent use of fetal MRI at our centre.

Diagnostic accuracy

The diagnostic accuracy of antenatal ultrasound alone was 60.1% in this study, which is comparable with the results from our systematic review in which ultrasound had 60.6% accuracy. The addition of fetal MRI led to increased diagnostic accuracy of 84.7% and this improved accuracy of 24.6% was statistically significant ($p<0.001$). These findings were again in concordance with our systematic review findings which found the diagnostic accuracy with the addition of fetal MRI to be 86.4% in those studies combined with an improvement of 25.8%.

When the diagnostic accuracy data was analysed in more detail in relation to the anatomical system of the individual anomaly and the specific diagnosis there was a wider range of diagnostic accuracy. Overall, the diagnostic accuracy for fetal MRI was comparable for the thoracic, genitourinary and head/neck cases with diagnostic accuracy of 88.2%, 89.9% and 86.7% respectively. This was lower in the musculoskeletal group (80%) and in the abdominal and GI tract group (77.2%). In the lymphovascular cases the MRI had 100% diagnostic accuracy, however there were fewer cases (n=9). These findings were better than what has been reported in the literature for thoracic anomalies [30,41,55] and lymphovascular anomalies [35], comparable for abdominal anomalies [32,36]and slightly lower for genitourinary and renal malformations [26–29,31,33,34] with around 4% difference from what has been previously reported.

In cases of thoracic anomaly there were two cases of pleural effusion which are likely to represent natural resolution over time, something which was discussed in the subsequent chapter by the professionals undertaking gradings of the utility of the MRI information, which will have impacted the diagnostic accuracy calculations. In this cohort, the MRI correctly identified a change in diagnosis from the ultrasound with significant impact on the management at birth and counselling for parents in two cases. One of these cases was a CPAM which had been thought to be a CDH on ultrasound and the other was a Pentalogy of Cantrell which was thought to be purely an exomphalos on the ultrasound.

In the subsection of abdominal and gastrointestinal cases MRI was seen to have overall improved diagnostic accuracy over ultrasound. However, diagnostic accuracy remains an issue for both imaging modalities in cases of TOF/OA with overdiagnosis made by both MRI and ultrasound. How this impacts clinical practice is discussed in the subsequent work with gradings by professionals and in the subchapter concerning the role of fetal MRI in the prenatal diagnosis of TOF/OA. In cases of gastroschisis both ultrasound and MRI were

shown to have 100% diagnostic accuracy which raises the question of whether MRI is of added value in these cases given its cost and limited availability. However, it may be of value from a surgical perspective in determining the size of the abdominal wall defect and potential assessment of bowel health. This is further discussed in the gradings and future research chapters.

Two important diagnoses were missed by both imaging modalities in a case of cloacal anomaly which was thought to be a cyst on ultrasound and an isolated anal atresia on MRI and a case of urethral obstruction thought to be a cyst by both imaging modalities. In this group there was also one case reported as normal on MRI which had liver calcification on a postnatal ultrasound. This case was initially referred for MRI due to a diaphragmatic lesion seen on ultrasound, however it is well recognised that MRI is less useful in detecting calcification than ultrasound [18].

Fetal MRI had an improved diagnostic accuracy over ultrasound of 24.7% in congenital anomalies of the kidneys and urinary tract. The advantages of using fetal MRI in cases of high maternal BMI and the use of DWI assessment of renal function were highlighted in the difference between positive predictive value of ultrasound and MRI in cases of suspected unilateral and bilateral renal agenesis. This was frequently seen in cases where one kidney could not be visualised on ultrasound but was seen on MRI in an ectopic position, the DWI imaging was useful in these cases to confirm presence of the kidney. Two cases of suspected bilateral renal agenesis on ultrasound were incorrect, for one patient a small amount of functional renal tissue was seen on MRI using DWI and after birth, and the other case had a high maternal BMI making visualisation of the fetal kidneys on ultrasound difficult, but both were seen on MRI and after birth. This improved diagnostic accuracy may influence the postnatal management of these babies as it allows decisions surrounding palliative care to be made in cases of bilateral renal agenesis, contributes to planning of the place of birth for example in cases of suspected posterior urethral valves and helps determine the frequency and nature of postnatal imaging in cases of hydronephrosis. Providing an accurate diagnosis will also enable appropriate genetic testing to be undertaken antenatally or in the early postnatal period where indicated. For example, in cases of suspected autosomal recessive polycystic kidney disease, an earlier confirmed genetic diagnosis enables accurate prognostication and counselling for parents.

The MRI diagnosis did not align with the final diagnosis in 7/69 (10.1%) of CAKUT cases. Two of these had normal MRI findings and a further two cases in which the MRI report was different to the final diagnosis may represent evolution of pathology in the time between fetal

MRI and postnatal ultrasound. One of these was a suspected unilateral MCDK which appeared as a unilateral renal agenesis on postnatal scans and the other was a dilated ureter on MRI which was an MCDK after birth. The likelihood of evolution over time was a significant point of discussion during the gradings by consultants which is discussed in the subsequent chapter.

In the cohort of fetuses with musculoskeletal anomalies there was a relatively large proportion of genetic conditions (12%). In these cases, the MRI was able to provide more detail, raising the suspicion of a genetic condition meaning genetic testing could be discussed prior to birth. This was seen in particular in the cases of limb deformity, where MRI frequently was able to provide more detail or additional information leading to a suspected genetic diagnosis. The role of MRI in suspected short long bones is discussed in more detail during subsequent work on the gradings by professionals but both imaging modalities had poor diagnostic accuracy in these cases. 60% of the cases in the musculoskeletal group in which the MRI was incorrect were cases of short long bones which were normal at birth.

Fetal MRI was able to refine the diagnosis for lymphovascular anomalies in two cases in which this had not been possible on ultrasound, meaning ultrasound had a diagnostic accuracy of 77.8% compared with 100% for MRI. These cases included a suspected neck mass which was a teratoma and the other was suspected chest wall mass which was a lymphatic malformation.

In this cohort there were five cases with a family history of a condition which were included in the referral for fetal MRI. Two of these were cases of severe vesico-ureteric reflux and the other three were genetic conditions. The genetic conditions included previous children with Fraser syndrome, Spinal Muscular Atrophy and an ITGA3 mutation. Fraser syndrome is an autosomal recessive disorder which comprises cryptophthalmos, syndactyly and renal agenesis. Spinal Muscular Atrophy causes progressive muscle weakness of varying severity due to loss of motor neurons in the brainstem and spinal cord, it is usually inherited in an autosomal recessive pattern. ITGA3 mutations cause ILNEB syndrome which is a rare genetic disorder characterised by interstitial lung disease, congenital nephrotic syndrome and epidermolysis bullosa and are also most commonly of autosomal recessive inheritance. All of these conditions can be fatal and their autosomal recessive inheritance equates to a 25% chance of the condition in subsequent pregnancies. In these cases fetal MRI may be able to yield the required phenotype to make a likely diagnosis, reducing the need for invasive genetic testing in the pregnancy which carries a risk of miscarriage, or to guide

rapid fetal exome sequencing in the form of the R21 test [56].

Study limitations

The study has some limitations, most of which are due to the methodology reflecting current clinical practice as the study was undertaken using patients having fetal MRI scans as part of their routine NHS care. For example, the ultrasound findings were available to the radiologist reporting the MRI scan meaning confirmation bias may have been a factor. However, this reflects clinical practice and the clinician performing the tertiary ultrasound in the Fetal Medicine Unit would have also had a report from the initial screening ultrasound when undertaking their scan. There was no normative data included in this study as patients were referred for fetal MRI following an abnormality detected on ultrasound, therefore we do not know the accuracy of ultrasounds which were reported as normal. As a result of this, sensitivity and specificity calculations were not performed.

The data set is at risk of selection bias as we do not know how many patients refused to have a fetal MRI scan, their demographics or why they decline the imaging. However, this was mitigated by using data from routine clinical practice, meaning the patients who decline to have a fetal MRI have declined part of their NHS care and not because they were asked to participate in additional research. Anecdotal findings from our qualitative study in the subsequent chapter found patient perceptions of fetal MRI to be acceptable, and the requesting clinicians felt that very few patients declined to attend.

We felt the overall sample size to be reasonable, with the maximum number of patients possible recruited in the time period. However, as the data we were using was from NHS patients, there is heterogeneity with limited data on some of the less prevalent conditions.

Conclusion

In conclusion, this study shows that fetal MRI has increased diagnostic accuracy when compared with ultrasound alone for congenital anomalies of the fetal body, not affecting the central nervous system. This data is in line with previous studies and adds weight to the current body of evidence for the use of fetal MRI as an additional diagnostic tool. Therefore, fetal MRI does not replace antenatal ultrasound but should be used as an adjunct to refine and/or confirm a diagnosis.

2.3 Fetal MRI for congenital anomalies of the fetal body: How useful is it in clinical practice?

Abstract

Introduction - Fetal MRI has been shown to have improved diagnostic accuracy when used in addition to ultrasound for congenital anomalies of the fetal body. However, a detailed understanding of how this information is used by medical professionals in clinical practice is lacking.
Methods - The utility of the information provided by fetal MRI was graded by specialists in fetal medicine and neonatology concerning the impact on antenatal counselling and postnatal management.
Results - 242 cases were reviewed. In 27.6% of cases the MRI provided additional information that could have affected management or counselling antenatally and in 19.9% of cases the antenatal diagnosis was changed on the basis of the MRI.
Conclusion - This study shows how the information from fetal MRI is used by health professionals and the impact it has on clinical management and the counselling of families.

Introduction

When evaluating the use of fetal magnetic resonance imaging (MRI) as an adjunct to the ultrasound scan (USS) in the diagnosis and management of congenital anomalies of the fetus it is important to not only consider the diagnostic accuracy in isolation. It is also crucial to understand the impact the fetal MRI reports have on the clinicians involved in the care of these women and their babies. For example, how the information provided by fetal MRI influences counselling of families and overall management decisions. It goes without saying that a technology which is highly accurate, but of little clinical value would not be cost-effective as a second line diagnostic investigation when resources are finite.

Previous studies have commented on how fetal MRI can provide important information that can be helpful in planning antenatal care and surgical procedures [57]. Furthermore, accurate interpretation of fetal MRI has been shown to provide valuable information that supports prenatal counselling, facilitates management decisions, guides therapy, and supports research studies [58]. However, the reasoning behind these statements has not been explored in great detail.

The influence of fetal MRI in cases of central nervous system anomaly has also been shown

to have an impact on counselling in 78% of cases, with it having a major influence in 15%. Fetal MRI was also reported to have some influence on patient management in 88% of these cases of brain and spine abnormality [19]. Although, there has been less detailed research concerning anomalies of the fetal body.

Aims

The aims of this study were to assess the utility of the information provided by fetal MRI for the medical professionals, both obstetric and neonatal specialists, looking after patients with a congenital anomaly of the fetal body. This was specifically concerning how the MRI report informs perinatal counselling and management decisions. The secondary aim was to assess whether these opinions change with experience.

Methods

Ethical approval for this study was provided by the Health Research Authority (IRAS project ID 222053 and REC reference 17/EE/0162). The database of all patients referred for fetal MRI between 1st December 2020 and 30th September 2023 used for assessment of diagnostic accuracy formed the basis for the assessment of the impact the fetal MRI information could have on patient care.

The utility of the information provided by the ultrasound and MRI was graded by five medical professionals, of which two were fetal medicine consultants and three were consultant neonatologists. Each professional graded the scans independently, except for two of the neonatologists who did this together and consensus gradings were recorded. Each clinician was blinded to the gradings by their colleagues, except for the two neonatologists who did the gradings together. For each specialty, i.e. fetal medicine and neonatology, clinicians with varying length of consultant experience were chosen to allow for an analysis of whether gradings changed with experience. The consultants fell into two groups, with the more experienced having over 15 years of consultant experience and the newer consultants having less than 10 years of consultant experience.

The fetal medicine consultants were asked to grade the information provided by ultrasound and MRI in terms of utility during the antenatal period and were blinded to the outcome of the pregnancy and overall diagnosis. The antenatal gradings were from 1-6 as shown in table 2.16.

Criteria	Score
Both USS and MRI gave comparable results	1
The diagnosis was not fundamentally changed but MRI provided extra information that would not have affected management or counselling	2
The diagnosis was not fundamentally changed but MRI provided extra information that could have affected management or counselling	3
The diagnosis was changed on the basis of MRI	4
USS provided more information than MRI	5
MRI gave incorrect information or uncertain clinical significance that required further clinical investigation or caused unnecessary anxiety.	6

Table 2.16. Grading criteria for utility of USS and MRI information antenatally

The neonatology consultants undertook the same gradings from 1-6 as shown in table 2.16 without knowing the postnatal diagnosis. They were then informed of the pregnancy outcome and final diagnosis and asked to grade the ultrasound and MRI separately in comparison with the final diagnosis. These gradings were from 1-4 as detailed in table 2.17.

Criteria	Score
Imaging agrees with outcome	1
Imaging missed information without effect on outcome	2
Imaging missed information that could have changed management or counselling	3
Imaging was incorrect	4

Table 2.17. Grading criteria for utility of USS and MRI compared with postnatal diagnosis, separate gradings undertaken for each imaging modality

Field notes were taken throughout the grading process, documenting any discussions around the reasons for certain gradings. The gradings were summarised alongside the narrative which developed throughout the grading process. Specific comparisons were made between the differences in gradings between the fetal medicine and neonatology professionals and the differences in gradings between newer and more experienced consultants.

Results

Gradings summary – overall

The gradings by all professionals combined based on the utility of the information antenatally (Grades 1-6) found that in 41.2% the ultrasound and MRI gave comparable results (Grade 1). In 11.1% the MRI gave additional information that would not have affected management (Grade 2) but in 27.6% the MRI provided additional information that could have affected management or counselling (Grade 3). In 19.9% of cases the diagnosis was changed on the basis of the MRI (Grade 4) and in 0.2% the ultrasound provided more information than the MRI (Grade 5). There were no cases where the MRI gave incorrect information or uncertain clinical significance that required further clinical investigation or caused unnecessary anxiety (Grade 6). The grading criteria for each case antenatally is shown in table 2.16.

The information provided by each imaging modality was then compared individually with the postnatal diagnosis and graded from 1-4 by the neonatal specialists as detailed in table 2.17. Overall, the postnatal diagnosis agreed with the MRI report in 19.7% more cases than ultrasound and the MRI information was incorrect in 11.6% fewer cases than ultrasound. The imaging agreed with the outcome in 64.2% for ultrasound and 83.9% for MRI (Grade 1). The imaging missed information without an effect on outcome in 9.6% for ultrasound and 6.5% for MRI (Grade 2). The imaging missed information that could have affected counselling or management in 9.4% for ultrasound and 4.4% for MRI (Grade 3) and the imaging was incorrect in 16.8% for ultrasound and 5.2% for MRI (Grade 4).

The gradings were analysed by each body system as discussed below and are summarised in figure 2.26, for the antenatal gradings from 1-6, and figures 2.27-2.28 for the postnatal gradings from 1-4 for ultrasound and MRI respectively.

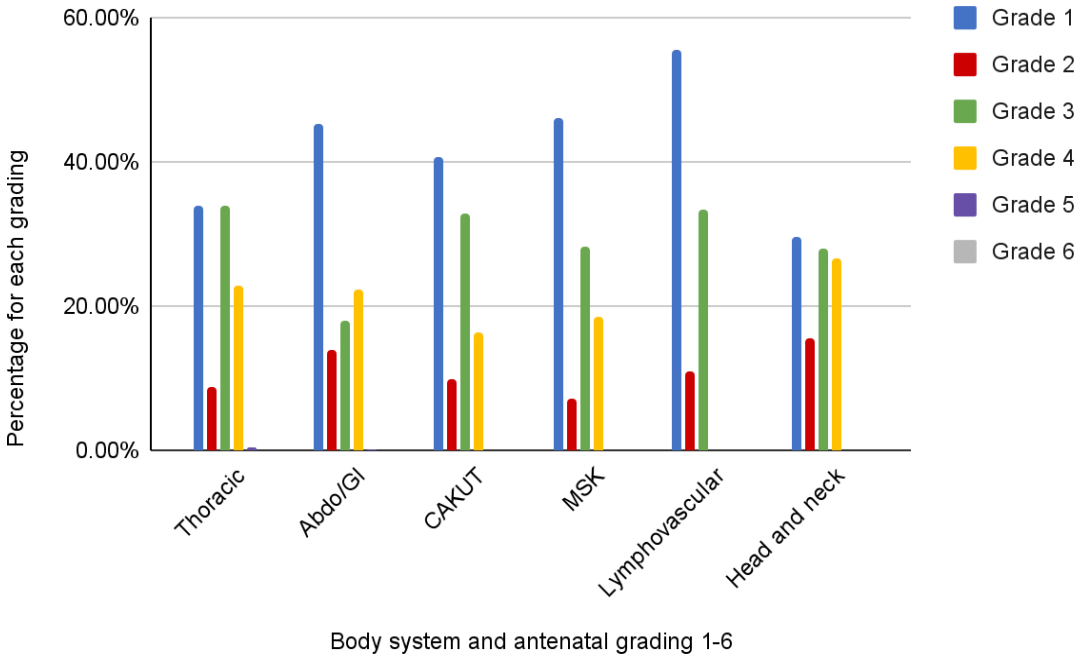


Figure 2.26 Comparison of antenatal gradings from 1-6 by body system

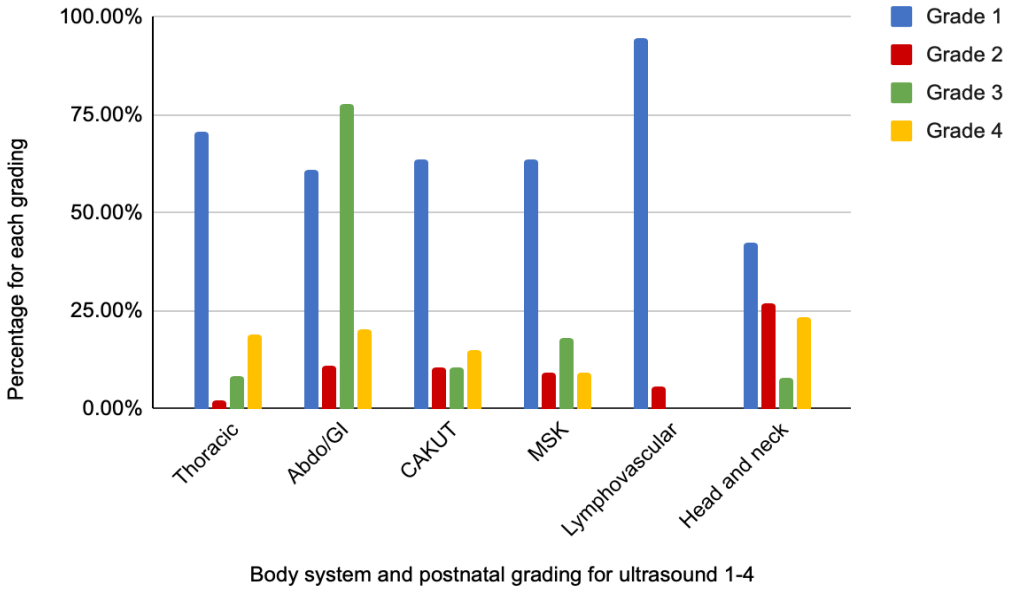


Figure 2.27 Comparison of postnatal gradings from 1-4 by body system for ultrasound

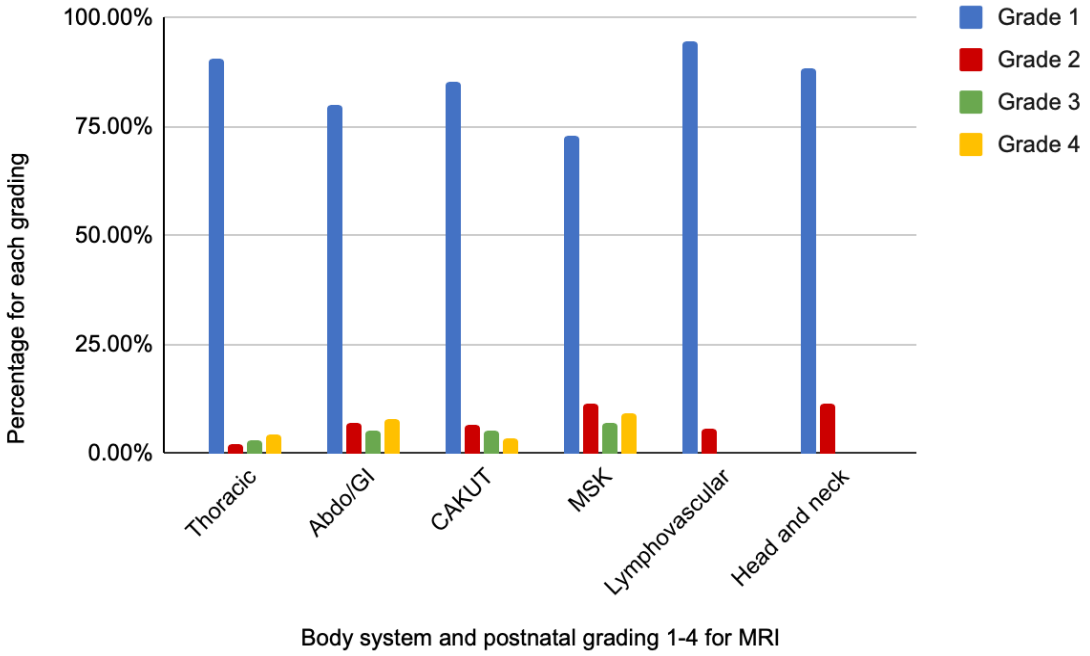
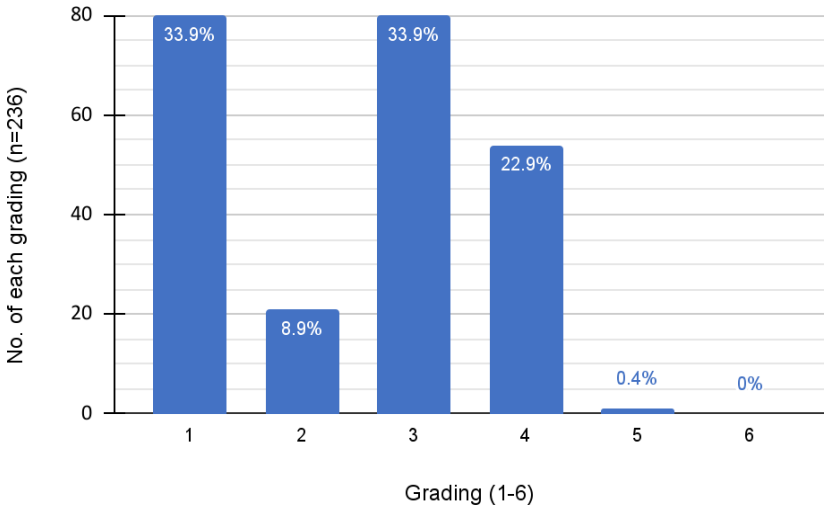


Figure 2.28 Comparison of postnatal gradings from 1-4 by body system for MRI

Gradings for thoracic cases

The impact of the information provided by fetal MRI on each case in the antenatal period was graded by all five fetal and neonatal professionals using the criteria in table 2.16. As four gradings were given for each of the 59 cases there were a total of 236 gradings undertaken. The overall summary of these gradings by all the professionals combined is shown in figure 2.29. In 33.9% cases the ultrasound and MRI gave comparable results, MRI provided extra information but did not affect antenatal counselling or management in 8.9%, MRI provided extra information that could have affected counselling or management in 33.9%, the MRI changed the diagnosis in 22.9% and ultrasound provided more information than MRI in 0.4%.



*F*igure 2.29. Overall antenatal gradings for thoracic cases

The comparison of antenatal gradings between the fetal medicine consultants and neonatology consultants is shown in figure 2.30. It shows that there were more cases graded as the USS and MRI giving comparable results (Grade 1) by the neonatologists when these cases were frequently graded as Grade 3, the MRI giving extra information which could have affected counselling, by the fetal medicine specialists. Both groups of professionals graded a similar number of cases where the diagnosis was changed by fetal MRI.

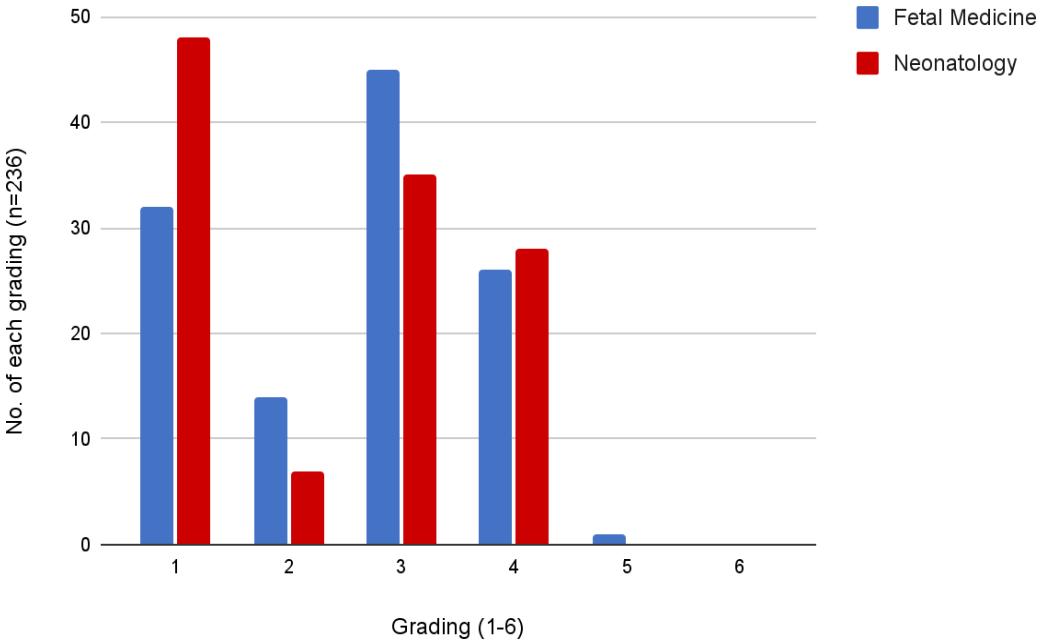


Figure 2.30. Comparison of antenatal gradings for thoracic cases between fetal medicine and neonatal specialists

The impact of clinician experience on their antenatal gradings is shown in figure 2.31. For the fetal medicine consultants, there were similar numbers of cases graded as Grade 1 where the USS and MRI results were comparable and Grade 4 where the diagnosis was changed by the MRI. However, there were more gradings of Grade 2 where the MRI provided additional information that would not change counselling by the newer consultant but more gradings of Grade 3 where the MRI provided extra information that could change counselling given by the consultant with more years of experience.

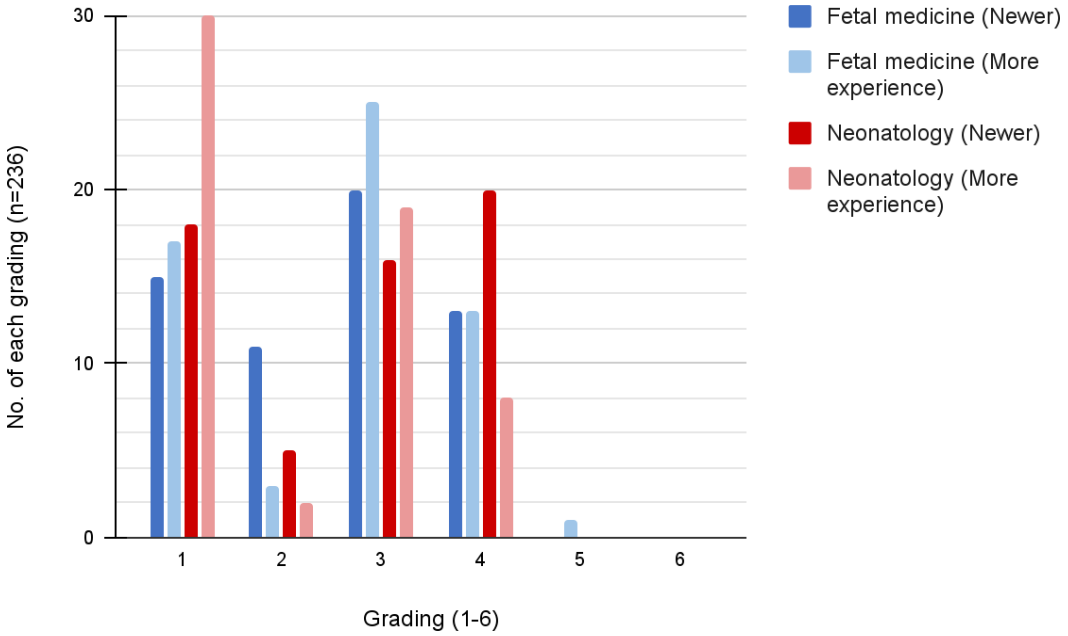


Figure 2.31. Comparison of antenatal grading between level of experience for thoracic cases

When comparing the gradings by the neonatologists with their experience, more cases were graded as Grade 1 (USS and MRI results comparable) by the more experienced consultant, compared with more gradings of Grade 4 (MRI changed the diagnosis) made by the newer consultant neonatologists.

The utility of the information provided by ultrasound and MRI was then graded again by the neonatologists with direct comparison to the final diagnosis provided by imaging, surgery or postmortem examination. These gradings were undertaken on 48 of the 51 cases with a final diagnosis as the postnatal diagnosis for three patients was not yet known at the time of grading. The focus for these gradings was how the imaging diagnosis compared with the final diagnosis and therefore how useful the imaging would have been in management of the baby in the neonatal period. The cases were graded from 1-4 using the criteria in table 2.17

and both imaging modalities were graded separately, two gradings were given for each case by the same two groups of neonatologists.

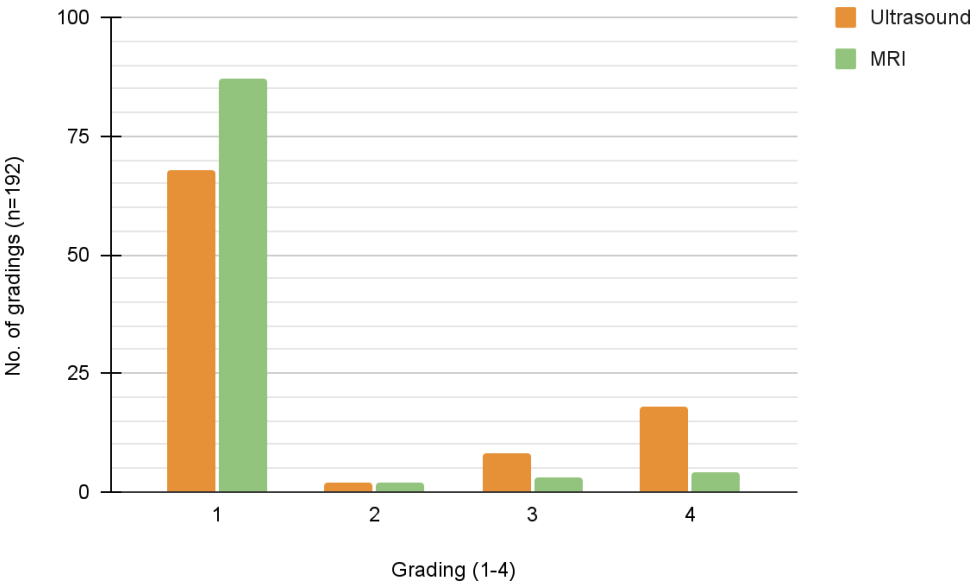


Figure 2.32. Grading of USS and MRI diagnosis compared with postnatal diagnosis for thoracic cases

The summary of these gradings is shown in figure 2.32. It highlights a higher percentage of cases graded as Grade 1, where the imaging agrees with the outcome, for fetal MRI (90.6%) compared with ultrasound (70.8%). Conversely more cases graded as Grade 4, where the imaging was incorrect, for ultrasound (18.8%) than MRI (4.2%). There was minimal difference in how the cases were graded by the newer and more experienced consultants as shown in figure 2.33.

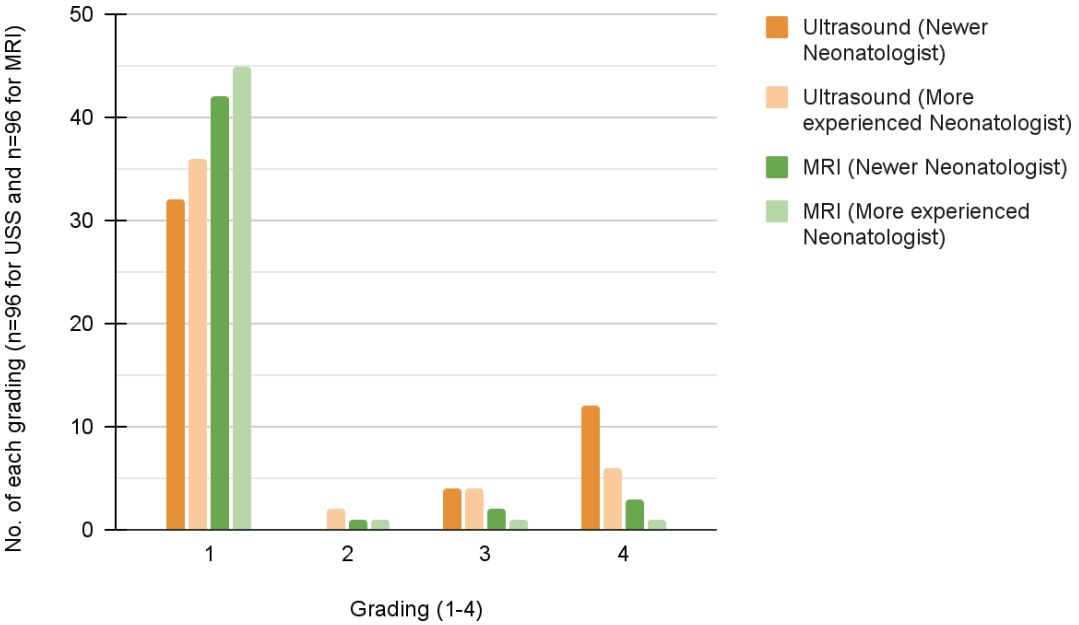


Figure 2.33. Comparison of postnatal grading and experience for thoracic cases

Gradings for abdominal and gastrointestinal tract cases

The influence the fetal MRI result may have had on each case in the antenatal period was graded by the five professionals using the gradings from 1-6 as listed in table 2.16. There were four gradings given for each case meaning there are a total of 392 gradings for each case. The overall results of the gradings combined are shown in figure 2.34. The majority of cases (45.5%) were graded as the ultrasound and MRI giving comparable results (Grade 1). In 14% of cases the MRI provided additional information that would not have affected counselling or management (Grade 2) but provided information that could have affected management in 17.9% of cases (Grade 3). 22.4% of cases had the diagnosis changed by the MRI (Grade 4) and there was one case (0.3%) where the ultrasound was felt to have provided more information than the MRI.

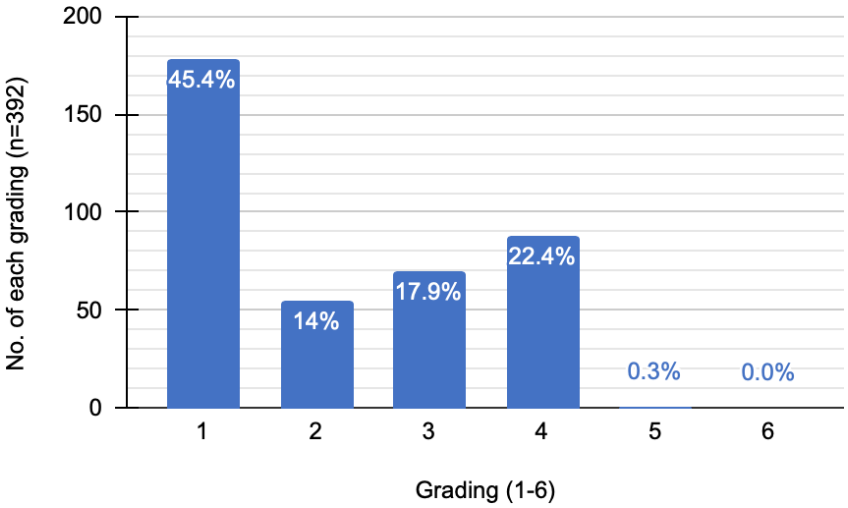


Figure 2.34. Overall antenatal gradings for abdominal and gastrointestinal tract cases

The differences in gradings between the fetal medicine and neonatology specialists are shown in figure 2.35. There were similar numbers of cases graded as the MRI having changed the diagnosis (Grade 4) in both groups. These tended to be in cases where there was a suspected anomaly on ultrasound but normal MRI or in cases where MRI provided significantly more detail allowing a less common or more complex diagnosis to be made such as Pentalogy of Cantrell or hepato-splenomegaly suggestive of haemophagocytic lympho-histiocytosis (HLH). All cases of gastroschisis were graded as 1 (USS and MRI results comparable) by all professionals.

However, the Fetal Medicine specialists graded more cases as Grade 2 or Grade 3 whereas the Neonatologists graded these cases more frequently as Grade 1. These discrepancies tended to occur in cases of suspected tracheo-oesophageal fistula/oesophageal atresia

(TOF/OA) on ultrasound in which the MRI findings were also suspicious of TOF/OA but not entirely diagnostic.

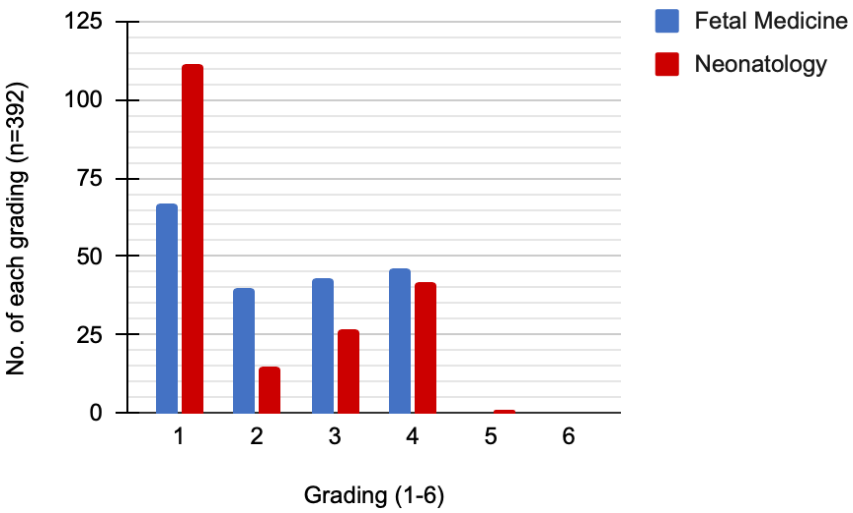


Figure 2.35. Comparison of antenatal gradings for abdominal/GI cases between fetal medicine and neonatal specialists

Figure 2.36 shows the comparison of individual clinician experience on their antenatal gradings. The Fetal Medicine consultants graded similar numbers of cases as Grade 3 and Grade 4. However, the consultant with more years of experience graded more cases as the imaging being comparable (Grade 1) and the newer consultant graded more of these cases as the MRI having provided additional information that would not have affected management or counselling (Grade 2).

For the neonatal consultants more cases were deemed Grade 4 by the newer consultants and more cases were graded as Grade 1 or Grade 3 by the consultant with more experience. Examples of these cases included suspected TOF/OA on ultrasound with normal MRI, abdominal cysts on ultrasound with normal MRI and cases where the terminology was changed slightly by the MRI for example an umbilical cord cyst which became an umbilical cord hernia.

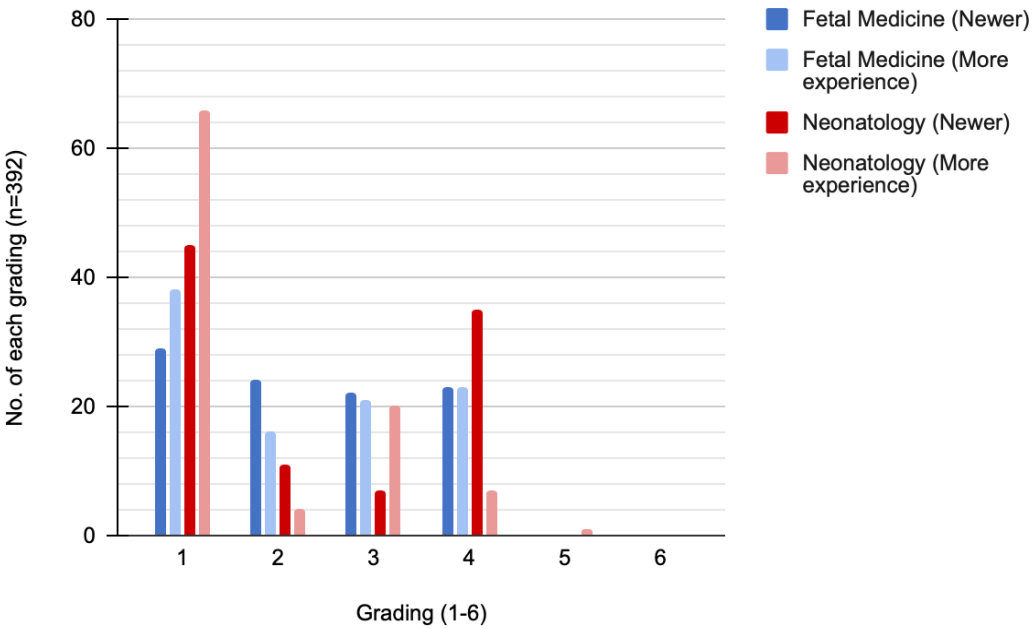


Figure 2.36. Comparison of antenatal grading between level of experience for abdominal/GI cases

The information from both imaging modalities was then graded again in comparison with the final postnatal diagnosis by the neonatologists. 77 cases with outcome data were graded by the two groups of neonatal consultants, one grading independently and a group of two, meaning there are 154 postnatal gradings for both ultrasound and 154 postnatal gradings for MRI. The cases were graded from 1-4 using the criteria in table 2.17 and are summarised in figure 2.37.

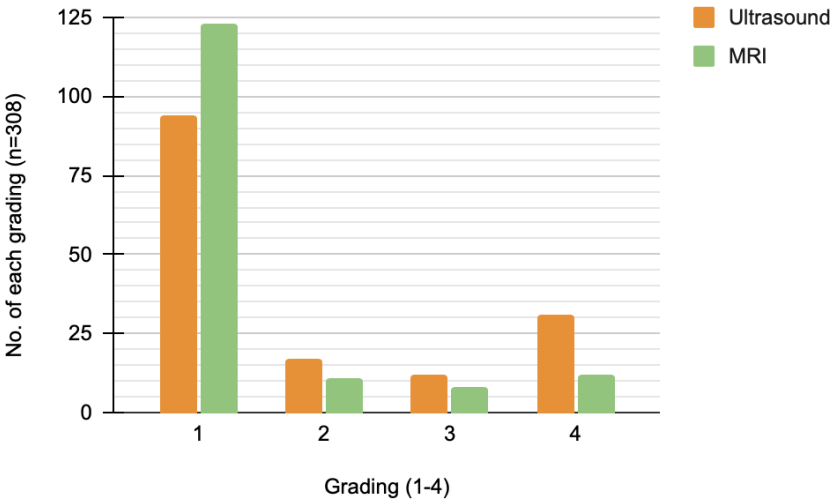


Figure 2.37. Grading of USS and MRI diagnosis compared with postnatal diagnosis for abdominal/GI cases

The grading of cases against postnatal diagnosis shows that for the majority of cases both imaging modalities agreed with the outcome (Grade 1). However, this was more pronounced

for fetal MRI as 79.9% of MRIs were Grade 1 compared with 61% of ultrasounds. There were more ultrasounds than MRIs graded as Grade 4 where the imaging was incorrect (20.1% vs 7.8%). Again, for all cases of gastroschisis both imaging modalities were graded as agreeing with the outcome (Grade 1).

These differences between the two imaging modalities were more pronounced when level of consultant experience was analysed, again with the newer consultants grading more cases as Grade 4. The impact of consultant experience on the postnatal gradings is shown in figure 2.38.

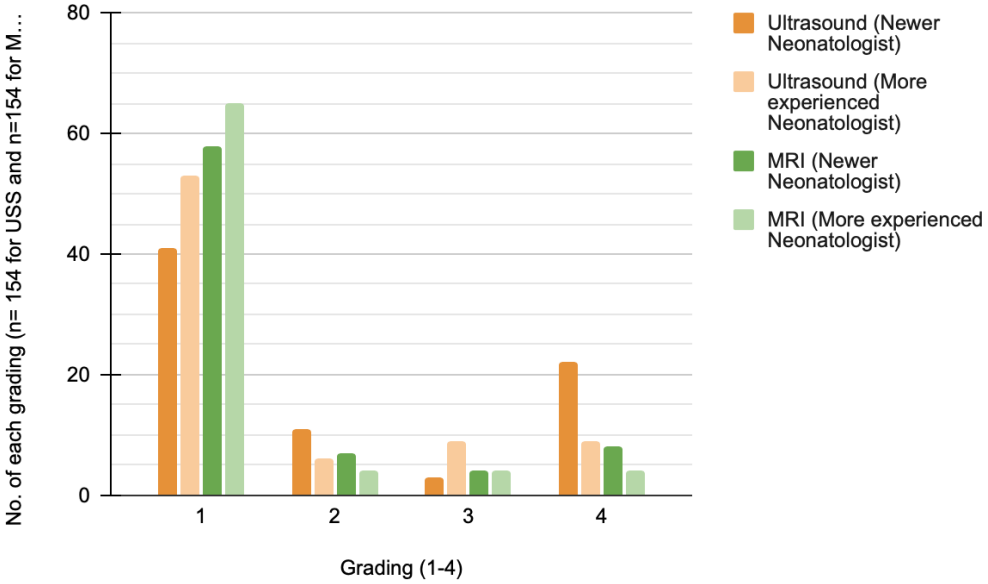


Figure 2.38. Comparison of postnatal grading and experience for abdominal/GI cases

The main themes from the discussions during the gradings of abdominal and gastrointestinal tract anomalies were frequently centred on the difficulties of both imaging modalities in diagnosis of TOF/OA.

Gradings for congenital anomalies of the kidneys and urinary tract (CAKUT)

The utility of the information provided by MRI in comparison to the ultrasound in the antenatal period was graded from 1-6 using the criteria listed in table 2.16. This was undertaken by the two Fetal Medicine consultants and three Neonatologists, of which two undertook the gradings together. Therefore, there were 364 gradings undertaken in total, the results of these are shown in figure 2.39. In 40.7% the ultrasound and MRI gave comparable results, in 9.9% the MRI provided additional information which did not affect management, in 32.9% the additional information from the MRI could have affected management and in

16.5% the MRI changed the diagnosis.

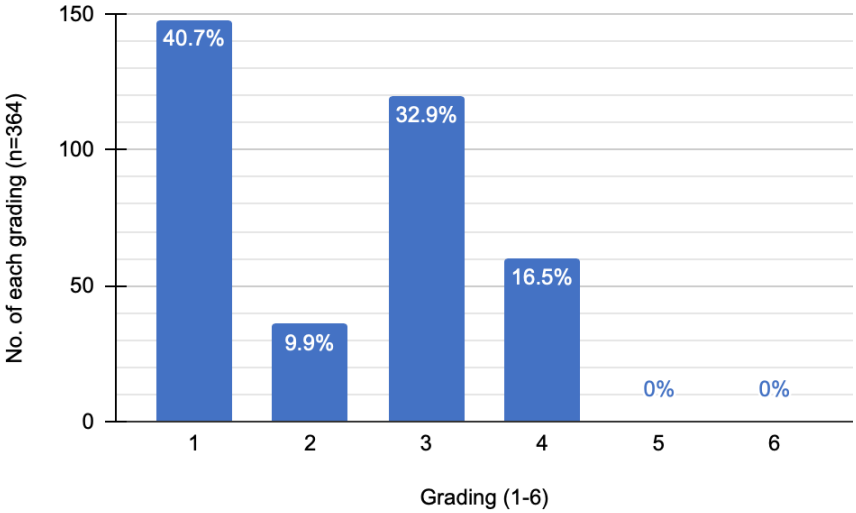


Figure 2.39. Overall antenatal gradings for CAKUT cases

When comparing the gradings made by the two different professions there were more cases where the fetal medicine consultants felt the additional information from the MRI could affect management or counselling (Grade 3) whereas the neonatal consultants felt the imaging modalities gave comparable results. The differences in gradings between professions are shown in figure 2.40.

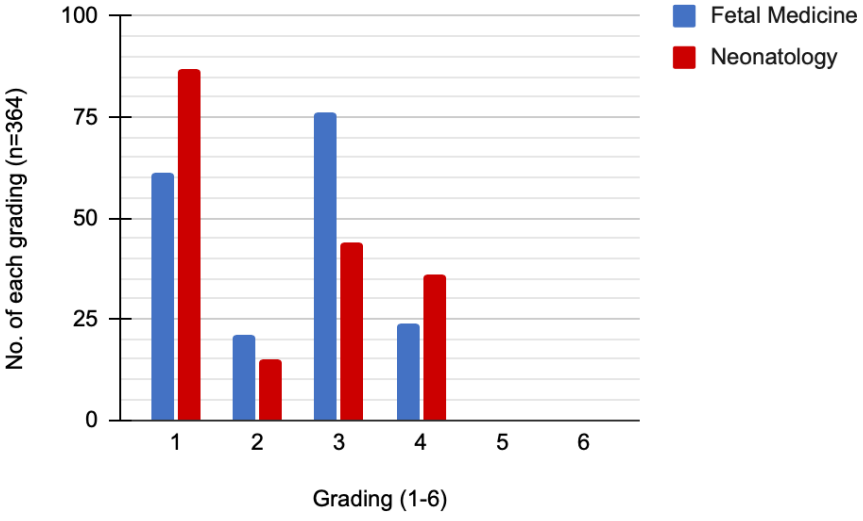


Figure 2.40. Comparison of antenatal gradings for CAKUT cases between fetal medicine and neonatal specialists

The impact of clinician experience on their gradings is shown in figure 2.41. For the fetal medicine specialists there were more cases where the newer consultant felt the MRI

provided additional information but did not alter the management (Grade 2) when the consultant with more years' experience felt the imaging modalities gave comparable results (Grade 1).

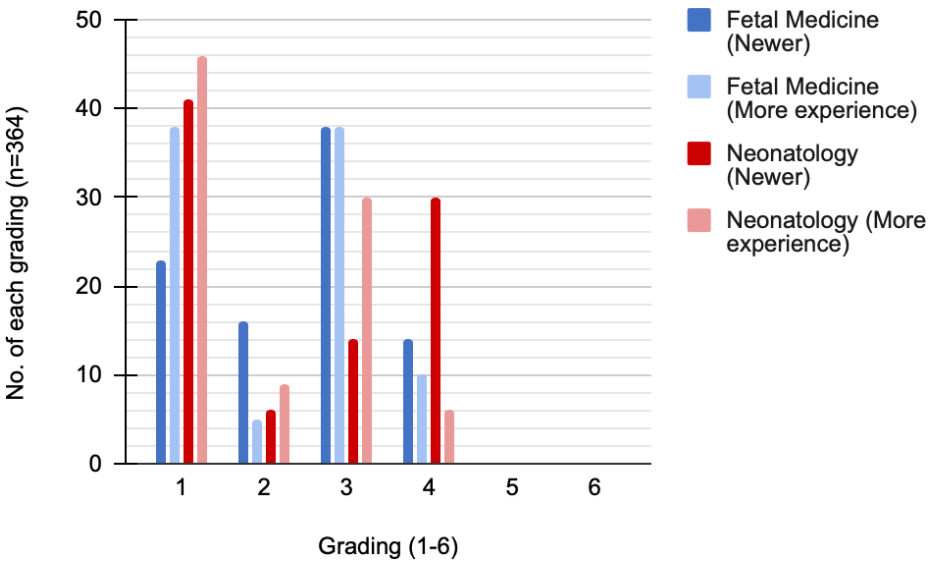


Figure 2.41. Comparison of antenatal grading between level of experience for CAKUT cases

The cases were graded again by the neonatal specialists in comparison with the final diagnosis made by postnatal imaging, surgery or postmortem examination. Two gradings were made for each of the 70 cases with a postnatal diagnosis by the three professionals, meaning there were 140 postnatal gradings in total for each imaging modality. These gradings were from 1-4 using the criteria in table 2.17. For both ultrasound and MRI, the majority of cases were Grade 1 where the imaging agreed with the final diagnosis. However, this was higher for fetal MRI than ultrasound (63.6% vs 85%) and there were more cases where the imaging was incorrect (Grade 4) for ultrasound than MRI (15% vs 3.6%). These findings are shown in figure 2.42.

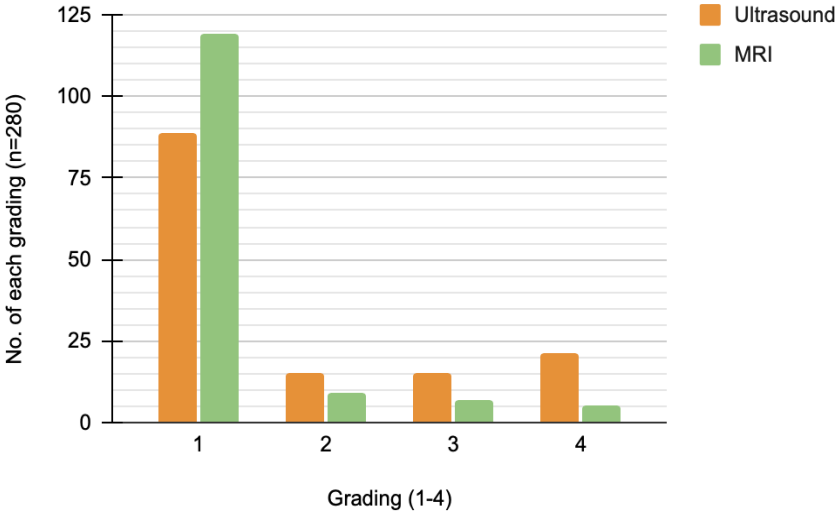


Figure 2.42. Grading of USS and MRI diagnosis compared with postnatal diagnosis for CAKUT cases

The level of professional experience did not appear to impact the gradings for fetal MRI compared to postnatal diagnosis. However, again there were more cases where the newer consultants felt the ultrasound was incorrect (Grade 4) which the consultant with more experience felt was information missed by the ultrasound which could have changed management or counselling (Grade 3). The impact of experience on grading the imaging against postnatal diagnosis is summarised in figure 2.43 below.

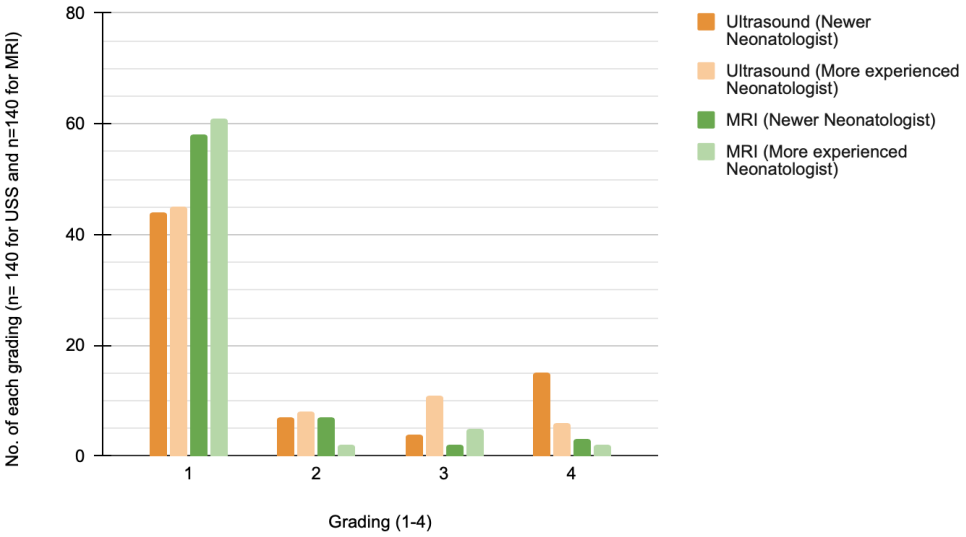


Figure 2.43. Comparison of postnatal grading and experience for CAKUT cases

Gradings for musculoskeletal (MSK) anomalies

The gradings for the utility of the information provided by the fetal MRI in the antenatal period in cases of musculoskeletal anomaly are shown in figure 2.44. They are based on the grading criteria in table 2.16 following review by the fetal medicine and neonatology specialists. The gradings were undertaken for 28/29 cases as the professionals felt one diagnosis was not possible from imaging therefore a grading was not applicable. Four gradings were undertaken individually for each case meaning there were 112 antenatal gradings in total. In 46.4% of cases both imaging modalities gave comparable results, in 7.1% the MRI provided extra information that wouldn't affect counselling or management but in 27.7% extra information was provided by the MRI that could have affected management or counselling. In 18.8% of cases the diagnosis was changed on the basis of the MRI.

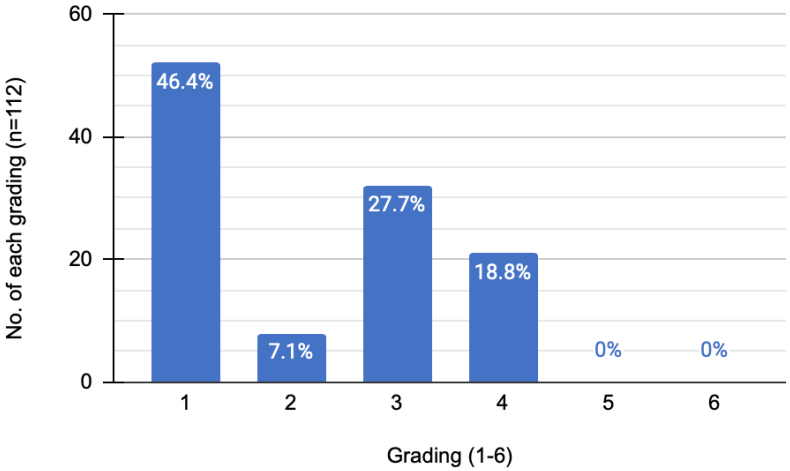


Figure 2.44. Overall antenatal gradings for MSK cases

The comparison between gradings by the fetal medicine and neonatology specialists on the impact of the MRI report antenatally is shown in figure 2.45. We found that the neonatologists considered a higher proportion of cases to have comparable ultrasound and MRI findings (Grade 1) than the fetal medicine consultants (55.4% vs 37.5%). This was frequently seen in cases of referral for MRI due to short long bones seen on ultrasound.

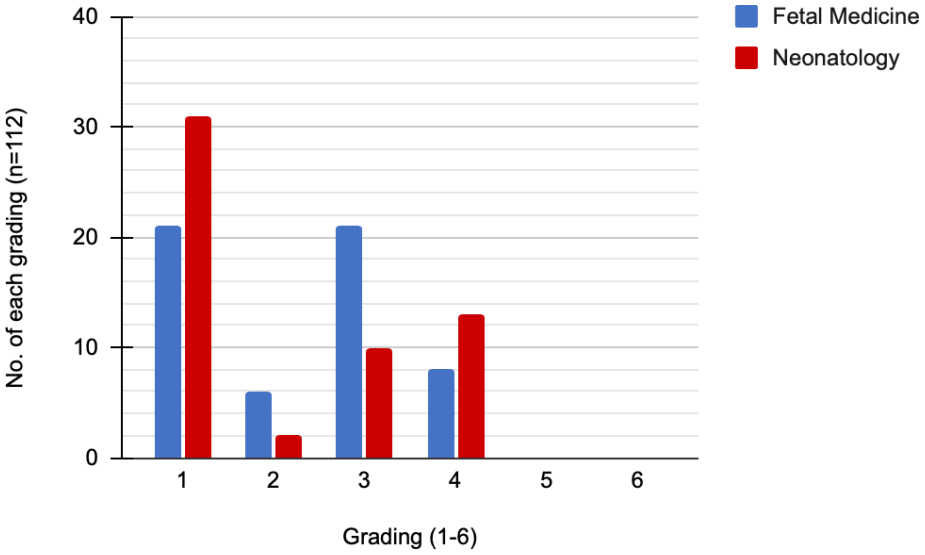


Figure 2.45. Comparison of antenatal gradings for MSK cases between fetal medicine and neonatal specialists

The impact of clinician experience on the differences in individual gradings is shown in figure 2.46. For the fetal medicine consultants, it shows more cases graded as Grade 2, where the MRI provided additional information which would not affect counselling or management, by the newer consultant. This was in cases where more detail on a specific anomaly, such as a forearm deformity, was provided in the MRI report compared with the ultrasound. As seen in

other body system anomalies, there were differences in gradings between the neonatologists based on their views on when a diagnosis was considered to have been changed.

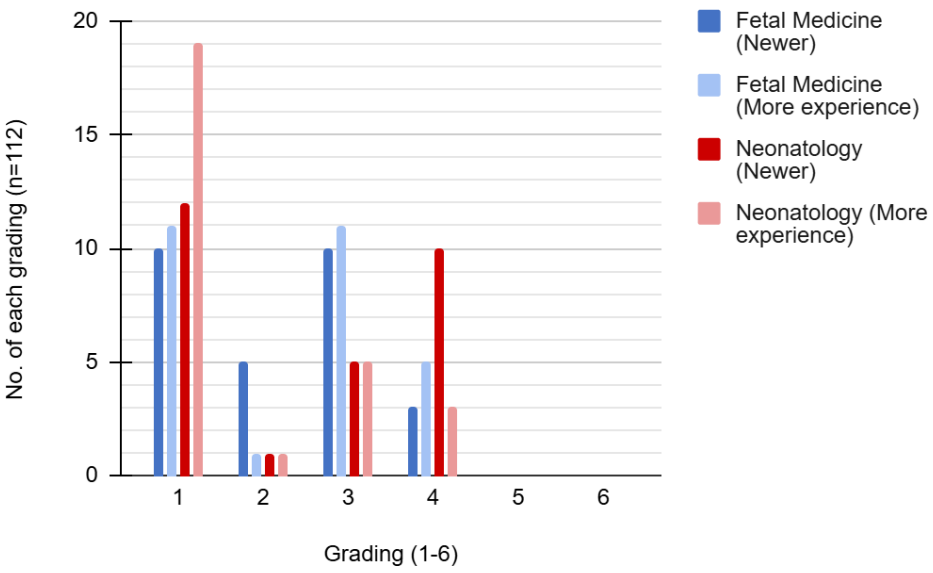


Figure 2.46. Comparison of antenatal grading between level of experience for MSK cases

The utility of the information provided by the fetal MRI was then compared with the final diagnosis made by postnatal imaging, surgery or postmortem examination. These gradings were undertaken by the neonatologists for 22/29 cases as at the time of grading a final outcome and/or diagnosis was not available for six cases and one was deemed to have a diagnosis which could not have been made by imaging alone. The cases were graded from 1-4 using the criteria in table 2.17. Each case was reviewed by the three neonatologists, the two newer consultants working together, with a separate grading given for ultrasound and MRI meaning there were 88 postnatal gradings.

The summary of these gradings, as shown in figure 2.47, shows fairly similar results for both imaging modalities but a slightly higher proportion of agreement between imaging and outcome for fetal MRI than antenatal ultrasound (72.7% vs 63.6%). Whereas there were more cases where the imaging missed information that could have affected management or counselling for ultrasound than MRI (18.2% vs 6.8%).

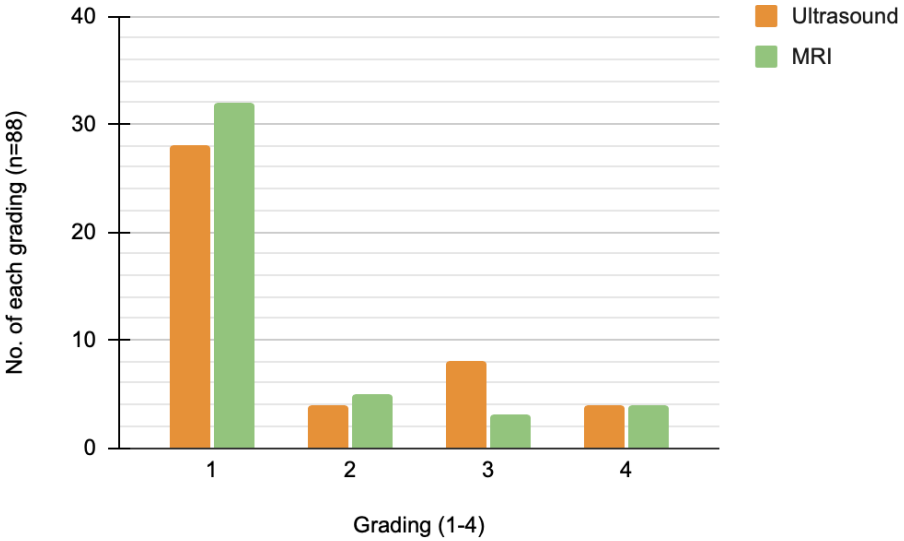


Figure 2.47. Grading of USS and MRI diagnosis compared with postnatal diagnosis for MSK cases

When comparing the impact of years of consultant experience on grading choices, there were similar results as seen in the antenatal gradings. This was in cases of suspected short long bones which were normal at birth. The difference in opinion on these cases as discussed above meant there were more gradings of the imaging being incorrect (Grade 4) made by the newer consultants and more gradings of the imaging agreeing with the outcome (Grade 1) made by the more experienced consultant. These findings are shown in figure 2.48.

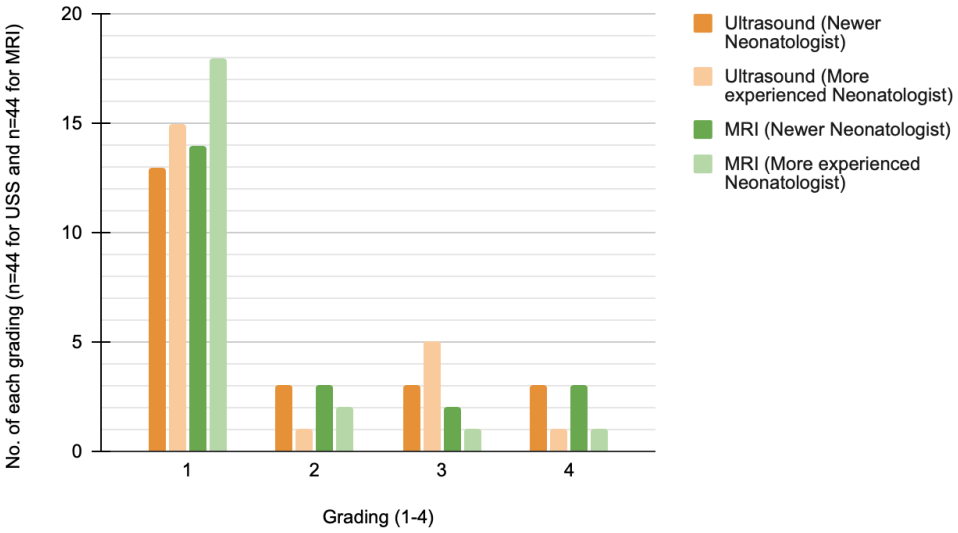


Figure 2.48. Comparison of postnatal grading and experience for MSK cases

For musculoskeletal anomalies, the gradings by the different professionals tended to be all in agreement in cases of isolated anomaly such as talipes or an absent hand. The biggest differences were seen in cases of suspected short long bones, as discussed, there were

differences between the professional groups on the role MRI plays in these cases and between level of experience as to whether the diagnosis is truly changed by a normal MRI.

Gradings for lymphovascular malformations

The impact of the information provided by fetal MRI on these cases in the antenatal period was graded by the two fetal medicine consultants and three neonatal consultants using the grading criteria from 1-6 in table 2.16. There were four gradings undertaken for each of the nine cases meaning there were a total 36 gradings, the results of which are summarised in figure 2.49. In 55.6% of cases the ultrasound and MRI gave comparable results, in 11.1% the MRI provided extra information which would not have affected antenatal management and in 33.3% the MRI provided information which could have affected management or counselling. There were no cases where the MRI was felt to have changed the diagnosis.

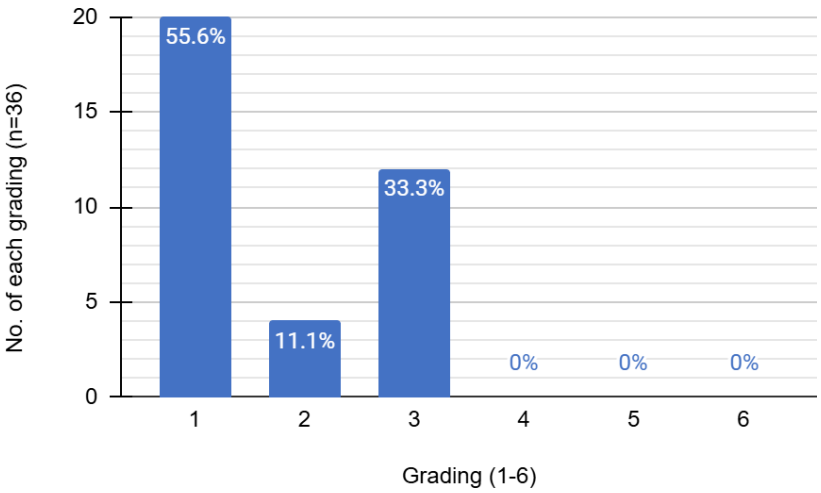


Figure 2.49. Overall antenatal gradings for lymphovascular cases

The comparison of gradings between specialities found that there were more cases where the fetal medicine consultants considered the MRI to have provided extra information (Grade 2 or Grade 3). This was seen most frequently in cases where anomalies diagnosed as cystic lesions on ultrasound were defined as lymphatic malformations by the MRI, in these cases the neonatologists considered the imaging findings to be comparable (Grade 1). This is summarised in figure 2.50.

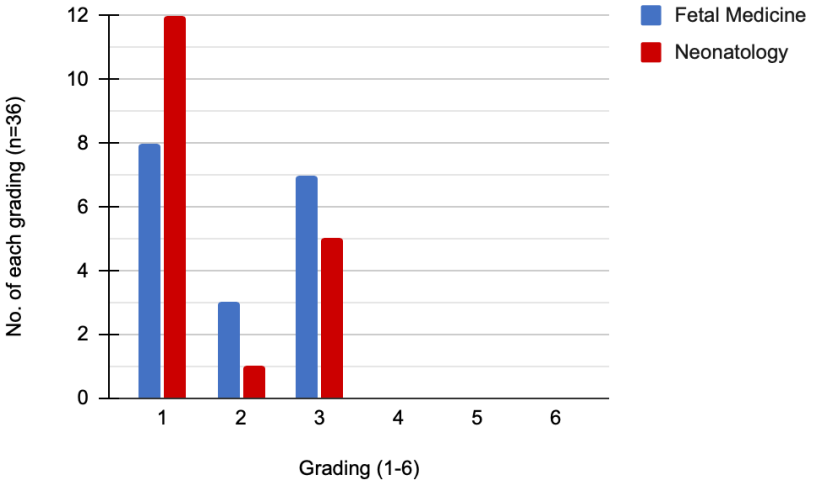


Figure 2.50. Comparison of antenatal gradings for lymphovascular cases between fetal medicine and neonatal specialists

When comparing the impact of clinician experience on their gradings there was minimal difference between the fetal medicine consultants. For the neonatologists, there were more cases felt to have comparable imaging (Grade 1) by the consultant with more experience whereas the newer consultants considered the MRI to provide more information. This is shown in figure 2.51.

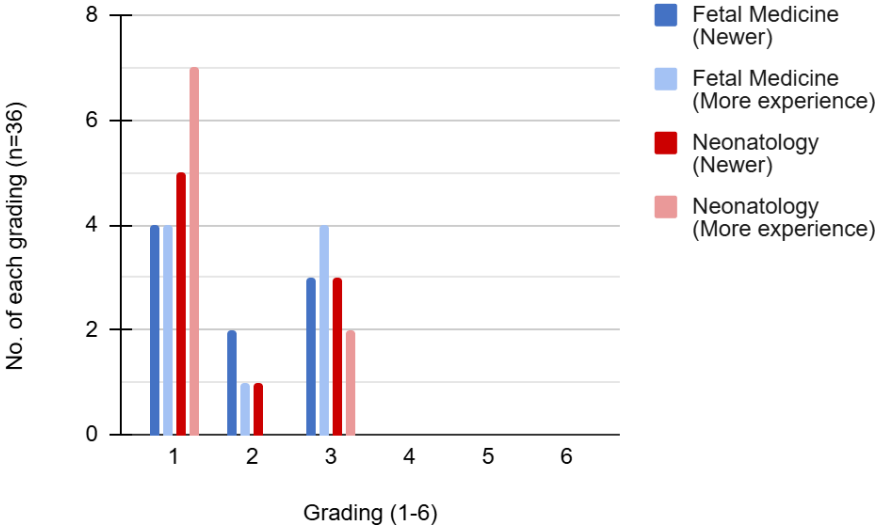


Figure 2.51. Comparison of antenatal grading between level of experience for lymphovascular cases

The information provided by both imaging modalities was then compared with the final postnatal diagnosis made by imaging, surgery or postmortem and graded again by the neonatologists from 1-4 using the criteria in table 2.17. For each case the ultrasound and MRI were graded separately by the neonatal specialist with more experience and the two newer neonatologists working together meaning there were two gradings for each imaging modality in each case. There were nine cases with a final diagnosis meaning each imaging

modality had 18 gradings and there 36 gradings overall.

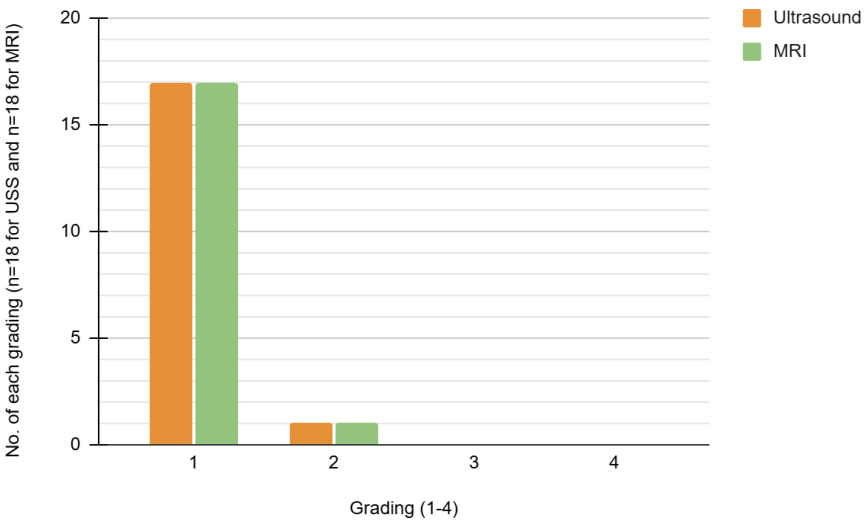


Figure 2.52 Grading of USS and MRI diagnosis compared with postnatal diagnosis for lymphovascular cases

The postnatal gradings are summarised in figure 2.52 and show identical gradings for both MRI and ultrasound with 94.4% cases where the imaging agreed with the final diagnosis. There was one case (5.6%) where both the ultrasound and MRI were felt to have missed information without an effect on the outcome. This was a case of a widespread lymphatic malformation which was more extensive on postmortem examination than suspected on antenatal imaging. There was minimal difference in these gradings between the level of consultant experience, as shown in figure 2.53.

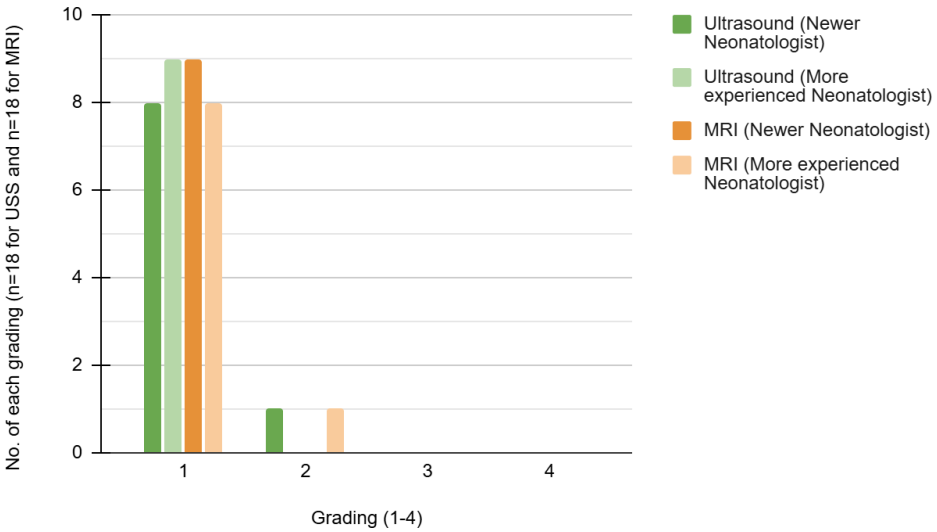


Figure 2.53. Comparison of postnatal grading and experience for lymphovascular cases

The gradings for these cases were fairly comparable both between imaging modality, profession and years of experience.

Gradings of head and neck anomalies

The impact of the imaging information on the antenatal management of these cases was again graded by the five professionals using the criteria from 1-6 listed in table 2.16. Four gradings were made for each of the 16 patients meaning there were 64 antenatal gradings in total which are shown in figure 2.54. In 29.7% of cases both imaging modalities gave comparable results, in 15.6% the MRI provided additional information which would not have affected management, in 28.1% however the MRI provided additional information which could have affected antenatal management and in 26.6% the MRI changed the diagnosis.

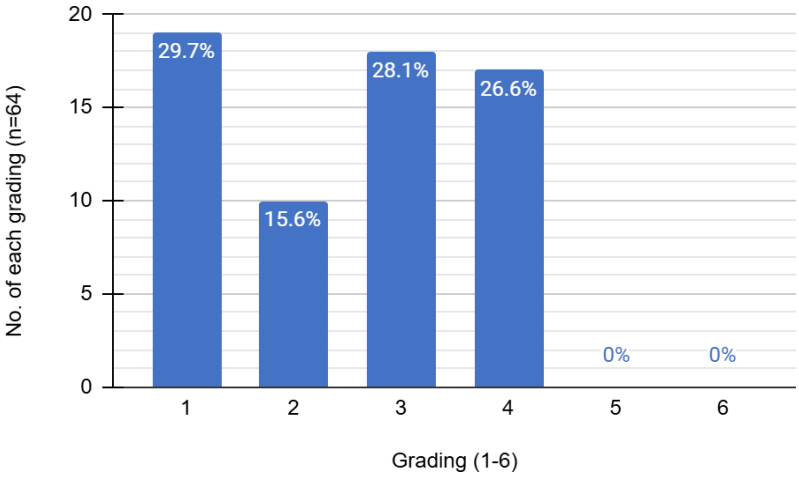


Figure 2.54. Overall antenatal gradings for head and neck cases

The comparison of gradings made by the specialists in fetal medicine and neonatology is shown in figure 2.55. There was a higher percentage of cases where the neonatal specialists considered the imaging to be comparable (Grade 1) and more cases where the fetal medicine specialists felt the MRI provided additional information. However, as the numbers were relatively small there was no clear pattern or explanation for the differences in these gradings between the two groups.

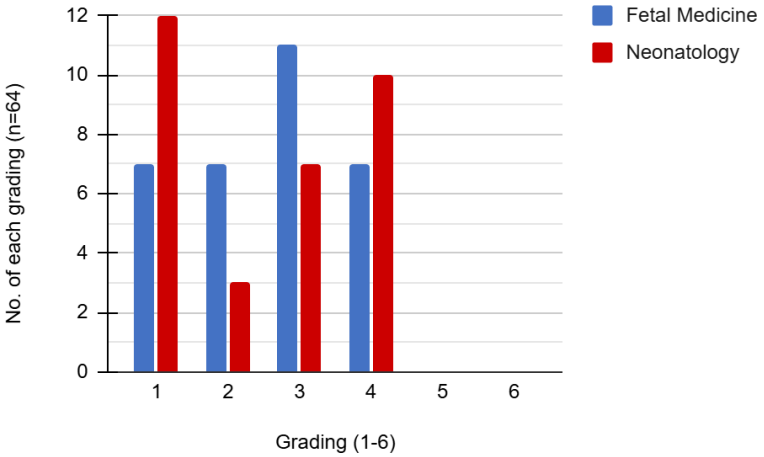


Figure 2.55. Comparison of antenatal gradings for head and neck cases between fetal medicine and neonatal specialists

When comparing years of experience and gradings, figure 2.56 shows how the newer fetal medicine specialist graded more cases as Grade 2 or Grade 3 than the consultant with more experience. This was due to a difference in opinion over what was considered to be more detail added by the MRI. These differences tended to occur in the more complex cases with multiple anomalies. The gradings made by the two groups of neonatologists with differing experience were fairly similar.

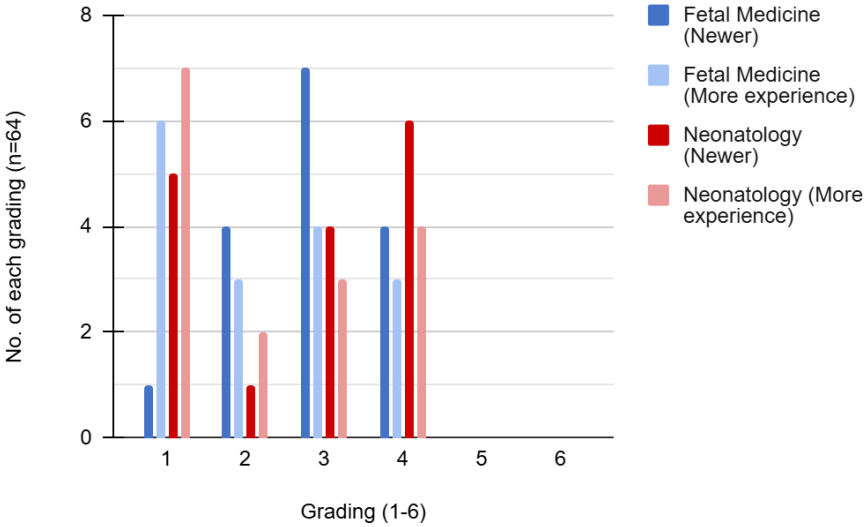


Figure 2.56. Comparison of antenatal grading between level of experience for head and neck cases

The information provided by both imaging modalities was compared with the final postnatal diagnosis and graded from 1-4 using the criteria in table 2.17 by the two groups of neonatologists. There were three patients with no outcome therefore the gradings were

undertaken on 13 patients; meaning there were 26 gradings for ultrasound and 26 gradings for MRI. Overall, there were far more cases where the MRI report was comparable with the final diagnosis than for ultrasound (88.5% vs 42.3%). There were no cases where the MRI diagnosis was felt to be incorrect, but the ultrasound diagnosis was incorrect (Grade 4) in 23.1% of cases. These findings are shown in figure 2.57.

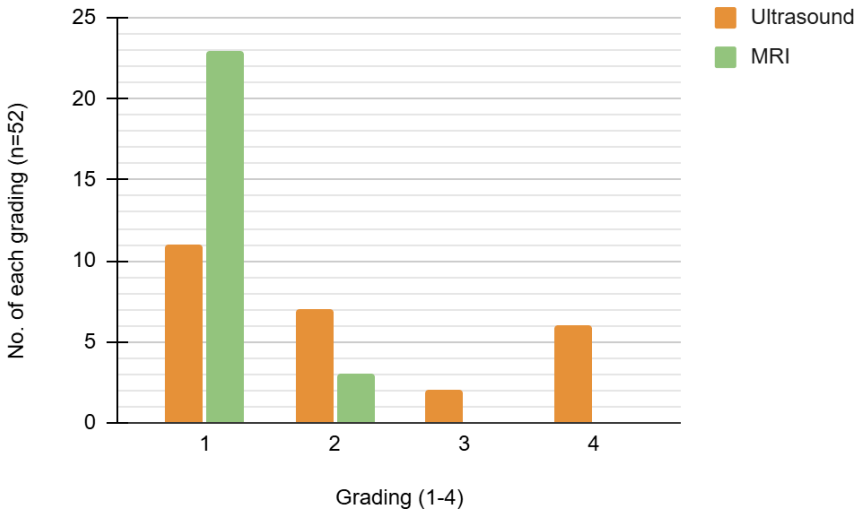


Figure 2.57. Grading of USS and MRI diagnosis compared with postnatal diagnosis for head and neck cases

When experience was compared with postnatal gradings by the neonatologists there was minimal difference between how the two groups graded the MRI information for each case. There was some difference in the ultrasound gradings, with the newer consultants considering there to be more cases where the ultrasound missed information without a clear effect on outcome (Grade 2) when the more experienced neonatologist considered the ultrasound to be in agreement with the outcome. This is shown in figure 2.58.

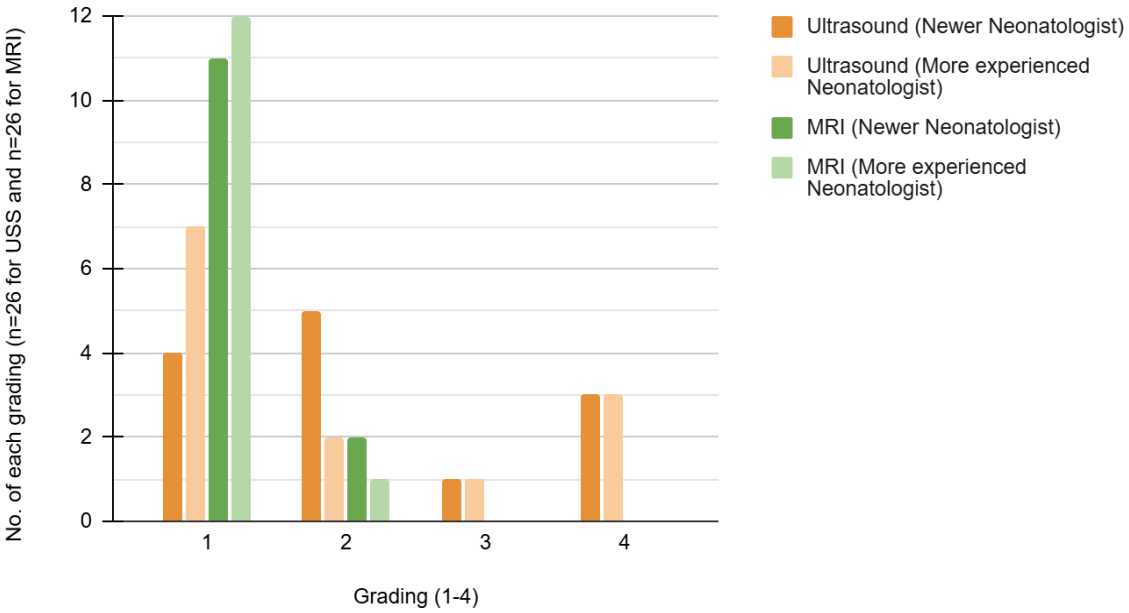


Figure 2.58. Comparison of postnatal grading and experience for head and neck cases

Discussion

The data from the gradings with fetal medicine and neonatology specialists is novel and allows direct comparison between the diagnostic accuracy of fetal MRI and its utility for the clinicians looking after these patients. As far as we are aware, this combined research has not been published in this research area before. The study was designed to include fetal MRIs performed as part of routine care following concerns on an antenatal ultrasound; therefore, reflecting clinical practice and not requiring any additional input from the patients. The narrative of the gradings highlights the areas and specific conditions in which the MRI information has the potential to impact antenatal management and/or changes the diagnosis as well as the conditions in which MRI has less value. The analysis also shows how the information from the fetal MRI is used and valued differently by professionals in different specialties and how this differs depending on the level of consultant experience.

Overall, the data from the gradings found the MRI information had the potential to change antenatal counselling and management in 27.6% and changed the diagnosis altogether in 19.9%. The specific conditions in which the fetal MRI was felt to be of the most benefit were prognostication using lung volume measurements in congenital diaphragmatic hernia and assessment of renal function and confirmation of bilateral renal agenesis. The fetal medicine consultants also commented on the role of fetal MRI in cases where patient factors may impact the accuracy of ultrasound such as raised maternal body mass index and oligohydramnios. In conditions such as tracheo-oesophageal fistula with or without

oesophageal atresia the MRI was felt to be less useful as it was unable to provide additional diagnostic clarity, as has been discussed in detail in the results for each body system. There were differences seen in the grading patterns between the fetal medicine and neonatal professionals, these tended to be specific to individual conditions and are discussed in more detail below. Overall, there was more discussion surrounding the importance of reassurance, especially reassurance of normality, and the role that fetal MRI plays as a second imaging modality from the newer consultants. There were other specific differences in how the newer consultants graded the cases compared with the more experienced consultants which are also discussed below.

The context of the set up at our centre is integral to explaining some of the grading patterns, this is also explored further in the qualitative study. The consultant radiologist reporting the fetal MRIs has many years of experience in this field and has developed the MRI service alongside the fetal medicine multidisciplinary team. The high level of trust and confidence the clinical teams place on the MRI reports was evident from the discussions during the gradings and the qualitative interviews discussed in the later chapter. The expansion of our fetal MRI service over the past 15 years means many of the professionals involved in the care of patients with fetal anomalies are used to requesting fetal MRIs and undertaking counselling with the information from the MRI in addition to the ultrasound, as this has always been present during their training. This is likely to have affected the difference in grading between the newer and more experienced consultants and was a frequent theme in the qualitative sub-study. This data is therefore specific to our centre, and we would expect the gradings and discussions during this research process to differ were they undertaken with clinicians working at a different centre.

Finally, the gradings undertaken by the professionals were based on summaries of the imaging reports and the images themselves were not reviewed during this time. As before, this was felt to represent clinical practice, and these clinicians would use the report information when seeing the families in clinic. Although, it was recognised that for the more complex cases, the images would be reviewed in clinical practice alongside the report as part of a multidisciplinary team meeting to discuss management planning.

The field notes taken of the discussions during the gradings by the different professionals are summarised below by body system, providing explanation for some of the differences in gradings.

Non-structural anomalies

The key themes identified from discussions during the gradings for the cases of MRI performed for a non-structural anomaly, such as family history of a condition or exposure to a teratogen, were of the importance of ensuring normality and the role of reassurance in these cases. For the fetal medicine consultants in particular, in the cases of oligohydramnios and polyhydramnios with no structural cause seen on ultrasound the role of the MRI was seen as a second opinion to rule out an underlying structural abnormality. For example, to ensure no features suggestive of oesophageal atresia or bowel obstruction in cases of polyhydramnios and to ensure presence and function of the kidneys in cases of oligohydramnios. The MRI was felt to add benefit to the diagnosis in these cases, especially where there was the presence of factors affecting accuracy of ultrasound such as raised maternal BMI or oligohydramnios. The fetal medicine consultants also reported referring women with oligohydramnios for fetal MRI specifically for assessment of lung volumes as this would impact how these patients are counselled regarding prognosis, for example following spontaneous preterm rupture of membranes.

Thoracic anomalies

The gradings of the thoracic anomaly cases found that there were more cases graded as Grade 1, comparable USS and MRI results, by the neonatologists than the fetal medicine specialists. This difference was seen predominantly in cases where one imaging modality diagnosed CPAM but the other diagnosed congenital lobar emphysema or another congenital cystic lung malformation. During the discussions both teams felt the diagnosis was not fundamentally changed however the fetal medicine consultant felt the information they would provide to expectant parents may change. The neonatal team explained they would provide parents with similar information during antenatal counselling as the initial management in the neonatal period is similar for all of these conditions.

There were a similar number of cases where both groups of professionals agreed that the diagnosis was changed by fetal MRI or more information was provided by fetal MRI. In specific conditions such as congenital diaphragmatic hernia, all clinicians consistently graded these cases as Grade 3 as the additional information on lung volumes provided by fetal MRI was likely to affect how families were counselled regarding prognosis. There were specific cases of rarer conditions, such as conjoined twins, where the additional detail provided by the MRI was felt by all clinicians to impact counselling by providing more information regarding the chance of survival.

There were differences seen in the grading patterns relating to the level of experience of the neonatologists, with the more experienced consultant grading more cases as Grade 1 which were graded as Grade 4 by the newer consultants. These differences were frequently seen in the cases where the ultrasound diagnosis was a relatively minor anomaly such as an accessory rib or sternal calcification, which were then normal on MRI.

The main themes of discussion by the clinicians during this grading process often centred on the additional information which can be provided by fetal MRI specifically in thoracic anomalies. Common examples include providing more detail in cases of mediastinal shift seen on ultrasound to enable counselling for a specific diagnosis such as lung aplasia or diaphragmatic eventration and the role of fetal MRI in measurement of lung volumes in congenital diaphragmatic hernia to enable prognostication.

Abdominal and gastrointestinal tract anomalies

The main themes from the discussions during the gradings of abdominal and gastrointestinal tract anomalies were frequently centred on the difficulties of both imaging modalities in diagnosis of TOF/OA. This is discussed in more detail in the subchapter discussing the role of fetal MRI in the prenatal diagnosis of TOF/OA. There were also discussions around gastroschisis as every case in this research was graded as both imaging modalities giving comparable results and agreeing with the postnatal diagnosis by all professionals. Therefore, the benefit of fetal MRI in these cases was brought into question, however it was felt the MRI may provide more detail on the size of the defect and possibly on bowel viability which may be of more use to surgical colleagues.

In the cases of TOF/OA the neonatologists graded these as Grade 1 more frequently than the fetal medicine consultants, this was most prevalent in cases where the MRI was also suspicious for TOF/OA but not diagnostic. The neonatal team felt their counselling of parents and management of the baby at delivery would be the same as based on the findings from both imaging modalities, whereas a second modality confirming findings or providing more detail was felt to have a possible impact on fetal medicine counselling.

There were also differences in grading between experience of fetal medicine consultants which occurred most frequently in cases of abdominal cysts where the MRI provided more information on the anatomical location of the cyst. The newer consultant graded these cases as Grade 2, where the MRI added information which did not affect management, whereas these were graded as comparable by the consultant with more experience.

There were discussions during these gradings around whether the abdominal cysts seen on ultrasound had resolved by the time of the MRI or whether they were cases where the fetal gallbladder was being misdiagnosed as a cyst. There was also a difference in opinion as shown by the difference in grading around cases where the ultrasound had some suspicions of TOF/OA for example due to a small stomach and whether a normal MRI is truly a change in diagnosis for these cases with softer features of TOF/OA.

Congenital anomalies of the kidneys and renal tract

In this group there were differences in gradings between the level of experience of the fetal medicine consultants. This was owing to the difference in importance placed on the role of reassurance of normality provided by MRI, for example in cases where there is difficulty visualising the kidneys on ultrasound due to maternal factors. These cases also caused discrepancies in grading between the newer and more experienced neonatologists as the newer consultants tended to consider the diagnosis changed when the MRI was able to visualise a previously unseen kidney (Grade 4).

In addition to what has already been discussed, a key theme identified during these gradings was the role of natural history of renal anomalies. For example, there is likely to be progression of some renal disease such as development of dysplastic kidneys following hydronephrosis and involution of multicystic dysplastic kidneys. Whilst the antenatal ultrasound and MRI are frequently within two weeks of each other, there is usually a much bigger time gap before postnatal imaging occurs which may explain some of the discrepancies between antenatal diagnosis and postnatal findings. The use of fetal MRI to determine renal function using diffusion weighted imaging was also frequently valued by the fetal medicine specialists in particular, to aid with confirmation of bilateral renal agenesis to allow appropriate counselling regarding the severity of this condition to be explained to expectant parents.

Musculoskeletal anomalies

Both imaging modalities had poor diagnostic accuracy in the cases of short long bones. During the discussions the fetal medicine consultants explained that the measurement of lung volumes on fetal MRI was one of the main reasons for referring these patients for MRI, in addition to confirmation of diagnosis. This is because in cases of skeletal dysplasia, observed-to-expected lung volumes are used to guide prognosis as smaller than expected

lung volumes are associated with poorer prognosis [59]. Therefore, following the addition of the information from the fetal MRI, the majority of the short long bone cases were graded as Grade 3 by the fetal medicine specialists as the MRI added information which could have affected counselling.

As seen in other body system anomalies, there were differences in gradings between the neonatologists based on their views on when a diagnosis was considered to have been changed. These differences occurred most frequently in the cases of short long bones seen on ultrasound which had a normal MRI. The neonatal consultant with more years of experience did not consider these cases to be a change in diagnosis, as the ultrasound was suspicious for a possible problem but not making an outright diagnosis of skeletal dysplasia. Therefore, the more experienced consultant tended to say the imaging modalities gave comparable results (Grade 1) in these cases, whereas the newer consultants considered the normal MRI to be a change in diagnosis (Grade 4).

Lymphovascular anomalies

This cohort was relatively small with only nine cases however which may have impacted the gradings and no clear themes were seen. The role of fetal MRI specifically in cases of neck masses including lymphovascular malformations is discussed in further detail in the pictorial review of neck masses.

Head and neck anomalies

Owing to the small patient numbers in this cohort, once again, the numbers of cases where there was a difference in grading were too small for any clear patterns to arise as there was heterogeneity between diagnoses. Overall, there were no clear themes other than what has already been discussed in the diagnostic accuracy chapter in terms of the ability of fetal MRI to accurately exclude craniofacial anomalies and the difficulties surrounding diagnosis of anomalies of such small structures such as cleft palates. This cohort contained a significant number of complex anomalies with genetic diagnoses, 26.7% of cases with a final diagnosis, which again highlights the role of fetal MRI in providing additional detail in complex cases.

Conclusion

This study contains novel data which highlights how the information provided by fetal MRI is

used by health professionals and the impact it has on clinical management and the counselling of families.

Chapter 3 – The application of fetal MRI in diagnosis and management of specific conditions

Context of the research

This chapter examines the role of fetal MRI in diagnosis of, prognostication and management planning for specific congenital anomalies of the fetal body. The anomalies studied are congenital diaphragmatic hernia, tracheo-oesophageal fistula and oesophageal atresia and masses of the fetal neck. These specific conditions were chosen as they comprise frequent referrals for fetal MRI, and they are conditions in which fetal MRI provides information pertaining to more than just diagnostic certainty. The subchapters aim to provide clarity on how useful fetal MRI is in these specific anomalies, with a view to providing evidence for efficient and cost-effective service delivery in the future.

This chapter comprises four manuscripts, of which two are published. The published manuscripts have been reproduced in line with journal permissions.

Author contributions

3.1 - MRI prediction of fetal lung volumes and the impact on counselling

Wilson L, Whitby EH. MRI prediction of fetal lung volumes and the impact on counselling. Clin Radiol. 2023 Dec;78(12):955-959. doi: 10.1016/j.crad.2023.09.006. Epub 2023 Sep 25. PMID: 37813756.

The planning of this research was undertaken by me and Dr Elspeth Whitby. I undertook the data collection, analysis and write-up prior to a final review by Dr Whitby. I submitted the research for publication and undertook the necessary revisions following peer review, under Dr Whitby's guidance. Prior to publication I have presented this work as a poster at the British Association of Perinatal Medicine (BAPM) spring conference in April 2023.

3.2 - MRI observed-to-expected lung volume in left-sided congenital diaphragmatic hernia - does the ratio change throughout pregnancy?

The planning of this research was undertaken by me and Dr Elspeth Whitby. I undertook the data collection, analysis and write-up prior to a final review by Dr Whitby. I have presented this work as a poster at the British Association of Perinatal Medicine (BAPM) annual

conference in September 2023.

3.3 - Prenatal diagnosis of tracheo-oesophageal fistula/oesophageal atresia: is MRI helpful?

Wilson L, Whitby EH. Prenatal diagnosis of tracheo-oesophageal fistula/oesophageal atresia: is MRI helpful? Pediatr Res. 2024 Aug 29. doi: 10.1038/s41390-024-03503-x. PMID: 39210049

The planning of this research was undertaken by me and Dr Elspeth Whitby. I undertook the data collection and we both undertook the stomach bubble measurements. I then completed the data analysis and write-up prior to review by Dr Whitby. I submitted the research for publication and undertook the necessary revisions following peer review, under Dr Whitby's guidance. Prior to publication I presented this research as an oral presentation at the UK Imaging and Oncology (UKIO) annual conference in June 2023.

3.4 - A clearer picture: Using fetal MRI to diagnose neck masses and predict airway compromise

The planning of this research was undertaken by me and Dr Elspeth Whitby. I undertook the data collection concerning the patient outcomes and final diagnoses with help from Dr Whitby in contacting external hospitals. The fetal MRI measurements and assessments were undertaken by Dr Elspeth Whitby and Dr Ashok Raghavan, and they generated the diagnostic pathway flow chart based on this information. I completed the overall write-up of the research, and this was then reviewed by both Dr Whitby and Dr Raghavan prior to completion.

3.1 MRI prediction of fetal lung volumes and the impact on counselling

Abstract

Introduction- Fetal magnetic resonance imaging (MRI) has become widely utilised in aiding the diagnosis of congenital diaphragmatic hernia (CDH) and in its prognostication, which is largely based on predicted lung volume. In the literature there are several recognised methods of calculating the expected lung volume for gestation in a healthy fetus. This study aims to assess whether lung volume percentages in CDH differ depending on which formula is used to calculate the expected volume for gestation and any potential impact this may have on perinatal counselling.

Methods - 47 cases of left-sided CDH which underwent fetal MRI at our centre were reviewed. The lung volumes were measured on MRI and compared with the volumes that would be expected at the given gestation for each patient. Expected values were calculated using four formulae from the literature and our own in-house method. These measurements were used to calculate the percentage total lung volume observed compared with the expected lung volume in a healthy fetus of the same gestation. The differences in percentage lung volumes using these five methods were then compared with how they relate to predicted rates of survival. We looked at how predicted survival would change depending on which formula was used to calculate the percentage lung volume with a view to how this may change the counselling given to a family.

Results - In 10/47 (21%) patients there was no change in the predicted survival depending on which formula was used to calculate the expected lung volume. In 37/47 (79%) the chance of survival changed depending on which formula was used to calculate the expected lung volume at the given gestation. In 20 (47%) of these cases the change in predicted survival depending on which formula used was 45% (i.e. from 25% to 70% survival in 4 and from 50% to 95% survival in 16) and in 2 cases (4%) this difference was 70% (i.e. from 25% predicted survival to 95% predicted survival).

Conclusion - There are several different methods for calculating expected fetal lung volumes for any given gestation. When used to estimate the percentage lung volume in patients with CDH there is a large difference in values depending on which method is used. This in turn leads to a large variation in predicted survival with some patients in this study having either a 25% or 95% chance of survival depending on which method is used. This has a huge impact on perinatal counselling and the difficult decisions made by families.

Introduction

Congenital diaphragmatic hernia (CDH) affects 2.96 per 10,000 births [17] with the majority of defects (85%) occurring on the left and 15% on the right [60]. Antenatal ultrasound remains the gold standard for detection of such anomalies and fetal magnetic resonance imaging (MRI) is used in addition to ultrasound when a more detailed evaluation is required. In particular, MRI allows for a more accurate assessment of structural volumes such as the lungs [61] meaning it has increasing use in not only the diagnosis of but also in the prognostication of CDH. The use of fetal MRI for lung volume measurement in CDH enables the prognosis to be determined by the degree of pulmonary hypoplasia, allows assessment for potential prenatal treatment, aids with parental counselling and planning for intervention after delivery [49].

Over the past twenty-five years there has been extensive research into methods for measuring and determining the extent of pulmonary hypoplasia using fetal MRI. This has involved work to develop formulae for what would be considered normal lung volume for gestation, research into using total fetal body volume as a comparator and using lung-to-head ratios to assess lung size [62]. The array of research means there are now multiple methods in practice for determining a percentage lung volume observed compared to what would be expected in a healthy fetus. This in turns leads to a variation in practice and a potential variation in counselling regarding prognosis if these methods give different values for percentage lung volume.

This study aims to explore how percentage lung volume estimates in patients with CDH would change depending on which method is used to calculate the expected volume for gestation. This is specifically with a focus on how counselling regarding survival prediction may change with a difference in percentage observed/expected lung volume.

Methods

All cases of left-sided CDH who underwent fetal MRI at our centre between January 2010-December 2020 were reviewed. Right-sided CDH patients were excluded as their numbers are much smaller, diagnosis is frequently made postnatally and prognostication is based on other factors in addition to lung volume [60]. Ethical approval for the study was given by the Health Research Authority as part of a larger study into outcome data from MRI scans of the fetal body.

The MRI scans were performed using a 1.5 Tesla Siemens Avanto scanner (Erlangen, Germany) and lung volume measurements were made from the T2 weighted SSFE sequence. The fetal lungs were then traced on each slice in the coronal orientation using the Agfa Healthcare (Mortsel, Belgium) Enterprise Imaging platform as shown in figure 3.1. The areas of each slice were then summed and multiplied by the MRI slice thickness to calculate the total lung volume.

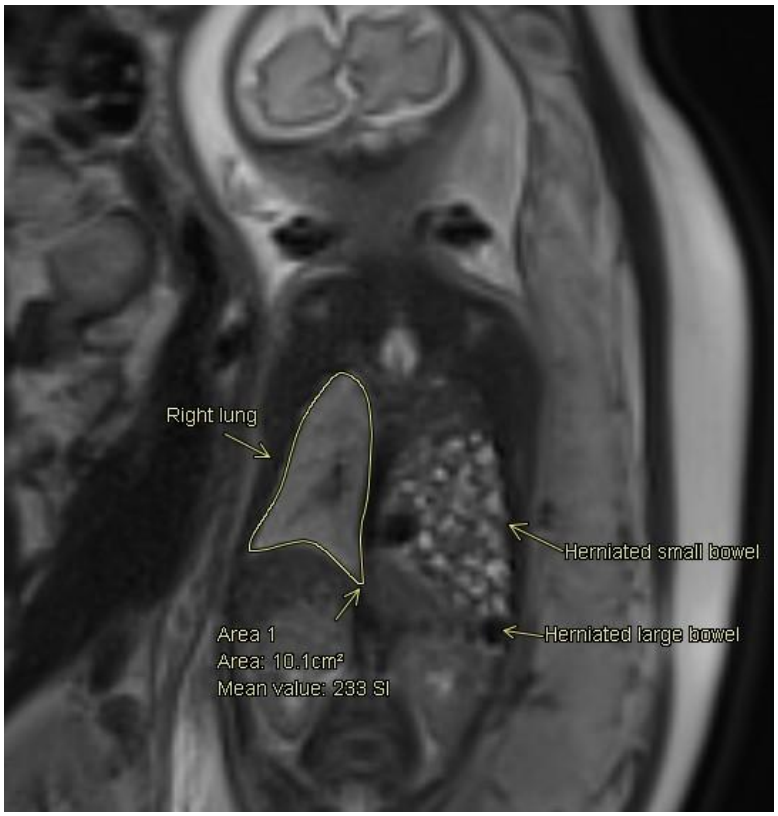


Figure 3.1. Coronal fetal MRI image of left-sided CDH and volume measurement of the right lung

The total lung volumes as measured by the radiologist reporting the MRI scan were used to calculate the percentage lung volume compared with what would be expected for the gestational age. Previous work, which is unpublished, has been undertaken at our centre to assess the repeatability of these measurements with assessment of inter and intra-observer variability using Cohen's Kappa coefficient which found them to be accurate and reliable. This has been undertaken using two separate data sets of 30 and 10 patients each. Intra (0.922) and inter observer variation (0.981) as determined by Cohen's Kappa was excellent. Five methods were used to calculate the expected lung volume; our own in-house method and four methods from the literature formulated by Rypens, Osada, Duncan and Mahieu-Caputo [62] as shown in table 3.1. A further published equation was not used as this had been previously reported as being very similar to the Rypens formula from beyond 23 weeks gestation [61].

Author	Year	Formula	Expected lung volume at 25 weeks (ml)	Expected lung volume at 35 weeks (ml)
Rypens et al.	2001	$V = 0.0033g^{2.86}$	32.8	86.0
Osada et al.	2004	$V = (2.41 \times g)$	22.6	46.75
Duncan et al.	1999	$V = 0.8375e^{0.1249g}$	19.0	66.3
Mahieu-Caputo et al.	2001	$V = \exp(1.24722 + 0.08939 \times g)$	32.5	79.5

V = fetal lung volume, g = gestational age

Table 3.1. Equations for calculating expected fetal lung volume [62]

The in-house method for calculating observed/expected lung volume from MRI involves comparing the measured values with a chart of what would be expected for any given gestation. This chart has been developed using data from hundreds of measurements of fetal lung volumes on MRI from fetuses from 19-39 weeks gestation without any lung pathology or any other condition which may affect fetal lung volume. The mean lung volumes for gestational age have been plotted on the chart and a curve of mean lung volume for gestation created. No specific formula for calculation has been generated. Previous work has been undertaken [63] to assess the accuracy of the in-house data which found it to be comparable to the published formulae for predicted fetal lung volume based on gestational age. In addition, in cases where a termination of pregnancy had occurred (in a previous cohort) the in vivo lung volumes from MRI were similar to the postmortem data obtained in the local centre.

For each patient five different values were calculated as a percentage observed/expected total lung volume using each of the formulae. These figures were then compared with how the predicted survival would change depending on which formula was used to determine percentage lung volume. Predicted survival was determined using survival rates in table 3.2, from the literature based on fetal body volume [12] as they are used locally for counselling.

Observed/expected total lung volume (%)	Survival (%)
<25	25
25-34	50
35-44	70
>45	95

Table 3.2 - Survival rate according to the percentage observed to expected total lung volume (O/E TLV) [12]

Results

Percentage observed/expected lung volumes

47 patients with left sided CDH underwent fetal MRI at our centre between January 2010 and December 2020. Figure 3.2 shows the observed/expected total lung volume (% O/E TLV) for each patient depending on which formula was used for calculation of expected lung volume for gestation. In general, the Rypens and Mahieu-Caputo formulae tended to give lower figures of percentage total lung volume than the others. The Duncan formula gave the highest values in 34 of the 47 cases (72.3%). Our in-house method of calculation frequently fell in the middle of the values in over half of the cases studied.

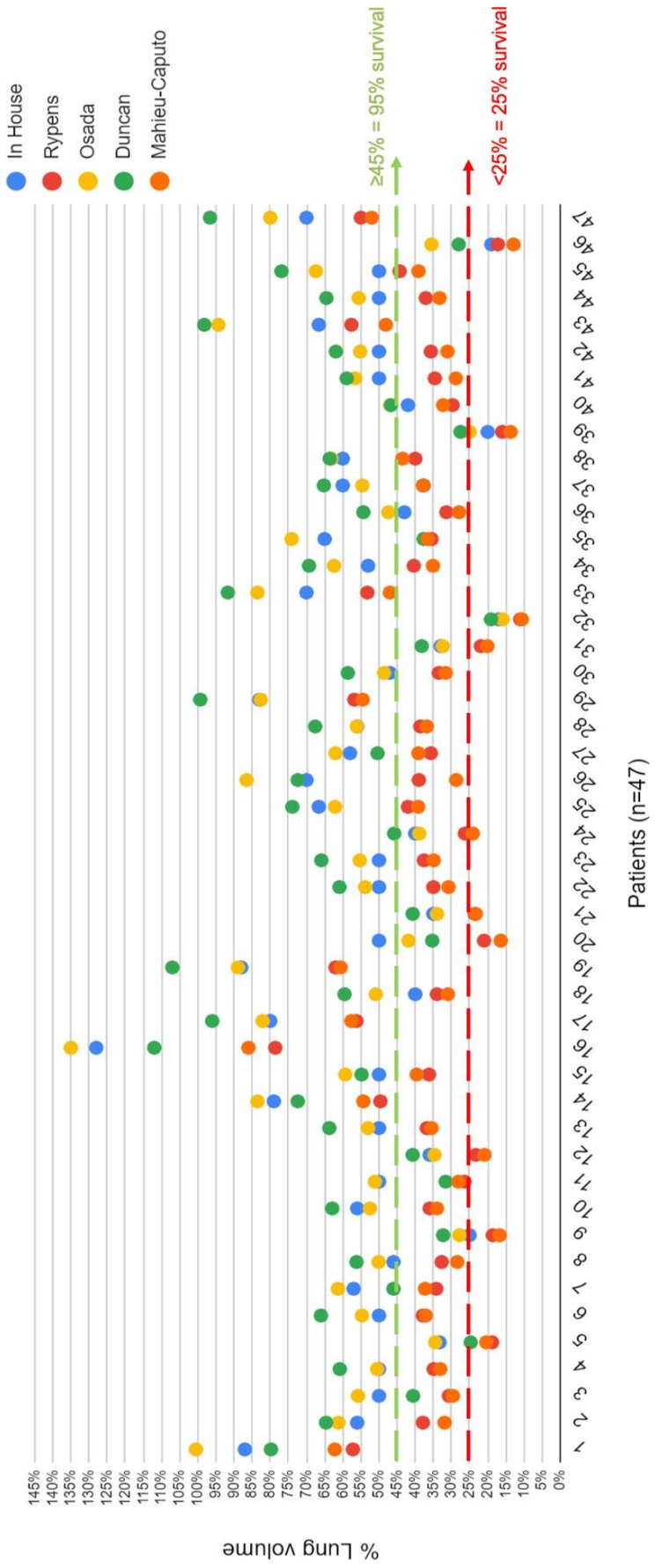


Figure 3.2. Percentage observed/expected total lung volume for each patient using each formula

In patients with smaller lung volumes the percentages of expected tended to be more narrowly distributed with less variation between formulae whereas cases with larger measured values showed a wider variation in percentage calculated.

Predicted survival and patient outcomes

Outcome data was available for 44/47 patients of which one underwent termination of pregnancy (TOP), and one was stillborn. There were 42 live births of which 32 are alive and well and, at the time of writing, unfortunately ten had died in the neonatal period.

The counselling of predicted survival rate would be changed in 37 patients (78.7%) depending on which formula was used to determine the lung volume as a percentage of what would be expected for the gestation. Figure 3.3 summarises the change in the prognostic group observed depending on which formula is used. The prognostic groups were survival of 25%, 50%, 70% or 95% as per table 3.2 [12].

In ten patients (21.3%) there was no change in predicted chance of survival regardless of which formula was used to calculate expected lung volume. Of these patients, one had an expected survival of 25% and the remaining nine had a predicted survival of 95%. The patient who underwent TOP had a predicted survival of 95%.

For two patients (4.3%) the predicted survival rate varied by 70% i.e. from 25%-95% survival depending on which method was used to calculate the percentage lung volume in comparison with what would be expected for gestation. Follow up of these patients found that one underwent successful repair and is fit and well but unfortunately the other died in the neonatal period and had suspected VACTERL although no post-mortem examination was undertaken.

The predicted survival varied by 45% in 20 patients (42.6%). For four of these patients their chance of survival varied from 25%-70% depending on which formula was used to calculate expected lung volume; two of these patients (50%) died in the neonatal period and the other two had successful repair and discharge from hospital. For 16 patients the chance of survival ranged from 50-95% of which the outcome is unknown for one, four died in the neonatal period and the remaining eleven are alive and well.

For the remaining 15 patients (31.9%) their predicted survival varied by 25% from either 25%-50% (three patients) or 70%-95% (twelve patients). In this group one patient was

stillborn, one died in the neonatal period, eight patients are alive and well and there was missing outcome data for the remaining two patients.

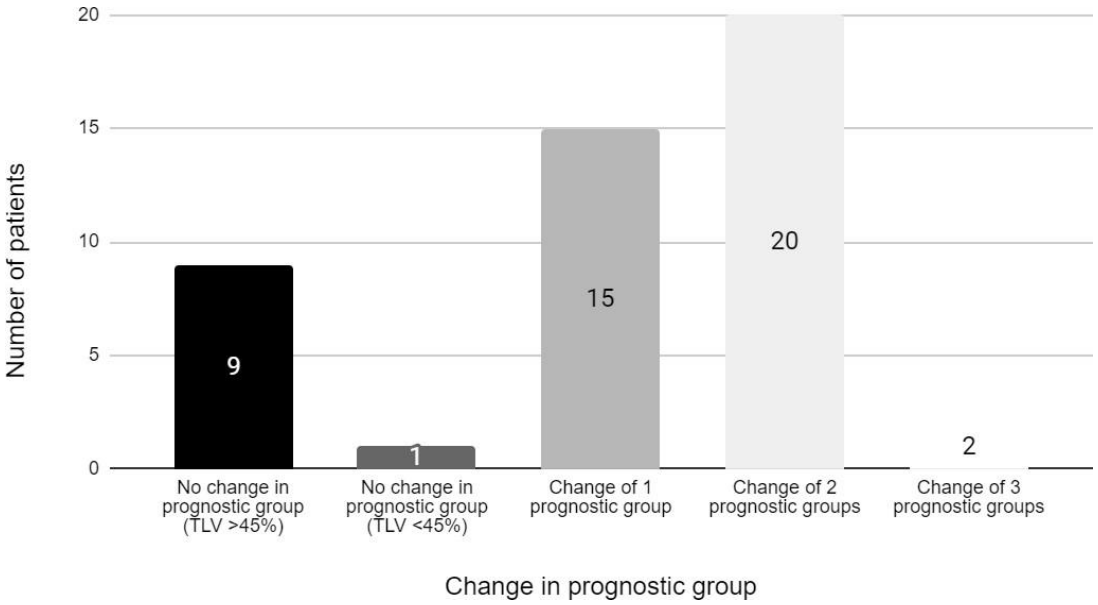


Figure 3.3. Change in the prognostic group observed depending on which formula for expected lung volume was used

For the ten patients who died in the neonatal period there was considerable variation between the ranges of percentage survival calculated using the five methods. One patient had 25% survival using all five methods, one had 25-50%, two had 25-70%, one had 25-95%, four had 50-95% and the remaining one patient had 95% predicted survival based on lung volume. Of these ten patients, the patient with 95% predicted survival using all methods of calculation had complex congenital heart disease which was inoperable and therefore a decision for palliative care was made. Three patients had a suspected VACTERL association noted after delivery but none of these patients underwent post-mortem examination.

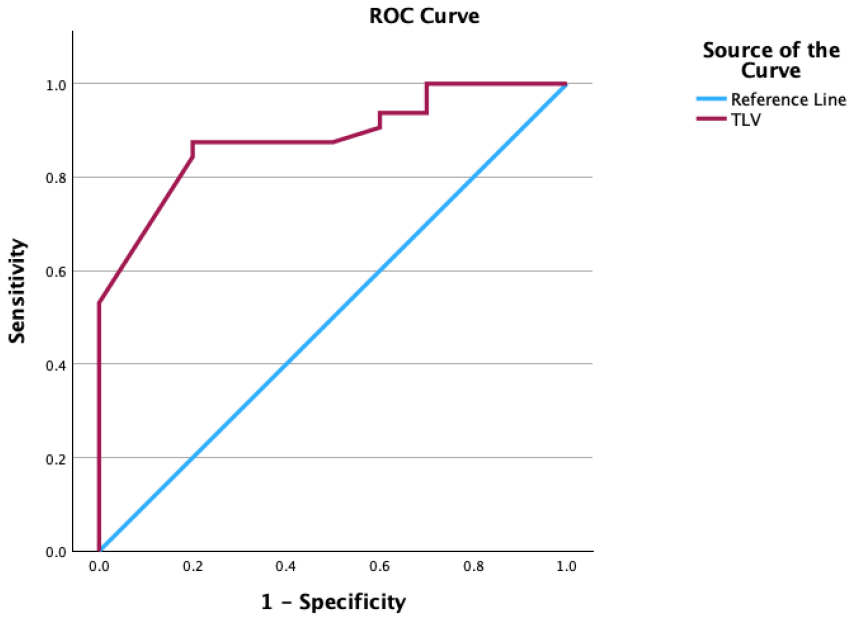


Figure 3.4. ROC curve of %TLV in relation to survival. Area under the curve = 0.883 (95% CI 0.778-0.988, p<0.001)

A receiver operating characteristic (ROC) curve was generated using the %TLV generated for each patient from our in-house method of calculation compared with survival as shown in figure 3.4. 42 patients were included as the patient who underwent termination of pregnancy and a patient who died in the neonatal period with comorbid complex cyanotic congenital heart disease were excluded from the analysis. The area under the curve (AUC) was 0.883, implying moderate accuracy of percentage lung volume in prediction of survival. Percentage total lung volumes of 35% had 94% sensitivity using our data, this is in correlation with more recently published literature suggesting 35% TLV should be used as a cut-off for survival prediction [64,65].

Discussion

This study shows the difference in percentage lung volume for patients with CDH depending on which method is used to calculate the expected volume for gestation. These differences in turn highlight the potential for significant variation in how parents are counselled when these percentage volumes are used to estimate chance of survival. This may impact on how decisions regarding the future of the pregnancy are made. These points also highlight the importance of verification by the reporting radiologist meaning that the value for percentage lung volume obtained should be viewed alongside the images afterwards to ensure it appears to be correct.

From this data we can see several examples of extreme differences in calculated percentage total lung volume which varied from 16.4%-50% in one patient and from 24.1-45.8% in another. This in turn leads to a difference in prognosis with survival varying from 25%-95% depending on which method is used. Whilst in other patients a larger variation in percentage volume was noted this did not impact the predicted survival or counselling as volumes were all over 45% meaning no change in the survival chance of 95% (n=9).

Upon initial review of this data, and its significant variation, there were concerns as to how decisions regarding the management of the pregnancy may potentially be influenced. However, in this cohort only one patient underwent termination, and they did not have any variation in their predicted survival (all 95%) but the question of how decisions made for this patient group may have changed if different formulae were used remains pertinent. Likewise, there is the possibility of counselling being more optimistic when certain formulae are used compared to others which raises concerns regarding potential false hope for parents. In addition to this, the impact that predicted lung volumes have on the teams looking after these babies after delivery must be considered. For example, whether plans for extent of resuscitation at birth, treatment on the neonatal unit and definitive surgery are altered by knowledge of the %TLV and likelihood of survival is a possibility.

In the literature, there are other methods of calculating expected lung volumes for gestation such as using total fetal body volume [66] from the MRI. These methods were not used in this study as this was a comparison of formulae using the same method. Furthermore, as far as we are aware, using total fetal body volume as a comparator is not widely used in clinical practice due to the extra images required to ensure that all the fetal body is imaged, including the limbs, and the time taken for calculation of the whole body volume.

The use of the degree of pulmonary hypoplasia in prognostication of survival unfortunately could not be supported by this study. For the patients who died in the neonatal period there was a wide variation in their chance of survival based on percentage total lung volume and with over 50% of them having a 50-95% chance of survival and one of these patients having a 95% survival chance regardless of which formula was used to calculate the expected lung volume. This may be reflected by the complex conditions frequently associated with CDH influencing morbidity and mortality [67]. However, when a ROC curve was used to determine a %TLV cut-off for survival, 35% had 94% sensitivity which is similar to other recently published studies [64,65] but we appreciate patient numbers for this analysis are small.

This study is limited by sample size and the missing outcome data for three patients.

However, it highlights the uncertainty of outcome in CDH and the importance of the provision of support for families following diagnosis [68].

Conclusion

In conclusion, there are multiple methods for calculating expected lung volume for gestation. When they are used to determine the percentage of total lung volume observed on MRI in patients with CDH there is a large difference in values between methods. As shown in this study, this leads to a variation in predicted survival rates which may have an impact on perinatal counselling and the difficult decisions made by families.

3.2 MRI observed-to-expected lung volume in left-sided congenital diaphragmatic hernia – does the ratio change throughout pregnancy?

Abstract

Introduction - Fetal MRI plays a role in diagnosis and prognostication of congenital diaphragmatic hernia. Prognosis is partly based on the observed fetal lung volumes as a percentage of what is expected for the gestational age. Most patients undergo two fetal MRI scans during pregnancy, however this is not always possible.
This study aims to assess whether percentage lung volume changes between MRI scans and whether prognosis would be affected.
Methods - Retrospective review of all patients with left-sided CDH who underwent fetal MRI at our centre between 2010-2023. Percentage observed-to-expected lung volumes at first and second MRI were compared with predicted survival rates to see if there was a change between scans.
Results - 58 patients underwent fetal MRI for left-sided CDH. 25 of these had two MRI scans. For 60% patients there was minimal change in their percentage lung volume between scans meaning their predicted survival did not change. For 40% patients there was a change in predicted survival rate between MRI scans. For 40% of these patients this was a reduction in predicted survival rate but for 60% there was an increase in observed-to-expected lung volume and predicted survival rate. When correlated with outcome the prognosis from the first MRI scan appeared to be more accurate.
Conclusions - This study shows observed-to-expected lung volume in left-sided CDH did not change enough between first and second MRI scans to alter the prognosis for 60% of patients. The initial MRI is important in prognostication for counselling families with the subsequent scan used for surgical planning.

Introduction

Congenital diaphragmatic hernia (CDH) is a rare congenital abnormality affecting 3 births per 10,000 within the UK [17]. The malformation most commonly occurs on the left [60] and is known to have significant morbidity and mortality. The diaphragmatic defect allows herniation of the abdominal contents into the thoracic cavity which compresses the lungs and prevents their normal development. CDH is characterised by pulmonary hypoplasia and pulmonary hypertension which are significant indicators of prognosis [21].

In recent years, fetal magnetic resonance imaging (MRI) has been shown to be increasingly

useful in accurate diagnosis and evaluation of the anatomical anomaly and any residual normal structures. This enables assessment of severity, estimation of prognosis and assessment for potential fetal therapy [69].

There are several factors which can be assessed with fetal imaging which are used to determine the prognosis for these patients; such as presence of significant liver herniation, lung-to-head (LHR) ratio predominantly used on ultrasound and observed-to-expected total lung volume ratio (O/E TLV) from fetal MRI [21,70,71]. Ultrasound assessment remains the gold standard for diagnosis of conditions such as CDH, it is widely available and low cost. However, it has some limitations especially where there is high maternal body mass index (BMI) and in cases of oligohydramnios or atypical fetal position [8]. Therefore, MRI is useful for supplemental imaging as it allows a more accurate measurement of structural volumes like the lungs [61]. There are multiple different methods for determining the expected lung volume for gestation on fetal MRI. Research has shown there can be a variation in the expected volume calculated depending on which method is used [72]. However, it is clear from all studies that outcome in CDH is not just dependent on lung volume.

In clinical practice many patients diagnosed with CDH undergo two fetal MRI scans during pregnancy for initial diagnosis and prognosis and later for re-evaluation and management planning. A second fetal MRI scan is not always possible for example in cases of diagnosis after 28 weeks gestation, in cases of preterm delivery and where there are logistical or personal barriers for the patient. However, if there are significant changes in scan findings between the initial and subsequent MRI there is a possibility of survival prediction and perinatal counselling being affected.

This study aims to assess whether the observed-to-expected lung volume ratio changes between the first and second MRI scans and whether prognosis and counselling could be affected by these changes.

Methods

This study had ethical approval from the Health Research Authority, IRAS no. 222053. This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

A retrospective review of all patients diagnosed with left-sided CDH who underwent fetal MRI between January 2010 and September 2023 at our centre was conducted. As cases of

right-sided CDH are significantly less common and often diagnosed postnatally [73], they were excluded from the study. Fetal MRI was performed in all cases of left-sided CDH following suspected or confirmed diagnosis made on antenatal ultrasound as is standard clinical practice at our centre. For each patient data was collected concerning the number of fetal MRI scans undertaken (one or two), the gestational age at the time of the scan(s), total lung volume in millilitres and as a percentage of expected volume for gestation.

The MRI scans were undertaken using a 1.5 Tesla Siemens Avanto scanner (Erlangen, Germany) and the T2 weighted SSFE sequence (repetition time 1000ms, echo time 91ms, 17 adjacent slices with a 3-5mm section thickness, flip angle 150°, field of view 288 x 288mm, and resolution 192/192) were used to measure lung volumes. During reporting of the MRI, the fetal lungs were measured on each slice of the coronal images using the Agfa Healthcare (Mortsel, Belgium) Enterprise Imaging platform as shown in figure 3.1. The slice measurements were summed and multiplied by the MRI slice thickness to calculate the total lung volume. Coronal measurements are used as they are less affected by motion artefact than the axial images.

However, total lung volumes were re-measured in the axial plane in cases where the coronal measurements were significantly different to the visual estimation or reported ultrasound volumes. These measurements were undertaken by the reporting consultant radiologist who has many years of experience in fetal MRI. Previous work has been performed at our centre using two separate data sets of 30 and 10 patients each to assess the repeatability of these measurements. An assessment of inter and intra-observer variability found the measurements to be accurate and reliable as intra-observer variation (0.922), and inter-observer variation (0.981) was excellent.

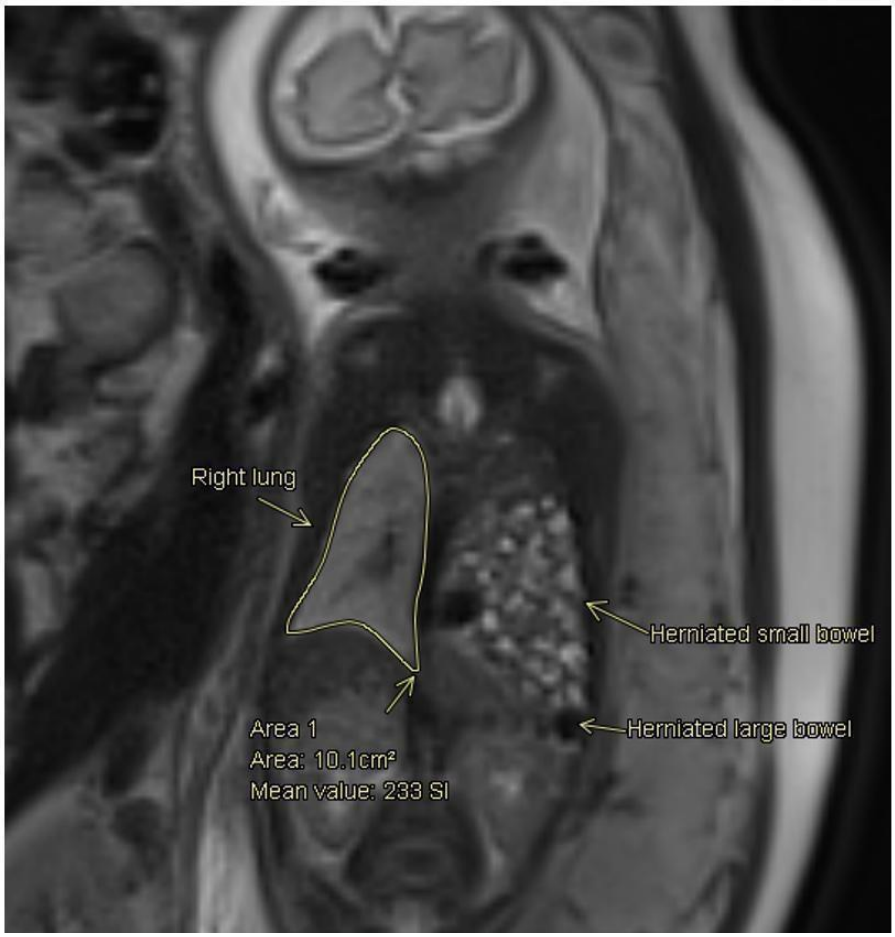


Figure 3.1. Coronal fetal MRI image of left-sided CDH with volume measurement of the right lung
Figure reproduced in line with journal permissions from: Wilson L, Whitby EH. MRI prediction of fetal lung volumes and the impact on counselling. Clin Radiol. 2023 Dec;78(12):955-959. doi: 10.1016/j.crad.2023.09.006.

These total lung volumes, as measured by the radiologist reporting the MRI scan, were used to calculate the lung volume as a percentage of what would be expected for the gestational age. The expected lung volumes for gestation are based on previous work within our centre to develop a chart based on the lung volumes seen in fetuses undergoing MRI for other reasons. The normative data has been substantiated both with comparison to other formulae in the literature [63] and post-mortem data as well as on phantom studies.

The observed-to-expected total lung volume ratio was then compared with predicted survival rates in the literature that are used for perinatal counselling at our centre as shown in table 3.2 [12]. For patients who underwent two MRI scans the values of observed-to-expected total lung volume ratio and predicted survival were compared to see if they changed between scans. Outcome data was collected where available for all patients.

Observed-to-expected lung volume (%)	Survival (%)
<25	25
25-34	50
35-44	70
≥45	95

Table 3.2. Survival rate according to the percentage observed to expected total lung volume (O/E TLV) [12]

The assessment of observed-to-expected lung volumes and their correlation with survival was chosen for this study as these are the measurements made using fetal MRI and are what is used clinically at our centre. The work uses gestational age to determine the observed-to-expected lung volume ratio as it is based on in-house data using gestational age to calculate the expected lung volume. Furthermore, data from the literature shows that when estimated fetal body weight is used instead of gestation to calculate the expected lung volumes discrepancies are more likely in women with a body mass index (BMI) >25 or if the estimated fetal weight is <10th centile or >90th centile [74]. The use of estimated fetal weight to determine the expected lung volume has not been established in clinical practice.

Results

A total of 58 patients with left-sided CDH underwent fetal MRI at our centre between January 2010 and September 2023. Of these 58, 25 patients underwent two MRI scans. The median gestational age at the time of the first scan was 21+5 weeks and 32+0 weeks at the second scan. Of the remaining 33 patients who only underwent one fetal MRI, 13 did not have their CDH detected on antenatal ultrasound until after 29 weeks gestation, two had preterm deliveries, five underwent termination of pregnancy, two had a stillbirth and one was a planned palliative delivery therefore a decision was made not to repeat the MRI. The reasoning for the lack of repeat MRI scan was not clear in the other ten patients, it was noted that all of these cases were prior to 2016.

A comparison was conducted between the observed-to-expected total lung volume ratios for each fetus. This was then correlated with survival rates based on percentage lung volumes in table 3.2 [12] to determine if predicted survival changed between the two scans. The change in lung volume and prognosis for each patient are shown in table 3.3.

Gestation (weeks + days)		Total lung volume (mls)		Observed-to-expected total lung volume (%)		Predicted survival (%)	
1st MRI	2nd MRI	1st MRI	2nd MRI	1st MRI	2nd MRI	1st MRI	2nd MRI
23+0	32+3	9	19	50%	45%	95%	95%
22+2	29+6	19.5	38.4	>100%	100%	95%	95%
21+3	31+6	7	26.5	44%	63%	70%	95%
22+2	31+6	4.5	40	28%	41%	50%	70%
23+1	33+1	6.4	12.7	40%	28%	70%	50%
20+1	33+4	6.7	24	56%	53%	95%	95%
23+0	35+2	9	42	50%	50%	95%	95%
23+4	32+0	10.5	22	50%	55%	95%	95%
21+4	31+4	4	16	25%	40%	50%	70%
22+5	31+5	9	38	56%	90%	95%	95%
21+4	32+0	5	20	36%	45%	70%	95%
23+3	32+0	10	42	50%	50%	95%	95%
25+5	32+0	20	40	80%	91%	95%	95%
21+5	32+0	7.5	15	40%	38%	70%	70%
18+4	32+0	3	11	50%	28%	95%	50%
24+1	32+0	7	18	35%	45%	70%	95%
21+0	29+1	7	15	50%	44%	95%	70%
22+2	34+0	10	24	66.6%	60%	95%	95%
18+0	35+5	5	25	70%	48%	95%	95%
23+0	34+4	10	27	56%	54%	95%	95%
22+6	35+6	8.5	34	47%	57%	95%	95%
21+2	32+0	6.5	18	43%	45%	70%	95%
20+0	32+0	6	17	50%	34%	95%	50%
20+6	28+0	7	20	50%	50%	95%	95%
20+0	31+0	10	26	66.6%	66%	95%	95%

Table 3.3. Change in lung volume between MRI scans and impact on predicted survival (n=25)

Reduced survival Improved survival

In 15/25 (60%) patients the change in the observed-to-expected lung volume ratio between the first and second scan was not significant enough to alter the predicted survival rate. For these patients predicted survival was 95% in 14 and 70% in one.

For 10/25 patients (40%) there was a change in predicted survival rate between the two MRI scans. For four of these patients this was a reduction in percentage observed-to- expected lung volume which was significant enough to reduce the predicted survival rate from 95% to 50% in two patients, from 95% to 70% in one and from 70% to 50% in one. The remaining six patients had an increased observed-to-expected lung volume ratio and improved predicted survival rate following the second MRI scan which increased from 70% to 95% in four and from 50% to 70% predicted survival in two patients. These findings are summarised in figure 3.5.

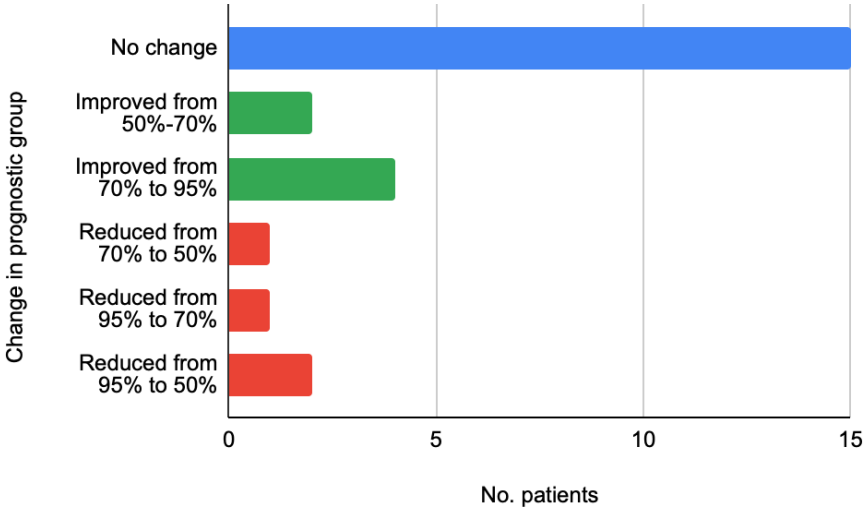


Figure 3.5. Summary of change in prognostic group between 1st and 2nd MRI scan (prognostic groups are 25%, 50%, 70% and 95% predicted survival)

Outcome data was available for all patients in the study. The survival rate was 63.8% for our cohort which is similar to a previous study in the literature with similar patient numbers [12]. Six patients were transferred for extracorporeal membrane oxygenation (ECMO) but two did not survive. The data concerning the outcome, associated comorbidities and cause of death is summarised in table 3.4.

Overall outcome (n=58)	**No. patients**
Termination of pregnancy	5
Stillbirth	2
Fit & well following repair	37
Died	14
Cause of death: (n=14)	**No. patients**
Pulmonary hypertension	8
Cardiac anomaly	3
Non-CDH related	3
Timing of death:	**No. patients**
Planned palliative delivery	2
Pre-operatively	8
Perioperatively	1
Post-operatively	3
Associated anomalies:	**No. patients**
VACTERL	3
Cardiac anomaly	6
TOF/OA	3
Other anomalies	2

Table 3.4. Outcome data for all patients with associated comorbidities and cause of death

All ten patients whose predicted survival changed following the second MRI scan were liveborn after 36 weeks gestation. The patient with reduced predicted survival from 95% to 70% required extracorporeal membrane oxygenation (ECMO) but underwent successful repair and is alive and well. One of the patients whose predicted survival decreased from 95% to 50% died on day one of life prior to surgical repair of the CDH. A formal post-mortem examination was not undertaken however features of VACTERL association such as oesophageal atresia, imperforate anus and cardiac abnormalities were noted, and the patient remained profoundly acidotic despite maximal therapy therefore care was

reorientated. The other patient with reduced predicted survival from 95% to 50% underwent successful CDH repair in the neonatal period but unfortunately passed away from a brain tumour during childhood. The patient with reduced predicted survival from 70% to 50% died in the neonatal period prior to surgery as a result of pulmonary hypertension and also had a diagnosis of encephalocoele.

Of the two patients whose predicted survival improved from 50% to 70% following the second scan both died in the neonatal period as a result of severe persistent pulmonary hypertension of the newborn (PPHN), this was despite one of them being transferred for ECMO. For the other four patients with improved predicted survival from 70% to 95% two underwent successful repair, one died post-operatively from E. coli sepsis and the other died pre-operatively from PPHN.

Further analysis was undertaken concerning the patient outcomes based on their prognostic group calculated from the observed-to-expected lung volume ratio on the first MRI scan. The percentage volumes from the first scan were used in this analysis as structural lung development is known to be complete by 24 weeks gestation although lung maturation has not yet occurred [75] and it is the volumes from the initial scan which are used clinically for perinatal counselling. These findings are summarised in table 3.5.

Prognostic groups (from 1st MRI):	**Fit & well**	**TOP**	**Stillbirth**	**Deceased**
25% (n=5)	0	1	1	3
50% (n=6)	2	2	0	2
70% (n=10)	3	1	0	6
95% (n=37)	32	1	1	3

Table 3.5. Patient outcome in relation to prognostic group from 1st MRI scan

Discussion

This study has shown that for 60% patients with left-sided congenital diaphragmatic hernia, observed-to-expected lung volume ratios did not change enough to affect predicted survival in the time between MRI scans. In 40% of cases the observed-to-expected lung volume ratio differed by 5% or less between the MRI scans. For the patients whose observed-to-expected lung volume percentage changed enough to alter their predicted survival this was a reduced

survival in 40% and improved predicted survival in 60%. It was reassuring, however, to note that the biggest change in prognostic groups was between the 50% and 95% predicted survival groups. There were no patients whose prognosis changed from one extreme to the other i.e. from 95% to 25% estimated survival and vice versa.

Our data did show that for some patients the observed-to-expected lung volume did change by a relatively high percentage. Although, using the survival predictions from table 3.2, the prognosis was unchanged as the volumes were sufficiently large meaning survival was 95% regardless of the change in percentage lung volume. At our centre this means counselling would not have been affected however, for centres using different prognostication methods the information given to families may be affected.

When outcome data is used in conjunction with the survival estimates the observed-to-expected lung volume ratio from the first MRI scan appears to have a closer correlation with survival rates than the volumes from the second scan in this cohort; especially for the patients whose observed-to-expected lung volume ratio increased. Based on this data, we would therefore suggest that the prognostic information determined by the observed-to-expected lung volume ratio from the initial MRI should continue to be used when counselling parents. The repeated MRI scan however remains an important investigation to allow planning for the surgical management of the baby after delivery.

The overall survival for our cohort was lower than predicted, when the outcome was compared with the prognostic value given by the observed-to-expected lung volume on the initial fetal MRI scan. When patients who underwent TOP were excluded the survival rates were 88.9% in the 95% predicted survival group, 50% in the 70% predicted survival group, 50% in the 50% predicted survival group and 0% in the 25% survival group. These results may be limited by the sample size of 25 patients, compared with 53 patients in the study the prognostic groups are based on [12] and because the spread of patients between the prognostic groups was not equal in our study. The use of a ROC curve from the data in the previous chapter on CDH and percentage total lung volume, alongside recent literature, suggests using 35% as a cut-off value for survival in left-sided CDH rather than separate prognostic groups [64,65].

These findings add weight to the view that lung volumes alone are not the sole indicator of survival in left-sided CDH and other factors such as the presence of liver herniation and associated comorbidities must be taken into account when counselling families. The impact of associated anomalies such as cardiac defects, tracheo-oesophageal fistula/oesophageal

atresia and VACTERL association was once again highlighted. Previous work has shown that comorbid anomalies are seen in up to 39% of patients with CDH and can impact overall outcome [76]. In this cohort 19% (11/58) patients had other congenital anomalies diagnosed and of these patients 54.5% (6/11) had a cardiac anomaly. These comorbidities were shown to impact the overall prognosis as 28.6% of liveborn patients who died after delivery had a cardiac abnormality in addition to their CDH.

This study is limited by sample size as despite a thirteen year period of data, the relative rarity of CDH meant the cohort only had 58 patients in total with 25 undergoing two MRI scans during pregnancy. There was missing data regarding the reason for an absence of second MRI in ten patients, however outcome data was available for all patients in the study. The non-uniformity of patient management may also be a factor limiting this study, although as all patients were born in the same centre and were managed by the same neonatal and surgical teams this was not felt to have had significant impact.

Conclusion

Assessment of pulmonary hypoplasia through calculation of observed-to-expected total lung volume ratios on fetal MRI has been shown to be an important indicator of prognosis in left-sided congenital diaphragmatic hernia. There has been debate concerning the best time to perform the MRI scan in order to obtain the most reliable results and whether multiple scans are more useful than one. This study shows observed-to-expected lung volume ratios from fetal MRI in left-sided CDH can change throughout pregnancy and influence the predicted survival rates for these patients. However, when this is correlated with outcome the prognostic information from the lung volumes on the initial scan appears to be more accurate, which is reassuring for patients who do not undergo a second MRI scan as a result of preterm delivery. It is evident that there are many other factors affecting prognosis in CDH, with associated anomalies having a significant impact on outcome. Therefore, we would suggest that data from the earliest MRI scan performed continues to be used to inform prognosis and counselling for families, and the information from any further MRI scan to be used for planning management after delivery.

3.3 Prenatal diagnosis of tracheo-oesophageal fistula/oesophageal atresia: is MRI helpful?

Abstract

Introduction - Oesophageal atresia (OA) with or without tracheo-oesophageal fistula (TOF) affects 2.75 per 10,000 births within the UK. It is most frequently suspected on antenatal imaging when the stomach is absent or appears small. Studies have shown fetal magnetic resonance imaging (MRI) has greater diagnostic accuracy than ultrasound, however, there remains uncertainty over what size constitutes a small stomach and how frequently this correlates with a diagnosis of TOF/OA.

Methods - A retrospective study of patients referred for fetal MRI due to suspicions of TOF/OA on antenatal ultrasound from 2011-2022. We also included patients with a fetal MRI suspecting TOF/OA who had been referred for other reasons. The indication, MRI findings and postnatal outcome were compared to assess diagnostic accuracy. For each case the size of the stomach bubble was measured on MRI and stomach volumes in a control group were measured for comparison.

Results - The diagnostic accuracy for USS was 45.5% and 51.7 % for fetal MRI. Fetal MRI had a negative predictive value of 100% (p=0.0001). The control group showed a strong positive correlation between stomach size and increasing gestational age (R^2 = 0.69, p<0.001), but this correlation was less positive in the TOF/OA group (R^2 = 0.26, p = 0.03) and the stomach volumes in TOF/OA were consistently lower than in the control group. The receiver operating characteristic curve illustrates that an absent or unmeasurably small stomach is more diagnostic of TOF/OA as volumes ≤0.06ml had 90% sensitivity.

Conclusion - Fetal MRI can accurately exclude TOF/OA but only has marginally improved diagnostic accuracy over ultrasound. Research with larger numbers is required to further aid development of a cut off value for what can be considered a pathologically small stomach.

Introduction

Oesophageal atresia (OA) with or without tracheo-oesophageal fistula (TOF) affects 2.75 per 10,000 births within the UK [17]. It is commonly suspected on ultrasound scans (USS) where the stomach bubble is difficult to visualise as filling of the stomach with amniotic fluid during fetal swallowing is disrupted. Over recent years there has been increasing use of fetal magnetic resonance imaging (MRI) clinically to aid with diagnosis of congenital anomalies. The importance of early and accurate diagnosis in TOF/OA is vital to aid counselling for parents and planning for management after delivery.

A recent systematic review found that a small or absent stomach was identified in half of cases of OA as shown in figure 3.6. This sign is subjective however, with no consensus on what constitutes a “small” stomach [77]. Research has shown that fetal stomach size increases with gestational age, this has been observed on both MRI and USS [78–80] and whilst a pilot study found that stomach size in fetuses with OA was smaller [80] there is no current cut-off value for normal. In addition, visualisation of the stomach bubble may occur intermittently in a healthy fetus due to the periodic nature of fetal swallowing. Furthermore, the presence of a distal tracheo-oesophageal fistula which is seen in 85% cases means the stomach bubble may be seen on scans and amniotic fluid volume may be normal [81]. In cases of pure OA with no fistula the stomach may still be visualised as a result of secretions produced by the gastric mucosa [82].

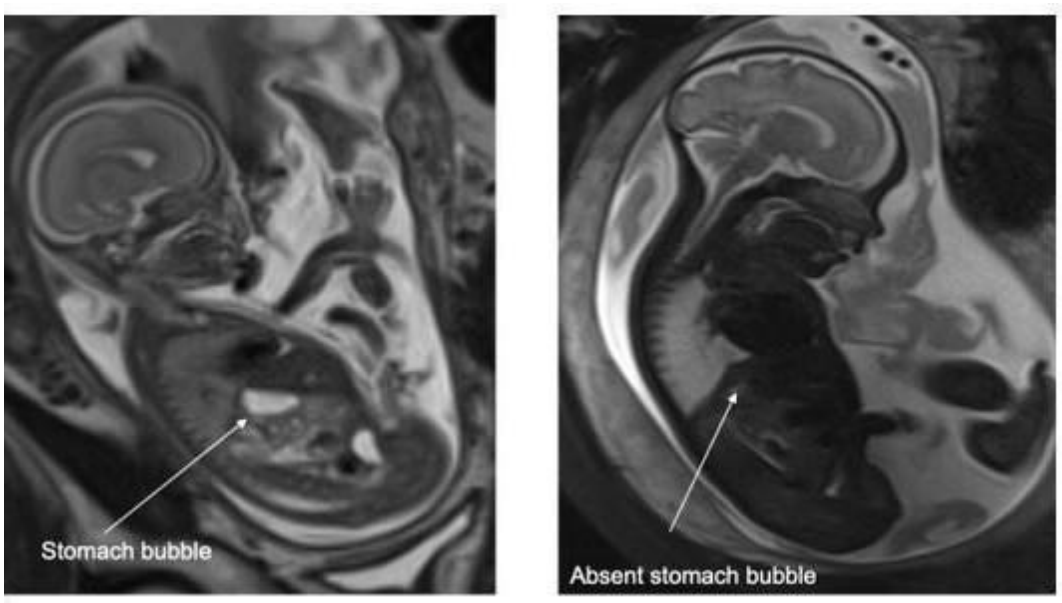


Figure 3.6. Sagittal T2 SSFSE fetal MRI images of normal stomach bubble size in 22 week fetus (left) in comparison with a small stomach bubble in a 30 week fetus with TOF/OA (right)

Other features seen on imaging such as the “pouch sign” [83] and the “distended fetal hypopharynx” [84] have been proposed as a more reliable sign for diagnosis of OA especially when using fetal MRI [85]. The pouch sign is visualisation of the dilated blind-ending upper oesophagus seen in the neck or mediastinum during swallowing as shown in figure 3.7. The pouch sign is seen most commonly in cases of pure oesophageal atresia, meaning MRI has an advantage in diagnosis of these cases. The distended fetal hypopharynx is seen as a result of amniotic fluid being forced upward into the mouth, distending the hypopharynx due to obstructed swallowing. Whilst these dynamic processes can be observed on real time fetal sonography, the cine mode of fetal MRI allows for better

dynamic studies. However, the pouch sign is not seen before 26 weeks of gestation [86] and although the distended fetal hypopharynx has been identified at an earlier gestational age it was less specific for OA than the pouch sign (67% vs 97%) [84].

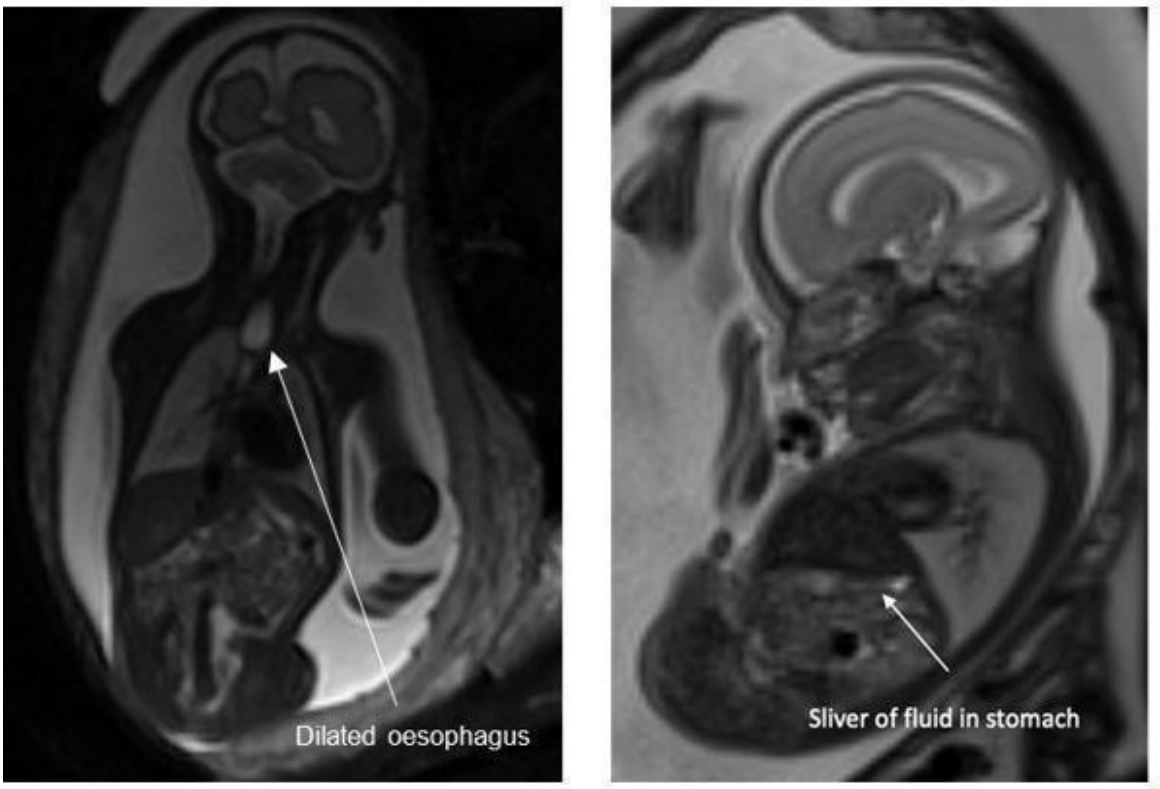


Figure 3.7. Coronal T2 SSFSE MRI image of dilated oesophagus (pouch sign) and small stomach in 30 week fetus with TOF/OA

In cases of oesophageal atresia with tracheo-oesophageal fistula, the pouch sign and distended fetal hypopharynx are less likely to be observed on antenatal imaging therefore stomach size is a key diagnostic indicator.

The aims of this study were to determine the diagnostic accuracy of fetal MRI in comparison with antenatal ultrasound in TOF/OA and to review the stomach bubble size to see if a range of normal values could be obtained.

Methods

The study had ethical approval from the Health Research Authority (HRA) as part of wider research into the use of fetal MRI in congenital anomalies of the fetal body (IRAS project ID 222053 and REC reference 17/EE/0162). As this is a study of diagnostic accuracy the Standards for Reporting of Diagnostic Accuracy Studies (STARD) guidelines were consulted

as a point of reference [87].

This study was a retrospective review of all patients referred to our centre for a fetal MRI between October 2011 and October 2022 due to concerns regarding possible TOF/OA on USS. Common reasons for referral included polyhydramnios and a small or absent stomach bubble. We also included cases which had been referred for a fetal MRI for a different indication, but possible TOF/OA was suspected following the MRI scan. Inclusion criteria for the study was patients with features suggestive of TOF/OA on USS referred for fetal MRI and patients with fetal MRI suggestive of TOF/OA who had been referred for other reasons. All antenatal ultrasounds were performed by consultant fetal medicine specialists with over three years consultant experience. A flow chart of patient recruitment is shown in figure 3.8 in the results section.

The MRI scans were performed using a 1.5 Tesla Siemens Avanto scanner (Erlangen, Germany). Stomach volume assessments were made from the T2 single shot fast spin echo (SSFSE) images (echo train length 117, repetition time 90, echo time 1000, number of excitations 1, matrix size 192x192, field of view 288x288mm, flip angle 150, slice thickness 4mm no gap).

Outcome data with overall final postnatal diagnosis made by imaging, surgery or post-mortem examination was collected for all patients and used as the reference standard to determine the diagnostic accuracy of the imaging. Diagnostic accuracy was determined by how frequently the ultrasound and MRI diagnosis aligned with the final postnatal diagnosis, i.e. the number of true positives and true negatives as a proportion of the total number of tests. For all cases, independent of outcome, the MRI scans were reviewed and stomach bubble size measured or documented as absent or unmeasurable in cases where only a sliver was visible. Other features such as presence of oesophageal dilatation, absence of the lower oesophagus, intermittent filling of the stomach, and regurgitation of fluid during fetal swallowing using the cine mode were also documented.

The fetal stomach volumes were traced on each slice in either the coronal or sagittal orientation (whichever it was most visible on) using the Agfa Healthcare (Mortsel, Belgium) Enterprise Imaging platform. The areas of each slice were then summed and multiplied by the MRI slice thickness to calculate the total stomach volume. The stomach volume measurements were undertaken by two researchers working independently and any discrepancies were then reviewed by the research team together. One of the researchers has many years of experience in reporting fetal MRI scans. Analysis of inter-observer

variation and intra-observer variation was then undertaken using the Cohen's weighted Kappa coefficient.

A second cohort of control patients was identified from fetal MRI scans which were undertaken for assessment of the placenta. These were healthy patients with no conditions which could affect stomach size. The stomach volumes for each of these patients were calculated using the method as described above, they were then plotted against gestation and compared with the stomach volumes in the cohort diagnosed with TOF/OA after delivery.

Results

Study characteristics

This study included a total of 51 patients, 46 of these were referred to our centre for fetal MRI due to concerns regarding TOF/OA on the ultrasound. The remaining 5 patients were referred for a fetal MRI due to different reasons, but the possibility of TOF/OA was raised following the MRI. The pathway of patient selection and follow-up is summarised in figure 3.8.

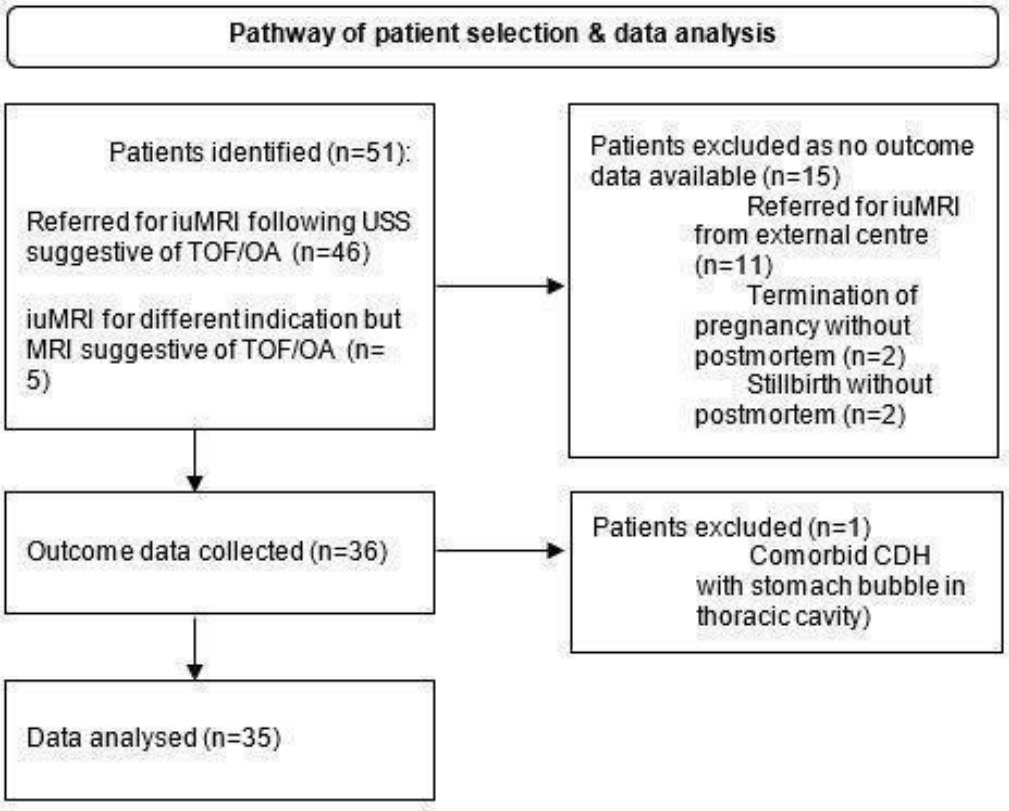


Figure 3.8. Patient selection and analysis

Abbreviations - iuMRI (in utero magnetic resonance imaging), USS (ultrasound scan) TOF (tracheo-oesophageal fistula), OA (oesophageal atresia), CDH (congenital diaphragmatic hernia)

The reasons for referral for fetal MRI to rule out TOF/OA (n=46) included polyhydramnios (n=12), a small/partially filled stomach (n=15), an absent stomach (n=18) and other associated anomalies (n=1) which were other features of VACTERL association. The indications for MRI referral in the other five patients were congenital diaphragmatic hernia (CDH), spina bifida, dextrocardia, Dandy-Walker malformation and a single kidney in each patient respectively.

The mean gestational age at the time of fetal MRI was 28.3 weeks. Outcome data with a final diagnosis was available for 36 patients. The remaining 15 patients with no outcome data of diagnosis were either referred from external centres (n=11) or underwent termination of pregnancy (n=2) or stillbirth (n=2) but declined post-mortem examination. One patient was excluded from the analysis as they had a congenital diaphragmatic hernia with the stomach herniated into the thoracic cavity which was felt to affect the reliability of stomach volume assessments. The patient characteristics and their MRI findings are summarised in table 3.6.

	TOF/OA (n=16)	No TOF/OA (n=20)
Mean gestation at iuMRI	28.4 weeks	30.1 weeks
Reason for iuMRI		
Polyhydramnios	5	5
Small stomach	0	10
Absent stomach	10	5
Associated anomalies	0	1
Other condition suspected	3	0
iuMRI findings		
Small stomach	7	12
Absent stomach	5	2
Dilated oesophagus/pouch	4	1
Lower oesophagus not seen	3	1
Mean gestation at birth	36.6 weeks	38.1 weeks

Table 3.6. Patient characteristics and fetal MRI findings of patients with outcome data (n=36).
NB Some patients had more than one finding. *Abbreviations - iuMRI (in utero magnetic resonance imaging), TOF (tracheo-oesophageal fistula), OA (oesophageal atresia)*

The 35 patients with outcome data who were included in the analysis were all liveborn with one death in the neonatal period in the confirmed TOF/OA group and three deaths from other causes in the patients without TOF/OA.

Diagnostic accuracy of USS and MRI

For the patients with outcome data TOF/OA was suspected on USS in 33/35 cases and on fetal MRI in 29/35 cases. As discussed above the differences in numbers are due to four patients being referred for fetal MRI due to other suspected diagnoses which were not TOF/OA and because six MRI scans were reported as normal.

The MRI findings suspicious for TOF/OA (n=29) included a small/underfilled stomach (n=16), an absent stomach bubble (n=6), a sliver of fluid in the stomach (n=5), intermittent filling of the stomach (n=1), evidence of oesophageal obstruction/dilatation (n=4) or absence of the lower oesophagus (n=4). There was some overlap between findings in cases. As there is no recognised cut-off value for what determines a ‘small’ stomach, this finding was based on

the opinion of the reporting radiologist who has many years' experience of fetal MRI. This was recognised as a study limitation due to its subjectivity; however, it reflects clinical practice and there is no objective definition of a small stomach at present. A sliver of fluid was defined as cases where the stomach was visible, but the area was too small to reliably measure on the MRI as shown in figure 3.9. Attempted measurement of the stomach volumes where only a sliver was visible were undertaken and these were all <0.2mls, however they were reported as unmeasurable as volumes were not felt to be reliable at this size.

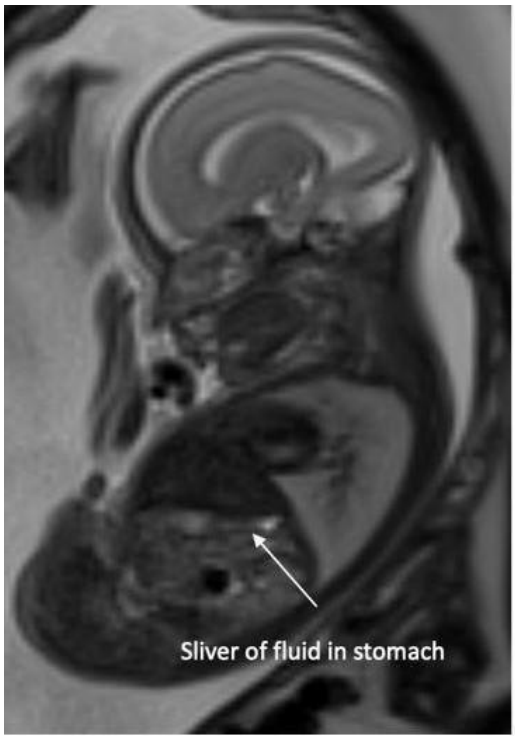


Figure 3.9. Sagittal T2 SSFSE fetal MRI image of 25 week fetus with a sliver of fluid visible in the stomach

Following delivery there were 15 cases of confirmed TOF/OA of which seven had pure OA, seven had TOF/OA and one had a complete laryngo-tracheo-oesophageal cleft. Fetal MRI findings for these patients are shown in table 3.7.

	Confirmed postnatal diagnosis		
iuMRI findings	**OA (n=7)**	**TOF/OA (n=8)**	**Complete cleft (n=1)**
Absent stomach	3	1	1
Small stomach	2	5	0
Oesophageal obstruction/dilatation	2	2	0
Lower oesophagus not visualised	3	0	0

Table 3.7. iuMRI findings in confirmed patients by diagnosis

Abbreviations - iuMRI (in utero magnetic resonance imaging), TOF (tracheo-oesophageal fistula), OA (oesophageal atresia). Overlap in cases - 2 patients had a small stomach & lower oesophagus not seen; 1 patient had small stomach & oesophageal dilatation.

Five patients had other associated congenital anomalies comprised of duodenal atresia (n=1), cardiac abnormalities comprised of a ventricular-septal defect (n=1), cardiac dextroposition (n=1) and Tetralogy of Fallot (n=1) and VACTERL (Vertebral defects, Anal atresia, Cardiac defects, Tracheo-oesophageal fistula/oesophageal atresia, Renal abnormalities, Limb Abnormalities) association (n=10). Of these 15 confirmed cases, 13 underwent MRI due to USS concerns regarding TOF/OA but the other two were referred for fetal MRI for a different indication. The other indications for fetal MRI which had confirmed TOF/OA were spina bifida and dextrocardia on antenatal ultrasound.

The overall diagnostic accuracy for USS was 45.5% (15/33) and 51.7 % (15/29) for fetal MRI. In this study fetal MRI had a negative predictive value (NPV) of 100% as all six MRI scans which were reported as normal did not have TOF/OA i.e. there were no false negative results as shown in table 3.8. Sensitivity was also 100% however, positive predictive value was only 53.3% and specificity 30%. These results were shown to be statistically significant with a p-value of 0.0001 using McNemar's test. The diagnostic value of specific fetal MRI findings is highlighted in table 3.9 and although certain findings such as an absent stomach and oesophageal pouch had specificity of 95%, not all of these findings were statistically significant when analysed in isolation.

	Sensitivity	Specificity	PPV	NPV	P Value
Diagnosis TOF/OA	100%	30%	53.3%	100%	p = 0.024

Table 3.8. Diagnostic accuracy of fetal MRI

Abbreviations - TOF/OA (tracheo-oesophageal fistula/oesophageal atresia), PPV (positive predictive value), NPV (negative predictive value). P value <0.05 considered statistically significant

	Sensitivity	Specificity	PPV	NPV	P value
Small stomach	37.5%	40%	33.3%	44.4%	p = 0.83
Absent stomach	31.2%	95%	83.3%	63.3%	p = 0.0063
Intermittent filling of stomach	6.25%	100%	100%	57.1%	p = 0.0001
Dilated oesophagus/pouch	25%	95%	80%	61.3%	p = 0.0034
Lower oesophagus not seen	18.8%	95%	75%	59.4%	p = 0.0018

Table 3.9. Diagnostic value of individual fetal MRI findings

Abbreviations - PPV (positive predictive value), NPV (negative predictive value). P value <0.05 considered statistically significant.

As this study was based on a cohort of patients identified through the use of fetal MRI, diagnosis was suspected on at least one imaging modality (ultrasound or MRI) prior to delivery. Further unpublished work was undertaken looking at all patients diagnosed with TOF/OA after birth who were managed at our centre from 2011 to 2023. A total of 48 patients were diagnosed with TOF/OA postnatally however only 33.3% were suspected on antenatal ultrasound and therefore referred for fetal MRI. 25% of this cohort were born in external district general hospitals. This highlights the importance of defining diagnostic criteria for TOF/OA to improve antenatal diagnosis.

Stomach volume measurements

The stomach volumes measured from the cohort with final outcome data (n=35) ranged from 0.085mls-6.04mls with a mean volume of 2.23mls (n=22) or were absent (n=6) or a sliver of stomach was visible, but it was unmeasurable (n=7). As previously discussed, measurements of these ‘slivers’ of fluid were made but they were all <0.2mls which was felt to be unreliable at such small volumes. For the patients noted to have a visually normal stomach with no other features suspicious for TOF/OA on the MRI report the measured

volumes were 2.24-6.04mls (mean volume = 4.02mls). As discussed above, all of the patients with normal fetal MRI scans did not have TOF/OA. Of the 15 patients with confirmed TOF/OA an absent stomach bubble was seen on MRI in five (83.3% of all absent stomach bubbles on MRI i.e. 5/6) and 75% patients with oesophageal obstruction/dilatation had TOF/OA confirmed after birth (3/4).

In the patients with confirmed TOF/OA after delivery (n=15) the stomach bubble on MRI was absent in five and unmeasurable in four. In the six patients in whom the volume could be measured it ranged from 0.349mls-3.55mls with a mean volume of 1.47mls.

The stomach volumes from the control patients (n=51) were plotted against gestation and showed a positive correlation between stomach size and advancing gestation ($R^2 = 0.69$) which was found to be statistically significant ($p < 0.001$) using the Pearson correlation coefficient. The stomach volumes for the patients with TOF/OA confirmed after delivery (n=15) were then plotted on the same chart for comparison with the control group. For these patients only six had a stomach volume which could be reliably measured as for the remaining nine patients, five had an absent stomach and four had only a sliver of fluid visible. Where the stomach bubble was absent this was plotted as zero and where only a sliver was visible this was plotted as 0.5mls. These results are summarised in figure 3.10 and show there is a less positive correlation between stomach volume and gestation in patients with TOF/OA ($R^2 = 0.257$, $p = 0.03$) and that the stomach volumes in TOF/OA were consistently lower than the control group.

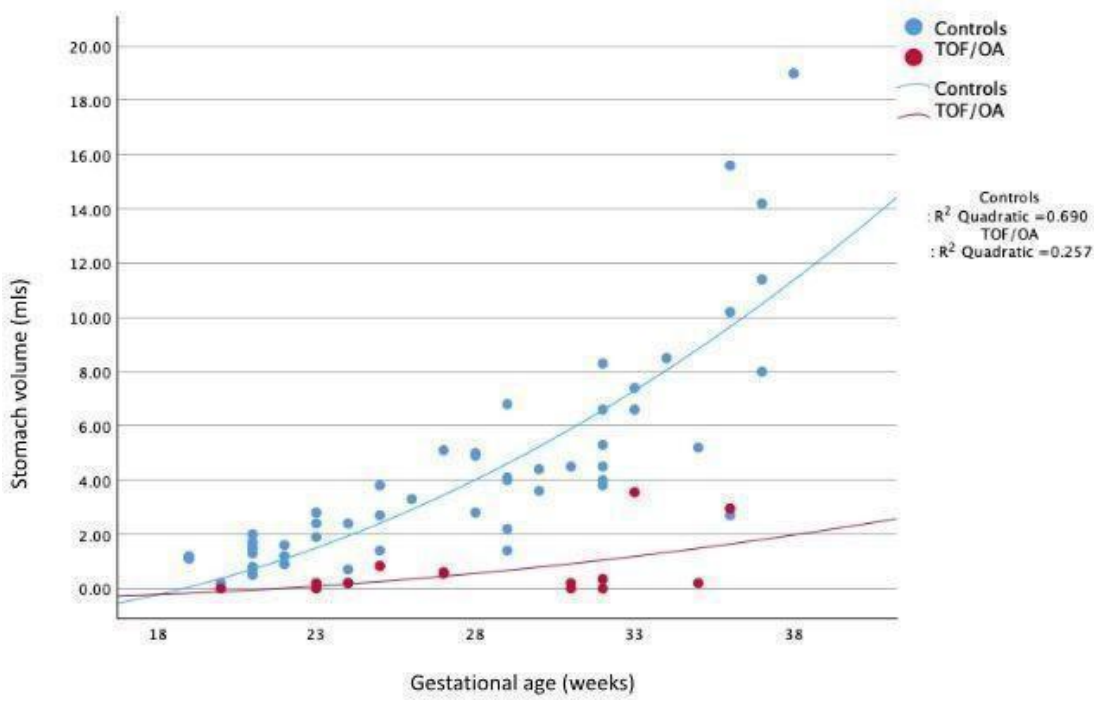


Figure 3.10. Scatterplot comparing the stomach size of controls and TOF/OA patients with increasing gestation

A receiver operating characteristic (ROC) curve was generated to see if a cut-off volume for stomach size indicative of TOF/OA could be determined. This data is limited by small numbers but shows an area under the curve of 0.79 as shown in figure 3.11. It shows that an absent stomach or unmeasurably small stomach (sliver) is more diagnostic of TOF/OA as volumes ≤0.06ml had 90% sensitivity and 67% specificity.

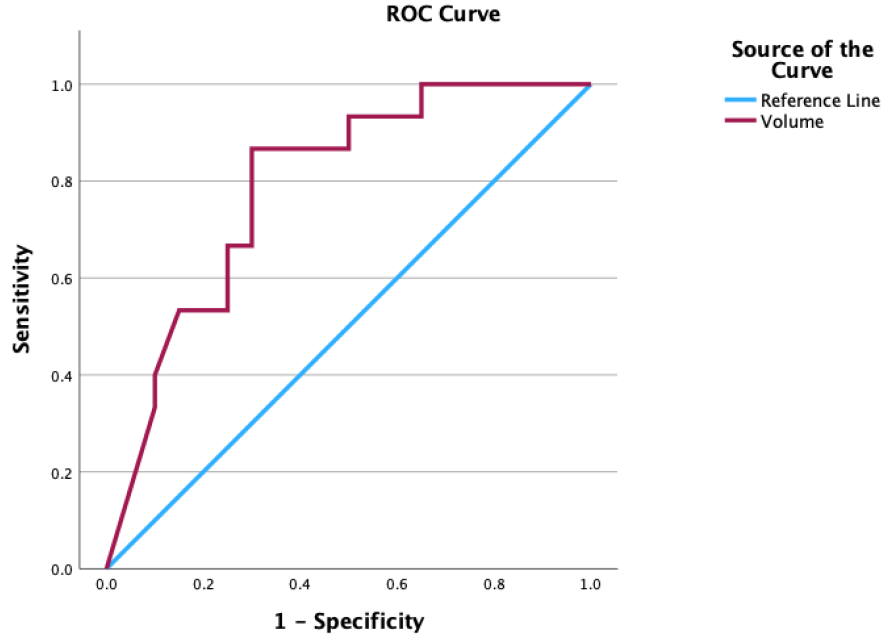


Figure 3.11. ROC curve of stomach volume, area under the curve = 0.79 (95% CI 0.64-0.94, p<0.001)

An assessment of inter-observer variation and intra-observer variation was undertaken using the Cohen's weighted Kappa coefficient. The weighted Kappa for was 0.818 for inter-observer variation and 0.883 for intra-observer variation, both of which showed excellent agreement.

Discussion

Accurate and early diagnosis of TOF/OA is vital for perinatal counselling for families and appropriate planning for place of delivery and surgical management. There are multiple signs cited in the literature seen on both ultrasound and MRI which raise suspicion of TOF/OA but larger studies of the diagnostic accuracy of these signs on fetal MRI is lacking [91].

This study has shown that fetal MRI has improved diagnostic accuracy over antenatal ultrasound alone, as seen in previous studies [85]. In addition, it highlights the use of fetal MRI to accurately exclude TOF/OA with 100% negative predictive value which was statistically significant ($p<0.05$). Evaluation of individual MRI findings has shown that absent stomach, dilated oesophagus and inability to visualise the lower oesophagus are highly diagnostic of TOF/OA with specificity of 95%. This is higher than in previous studies [88] and most useful when these findings are seen in combination, although the specificity of these signs was not consistently statistically significant when reviewed separately.

However, the overall diagnostic accuracy of fetal MRI in comparison with ultrasound was only marginally better in this study (51.7 % for MRI compared with 45.5% for USS). This is lower than previous studies which suggest MRI to be much more accurate at correctly diagnosing TOF/OA antenatally [77]. Therefore, this study raises the question of whether the additional costs and stress for the patient can be justified for only a marginal improvement in diagnostic accuracy. As discussed in the literature, many of the signs of TOF/OA seen on both ultrasound and MRI, such as a small stomach, are subjective and fetal stomach size will vary with time in relation to swallowing and gastric emptying [77]. Several of the signs seen on MRI such as the pouch sign and distended fetal hypopharynx relate to obstructed swallowing and therefore will not always be seen during the scan [83–85]. The presence of a distal tracheo-oesophageal fistula may mean there is fluid seen in the fetal stomach even when there is an oesophageal atresia [81] and the gastric mucosa produces secretions which may also make the stomach size appear normal on imaging [82]. All of these factors combined make accurate prenatal diagnosis of TOF/OA significantly challenging.

The use of control data to show increasing stomach size with gestational age has only been published in one previous study using fetal MRI to conduct the measurements [80]. Our data is consistent with what has previously been reported that there is a positive correlation between stomach volume and increasing gestation ($R^2 = 0.69$). The comparison of these controls with a cohort of 15 patients with TOF/OA supports the evidence that stomach size in TOF/OA is consistently smaller than in the control group and the stomach size has a less positive correlation with advancing gestation ($R^2 = 0.26$).

It seems that stomach size alone is unlikely to be the only determinant of diagnosis as we have shown there are multiple factors involved and cases which are more complex i.e. those with an absent stomach in addition to oesophageal dilatation or non-visualisation have a much higher likelihood of TOF/OA. The ROC curve further confirms that an absent or unmeasurably small stomach on fetal MRI is indicative of pathology, however a measurably but visually small stomach is less reliable in diagnosis of TOF/OA.

In this cohort there was only one patient with the combined features, an absent stomach and oesophageal dilatation, who did not have TOF/OA but was diagnosed postnatally with a complex upper airway anomaly (CHAOS syndrome). In addition to this, one of the patients in the cohort who had a visually small stomach on MRI which was too small to be measured was postnatally diagnosed with a congenital myopathy and although TOF/OA could not be ruled out based on the MRI findings there was family history of congenital myopathy meaning this was felt to be the most likely diagnosis antenatally.

It is important to note the patient who was excluded from the study prior to analysis, due to presence of left-sided congenital diaphragmatic hernia with the stomach bubble visible within the thorax as there was a concern this may have affected measurement of stomach volumes, was diagnosed postnatally with TOF/OA. Their stomach volume was a significant outlier when compared with the data set with a volume of 12.45mls. For this patient a bolus was seen in the oesophagus raising the suspicion of TOF/OA from the fetal MRI as shown in figure 3.12.

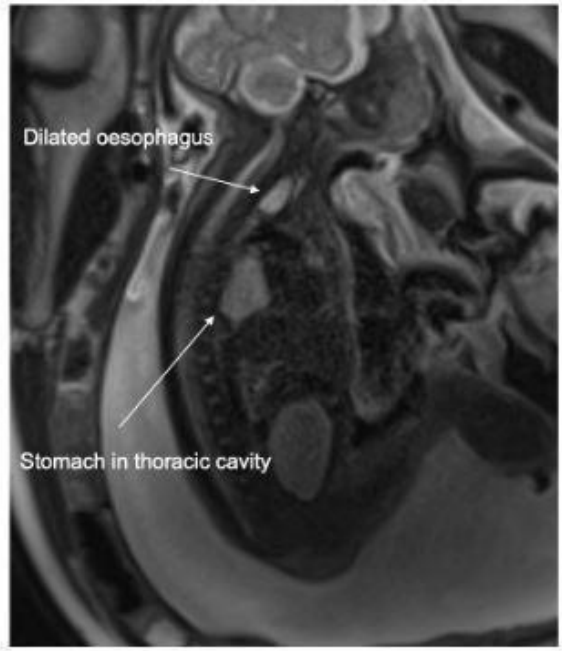


Figure 3.12. Sagittal T2 SSFSE fetal MRI image of 35 week fetus with CDH and TOF/OA with rotated stomach bubble in thoracic cavity and oesophageal pouch

This study also highlights the prevalence of comorbidities associated with TOF/OA such as cardiac abnormalities, congenital diaphragmatic hernia, VACTERL association and duodenal atresia. Research has shown that 55% of patients with TOF/OA have associated anomalies forming the VACTERL spectrum [89] including cardiac anomalies in 29%, gastrointestinal anomalies such as anorectal malformation in 16%, renal anomalies in 16% and musculoskeletal anomalies in 13%. The outcomes for these patients have been shown to be impacted by the presence of comorbidities with rates of termination of pregnancy ranging from 3-8% in isolated TOF/OA [90] but rising to 27% in the presence of other congenital anomalies [91]. Survival rates have also been shown to be impacted by comorbidities with rates of survival >90% in isolated cases and up to 87% in high risk cases such as where there are cardiac anomalies. The role of fetal MRI in these cases is vital for comprehensive diagnosis to enable appropriate discussions with parents and within the wider multidisciplinary team.

The study is limited by sample size, which is further impacted by missing outcome data regarding the final diagnosis for 15/51 patients. As previously discussed, many of the signs suggestive of TOF/OA such as a small stomach are subjective, meaning there are no specific definitions in the literature. However, the lack of definition of a pathologically small stomach was one of the areas this study aimed to address. As a measurable stomach volume was seen in only six of the confirmed TOF/OA patients a reliable cut off value for a

pathologically small stomach could not be determined by this data. The analysis using a ROC curve demonstrated that stomach volumes ≤0.06ml, i.e. where there is an absent stomach or unmeasurable sliver of stomach seen on fetal MRI, have a sensitivity of 90%.

Conclusion

In conclusion, this study has shown that fetal MRI has some improved diagnostic accuracy over antenatal ultrasound alone in diagnosis of TOF/OA. It has a higher diagnostic specificity when findings such as an absent stomach bubble, oesophageal dilatation and non-visualisation of the lower oesophagus are present, especially when in combination. However, this improvement in accurate diagnosis is only marginal which raises the question of whether a fetal MRI scan for suspected TOF/OA can be justified both in terms of the cost and stress for the family. This study shows that fetal MRI is accurate at ruling out TOF/OA as all MRIs reported as normal were confirmed as normal after delivery meaning there were no false negative results.

3.4 A clearer picture: Using fetal MRI to diagnose neck masses and predict airway compromise

Abstract

Introduction - Fetal neck masses are rare but can be life-threatening if causing airway compromise. Early and accurate diagnosis of these masses allows life-saving interventions to be undertaken at birth in the form of the EXIT procedure.
Methods - A single institution case series of all patients referred for fetal MRI to a tertiary centre in the North of England due to presence of a neck mass on antenatal ultrasound. Data was collected concerning the MRI findings for each patient and their final diagnosis to create a flow chart proposing the most likely diagnosis based on fetal MRI features.
Results - 13 patients who underwent fetal MRI for a neck mass with a final diagnosis available were included in the analysis. This review shows the range of diagnoses in these patients and that MRI was accurate in prediction of airway compression and the need for EXIT procedure.
Conclusion - Fetal MRI is a valuable tool in addition to ultrasound for refining the diagnosis of masses of the fetal neck and assessment of airway patency to allow planning for management at birth.

Introduction

There are several different pathologies which present as masses in the fetal neck. The most common include lymphatic malformations and teratomas as well as less frequently seen pathologies such as malignant tumours including rhabdomyosarcomas, and goitres caused by thyroid problems.

Cervical lymphatic malformations are the most common type of lymphatic malformation seen in infants, affecting 1.2-2.8/1000 live births [92]. They are low-flow vascular malformations that do not communicate with normal lymphatic vessels. Head and neck malformations account for 70-80% of all lymphatic malformations [93]. The International Society for the Study of Vascular Anomalies (ISSVA) updated the nomenclature for such malformations in 2018 and, in the new classification, the terms ‘lymphangioma’ and ‘cystic hygroma’ have been replaced with ‘lymphatic malformation’ and ‘cavernous haemangioma’ has been replaced by ‘venous malformation’. This is owing to potential confusions with the older terms as the suffix ‘oma’ implies a tumour rather than a malformation [93,94].

Teratomas are congenital tumours containing tissue from all three germ cell layers (the mesoderm, ectoderm and endoderm) [95]. Cervical teratomas are rare and account for 3-5% of all teratomas with an incidence of 1 in 20,000-1 in 40,000 live births [96], with the most common sites for fetal teratoma being in the sacrococcygeal region. In the head and neck teratomas are usually benign [97].

Early and accurate diagnosis of fetal neck masses is important as it allows appropriate antenatal counselling for families and planning for management at delivery and in the postnatal period. Ultrasound remains the imaging modality of choice for screening for fetal anomalies but further imaging with magnetic resonance imaging (MRI) and genetic testing may be undertaken to further refine the diagnosis.

Fetal MRI has been shown to be highly accurate in the diagnosis of mass nature and assessment of the fetal airway, allowing for planning of management at the time of delivery [98]. Whilst other studies have shown the diagnostic accuracy of fetal MRI in diagnosis of lymphatic and venous malformations to be no better than ultrasound, they further highlight the complementary role of MRI in providing more anatomical detail to anticipate the required intervention and risk of complications at birth [35,99].

The primary role of fetal MRI in clinical practice for the assessment of neck masses is to assess for airway patency and to help refine a diagnosis in cases where ultrasound is technically challenging, such as high maternal body mass index (BMI) or unfavourable fetal position [100]. In cases with airway compromise, significant multidisciplinary team (MDT) planning is required prior to delivery to prepare for advanced airway intervention at birth [101]. For the most severe cases, this intervention is the ex utero intrapartum treatment (EXIT) procedure. The EXIT procedure involves securing the airway via endotracheal intubation or tracheostomy in a controlled manner whilst the fetus is only partially delivered and remains attached to the placenta [102]. EXIT procedures are relatively uncommon, require an experienced MDT in a tertiary centre and are associated with both maternal and fetal risks [103].

The aim of this study was to present a series of patients with fetal neck masses as a pictorial review of the different diagnoses. Secondary aims were development of a pathway of the most likely diagnosis based on MRI findings and to assess the accuracy of MRI in assessment of airway patency.

Methods

This study was a retrospective case series from a single institution. Ethical approval was given by the Health Research Authority (HRA) for retrospective data collection and analysis (IRAS project ID 222053). The study included all patients referred to our centre for fetal MRI with a neck mass from January 2011 to March 2023.

The MRI scans were performed using a 1.5 Tesla Siemens Avanto scanner (Erlangen, Germany). The assessment of the neck mass and surrounding anatomical structures was made using the Agfa Healthcare (Mortsel, Belgium) Enterprise Imaging platform. The assessments were made predominantly from the T2 weighted images, with the diffusion weighted imaging (DWI) sequences used to assess for any restricted diffusion within the masses. The MRI findings were reported independently by two consultant radiologists each with over 20 years' experience of fetal MRI. Each radiologist reported the size of the neck mass in terms of antero-posterior (AP), medio-lateral (ML) and cranio-caudal (CC) dimensions. They also commented on airway patency, location of the mass within the neck, the nature of the mass i.e. heterogeneity and whether it was solid or cystic, presence of restriction on diffusion weighted imaging and the most likely diagnosis. A weighted Cohen's Kappa was then undertaken on this data using IBM SPSS Statistics for Macintosh version 29.0.1.0 to determine the degree of inter-observer reliability.

Data was collected concerning the ultrasound findings prompting referral for MRI, gestation at the time of MRI scan and the fetal MRI findings. Patient outcomes, including the outcome of the pregnancy and the final diagnosis made by imaging, surgery or postmortem were collected. Additional information concerning whether an EXIT procedure was undertaken and the type of airway and respiratory support needed after birth were also examined in detail. Where patients had been referred from external sites, these centres were contacted directly for this information. The diagnosis, as written in the patient notes, was documented in the analysis, alongside the most up-to-date terminology as listed in the ISSVA classification [94].

A flow chart detailing the most likely diagnoses based on the fetal MRI findings was then developed using data from the MRI reports and the final diagnosis for the patients. This was created independently by each consultant radiologist and the charts were then combined following discussion. The main MRI findings used to develop the flow chart were the nature of the mass, i.e. whether cystic or solid, the location of the mass within the neck, its heterogeneity and the presence or absence of restriction with DWI.

Results

There were 20 patients who met the inclusion criteria of having undergone fetal MRI at our centre due to presence of a neck mass seen on antenatal ultrasound. Outcome data was available for 18 patients, as two were referred from external centres who did not respond to the requests for outcome data. A final diagnosis made by imaging, surgery or post-mortem was available for 13 patients, and this was included in the final analysis. The seven patients with no final diagnosis had no outcome data available (n=2), underwent termination of pregnancy without postmortem examination (n=3) or were stillborn but did not undergo postmortem examination (n=2). The 13 patients with a final diagnosis available were used in the analysis.

The mean gestational age at the time of fetal MRI was 28.5 weeks with a range of 21-36 weeks. Of the 13 patients included in the final analysis five were referred for fetal MRI from external tertiary centres. Four patients underwent two fetal MRI scans during pregnancy, the MRI findings listed below for these patients are from the first MRI scan.

Fetal MRI findings

The fetal MRI findings for each patient alongside their final diagnosis are shown in table 3.10. There were five cases with airway compression (n=3), or displacement (n=2) seen on the MRI.

Postnatal diagnosis	Gestation at MRI	Mean AP (mm)	Mean ML (mm)	Mean CC (mm)	Solid/ Cystic	Hetero/ homogeneity	DWI	Airway patency
Rhabdomyosarcoma	33 weeks	41	42	33.5	Solid	Homogeneous	Not done	Patent but displaced
Teratoma	22 weeks (Repeat at 29 weeks)	50.5	52	51.5	Mixed	Heterogeneous	Restriction in solid area	Patent but displaced
Kaposiform lymphangiomatosis	27 weeks	29.5	28	34	Cystic	Heterogeneous	No restriction	Patent
Teratoma	36 weeks	54.5	64.5	53	Mixed	Heterogeneous	No restriction	Compressed
Lymphatic malformation	31 weeks	68.5	37	68.5	Cystic	Heterogeneous	No restriction	Small compressed area
Lymphatic malformation	35 weeks	96	51	79.5	Cystic	Heterogeneous	No restriction	Patent
Lymphatic malformation	21 weeks (Repeat at 31 weeks)	27	19	21.5	Cystic	Heterogeneous	No restriction	Patent
Macrocystic lymphatic malformation in posterior neck (documented as hygroma)	36 weeks	51.5	39.5	80.5	Cystic	Homogeneous	No restriction	Patent
Kaposiform haemangio-endothelioma	22 weeks	7	11	7.5	Cystic	Heterogeneous	No restriction	Patent
Lymphatic malformation	25 weeks	80	79	51	Cystic	Homogeneous	No restriction	Patent
Teratoma	31 weeks (Repeat at 34 weeks)	64	69.5	56	Mixed	Heterogeneous	Restriction in solid area	Patent
Rhabdomyosarcoma	30 weeks	59	56.5	50.5	Solid	Homogeneous	Restriction	Compressed
Goitre from thyroid dyshormonogenesis	21 weeks (Repeat at 30 weeks)	9.5	9.25	18.25	Solid	Homogeneous	No restriction	Patent

Table 3.10. Fetal MRI findings and postnatal diagnosis for each patient

Abbreviations - AP (antero-posterior), ML (medio-lateral), CC (cranio-caudal), DWI (diffusion weighted imaging)

The weighted Cohen's Kappa, which was undertaken to assess degree of inter-observer reliability, was 0.769 which showed good agreement between the two clinicians measuring the size of the neck masses from the MRI.

Postnatal outcomes and diagnoses

All 13 patients with outcome data available and a final diagnosis who were included in the final analysis were liveborn. The mean gestational age at delivery was 35.7 weeks. Unfortunately, two patients died in the neonatal period. One of these was following a planned palliative delivery and the other from Kasabach-Merritt phenomenon which is a disorder of thrombocytopenia and haemorrhage secondary to a Kaposiform haemangioendothelioma, a locally aggressive rare vascular tumour. As far as we are aware, the remaining patients are alive and well, having undergone treatment after birth or are still receiving treatment.

The final diagnoses for these patients included lymphatic malformation (n=5), of which one was documented as a cystic hygroma, teratoma (n=3), rhabdomyosarcoma (n=2), Kaposiform haemangioendothelioma (n=1), Kaposiform lymphangiomatosis (n=1) and goitre secondary to congenital hypothyroidism caused by thyroid dyshormonogenesis (n=1). Rhabdomyosarcomas are rare malignant soft tissue tumours arising from the embryonal mesenchyme, they require complex oncology management including surgery, chemotherapy and radiotherapy [104,105]. Kaposiform haemangioendotheliomas are rare, locally aggressive vascular tumours with significant morbidity and mortality due to local invasive and compression as well as the consumptive coagulopathy Kasabach-Merritt phenomenon [106]. Kaposiform lymphangiomatosis is a rare lymphatic anomaly characterised by abnormal lymphatic channels and clusters of lymphatic endothelial cells with a spindled or 'Kaposiform' morphology [107].

Four of the patients underwent EXIT procedure at delivery, with two of these patients requiring a tracheostomy in the delivery room. One of the EXIT procedures was performed at our centre, and the other three were at two other tertiary centres. As expected, the four patients who underwent EXIT procedure all had airway compression or displacement seen on MRI. One other patient required intubation after birth due to poor respiratory effort, they had a small area of airway compression noted on fetal MRI but were not felt to have airway compromise at birth and underwent a straightforward intubation by the neonatal team. One patient was electively intubated for a postnatal MRI scan who had previously required non-invasive ventilation, but as they were born at 33 weeks the need for non-invasive ventilatory

support may have been secondary to prematurity. None of the other patients required airway support or invasive ventilation after birth. Two other patients briefly required low flow oxygen therapy.

The four patients who underwent EXIT procedure had diagnoses of rhabdomyosarcoma (n=2), lymphatic malformation (n=1) and teratoma (n=1). The fetal MRI images for each of the diagnoses are shown in the figures 3.13-3.19 below.

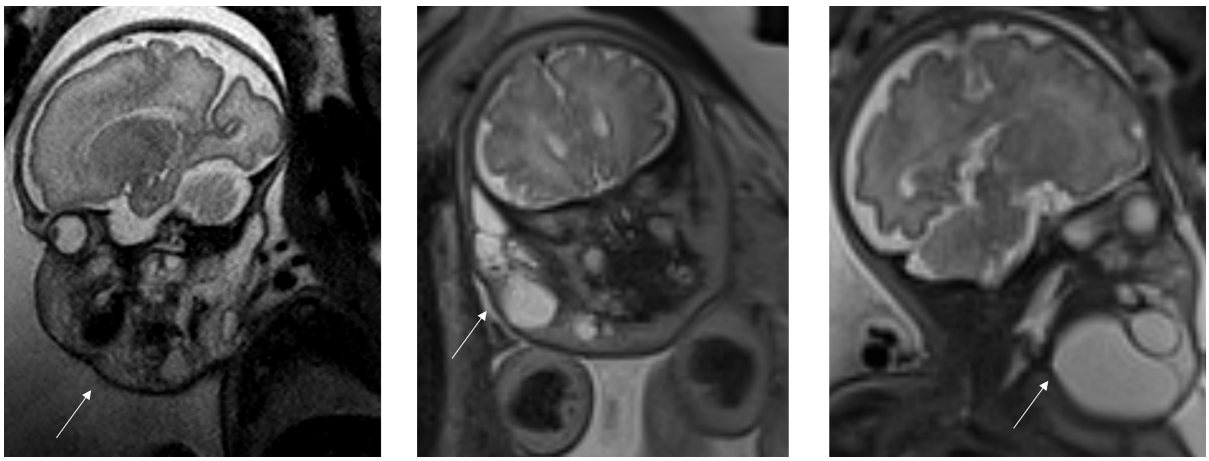


Figure 3.13. Fetal MRI images of lymphatic malformation
Left image - T2 HASTE sagittal image of a 31 week fetus showing a multi-septated cystic mass from orbit to upper thorax which infiltrates into the face with airway compression.
Middle image - T2 HASTE coronal image of a 35 week fetus showing a septated multicystic subcutaneous lesion right side of face from orbit to neck.
Right image - T2 HASTE coronal image with head turned to the left of a 25 week fetus with an anterior cystic neck mass.

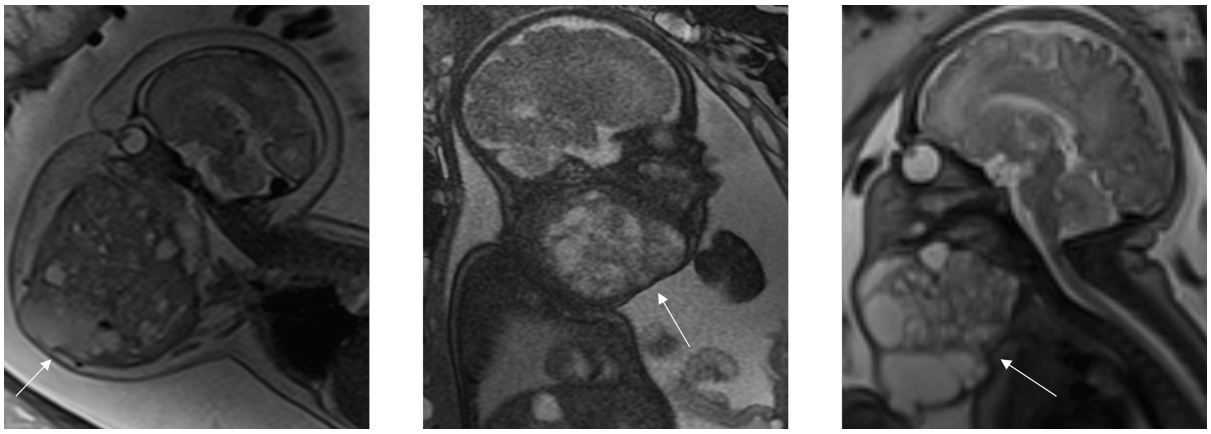


Figure 3.14. Fetal MRI images of teratoma

Left image - T2 HASTE sagittal image of a 22 week fetus with an extensive neck and facial mass with solid and cystic components and airway displacement

Middle image - FIESTA (Fast Imaging Employing Steady-state Acquisition) 60 sagittal imaging of fetus with a large cystic/solid mass on the left side of the neck, crossing over midline with Compression of the vessels and trachea

Right image - T2 HASTE sagittal image of a 31 week fetus with an anterior cystic neck mass with some solid components

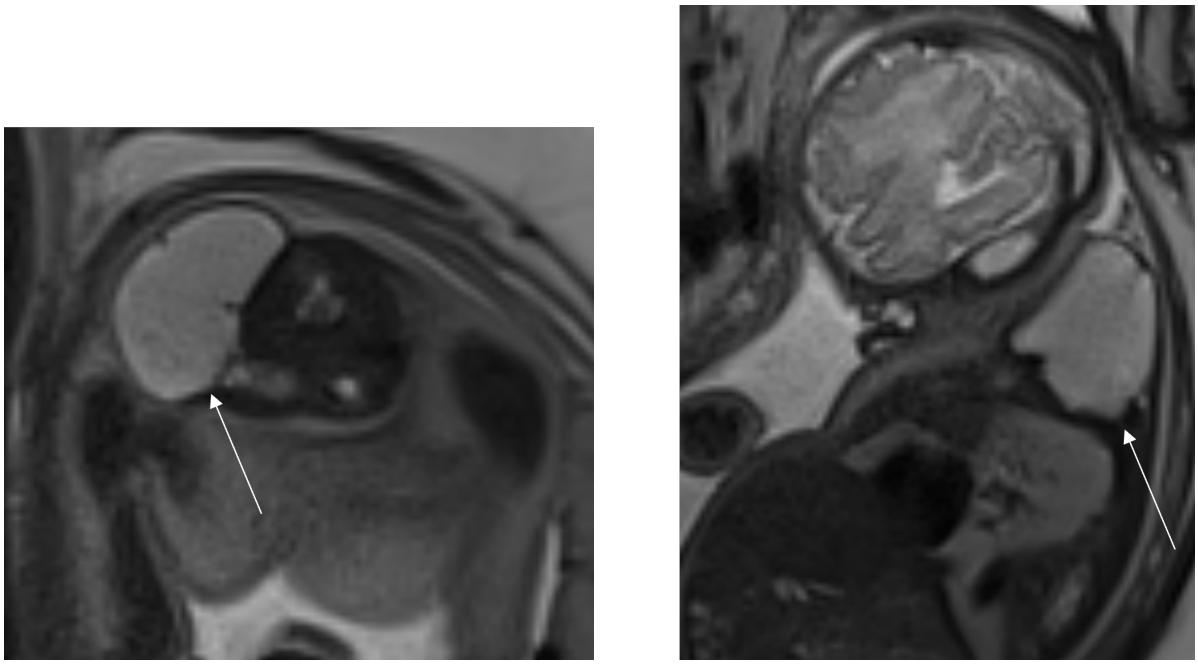


Figure 3.15. Fetal MRI images of a macrocystic lymphatic malformation (documented as cystic hygroma)

T2 axial (left) and sagittal (right) images of a 36 week fetus with a right sided homogeneous macrocystic cystic neck mass

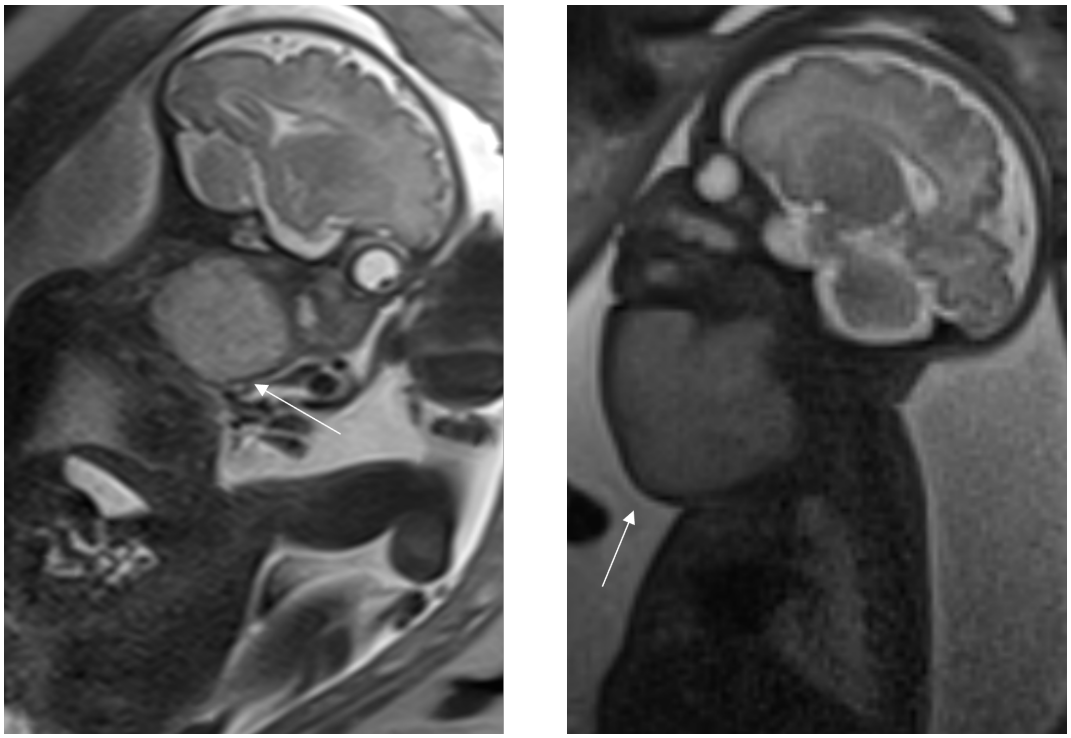


Figure 3.16. Fetal MRI images of rhabdomyosarcoma

T2 haste sagittal images of a 33 week fetus (left) and a 30 week fetus (right) both with a solid anterior neck mass causing airway compression/displacement

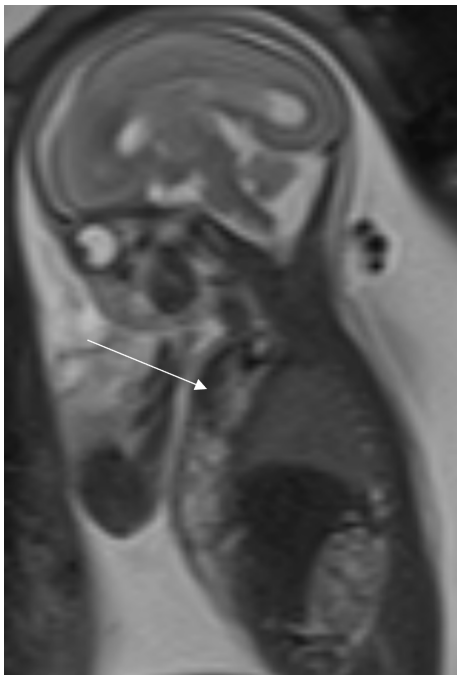


Figure 3.17. Fetal MRI image of a Kaposiform haemangioendothelioma

T2 HASTE sagittal image of a 22 week fetus with extensive subcutaneous mixed venous and lymphatic malformation, extension into the neck and anterior aspect of the mediastinum consistent with the known lymphatic drainage pattern.

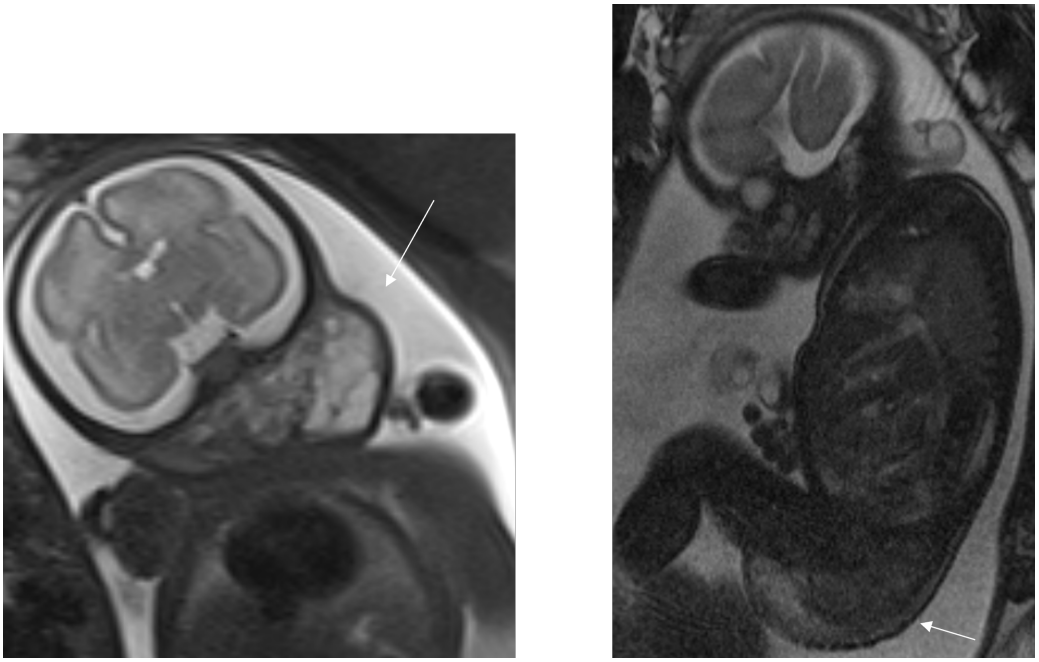


Figure 3.18. Fetal MRI images of Kaposiform lymphangiomatosis

Left image - T2 HASTE coronal image of 27 week fetus with a multiloculated fluid filled cystic lesion that extends from the subcutaneous tissues on the left side of the neck anteriorly and posteriorly towards the midline. Extends from shoulder to ear with possible areas of haemorrhage.

Right image - T2 sagittal image of the same fetus showing a similar cystic lesion over the left buttock and thigh.

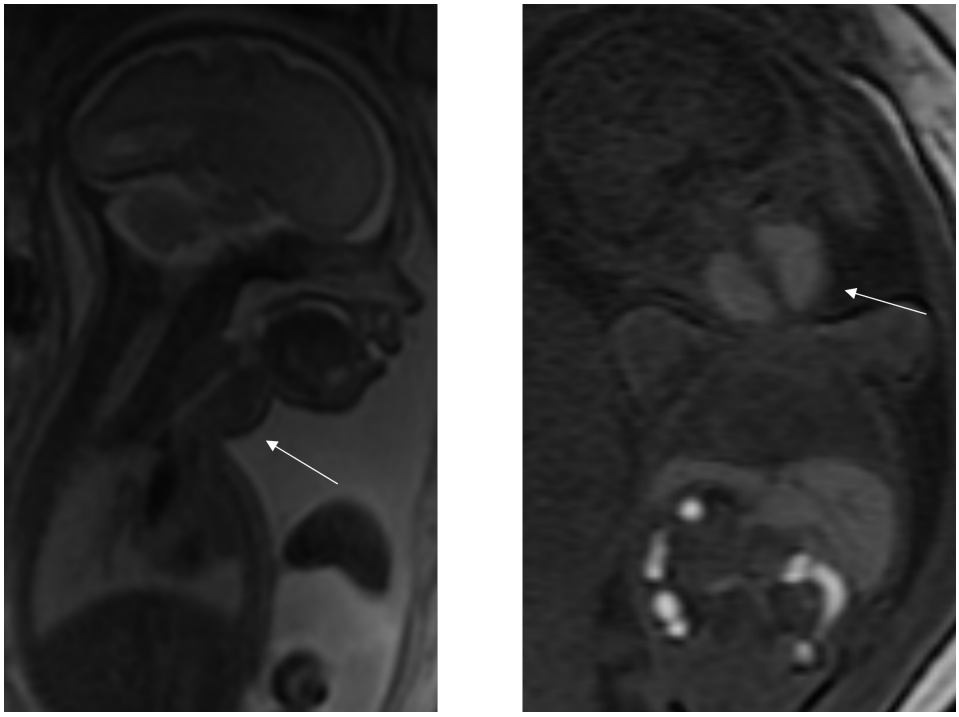


Figure 3.19. Fetal MRI images of a goitre

Left image - T2 SSFSE sagittal image of 21 week fetus showing a solid homogeneous anterior neck mass. Right image - T1 coronal image of the same fetus showing increased signal in the thyroid (goitre) and the meconium in the bowel

Diagnostic flow chart

The diagnostic flow chart was developed using the MRI findings from this cohort compared with the final diagnosis and other research reported in the literature. Figure 3.20 highlights the most likely diagnosis based on the MRI findings, including the nature of the neck mass, i.e. whether cystic or solid, the site of the mass, the heterogeneity and MRI signal uptake.

Whilst there was some overlap between the MRI findings for different diagnoses, the most common diagnoses had key defining features on MRI. Lymphatic malformations were cystic or mixed cystic and solid lesions, which could be homogeneous or heterogeneous, but there was no restriction seen on diffusion weighted imaging. Teratomas were mixed cystic and solid lesions with restriction on DWI. Restricted diffusion on DWI implies the water molecules in that specific area are less free to move around for example due to increased cellular density, cellular swelling or tissue damage. The patient recorded as having a cystic hygroma, now known as macrocystic lymphatic malformation, had a cystic lesion only seen in the posterior neck. Rhabdomyosarcomas were solid, homogeneous lesions with mid-signal and restriction on DWI.

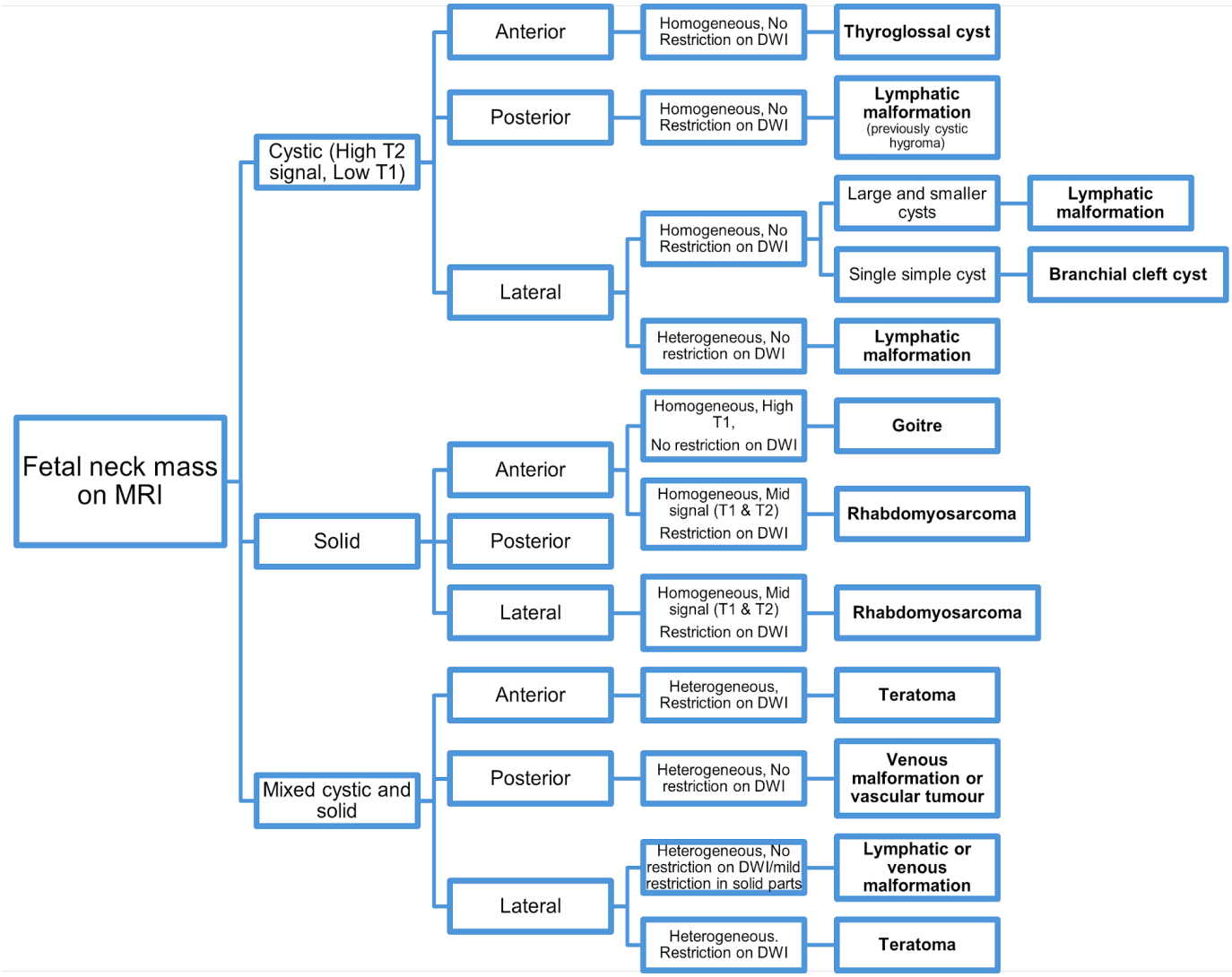


Figure 3.20. Flow chart of most likely diagnosis of neck mass seen based on fetal MRI findings

Discussion

This study presents the range of 13 neck masses referred for fetal MRI to a tertiary fetal and neonatal centre in England over a twelve year period. It showcases the different diagnoses seen including the more common lymphatic malformations and rarer conditions such as teratomas and vascular tumours and their appearances on MRI in utero. The MRI findings have been used to propose a pathway indicating the most likely diagnosis.

This research highlights the role of fetal MRI in addition to antenatal ultrasound in these cases predominantly in helping to refine the diagnosis and assess the patency of the airway. A better understanding of the most likely diagnoses prior to delivery enables planning for the management of these babies after birth to begin antenatally, ensuring thorough counselling of parents and allowing for earlier multidisciplinary team (MDT) discussions. Several of these cases were complex, with extensive lymphatic lesions and some with lesions at multiple

sites. The fetal MRI was able to provide detailed additional information on the sites of lymphatic lesions and potential metastatic sites of malignant lesions and to look for other structural anomalies of the fetus which impact morbidity and mortality.

This use of fetal MRI could be integrated with early genetic testing, for example fetal exome sequencing, to differentiate between the various syndromic and non-syndromic causes of neck masses. The R21 rapid prenatal exome sequencing can be requested as part of NHS care in the UK in cases where a fetus has multiple anomalies affecting multiple systems and/or where the presentation is suggestive of an underlying monogenic disorder in which a genetic diagnosis may influence management of the pregnancy or the baby in the neonatal period. Several of the diagnoses in our cohort are associated with genetic mutations, for example Kaposiform lymphangiomatosis is most often due to NRAS mutations [108], Kaposiform haemangioendothelioma may be related to PIK3CA mutations which influence response to certain treatments [109] and rhabdomyosarcomas have significant genomic heterogeneity [110]. The phenotype, and most likely diagnosis, as determined by fetal MRI would be able to guide appropriate genetic testing both antenatally and postnatally as whilst some of these genetic variants can be diagnosed using exome and whole genome sequencing (R14 testing), others such as the PIK3CA mutations are better diagnosed from biopsy samples [111]. The use of fetal MRI in combination with genetic testing would allow earlier confirmation of diagnosis which would enable more precise prognostication and appropriate counseling for families, in addition to management planning for the baby after birth.

As shown in other studies [98,102], a significant advantage of using fetal MRI in these cases was the accurate prediction of airway patency in advance of delivery. This allowed complex MDT planning for management at birth, including EXIT procedures. The MRI prediction of airway patency remained accurate even when the MRI had been performed several weeks prior to delivery. In this cohort, the overall size of the mass did not relate to presence of airway compression.

The study is limited by the relatively small cohort and the missing data concerning the final diagnosis for seven of the twenty patients initially identified from the MRI database. As this patient group underwent their MRI scans as part of their routine National Health Service (NHS) care, the MRI scans were all performed at different gestations meaning measurements cannot be standardised.

Conclusion

In conclusion, this study shows the heterogeneity of neck masses diagnosed in utero and

the role of fetal MRI in refining the diagnosis and predicting airway patency to guide management at birth.

Chapter 4 – The utility and experience of fetal magnetic resonance imaging

Context of the research

This chapter of research is focused on the experiences of patients who undergo MRI during pregnancy to explore how, if at all, fetal MRI helps with their understanding of the anomaly and with any decision making for the pregnancy. This is with the aim to improve our understanding of the patient pathway when undergoing fetal MRI, from initial referral to the birth of their baby. We also explored the views of a variety of healthcare professionals involved in the care of these families regarding how useful they consider the information provided by fetal MRI to be in clinical practice. This qualitative research aims to bring together the role fetal MRI has in current clinical practice and the patient journey in addition to its diagnostic accuracy and role in prognostication and management of congenital anomalies of the fetal body.

This chapter comprises one manuscript.

Author contributions

4.1 - “This was the first time we were properly seeing our baby” - Patient and professional perspectives on the role of fetal magnetic resonance imaging

For this research Dr Elspeth Whitby and I undertook the initial planning of the project, and I completed the applications for the required ethical approvals by IRAS, the university and the hospital trust. Prior to commencement of the patient and professional interviews the topic guides were reviewed by Prof Kate Reed, who gave her expert opinion on conducting qualitative research with semi-structured interviews and thematic analysis. The patient recruitment and consent were undertaken by both me and Dr Whitby and I undertook the recruitment of healthcare professionals. I undertook the interviews, transcribed the recordings and undertook the thematic analysis. The analysis was reviewed by Dr Whitby prior to the write-up of the research, which was then reviewed by both Dr Whitby and Prof Reed prior to the final completion of the work.

4.1 "This was the first time we were properly seeing our baby" – Patient and professional perspectives on the role of fetal magnetic resonance imaging

Abstract

Introduction - As fetal magnetic resonance imaging technology improves, its use in clinical practice continues to expand. This work aims to add to previous research exploring the views of expectant parents undergoing fetal MRI scans due to a suspected congenital anomaly and the views of the professionals looking after them.

Methods - Semi-structured interviews with 12 patients who had undergone fetal MRI and 15 professionals who work within fetal and neonatal medicine were undertaken and thematic analysis was performed.

Results - Patient themes included the misconceptions of antenatal screening, perceptions of MRI and its safety, interaction with the MRI image and the importance of healthcare provider empathy. Professional themes comprised the role of reassurance, how MRI informs clinical practice and multidisciplinary professional collaboration. The patient themes have led to changes in our department and plans for future work to improve multidisciplinary team working.

Conclusion - Fetal MRI is seen as a valuable tool in addition to ultrasound by both patients and the professionals involved in their care.

Introduction

Congenital anomalies affect 2-3% of pregnancies within the United Kingdom and account for approximately 30% of neonatal and infant mortality [112]. The National Health Service (NHS) fetal anomaly screening programme offers screening for genetic and structural problems to all women as part of their routine antenatal care in the form of blood tests and ultrasound scans [113]. In some centres, fetal magnetic resonance imaging (MRI) is offered in addition to ultrasound scans when a congenital anomaly is suspected. This means that whilst ultrasound is expected by patients as part of routine pregnancy screening, fetal MRI is only performed when a problem is identified [114]. Antenatal imaging has been shown to be of importance in enhancing fetal-parent bonding [115] and fetal MRI has been shown to have both an emotional and practical value for expectant parents [114].

Previous sociological research has been undertaken to examine women's views on the role fetal MRI plays in managing and mediating uncertainty [45]. This work found that the detailed information provided by fetal MRI helps women navigate through the stress of diagnostic

uncertainty during pregnancy, especially when combined with skilled interpretation and communication of MRI findings. Further evidence suggests that pregnant women and their families are accepting of the procedure of a fetal MRI scan [116], but that it can be associated with higher levels of psychological distress [117] and emotional support from care providers during this time is paramount [118].

Research on the views of health professionals regarding fetal MRI is more limited, but has shown that they perceive MRI to be of value in refining the diagnosis of brain anomalies and that fetal MRI can act as a bridge for clinicians working across specialties [116,119].

There have been significant technological advances in antenatal screening and management over the past decade. This includes advances in obstetric ultrasound, next generation genetic testing, increasing use of fetal MRI and development of fetal surgery.

Aims and objectives

The project aims to explore the fetal MRI service at a tertiary fetal and neonatal medicine centre from a variety of perspectives. The primary objective of the research is to improve understanding of the patient journey from suspected fetal anomaly, being seen by the fetal medicine team and attending the fetal MRI scan, through to the outcome of the pregnancy. This included assessment of the patients' experience throughout this process. The secondary objective is to gauge professional opinions on the technology and the fetal MRI service as a whole.

A better understanding of service users' and healthcare professionals' experience of the technology and service would enable improvement of the service to enhance the benefits of fetal MRI in perinatal management. It would help us to understand the value of the imaging and explanation for patients and the impact this has on professionals involved in their care.

Methods

This study has ethical approval from the Health Research Authority, IRAS no. 321622 and REC reference 23/SC/0250. This project was undertaken as part of wider research into the role of fetal MRI in the diagnosis and management of congenital anomalies of the fetal body.

This study involved semi-structured interviews with patients who had undergone MRI during pregnancy and medical professionals who utilise the information from fetal MRI in their practice. The topic guide for the interviews was developed following a review of the literature

and discussion within the research team which included a consultant fetal MRI radiologist and professor of sociology.

The inclusion criteria for patients were pregnant women over 18 years of age who had undergone a fetal MRI scan at our centre as part of their National Health Service (NHS) care due to a suspected structural anomaly of their baby. This study was undertaken at a teaching hospital in the North of England which has tertiary fetal medicine and neonatal care, including surgical care. It undertakes fetal MRI scans for patients from across the region and is involved in the reporting of scans from multiple other tertiary centres across the United Kingdom. As this study was part of wider research looking at the use of fetal MRI for congenital anomalies of the fetal body, women undergoing fetal MRI due to a suspected fetal central nervous system malformation were excluded. For the medical professionals, inclusion criteria comprised healthcare workers involved in the care of women and their babies who undergo fetal MRI.

The patients were recruited to the study on the day they attended for their fetal MRI. Letters introducing the study were sent out to all eligible patients alongside their appointment letter. Patients were approached by the research team once they had been given the results of their fetal MRI by the reporting consultant radiologist. Informed written consent was obtained and consenting patients were then contacted by email to arrange the interview at a later date. The decision was made to conduct the interviews on a separate day after the MRI scan to allow the participants time to reflect on their feelings regarding the whole process and to enable them to withdraw from the study if they wished.

The patient interviews were conducted via telephone at a date and time most convenient to the patient. All interviews were conducted by the same researcher who was not involved in clinical care of the women. The audio from these interviews was recorded ensuring participant anonymity and was then transcribed verbatim by the same researcher. Demographic data was collected from each participant at the start of the interview.

The medical professionals approached to take part in the study included all those at our centre who come into contact with fetal MRI as part of their daily clinical practice. Professionals who do not work at our centre but utilise our fetal MRI service, either through referring patients for MRI scans or having MRIs undertaken locally reported at our centre, were also contacted. Invitations for study participation were sent via email, and interviews were arranged either face to face or via virtual online meeting. The audio from the interviews was recorded and transcribed by the same researcher conducting the interviews.

Recruitment of both patients and medical professionals was undertaken from February

2024-June 2024, all the interviews and transcriptions were also conducted during this time. The thematic analysis was undertaken from July 2024-August 2024.

Thematic analysis was undertaken using the six-step approach as described by Braun and Clarke [120] using reflexivity and an iterative approach [121]. The quotes from the transcribed interviews were used to generate codes from the data which enabled the development of overall themes. The development of themes was undertaken by the research team, without the use of specifically designed computer software.

Results and discussion

Patient characteristics

A total of 24 patients consented to take part in the study, however only twelve patients were interviewed as the remaining twelve did not respond to the invitation to interview sent via email. The twelve patients interviewed were all included in the final thematic analysis.

The age of patients interviewed is shown in figure 4.1, their age ranged from 19-40 years and the mean age was 30 years. 75% of patients were White British, as shown in figure 4.2, and 58.3% identified as Christian. 75% of patients were employed, with 44.4% of these working in the healthcare sector. Data from the Office for National Statistics (ONS) Census 2021 was used to analyse patients by socio-economic group using their postcode. The National Statistics Socio-Economic Classification (NS-SEC) analytic class [122] was group 7 for 45.5% (routine occupations), group 2 for 45.5% (lower managerial, administrative and professional occupations) and group 1 for 9% (higher managerial, administrative and professional occupations).

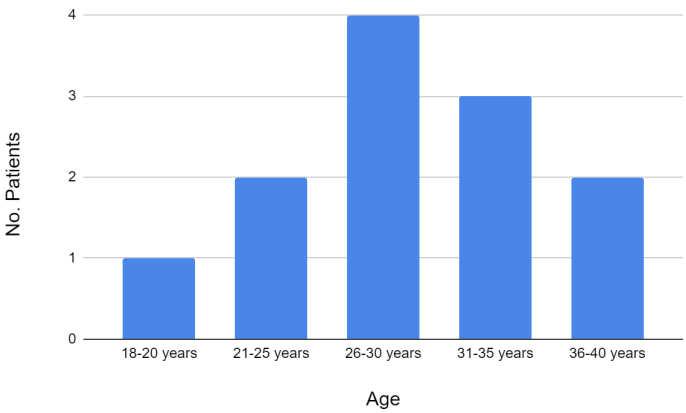


Figure 4.1. Age of interviewed patients

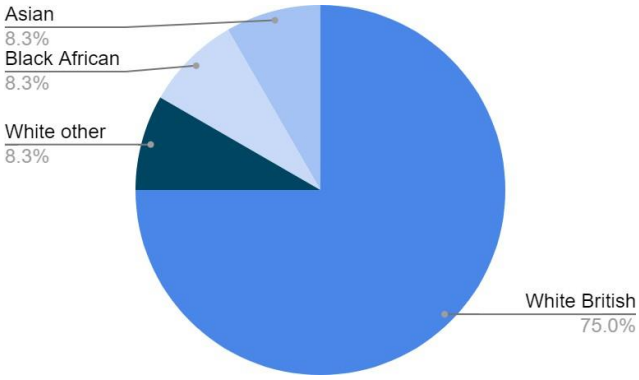


Figure 4.2. Ethnicity of interviewed patients

In this cohort there was one twin pregnancy. For 41.7% of women interviewed this was their first pregnancy. Of the remaining 58.3% who had been pregnant before 42.9% had experienced a previous fetal or neonatal loss. Following the MRI scan, 7/12 (58.3%) had an anomaly confirmed and the remaining 5/12 (41.7%) had a reassuring result.

Characteristics of patients consented but not interviewed

The patients who consented to take part in the study but did not respond to invitations to interview were of a similar age, ethnicity and socioeconomic status to those who took part. Their ages ranged from 25-39 years with one patient aged 20-25 years, four patients aged 26-30 years, six patients aged 31-35 years and one patient over 35 years old. Ten of the twelve patients (83.3%) were White British, one was White other and the other was Black African. The NS-SEC classes were group 2 for 50% (lower managerial, administrative and professional occupations) and group 7 for the other 50% (routine occupations).

One third of these patients had had a reassuring MRI result, with the remaining two thirds having had an anomaly confirmed on MRI. The pregnancy outcome is unknown for four of these patients as they were referred from external centres. There was one termination of pregnancy, one stillbirth and one preterm delivery with subsequent neonatal death. The remaining five patients delivered at term after the interview period had ended, with two of the babies requiring intensive care admission.

Medical professional characteristics

15 professionals were approached and consented to participate, all 15 participants were

interviewed and used for the analysis. A range of professionals from different backgrounds were included as shown in figure 4.3. Seven participants were fetal medicine specialists including two consultants, one subspeciality trainee and four midwives. There were three consultant neonatologists, three consultant paediatric surgeons (one general surgeon, one urologist and one neurosurgeon), one consultant geneticist and one consultant perinatal and paediatric pathologist.

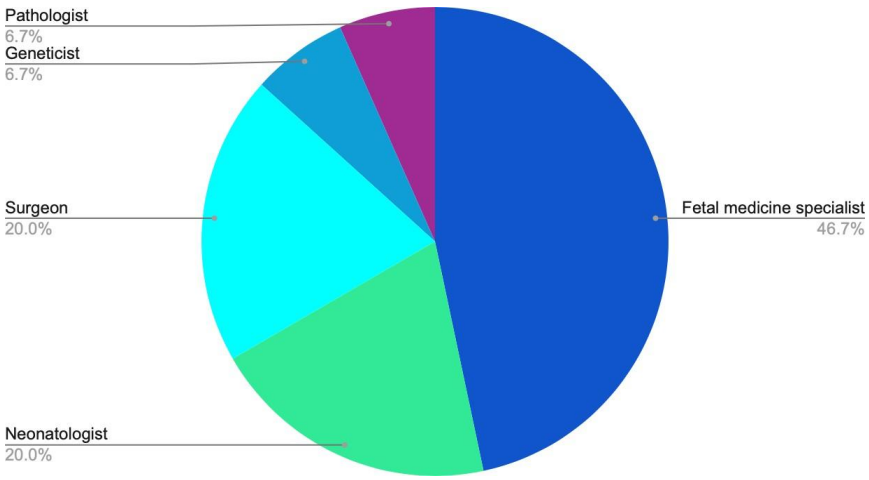


Figure 4.3. Clinical specialities of included professionals

There was a range of experience from 1-27 years in their current professional role with a mean experience of 9 years, more detail is shown in figure 4.4. The professionals interviewed worked at three different centres, of which 13/15 work at our centre. The two clinicians who worked at other centres were a fetal medicine consultant who refers patients to our centre for fetal MRI and a paediatric surgeon whose centre has their MRI scans reported by our consultant radiologist.

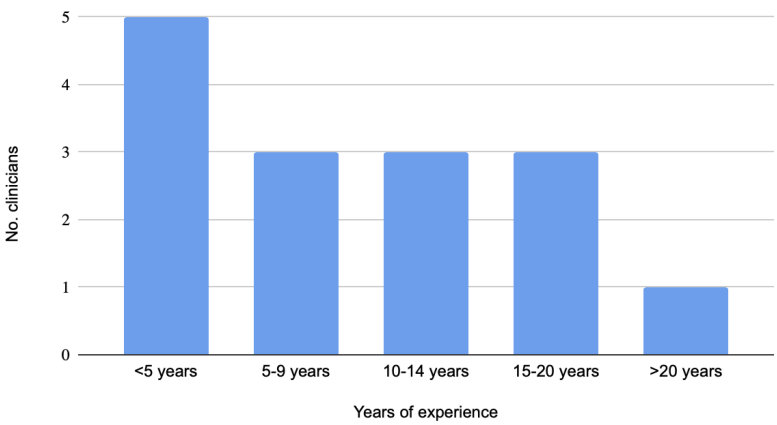


Figure 4.4. Years of experience in current role of professionals interviewed

Results and discussion – Patient themes

A change in thinking at 20 weeks - the misconception of antenatal screening

In this cohort, for the majority of patients the fetal concerns were detected after their anatomy scan, also referred to as the 20 week scan as it usually takes place at 18-20 weeks gestation. Most of the patients interviewed described a change in their emotions and way of thinking about the pregnancy after their fetal anatomy ultrasound. This led to discussions around the misconceptions some patients may have about the role of antenatal screening ultrasound scans.

> *Patient 12: "So up until the 20 week scan it was a dream. You know, I felt exactly the same as I did with my first born and a bit naively, we went to the 20 week scan oblivious to what that actually entails. I just thought we would find out the gender."*

Previous research has also drawn on these misconceptions in which interviews with sonographers highlighted their frustration and disappointment at public misunderstanding of the role of the sonographer. In this research sonographers described feeling as though the anatomy scans were 'entertainment' for patients and families rather than a diagnostic test with a purpose [123].

Our patients understandably described feelings of shock and fear at being told there was a potential fetal abnormality on their ultrasound scan and when being advised that an MRI scan would be useful in understanding the problem in more detail. We saw how the 20 week ultrasound was a real turning point of emotions in the pregnancy for these women as things became more medicalised.

> *Patient 12: "The wind had been taken out of my sails, I was frightened and didn't know what to think. It just hit me in waves and waves".*
>
> *Patient 5: "Everything has become so hectic; it's gone from enjoying a pregnancy to worrying about a pregnancy now".*

When discussing the role of the MRI and the impact of increasing medical care at this point in the pregnancy, our patients described a real mix of emotions. Most of the patients talked

about their feelings of devastation after being told there was a problem but also feelings of relief with regard to the fetal MRI, as well as other tests such as genetic investigations, to aid confirmation of a diagnosis.

> *Interviewer: “How did you feel when you were told about going for the MRI scan?”*
>
> *Patient 7: “I was scared and relieved at the same time, it felt like a step in the right direction to know what was actually going on.”*
>
> *Patient 10: "I felt reassured because it was another step in terms of checking the baby".*
>
> *Patient 6: "I was almost reassured that we were being investigated a little bit further".*

Preconceptions of MRI and its safety

The association between MRI scans and serious illness such as cancer has been explored in previous research [45] and was a factor for our cohort. When patients were asked about their understanding of why a fetal MRI was being advised as the next step in their care, many disclosed feelings of apprehension at the thought of the scan itself.

> *Patient 7: "An MRI sounds scary in itself, doesn't it? You assume, I don't know how to describe it, that it's for really poorly people".*

We explored the patients’ understanding of MRI safety in pregnancy and found that most of our patients did not feel they had been given much information regarding the process of having an MRI scan in pregnancy, including the safety for their baby. It is widely recognised that patients struggle to retain information once bad news has been given; many of the women interviewed disclosed feeling unprepared for the MRI scan prior to attending. They described assuming it was safe as it was being offered to them as a National Health Service (NHS) investigation and undertaking their own internet research.

Patient 10: "I only found out from Googling it that having an MRI doesn't harm your baby in any way, but I wasn't told that. Although when your baby is poorly you want to do everything you can anyway. I guess some people might have just asked".

Patient 8: "I gathered it was safe, but I didn't have any idea. Until I got home and started Googling it, I didn't know what it was".

Patient 3: "I just went with it, assuming that the NHS wouldn't do something that wasn't ok. Like you know, they wouldn't offer a service for babies that would be unsafe".

This highlights the trust patients place in the healthcare professionals looking after them as well as the ever increasing role of the internet for personal health research.

The resilience of expectant parents

When discussing the patient experience during the MRI scan, the sense of resilience in these women and their families was overwhelming. Many of the patients described feelings of claustrophobia and fear due to the noises made by the scanner or pre-existing anxiety due to a lack of information prior to attending for the scan. During several of the interviews the women described expecting the MRI scan to be worse than it actually was in terms of claustrophobia or noise and overall, the majority of patients interviewed found the MRI to be an acceptable investigation.

Interviewer: "How did you find the MRI scan itself?"

Patient 5: "Sheer panic took over in the room, I didn't realise I was claustrophobic at the time but I think that's what it was".

Patient 6: "It was loud, and the baby feels like it's very active. But I would say I'd built it up in my head to be more scary than it actually was. It was actually fine".

Despite these feelings of fear and anxiety however, the women interviewed repeatedly talked about how they coped during the scan by focusing on their baby. Although the patients had freely consented to the MRI and knew they could stop the scan if needed, there

was a sense of determination to get through the scan and get more answers for their pregnancy.

> *Patient 12: “Being in there felt a bit claustrophobic the first time, I felt anxious. I needed to be there, and it had to be done, and I would go through anything for my children”.*
>
> *Patient 11: "I was scared about the MRI scan because I'd never had one and I don't like being in small spaces, but I had to think about my son and put my son first because it wasn't about me. It was about him.”*
>
> *Patient 10: "When your baby is poorly you want to do everything you can".*

Coping with uncertainty and risk

Several of the patients interviewed had reassuring news following their MRI scan which is likely to have influenced how they viewed the experience as a whole. However, even for patients who had an anomaly confirmed with MRI, the majority of women interviewed talked about a greater understanding of the problem following the MRI.

> *Interviewer: “How did you feel after being given the MRI scan results?”*
>
> *Patient 2: "Because I had good news, I was a bit relieved. I can't imagine if it had been something negative, I wouldn't be feeling the way I feel."*
>
> *Patient 9: "They looked a lot more in depth at the baby than I thought they would be able to, which was quite reassuring".*

The interaction between the families involved and the MRI images of their baby seems to have played a significant role in their understanding of the anomaly as well as feelings of reassurance. On the day of the MRI scan, the patients meet with the reporting radiologist after their scan and are shown the images whilst the findings are discussed. The patients are then sent copies of their MRI images with labels via email if they wish. The majority of patients interviewed responded positively to this aspect of attending for the scan, they reported that seeing the images helped their understanding of what was wrong as well as

providing enjoyment when seeing a recognisable image of their baby.

Interviewer: “How did you find seeing the MRI pictures of your baby?”

Patient 4: "That was the best part of the scan, seeing the pictures of my baby was really exciting. This was the first time we were properly seeing our baby”

Patient 10: "It's so much clearer than the normal black and white scan pictures. Seeing all the organs inside and stuff was quite interesting. Luckily because nothing was wrong, I could enjoy looking at them."

Patient 1: "I was pleased to be able to see the pictures, I was able to understand and see clearly where the problem is".

Many of the families interviewed discussed using technology to manage their feelings of uncertainty, frequently in the form of doing their own research online about the suspected anomaly and the process of fetal MRI prior to attending the MRI appointment. Whilst this may somewhat reflect the lack of information given to families before the scan, it also shows how patients are utilising the readily available information online as a means of reassurance. The women often acknowledged they knew looking things up online was not necessarily a good thing in terms of alleviating worry, but several had found useful information and advice from appropriate resources.

Patient 12: "My wife went a bit crazy on Google. She researched like you wouldn't believe, I know it's probably the worst thing ever".

Patient 8: "It was just me Googling things to make me feel better. I found some information from an American hospital that comforted me and made me feel better".

One of the women interviewed, who’s baby was diagnosed with a cleft palate antenatally, described the support she has received online and the support she has been able to offer others virtually.

Interviewer: “Had you come across the concept of some pregnant women having

MRI scans?"

Patient 5: "Erm, I'm in a few groups on Facebook and it was just after I'd had mine done actually a lady had said that she'd had to go for hers. And she was worried about everything going off. I sort of said 'look it's over within 25-30 minutes, you'll be fine'. So before having it no, but then everybody seems to have come out of the woodwork afterwards, if that makes sense."

The way in which uncertainty is conveyed to patients and their perception of the information they are given by health professionals was also frequently mentioned by the families interviewed. For example, discussions regarding termination of pregnancy were an understandably emotive topic. With hindsight the patients explained they knew their doctors were giving them options, but at the time of these discussions the mention of termination was not well received by the families who talked about it in their interviews.

Patient 12: "He used the word, I can't even say it out loud, 'T'. I just ushered him off like 'don't insult me'."

Patient 10: "They mentioned I could terminate due to the uncertainty. I thought because they've brought it up it must mean it's bad, I lost all hope and positivity about it. I don't think they meant to upset me and were just giving me my options but that's the last thing I would want".

The discussions around uncertainty also frequently involved the possibility of a genetic problem and the options for prenatal genetic testing. Whilst the evolution of technology including advances in imaging and genetic testing allows more information to be provided to families before their baby is born, uncertainty often still remains, and more potential risks are introduced. The explanations of antenatal genetic testing and its implications can be complex and challenging [124]. This patient was describing their feelings surrounding amniocentesis.

Patient 3: "I was struggling with the risks of the procedure but equally my mental health wasn't good because I didn't know. I wouldn't want to have a baby with a trisomy and watch it suffer but equally I didn't want to terminate the pregnancy. It was

a difficult decision to make but for my mental health I needed to know. It was a really hard time".

When thinking about the future of their pregnancy uncertainty was still at the forefront for most of the families interviewed, even following reassuring MRI results. However, most of the patients felt the MRI had helped with some of their anxiety.

Patient 5: "They've just got to monitor and see; I'm taking each day as it comes. So, we're still unsure but we've got a plan in place."

Patient 6: "It has given us a lot of reassurance, but I guess we probably won't know until they're born".

Patient 9: "I think if there had been something else that was discovered I would have liked to know sooner. Just having that information, you can make a more informed decision and be better prepared".

Empathy and effective communication are key

The overarching theme throughout all of the interviews was the importance of good care and communication for these families. The times where our patients were unhappy with their care related to not feeling listened to or feeling rushed when information was being given. The women interviewed responded positively to being given their MRI results immediately after the scan by an experienced clinician.

Patient 6: "It was really detailed and really thorough, she gave us loads of time to ask questions. The fact you get the results there, on the same day, is remarkable, unbelievable."

Patient 12: "It was just so valuable having someone sitting less than a foot away telling me what they've seen, being confident of what they've seen and having the back-up of a second opinion".

Patient 10: "I just feel like I've been well looked after, I've got peace of mind that they

are keeping a close eye on me. They genuinely care, so I'm glad I've had that."

Even in the cases where the MRI results confirmed an anomaly and a potential poor outcome, the women we interviewed still seemed to appreciate the time taken to explain the problem in detail using the MRI images.

Patient 11: "I was relieved when I got told from the MRI what it was. Instead of being told what it could be".

We received useful feedback regarding how to improve the communication within the service, largely by providing more information about the process of coming for an MRI prior to the day and other places to go for support following a diagnosis.

The discussions regarding feelings of uncertainty, especially when they involved conversations around antenatal genetic testing and termination of pregnancy, further highlight the importance of sensitive yet clear communication from healthcare professionals and emotional support during this time. We therefore recommend a multidisciplinary team based approach to this process, combining the expertise of multiple professionals including the fetal medicine, neonatal, surgical and clinical genetics teams. This would be to ensure a consistent counselling approach from all teams, reducing potential confusion for parents during this difficult time. Furthermore, we would suggest all clinicians involved in the care of these women have specific training regarding the breaking of bad news and conveying complex information in an accessible format. Providing psychological support during this process is paramount and we would encourage, where appropriate, referral to specialist perinatal psychologists and mental health teams to reduce distress and allow families to make informed decisions [125].

Results and discussion – Medical professional themes

The evolution of technology

The professionals interviewed from across a range of specialties all agreed they had seen an increase in the use of and reliance on fetal MRI at our centre in recent years. There was frequently a feeling of increased acceptance locally of the utility of fetal MRI in suspected congenital anomalies which has led to increasing use of the technology and the service.

Neonatologist: "It's a lot more frequent now. I think the more people find out about it and the more people have experience of interpreting it the more likely it is to be done. So, it's becoming more common".

Fetal medicine specialist: "I think there is a general acceptance in obs and gynae and fetal medicine at large of the utility of MRI and therefore our threshold for asking becomes lower".

This increased use and acceptance has in turn led to feelings of some reliance on the technology, especially for the clinicians for whom fetal MRI has always been a part of their practice throughout their training.

Neonatologist: "I think it's invaluable, I can't imagine life without it now. If I was asked to counsel a woman with a structural abnormality on ultrasound, I would be very surprised not to have an MRI".

Those interviewed recognised that their experience is likely to differ from colleagues working in different centres and there will be geographical differences in the use of fetal MRI nationally.

Fetal medicine specialist: "I'm very mindful that there will be regional variation. Because I trained in a unit that uses MRI quite heavily, I'm aware I probably request MRIs more than if I had trained elsewhere".

Collaborative working

Along with evolution of the technology, the ways of working in an ever-expanding multidisciplinary team have also evolved. The counselling and care of families with a fetal anomaly involves many people from multiple medical specialities. The size of this team will be dictated by the nature of the anomaly but will usually include midwives, fetal medicine specialists and neonatologists. In addition to this core team, surgeons of varying specialties, geneticists and other paediatric specialities such as nephrology or neurology may also be

involved.

During the interviews the participants frequently discussed the collaborative working they undertake when looking after these families. However, many recognised that the way this is done could be improved, as often professionals from individual teams will meet the patient separately. Therefore, improved collaboration would reduce the number of appointments for the families involved.

> *Neonatologist: "The idea of everyone seeing the family together would be the best".*
>
> *Neurosurgeon: "I think in an ideal world we should see them the same day really, as a one-stop shop. I don't think it's nice for them to wait for the MRI, for the results and then to see us".*
>
> *Neonatologist: "That's where I sometimes find it difficult as their surgical appointment will be separate from ours. That's maybe something we can look at for the future is to combine those appointments so that we're all talking together as an MDT".*

The role of reassurance

As seen in the patient interviews, uncertainty around diagnosis and prognosis was frequently mentioned in the interviews with professionals. When discussing uncertainty, several of the participants acknowledged that within medicine uncertainty is often something that is accepted by healthcare professionals more readily than patients.

> *Neonatologist: "Anything we do is always going to have an element of uncertainty, I think as doctors we get used to accepting uncertainty."*
>
> *Neonatologist: "I think the biggest thing with counselling antenatally is the uncertainty. Knowing what you're certain about and what you're certain you're uncertain about".*
>
> *Neonatologist: "It gives me a better idea about prognosis and how sick this baby might be but all of that is understanding that there is uncertainty, you know we get used to that in our daily lives don't we."*

Following on from this, the role of the fetal MRI was seen by some of those interviewed as a means of reducing the uncertainty for the patients. In some cases, this was in ensuring normality using two different imaging techniques, for example in cases of significant family history or concerns raised on ultrasound scans performed in non-tertiary units.

> *Specialist midwife: "I think families gain a lot from having a more in depth, or a different modality, that can tell them there's a seemingly normal appearance. I think it provides reassurance."*
>
> *Fetal medicine specialist: "So actually having the double reassurance of a normal ultrasound and MRI is helpful when concerns have been raised by the local team".*
>
> *Specialist midwife: "I think we use it well for reassurance".*

The fetal medicine specialists in particular discussed the use of MRI to rule out additional structural abnormalities, for example if a condition with known associations had been diagnosed.

> *Fetal medicine specialist: "Sometimes it does help to have an additional modality confirming there is nothing else going on, it is reassuring for the parents".*

Informing clinical practice

When asked about how, if at all, the information from the fetal MRI impacts on their clinical practice, most of the professionals described it as either confirming a diagnosis made by ultrasound or providing complimentary information to refine a diagnosis or inform prognosis.

> *Neonatologist: "The diagnosis is often made, it's more a case of the certainty and severity".*
>
> *Fetal medicine specialist: "It's useful for those challenging to refine cases where you're worried, you're missing something".*

Neonatologist: "It's more information that I can add to my clinical plan, I can explain the prognosis to parents and draw pictures to explain."

This was seen to be of benefit both in terms of aiding the clinician's own certainty in the information they are providing families as well as enabling them to give the families more information, especially if difficult decisions need to be made.

Specialist midwife: "Sometimes it can be really devastating news, but it confirms a diagnosis to help parents make a really difficult decision".

Specialist midwife: "I think it's a really significant part of the diagnostic process purely because the families that come through our service are making some huge life-changing decisions and I think if we can provide as much information as possible, they prefer that. It's almost like it provides further clarity".

The consultant surgeons and the pathologist interviewed also discussed how the information from the fetal MRI informs their management in addition to how they would counsel families. For example, decisions regarding the place of delivery and the immediate postnatal management may change depending on MRI findings or the approach to a postmortem examination may be influenced by what is already known antenatally.

Paediatric surgeon: "The main thing is making that postnatal plan and where they can deliver is the most useful aside from the normal counselling elements".

Paediatric surgeon: "The MRI gives you enough information to decide whether you need to operate postnatally. It's smaller numbers but personally I have found it useful seeing the MRI images and correlating them with what I've found intraoperatively, it has been a real eye-opener".

Neurosurgeon: "They don't always have a postnatal scan prior to surgery but we do need to see them clinically".

Pathologist: "If someone had an MRI antenatally and they wanted a full post-mortem the MRI influences my approach and how I might do an incision for example".

General discussion

This qualitative study involved semi-structured interviews with women attending for a fetal MRI scan due to a concern on their antenatal ultrasound regarding a structural anomaly of the fetal body. Interviews with the healthcare professionals involved in the care of these women and their babies were also conducted, and both sets of interviews have generated several themes. For the patients these themes centred around the emotional impact of the process of having a fetal anomaly diagnosed, the strength and resilience of these women and their families, how risk and uncertainty are managed including the interaction with technology and the importance of empathy and good communication from care providers. The themes generated by the healthcare professional interviews focused on the evolution of the fetal MRI technology and service and its current place in clinical practice locally, informing some of the practical aspects of management of these babies in addition to how the expectant families are counselled. Similar themes have been seen in previous research on fetal MRI both with patients [45] and healthcare professionals [119], it is interesting to see how these themes have evolved over recent years as the MRI technology and its role in clinical practice has evolved.

This study is limited by the risk of bias introduced through the kinds of patients who consented to be interviewed. Understandably, we did not collect any data on the demographics, MRI result or pregnancy outcome for the patients who did not consent to be involved in the study. Whilst all were patients attending for fetal MRI due to an anomaly of the fetal body, we accept that patients given positive news are more likely to have agreed to be involved than those who received bad news. There was felt to be little that could be done to mitigate this risk however, and the interviews from the patients with reassuring MRI results still provided valuable insight into the patient journey following a concerning antenatal ultrasound scan.

The analysis of the patients who consented and were interviewed in comparison with the patients who consented but did not respond to the invitations to interview showed similar demographics and proportions of reassuring MRI results, therefore we do not feel this significantly impacted their reasons for participation. A quarter of those who did not respond to invitation to interview had undergone pregnancy loss or preterm delivery shortly after their MRI scan which we appreciate will have impacted their likelihood of taking part.

The findings from this study have had real-world impact at our centre as the findings from patients concerning a lack of accessible information about the process of attending for a fetal

MRI scan have been used to implement change. For example, a new patient information leaflet with an overview of the process of undergoing a fetal MRI scan, as well as safety information, has been developed for the fetal medicine specialists to provide to patients when their MRI scan is requested. This is shown in appendix 6.3. A quick-response (QR) code has been created to provide a clear link to our centre's fetal MRI website which also contains all the relevant information about attending for a fetal MRI scan as well as useful links to support for specific conditions. Business cards with this scannable link have been implemented so patients do not feel overloaded by information at their fetal medicine appointment but can access the information in their own time. These business cards have also been shared with other hospitals in the region who refer to our centre for fetal MRI. Most recently, a video has been developed detailing the patient journey through the MRI department when attending for a scan. This was undertaken alongside a wider project providing patient information for different types of MRI scan to familiarise patients with the environment, including what it is like inside the scanner itself, before they attend their appointment. We hope these changes will provide patients with more safety information and a realistic idea of what to expect, in order to alleviate some anxiety during the process.

The future directions from this project aim to improve some of the challenges described from the professional interviews. This was mainly the lack of multidisciplinary working when speaking with families. The team recognised good collaborative working when having discussions about and making plans for these patients, however they were frequently unable to meet the patient all together at the same time; meaning multiple patient appointments are often required to meet the entire team. We plan to explore how complex perinatal counselling requiring multiple healthcare professionals from different medical specialities is undertaken at other centres to see how change can be implemented locally.

Conclusion

In conclusion, this research shows the value expectant parents feel fetal MRI adds to their journey when a fetal anomaly is diagnosed in terms of aiding their understanding and how they interact with the MRI image. It also highlights the importance of empathy and clear communication from care providers during this turbulent time for families. For healthcare professionals, fetal MRI has a role for providing reassurance, informing management decisions and prognostication as well as providing a focal point from which multidisciplinary teams can work.

Chapter 5 – Concluding comments, impact and future directions

This research aimed to investigate the diagnostic accuracy of fetal MRI in congenital anomalies of the fetal body when used in addition to antenatal ultrasound. We further aimed to explore the role of fetal MRI for both clinicians and parents in the prognostication and management of these anomalies. The work focused on four main objectives which have been addressed in chapters 2-4. Whilst the research in each subchapter has been discussed already; this final discussion aims to bring together the overall research findings, examine their impact and consider future directions for this research.

1. Firstly, we studied the diagnostic accuracy of fetal MRI in addition to antenatal ultrasound alone in both the literature and our own patient cohort. We explored how frequently the overall diagnosis was changed following the addition of fetal MRI and how specialists in both fetal medicine and neonatology use the information provided by fetal MRI and how useful they consider it to be. (Chapter 2)
2. We then examined the role of fetal MRI in specific congenital anomalies in more detail including congenital diaphragmatic hernia, tracheo-oesophageal fistula and/or oesophageal atresia and fetal neck masses. This research specifically concerned the different ways in which fetal MRI is used for these conditions such as to aid diagnosis, for prognostication and for planning of management both in utero and after birth. (Chapter 3)
3. We explored the views of the parents who undergo fetal MRI following a suspected anomaly seen on ultrasound. This was undertaken in order to improve understanding of the patient experience during this difficult time and to examine how, if at all, the fetal MRI findings help patient understanding and decision making regarding the pregnancy. (Chapter 4)
4. We also explore the views of a variety of healthcare professionals involved in the care of the women and babies with a fetal anomaly who undergo MRI during pregnancy. This was to further understand how different specialities use the information provided by fetal MRI and the utility of this information. (Chapter 4)

5.1 The diagnostic accuracy of fetal magnetic resonance imaging

The systematic review findings showed a statistically significant improvement in diagnostic accuracy of 25.8% when fetal MRI was used in addition to ultrasound. It also found that the fetal MRI provided additional information in 26.8% and the management was changed in 14.9% of cases. The findings from our own patient study showed a similar improvement of diagnostic accuracy with the addition of fetal MRI of 24.6%. Owing to the heterogeneity of the pathology studied there was, however, variation in this improved diagnostic accuracy with fetal MRI depending on the anatomical system and individual congenital anomaly studied.

The work with fetal medicine and neonatal consultants grading the utility of the information provided by fetal MRI found that additional information was provided by the MRI in 27.6% of cases and the diagnosis was changed antenatally in 19.9% of cases. This data is novel and highlights how this information can be used in combination with the overall diagnostic accuracy of fetal MRI. Whilst there was a variation in opinions, largely based on field of speciality and years of consultant experience, this work provides an insight into how the different professions use the information provided by fetal MRI.

These findings confirm that fetal MRI is a useful additional diagnostic tool for the diagnosis of congenital anomalies of the fetal body. It compares with existing research on the role of fetal MRI in diagnosis of fetal central nervous system anomalies and adds data to the smaller body of evidence for use of this technology in non-CNS anomalies. We hope that this work will add to the evidence base which encourages standardisation in defining the scope for fetal MRI as an additional diagnostic tool to ultrasound. There is a wide variation in practice both within the United Kingdom and internationally meaning there is somewhat of a ‘postcode lottery’ regarding the antenatal imaging that pregnant women receive, which may impact decision making for the pregnancy and overall management.

We propose the future directions of this field of research to include further collaboration between different centres both within the UK and the wider international community. The aim of this would be to generate studies with larger patient numbers to avoid the potential bias introduced by smaller studies with limited patient numbers owing to the relatively rare and heterogeneous pathologies being studied. This would include larger panels of specialists reviewing the MRI findings and commenting on the utility of the information provided by fetal MRI, with the aim of involving centres which do not routinely use fetal MRI at all to gain their insight into the differences in clinical practice.

The improved diagnostic accuracy of congenital anomalies of the fetal body with the use of fetal MRI and the significant proportion of genetic anomalies seen in our diagnostic accuracy study (26.7%) raises the question of how fetal MRI should be further integrated with genomic data. This so-called ‘radiogenomics’ approach could have several applications including improved prenatal counselling, more personalised treatment strategies and earlier detection of more subtle fetal anomalies seen on imaging as well as enabling further research into fetal development. A truly combined approach would have practical challenges as both technologies are expensive and currently have limited use within the NHS. There would be ethical challenges as increasing genetic testing would increase the numbers of variants of unknown significance which can be a difficult concept for both clinicians and families. We would propose future research in this field to involve the use of fetal MRI in providing the phenotypic picture of a structural anomaly to enable appropriate genetic testing to be undertaken. There may also be a role for using genetic results to re-examine subtle MRI findings retrospectively, however this role may be more limited and have less influence on perinatal counselling and management planning. This area of fetal research is continually expanding with improvements of MRI and significant developments in both fetal exome and neonatal whole genome sequencing and has exciting future prospects.

5.2 The application of fetal MRI in diagnosis and management of specific conditions

The research concerning the use of fetal MRI in prognostication of congenital diaphragmatic hernia through the measurement of lung volumes and use of observed-to-expected total lung volume showed a significant potential variation in practice. Depending on which formula is used to calculate the expected lung volume for gestation we saw a large difference in expected survival rates which could in turn create differences in the counselling information given to families. We have also shown that for more than half of the patients studied the observed-to-expected total lung volume did not change enough between fetal MRI scans performed in the second and third trimester to alter the prognosis. However, when this data was correlated with the pregnancy outcome we found the first MRI scan to be more accurate in predicting survival, although the scans in later pregnancy remain an important tool for surgical planning. These two studies illustrate the need for consensus on both time of imaging and method of calculating percentage lung volume. The current large consensus data has been gathered from multiple studies from across the globe, all with different methodology and findings, affecting the quality of the data clinical practice is based upon.

We feel there is potential for further research regarding congenital diaphragmatic hernia using fetal MRI, specifically in assessment of the lung tissue which is in direct contact with the hernia. Even in patients with good percentage lung volumes, there is still significant morbidity and mortality and this may be because the lung tissue which has come into contact with the abdominal contents may not function as expected even when it expands following corrective surgery. We propose that research using magnetic resonance spectroscopy may provide some insight into these differences at a tissue level.

The examination of the diagnostic accuracy of fetal MRI in cases of tracheo-oesophageal fistula and/or oesophageal atresia demonstrated a relatively poor diagnostic accuracy of both ultrasound and MRI (PPV 45.5% and 51.7% respectively). We did however show the utility of fetal MRI in accurately excluding TOF/OA. We explored the multiple different diagnostic signs reported in the literature but found that a combination of these features had the highest diagnostic accuracy. This study was limited by small sample size, and we were unfortunately unable to provide a quantifiable definition of an objectively small stomach on antenatal imaging. This work raised the question of whether fetal MRI is useful as an additional diagnostic tool in cases of suspected TOF/OA on ultrasound as it only had a marginally improved diagnostic accuracy. However, the MRI was able to accurately refute a suspected diagnosis and examine the fetus in detail for presence of associated congenital anomalies such as those comprising VACTERL association. The most logical way to

improve the data is to establish a multicentre study using retrospective and prospective data to increase the numbers. The aim of this would be to assess not only the diagnostic accuracy of antenatal imaging, but also to assess if the type of TOF at the time of surgery correlates with specific antenatal imaging findings such as an absent stomach. Large numbers would allow generation of a ROC curve for stomach size and more control data would also be beneficial.

The study of the role of fetal MRI in refining the diagnosis of fetal neck masses and predicting airway compression requiring intervention at birth showed that MRI was a valuable tool in both diagnosis of the specific type of mass and in predicting airway compromise. This research provides evidence for the use of fetal MRI in all cases of fetal neck mass to enable appropriate planning for the delivery of these babies, including whether delivery in a tertiary centre with the ability to perform an EXIT procedure is required.

These findings help define the role for fetal MRI in specific conditions and explore some areas where it may be less useful. However, once again, larger studies are required to confirm these findings. This is especially important for the work on TOF/OA as our findings differed from what has previously been reported in the literature. We hope larger studies providing evidence to support a standardised use of fetal MRI in addition to ultrasound for specific congenital anomalies could again be used to develop consensus and national guidelines.

The interviews with different healthcare professionals also allowed us to explore more specific potential future research applications of fetal MRI. For example, we had discussions with our surgical colleagues concerning the use of fetal MRI in gastroschisis. The diagnostic accuracy study showed both ultrasound and MRI have good accuracy in diagnosis of gastroschisis, however MRI may be able to provide more detailed information regarding the health of the bowel, for example using diffusion weighted imaging and spectroscopy of the amniotic fluid to assess metabolite change. The most likely metabolite to change would be lactate and we would expect an increased lactate in cases where the bowel was less healthy due to cell necrosis.

During the interview with the consultant urologist we also discussed the role of fetal MRI in diagnosis and prognosis of pelvicalyceal dilatation and its causes. At present, ultrasound is used to sequentially monitor hydronephrosis and antero-posterior diameter (APD) measurements of the renal pelvis are well validated for ultrasound. This validation does not currently exist for fetal MRI however, and we have therefore commenced measurement of

APD of all renal pelvises imaged on fetuses with non-renal problems. The aims of this are to provide a control database with a normal range of renal pelvis measurements which could be compared with ultrasound measurements to see if the two align. This would allow future research to provide validation for the measurement and monitoring of hydronephrosis using fetal MRI. There is also the potential to try and quantify the DWI. Currently the DWI is used to predict renal function and is usually present or absent. However the signal intensity can vary and this might reflect different degrees of renal function. Quantification prior to birth would allow more accurate counselling and also planning for postnatal management.

5.3 The patient experience of fetal magnetic resonance imaging

The qualitative work concerning the semi-structured interviews with women who have undergone fetal MRI and the thematic analysis of this data highlights the experience of the families throughout the process. This work gave insight into some of the misconceptions patients may have of the role of antenatal screening and how they interact with the physical MRI images and the positive effects of seeing a more detailed image of their baby. We saw, understandably, how difficult this time of uncertainty is for families, their resilience and the importance of good communication and empathy from care providers. We also gained insight into some of the areas of our service which could be improved and have made changes to address this.

This research has allowed us to make changes to our own service, predominantly focused on providing additional patient information prior to attending a fetal MRI scan. As discussed in the subchapter we have since provided a patient information leaflet, business cards with a QR code to our fetal MRI website and a patient information video detailing the whole process. It is also now routine practice for our fetal medicine colleagues to discuss claustrophobia with the patients and reference raised BMI when requesting the fetal MRI, this allows the MRI team to book patients onto the larger MRI scanner if needed. We hope these changes will help alleviate some of the anxiety during this process.

We propose future research in this area to include interviews with a larger cohort of patients and their families to gain a more in depth insight into their journey and experiences of stress and uncertainty when having a fetal anomaly suspected. It would be useful to interview the patients at different time points during this journey, including after their baby has been born to assess how feelings change with time. This could include speaking with families in the postnatal period, either through approaching them on the neonatal unit, in neonatal outpatient clinic settings or through advertising with national charities such as CDH UK, antenatal results and choices, Sands and Bliss. Our research mainly focused on the women undergoing the fetal MRI scans, however separate interviews with their partners and wider family may also provide new insights into the journey.

5.4 Health professional views on fetal magnetic resonance imaging

The thematic analysis of qualitative interviews from a variety of healthcare professionals involved in the care of pregnant women and babies with congenital anomalies provided insight into the variety of ways in which fetal MRI is valued. We have shown how the technology has evolved throughout many people's careers and the reliance that is now placed on fetal MRI by many professionals, as it is a modality they have always worked with. We recognise this work has some bias as all the professionals interviewed use fetal MRI in some aspect of their clinical practice and therefore know that these results would differ if similar research was undertaken at other centres.

This research highlights the importance of multidisciplinary team working in cases of fetal anomaly and explores some of the barriers to seamless collaboration. As discussed in the associated subchapter, we feel further work exploring how MDTs at other centres operate to deliver streamlined multi-professional antenatal counselling to see how improvements in our local service can be made.

5.5 Conclusions

Overall, this research shows that whilst antenatal ultrasound remains the gold standard for diagnosis of structural fetal anomalies, the use of fetal MRI as an additional diagnostic tool improves overall diagnostic accuracy. Therefore, we suggest that best practice would require a combination of these imaging modalities. The heterogeneity of pathology which comprises congenital anomalies of the fetal body means that use of fetal MRI may not be of additional benefit in every case. However, we have shown multiple specific conditions in which fetal MRI aids diagnostic precision, enables prognostication which can inform antenatal counselling of families and can inform management planning for the time of birth and in the neonatal period. In isolation many of the pathologies discussed are relatively rare, meaning that collaboration to enable large multi-centre studies, ideally internationally, is required to increase the evidence base for fetal MRI use further.

This research has shown high levels of acceptability of fetal MRI by the patient population and has explored the perceived benefits patients who have undergone fetal MRI feel. Whilst fetal MRI as an additional imaging modality in pregnancy is now a part of antenatal care for many patients, its use is not yet standardised and further work is needed to explore the barriers to a nationally unified pathway.

Chapter 6 – Appendices

6.1 – Search strategy for systematic review

6.2 – Data collection tool for systematic review

6.3 – Patient information leaflet for fetal MRI

6.1 Search strategy for systematic review

Medline (via Ovid 1966-present)

Search no.	Query	Results (n)
17	#16 AND congenital anomaly	392
16	#8 AND #15	698
15	#11 OR #12 OR #13 OR #14	5,324,440
14	abdomen OR abdominal OR gastrointestinal OR GI tract	1,494,932
13	thoracic OR Chest OR Lungs	1,563,924
12	renal OR kidney	1,259,757
11	body	1,569,160
10	#8 NOT #9	1,391
9	cardiac OR heart OR Cardiovascular system	2,739,995
8	#6 NOT #7	1,700
7	CNS OR central nervous system OR Brain OR Spine	2,758,241
6	#4 AND antenatal diagnosis	2,989
5	#4 AND prenatal diagnosis	2,928
4	#1 AND #2 AND #3	4,903
3	ultrasound or ultrasonography	1,910,881
2	MRI OR Magnetic resonance imaging	723,986
1	fetal [Title/Abstract] OR fetus [Title/Abstract]	307,483

6.2 Data collection tool for systematic review

- Author & Year
- Title
- Journal of publication
- Country of study
- Target population
- Study characteristics:
    - Participant selection (consecutive, random or unclear)
    - Retrospective or prospective
    - Total no. in study
    - No. excluded by study authors + why
    - Total no. included in study report
    - Total no. included in systematic review
    - Gestation at USS
    - Gestation at MRI
    - Outcome reference standard used
- Results:
    - USS result (% correct compared with outcome)
    - MRI result (% correct compared with outcome)
- Analysis:
    - USS & MRI agreed + correct
    - USS & MRI agreed but wrong
    - MRI changed diagnosis (USS wrong)
    - USS changed diagnosis (MRI wrong)
    - Additional info given by MRI
    - Management changed by MRI
    - Specific anomaly where was MRI most useful

6.3 Patient information leaflet for fetal MRI

Sheffield Teaching Hospitals NHS
NHS Foundation Trust

WHERE CAN I GET MORE INFORMATION?

The website www.fetalmri.co.uk has been created by the Fetal MRI team at Sheffield Teaching Hospitals and contains further information about the team, appointments, what to expect and FAQs.

It also has reliable information about common reasons for referral for MRI during pregnancy and links to support charities that may be useful to you.

QR code for website

You can also discuss your referral with your doctor or contact the department using the number on the appointment letter.

There are more patient information leaflets on The Sheffield Teaching Hospital website, including a leaflet called "Magnetic resonance imaging (MRI)". This leaflet contains more general information about MRI scans.

https://www.sth.nhs.uk/patients/patient-information/find-a-leaflet/search-for-a-leaflet

Sheffield Teaching Hospitals NHS
NHS Foundation Trust

MRI scans during pregnancy

Sheffield Teaching Hospitals NHS
NHS Foundation Trust

WHAT IS AN MRI SCAN?

MRI stands for Magnetic Resonance Imaging which is a scan that uses a powerful magnet to obtain images of your body.

WHY DO I NEED AN MRI SCAN?

MRI can take pictures of almost all parts of the body and shows many different diseases. Your doctor should have discussed with you their reason for wanting a scan.

MRI of the unborn baby is usually requested when the ultrasound scan of your baby has detected a problem or there is a family history of previous problems.

WHAT SHOULD I WEAR?

It makes it easier and quicker if you can wear clothing without metal parts e.g. sports bra without underwires and metal fastens. This means you will be able to wear your own clothes for the scan and not need to change into a hospital gown.

Please remove all hair clips, you can leave head scarves on. Ideally leave your jewellery at home.

HOW LONG DOES THE SCAN TAKE?

The scan takes around 20-30 minutes. Twins will take longer. Your baby will move when they first hear the noise but then will settle again as the noise is repetitive.

IS MRI SAFE DURING PREGNANCY?

There have been several laboratory and clinical research studies conducted to look at the effects of MR imaging in pregnancy. To date, there is no indication that the use of clinical MRI during pregnancy has produced any harmful effects to the unborn baby. MRI does not use ionising radiation (e.g. X-rays).

There are two things we are careful about:

- The radio signals used during the scan can cause you to feel warm. As you will be aware, too much heat is not good for the baby. We use very low levels when scanning during pregnancy in order to keep any heating to a minimum.

- MRI scans are very noisy and we will give you earplugs and headphones to protect your ears. Some studies have looked at whether the noise can affect your baby's hearing. These studies have shown no effect on the hearing of newborn babies who have been exposed to MRI during pregnancy. We will choose quieter scans to minimise the noise to your baby as far as possible.

WILL I NEED AN INJECTION?

You will not normally need an injection.

Chapter 7 - References

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