1. Introduction

Magnetic resonance imaging (MRI) has been well established for the detailed depiction of developmental anomalies of the fetal brain for several decades. More recent applications also include the investigation of congenital cardiac lesions, the results of which have significantly enhanced the counselling of affected pregnancies[1].

MRI has several conceptual advantages over ultrasound (US). Ultrasound is operator dependent and images acquired can be limited by maternal habitus, oligohydramnios and fetal lie. MRI can obviate these issues especially with recent post-acquisition processing that allows for motion correction, applied not only to the brain but also the abdominal cavity[2,3]. Since most published series report cases where an ultrasound has been performed prior to MRI and therefore produced unblinded reports, we anticipate a potential overemphasis on the diagnostic value of MRI. This study explored the information made available on contemporary MRI and ultrasound of the fetal body in a cohort of fetuses with identified anomalies of varying severity: including anomalies that were identified *de novo* in the MRI study. The study population also included a large cohort of low-risk fetuses who were recruited as controls and therefore it was possible to study incidental findings in healthy pregnancies.

2. Methods

This study was a retrospective analysis of data already acquired as part of the iFIND imaging study which had full ethical approval (14/LO/1806). The study recruited pregnant women with anomalies identified on their 18-20 antenatal US who had then been seen in the regional

fetal medicine unit at St. Thomas' Hospital, London for a specialist ultrasound +/- fetal echocardiogram. Healthy controls were recruited through the antenatal services at St. Thomas' Hospital. Patients subsequently underwent MRI and US at the same time and these were reported by separate individuals, however MRI reports were not blind to findings from initial anomaly scan or any subsequent clinical US findings.

All patients within the study with complete postnatal outcome data from delivery and newborn assessment were eligible for inclusion. Analysis was performed on three groups of patients: those with pre-identified body anomalies, those with brain or cardiac anomalies, and normal controls. Incidental findings of additional anomalies, and additional information made available from MRI were noted.

Each case included was examined by three independent clinicians with a background in antenatal counselling and clinical practice pertaining to the system of interest (i.e. Maternal-Fetal Medicine, Perinatal Neurology, Neonatal and Paediatric General Surgery and Cardiology). Imaging reports and clinical notes for mother and newborn were assessed. Consensus was reached on whether the information available from the MRI would modify the antenatal management (i.e. change of counselling, increased frequency of appointments, change to the birth plan or prompting a termination of pregnancy) or the postnatal management (i.e. prompting investigation, early intervention or redirection of care in the neonatal period). This was summarised by grading the anomaly (1-5): 1. No consequence, no follow-up; 2. Further imaging / monitoring; 3. Needs postnatal intervention - not life threatening; 4. Needs fetal or neonatal intervention - life threatening; 5. Lethal.

As the descriptive data obtained were not strictly quantitative, it was not deemed appropriate to perform statistical analyses.

3. Results

Among 531 fetal MRI performed in 522 mothers (9 twin pregnancies); there were a total of 54 body anomalies identified on fetal MRI; 37 of which had been identified prior to inclusion listed as identified body anomalies in Figure 1. A further 17 body anomalies were found at the time of the MRI scan and were not detected on US, these have been classed as incidental findings.

3.1 Incidental Findings

Seventeen anomalies were identified incidentally (i.e. not noted on clinical or contemporaneous research ultrasound); five of which were identified in 329 normal volunteer pregnancies, giving a rate of detection 1.5% (Table 1). All five of these anomalies were judged to be of minimal significance: 80% were in the renal system with unilateral borderline pelvicalyceal dilatation or uncomplicated duplex system. There was also a finding of a sub-centimetre nasolacrimal cyst.

Twelve of 171 (7%) of patients with identified cardiac / CNS lesions had body findings on their MRI that were discrepant with their contemporary USS (Table 1). Again, the main system affected was the renal tract and bladder (5/12, 42%). Importantly, specific information on MRI of the fetal brain led to termination of pregnancy in one case with open spina bifida (myelomengingocele – MMC) and one with skeletal anomalies and USS identified cerebellar anomaly (Table 2).

In 3 cases, abnormal anatomy considered to be an additional body anomaly had been suspected based upon USS findings at the FMU scan (central heart giving suspicion for CDH or congenital lung lesion; bilateral talipes; large stomach suggesting bowel obstruction) in

these cases, MRI reported completely normal anatomy – which meant counselling could be modified just to concern the previously identified anomaly.

3.2 Recognised Body Anomalies

Fetal MRI was also performed in 37 cases with USS detected body anomalies (18% of the 208 recruited patients with fetal anomalies); additional or more detailed body findings were demonstrated with MRI in many of these (Table 1+2). MRI depicted more concerning features for prognosis in 10 cases. This included definitive diagnoses of suprarenal neuroblastoma, bronchopulmonary sequestration (BPS) with an identified systemic feeding vessel from the thoracic aorta, intestinal malrotation with likely distal intestinal obstruction, bilateral complicated duplex kidney, posterior urethral valves and long-gap oesophageal atresia. TOP was opted for once further delineation of anatomy was made available in 2 cases of massive exomphalos with abnormal brain findings of ventriculomegaly, and thoracolumbar MMC with an anterior cystic mass.

In 25 of the 37 cases, the MRI findings did not change the severity of prognosis; however, there were 5 cases in which the additional information would have modified the antenatal course (i.e. additional counselling in 3 cases plus further MRI of renal dilatation in suspected PUV with oligohydramnios, and confirmation of separation from the airway in a neck mass assuring no need for an EXIT procedure). There were 2 cases in which postnatal management was modified (renal ultrasound for hydronephrosis and contrast study on day one of life).

In the 2 remaining cases, MRI demonstrated normal anatomy where cervical lymphatic malformation (diagnosed nuchal oedema) and intestinal obstruction (due to echogenic bowel) had been suspected on US at referral and ongoing study with US at the time of MRI.

In both cases, there was hence no need for further antenatal counselling nor postnatal follow-up.

3.3 Changes to the antenatal or postnatal course

Regarding the incidental or newly discovered anomalies, there were no severe abnormalities diagnosed *de novo* on MRI, however MRI gave additional prognostic information that modified the clinical course in 5/17 pregnancies (29%, Table 2); these were all cases of additional findings in patients with recognised cardiac or CNS anomalies. Comparatively, in the 37 patients with body anomalies at entry into the study, information was made available that led to a change in the prenatal or postnatal course in 21 patients (59%, Table 2).

3.4 Cases that were missed

Important to note were cases within the series where neither US nor MRI made a complete diagnosis. One was a diagnosis of oesophageal atresia in a fetus scanned for bilateral superior vena cava but no other anomalies. A distal trachesophageal fistula was identified at the time of primary repair aged 2 days. Retrospective review of the images suggested a possible discontinuity of the oesophagus (Figure 3A) as well as enlargement of the upper oesophagus (not shown). There were also cases of antenatally-undetected anorectal malformation (ARM) in two unrelated fetuses with multiple identified anomalies, including major cardiac and suspected intestinal malrotation. The first underwent exploratory laparotomy after bilious emesis on day 1, having also been noted to have an abnormal perineal opening. Retrospective review of images could detect an anterior deflection of the rectum (Figure 3B), however the lack of mixed signal as would be expected in a fistula to the urinary tract makes the diagnosis very challenging. The second fetus had antenatally suspected upper GI obstruction

(confirmed at neonatal laparotomy), and a subsequently diagnosed bulbar urethral fistula. The antenatal high obstruction would have limited the volume of meconium in the distal bowel, thereby making diagnosis on fetal MRI extremely difficult even on retrospective review of the images.

4. Discussion

We have demonstrated notable benefit to performing MRI in cases of US-identified body anomaly; with MRI providing clinically relevant complementary information in over half of the cases scanned. We reported additional information on MRI in 59% of USS pre-diagnosed body anomalies, as well as new body anomalies in 7% of pre-diagnosed cardiac/CNS and in 1.5% of healthy control fetuses. Overall, in cases with confirmed body anomalies at enrolment, MRI provided additional information in 57% of fetuses, and was able to refute a diagnosis in five cases (9%). This is considerably higher than the reported yield by some previously published retrospective series; Amini et al. reported new information from MRI available in just one third of patients with suspected body anomaly, with very few new findings changing management[4]. Manganaro and colleagues reported very similar results to our study in a prospective series of 38 fetuses with US suspected intra-abdominal anomalies[5]; with 60.6% of MRI examinations providing additional information, and 5% of cases where MRI was able to refute a diagnosis suggested by US. We anticipate this discrepancy may represent a difference in definitions based on retrospective data collection: we regarded antenatal management to be altered if further scans were performed, if counselling were changed or if the delivery plan might be altered. Postnatal management was judged to be changed if the MRI findings dictated investigations in the neonatal period: in our

series, two neonates underwent investigation to rule out suspected malrotation or posterior urethral valves.

We also report within this series, a 1.5% rate of incidental fetal abdominal findings in healthy control pregnancies. Our previous exploration of 2,569 retrospective cases undergoing fetal MRI has suggested that the rate of detection of additional incidental anomalies in fetal MRI may be considerably higher when identified CNS and cardiac anomalies are included[6]. It should be recognised that many of these are clinically insignificant but might warrant further investigation and occasionally incidental findings in healthy pregnancies may have major significance (i.e. congenital lung lesions, cerebral haemorrhage, polymicrogyria) therefore, the possibility of incidental findings and how these will be managed should always be discussed at recruitment and prior to consenting for research MRI.

Valid comparisons between clinical USS and later MRI are difficult as many anomalies such leading to hollow viscus dilatation or changes in liquor volume may evolve over time and hence be more or less evident at later gestations. We feel that the ability to compare MRI-derived information with US performed at the same gestation is therefore a strength of this study.

While this study is able to provide information from a large number of pregnancies undergoing contemporary US and MRI, the low prevalence of specific regional anomalies mean that the data here cannot produce meaningful information regarding diagnostic accuracy or sensitivity, furthermore the majority of cases reported here would have been recruited to the study with an anomaly already suspected. It should also be noted however, that those studies reporting larger retrospective series of prenatally evaluated lesions also will be subject to selection bias and review bias owing to the pre-selection of higher severity cases to undergo MRI. This could lead to an overestimation of the sensitivity and specificity

of MRI for diagnosis of specific lesions and should be regarded as an inherent limitation even when assessing meta-analyses as have been published for prenatal diagnosis of orofacial cleft[7] or oesophageal atresia[8]. This is reinforced from our own dataset, whereby a fetus with oesophageal atresia was not diagnosed despite fetal MRI, however this fetus also lacked the imaging features of polyhydramnios or microgastria. We must also acknowledge that certain anomalies may be particularly challenging to diagnose on MRI; as is demonstrated by two cases of ARM in fetuses with multiple anomalies.

Despite the widespread use of fetal MRI in the clinical setting for over a decade, there are few studies previously published that have attempted to explore the added benefits of MRI to the routine US that might be performed in the antenatal monitoring of identified congenital body anomalies. We anticipate that further evidence to demonstrate clinical effectiveness will strengthen recommendations made by expert bodies proposing the use of fetal MRI in these cases, which are poorly adhered to at present[9]. Furthermore, with improved diagnostic and prognostic value, fetal body MRI is likely to return similar benefits to that which have been shown for MRI of the fetal brain – where the cost of scanning is considered to be justified by the alterations to management[10]. It should be reinforced that expert US represents an excellent modality for the diagnosis and prognostication of many congenital anomalies, and owing to cost and access implications would likely continue as the mainstay of antenatal imaging, especially in conditions which might require serial monitoring such as congenital lung lesions[11], or gastroschisis[12]. On the basis of our data presented here, we would recommend that any fetus with an US-identified anomaly (including CNS/cardiac anomalies) ought to undergo fetal MRI with specific sequence acquisition to allow examination of the fetal body. Standardised, prospectively imaged cohorts will allow diagnostic sensitivity and specificity to be calculated; to further add to ultrasound-based metrics[13,14].

Figure Legends

Figure 1. Study Enrolment

Figure 2. Timing of study scans

Figure 3 – Cases missed on initial MRI

- **a- B-TFE (balanced turbo field echo) image of fetus at 30+5w scanned because of bilateral SVC. A lack of continuity of the oeosphagus can be appreciated (*) as well as dilatation of the upper oesophagus on other sequences that were taken (not shown).**
- **b- T2-weighted image of fetus at 32+3w scanned for cardiac concerns; the bladder and posterior urethra are distended (*) the distal rectum which could be seen to have a slight anterior angulation (arrow). The postnatal evaluation demonstrated an anorectal malformation with perineal fistula, the urethra was confirmed to be normal.**
- **c- T2-weighted MRI of fetus at 31+3w scanned for cardiac concerns; dilated stomach and duodenum are clear (*) with a paucity of meconium in the distal bowel. Postnatal evaluation suggested an anorectal malformation with bulbar fistula as well as duodenal atresia.**

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