Fetal magnetic resonance imaging in the confirmation of congenital anomalies found on routine mid-trimester ultrasound

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Objective. To determine the added value of fetal magnetic resonance imaging (MRI) when clarifying a suspected anomaly detected by mid-trimester scan.
Methods. Women attending two centers of fetal medicine between January 2017 and December 2021 were identified. The centers carried out routine mid-trimester ultrasound scans to detect fetal anomalies. Those with a suspected anomaly which required further clarification were referred for fetal magnetic resonance imaging (MRI). The medical records of all referred women were examined to determine the anomalies found at scan, MRI and termination of pregnancy or delivery. A total of 9571 women had a routine mid-trimester scan and an anomaly was either diagnosed or suspected in 449 (4.7%); an MRI examination was made in 76 cases (0.79%).
Results. MRI confirmed the presence of an abnormality in 61 referrals (80%) and failed to yield a result in one case. Outcome information was available for 69 cases: the MRI confirmation rate was 89% (48/54) in those with abnormal outcome and 40% (6/15) if the outcome was normal, $P<0.0001$. Among defects in the most common anatomical systems identified at ultrasound, the highest confirmation rates were for urinary tract abnormalities (94%, 15/16) and facial abnormalities (100%, 8/8). Results in other systems varied according to the specific defect but the confirmation rate was high for ventriculomegaly (86%, 6/7) and neural tube defects (83%, 5/6).
Conclusions. We have shown that in women with suspected anomaly scan results, requiring further clarification, MRI confirmed ultrasound at a high rate, particularly for urinary tract and facial anomalies.

Key words: magnetic resonance imaging, anomaly scan, mid-trimester, prenatal diagnosis, developmental

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INTRODUCTION

Prenatal diagnosis of fetal developmental abnormalities relies mainly on routine ultrasound examination[1]. Most centers carry out a routine "anomaly" scan in the second trimester. Some of the anomalies observed at the scan are related to chromosomal and genetic disorders. These can be confirmed by fetal DNA obtained by invasive procedures such as amniocentesis, chorionic villus sampling and, more rarely, cordocentesis. However, the majority of anomalies cannot be resolved in this way. In some cases, the ultrasound finding alone, or combined with more targeted scanning or close ultrasound follow-up later in pregnancy, are sufficient for a reliable prenatal diagnosis. But in many cases the anomalies are subtle or inconclusive and fetal magnetic resonance imaging (MRI) has a role in providing more definitive information leading to prenatal diagnosis[2-14].

The added value of MRI will be dependent on the proportion and type of ultrasound anomalies referred for examination. In this paper a large series of cases are described and the outcomes assessed among women having a routine anomaly scan at two Czech centers over a four year period.

METHODS

Women attending two centers of fetal medicine, in Zlin and Olomouc, between January 2017 and December 2021 were identified. Prenatal screening in these centers is routinely carried out in the first trimester to detect common aneuploidies using the combined test and at mid-trimester using ultrasound scans to detect fetal anomalies. These scans were performed by physicians with ultrasound certification from the Fetal Medicine Foundation (FMF) using General Electric Voluson E10 and S10 Expert, and Mindray Neuwa 19 scanners. The examination was carried out using a transabdominal probe. Women with a suspected fetal anomaly which requires further clarification are referred for fetal MRI carried out by radiologists using Siemens Magnetom scanners: Prisma, with an 18-channel

body coil and XA 31 software, in one centre; and Avanto 1.5T, with a body coil, in the other centre.

The medical records of women referred for MRI were examined to determine maternal age, parity, method of conception, number of fetuses, maternal weight and the first trimester combined test results. The information was also abstracted on the findings of the anomaly scan, MRI, pathological results of any terminations of pregnancy and pediatric findings after delivery. All those referred for MRI were included in the study. Technical difficulties with the MRI scan and incompleteness of information on the outcome of pregnancy were not exclusion criteria.

During this period a total of 9571 women had an anomaly scan. One or more fetal anomaly was found in 449 (4.7%) and a referral for MRI was made in 76 cases (0.79%).

RESULTS

The characteristics of the 76 referred women are shown in Table 1. These characteristics are pregnancy related factors, as well as those associated with the combined test and the anomaly scan.

The MRI examination confirmed the presence of an abnormality in 61 referrals (80%) and in one pregnancy the MRI examination failed (1.3%). Table 2 shows the association between MRI results (abnormality reported or not reported) and the outcome of pregnancy (abnormality found, not found or unavailable). Information on the outcome of pregnancy was available in 69 cases, obtained from different sources: livebirth (48); termination of pregnancy (20), including selective feticide in one set of twins; and infant death (1). Among 54 cases with a proven abnormal outcome the MRI confirmed the presence of an abnormality on ultrasound in 48 (89%) and in the 15 with proven normal outcome the MRI incorrectly confirmed the ultrasound or failed in 6 (40%), a highly statistically significant difference (P<0.0001). When outcome was unavailable, the proportion with MRI confirmation of the ultrasound finding was 71% (5/7), not significantly different from the proportion in those with available outcomes (P=0.68).

The anatomical systems according to ultrasound were: 33 (43%) central nervous system (CNS); 16 (21%) urinary tract; 11 (14%) thorax; 8 (10%) facial; 5 (7%) gastrointestinal; and three were in more than one system. One twin pregnancy had a CNS anomaly and in the other twin pregnancy it was thoracic. The specific ultrasound abnormality for each case is shown in supplementary Table S1, together with MRI finding, outcome and source.

Table 3 shows the proportion confirmed by MRI according to the anatomical system identified by ultrasound. The highest confirmation rate was achieved in the urinary tract abnormalities, facial anomalies (all cleft lip/palate) and those involving more than one system, totaling 36% (27/76). Of these, the only discrepancy was in a single case of bladder extrophy, a very rare finding – in this case, the MRI was not able to rule out an abdominal or bladder wall defect due the fetal position (hip flexion); but a post mortem validated the original ultrasound result. The other urinary tract abnormalities relating to the kidney: multi-cystic dysplasia kidney (5); duplex (4); posterior valves (3); single cyst (2); and agenesis (1). In this case, the MRI was not able to rule out an abdominal or bladder wall defect due the fetal position (hip flexion); but a post mortem validated the original ultrasound result.

Table 4 shows the proportion confirmed by MRI for the most common types of CNS and thoracic abnormalities. In those with an ultrasound finding of corpus callosum agenesis or anomaly, the overall confirmation rate was low but it reached 100% in four cases with proven abnormality. In those with ultrasound finding of ventriculomegaly or a neural tube defect the confirmation rate was high. Among the thoracic abnormalities, the confirmation rate reached 100% for congenital cystic adenomatoid malformation.

Table 1. Characteristics of the 76 women referred for MRI because of an ultrasound abnormality.

Characteristic	Value
Pregnancy	
Maternal age:	
Median (IQR)	30 years (27–33 years)
≥35	12 (16%)
Nulliparous – number (%)	19 (25%)
IVF – number (%)	3 (3.9%)
Twins – number (%)	2 (2.6%)
Maternal weight – median (IQR)	67 kg (61–74 kg)
Tests	
Combined test – number (%):	
Done	73 (96%)
Positive	4 (5.5%)
Scan gestation – median (IQR)	144 days (142–156 days)

*Information missing for two women; IQR, inter-quartile range.

Table 2. Association between MRI results and outcome of pregnancy.

MRI finding	Outcome of pregnancy	Number (%)
Abnormality	Abnormality	48 (63%)
Abnormality	None	8 (10%)
Abnormality	N/A	5 (6.6%)
None	Abnormality	6 (7.9%)
None	None	6 (7.9%)
None	N/A	2 (2.6%)
Failed	None	1 (1.3%)

N/A, not available.

DISCUSSION

We have shown that overall MRI had good concordance with the ultrasound scan findings at 80%. MRI confirmed the ultrasound findings at a very high rate in those with proven abnormal outcome and relatively low if proven normal (89% and 40% respectively).

Table 3. MRI confirmation of an abnormality according to anatomical system of ultrasound abnormality.

Ultrasound abnormality	All	Proven outcome	
		Abnormal	Normal
Central nervous system	73% (24/33)	93% (14/15)	45% (5/11)
Urinary tract abnormality	94% (15/16)	94% (15/16)	–
Thoracic	73% (8/11)	67% (6/9)	100% (2/2)
Facial	100% (8/8)	100% (8/8)	–
Gastro-intestinal	60% (3/5)	67% (2/3)	50% (1/2)
More than one system	100% (3/3)	100% (3/3)	–

Table 4. MRI confirmation of an abnormality for common types of central nervous system and thoracic abnormalities on ultrasound.

Ultrasound abnormality	All	Proven outcome	
		Abnormal	Normal
Central nervous system			
Corpus callosum agenesis/anomaly	62% (8/15)	100% (4/4)	25% (1/4)
Ventriculomegaly	86% (6/7)	100% (3/3)	75% (3/4)
Neural tube defect	83% (5/6)	83% (5/6)	–
Thoracic			
Diaphragmatic hernia	67% (2/3)	67% (2/3)	–
CCAM	100% (3/3)	100% (3/3)	–

CCAM, Congenital cystic adenomatoid malformation,

The median maternal age, weight and proportion conceived using in-vitro fetilisation (IVF) were similar to those reported in a series of 1684 women with singleton pregnancies having combined tests at one of the centres[15]. The median age was 30 years in both series; median was 66 kg compared with 65 kg (ref.[15]); and the IVF rate was 3.9%, in both series, although the proportion of nulliparous pregnancies was lower – 25%, compared with 42% (ref.[15]).

The highest concordance was achieved in the urinary tract abnormalities, facial anomalies and those involving more than one system. The only discrepancy was the single case of bladder extrophy in the series, where the MRI was compromised by the fetal position.

CNS abnormalities were the most common indication for MRI and had a lower concordance but this varied according to the specific disorder. Ultrasound is not able to clearly describe disorders of the corpus callosum and MRI is of great importance in the evaluation, in contrast to neural tube defects. Among referrals because of ultrasound suspicion of ventriculomegaly both ultrasound and MRI findings may not, as in this series, be confirmed at postnatal examination. This may reflect the dynamic nature of ventriculomegaly in that mild or borderline cases can resolve by the time of the delivery. An important role of MRI in ventriculomegaly is the detection of additional CNS abnormalities in the foetus[2].

In 2006 a workshop was held by the Eunice Kennedy Shriver National Institute of Child Health and Human Development to summarize the available data on different fetal imaging technologies[3]. The workshop conclusion regarding MRI was that, compared with ultrasound, it could improve characterization of CNS abnormalities, particularly ventriculomegaly. Whilst there was insufficient data available for non-CNS defects the workshop suggested that for congenital diaphragmatic hernia MRI might be better than ultrasound at delineating the remaining normal lung.

In the following decade there were a large number of publications on the subject. Some studies compare the detection and false-positive rate using ultrasound and MRI in the same or a separate series of pregnancies. Others compare the findings within the same series in which the MRI was carried out because of abnormal or suspicious ultrasound findings. Systematic reviews with meta-analyses have been performed for specific disorders.

A systematic review summarized the findings on CNS defects[4]. In 13 publications there were a total of 710 fetuses with a CNS abnormality diagnosed or suspected by ultrasound and subsequently examined by MRI. The presence of such an abnormality was found in 464 (65%) by MRI; postnatal or postmortem examination confirmed the MRI result in 630 (89%). A specific systematic review of brain imaging in five studies found detection rates of 85% and 95% for ultrasound and MRI with false-positive rates of 23% and 20%, respectively[5].

Several studies have indicated that MRI performs better than ultrasound in the detection and assessment of facial clefts[6-10]. A systematic review of MRI alone included eight studies and a total of 334 fetuses[11]. The detection rate was 97% and false-positive rate 6%. A more recent systematic review comparing the two techniques confirms that MRI is a useful adjunct to ultrasound[12].

A systematic review of prenatal imaging and amniocentesis for esophageal atresia included twenty studies[13]. Eleven studies could be used to compute the detection

rate of ultrasound, which was low at 32% and in two of these studies, with detection rate 42%, the false-positive rate was very low at 0.1%. Among five studies that included MRI for women with suspicious ultrasound findings the detection rate was 95% and false-positive rate 11%.

Many of the prospective studies included in the systematic reviews, like our own, are biased in favour of MRI since knowledge of the ultrasound findings is available when carrying out the MRI and interpreting the results. To overcome this bias a blinded case-control study was carried out in 58 pregnancies with ultrasound anomalies and 90 gestation matched unaffected pregnancies[14]. The detection rates for 2D-ultrasound (3D-ultraound) compared with MRI were 86% (79%) and 84% and the false-positive rates 7.8% (5.6%) and 14%, respectively. The only statistically significant difference between ultrasound and MRI was for the lower false-positive rate of 3D (P<0.05); among the 18 cases with CNS disorders the detection rate for MRI, 89%, was higher than for 3D, 67%, a statistically significant difference (P<0.05).

Despite bias in favour of MRI when performed selectively because of abnormal or suspicious ultrasound findings, this is clinical practice. The practical question to be answered concerns the benefits and losses associated with contingent use of MRI rather than as a replacement for routine ultrasound. But this cannot be answered by meta-analysis since each centre is likely to select for MRI a different range of disorders depending on confidence in the ability to interpret the ultrasound findings alone.

The results of our study may be applicable in other centres which refer for MRI, as we have done, about one in six women with ultrasound abnormalities.

CONCLUSION

In women referred for MRI because of suspected anomaly following a routine second trimester scan, concordance with MRI results is very high. Concordance is particularly good for urinary tract and facial anomalies. Among CNS abnormalities, the most common indication for MRI in this series, concordance varied according to the specific disorder, being highest for ventriculomegaly and neural tube defects.

Author contributions: ID, HC, MG: participated in the creation of the text of the article almost equally and actively collaborated on all modifications; JH supplemented, according to their experience, the parts of the article concerning the collection of data and follow up of the patients; PH, KM, LBZ, JC provided the MR examination and supplemented, according to their experience, the parts of the article concerning the case analysis.
Conflicts of interest statement: None declared.

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Table S1. Detailed breakdown of the anomalies found at the mid-trimester scan, MRI findings and, where available, outcome.

Anomaly	MRI	Outcome	Source of outcome
Central nervous system			
Corpus callosum agenesis	Abnormality	Abnormality	Birth
Corpus callosum agenesis	Abnormality	Abnormality	Termination
Corpus callosum agenesis	Abnormality	Abnormality	Termination
Corpus callosum agenesis	Abnormality	Abnormality	Termination
Corpus callosum agenesis	Abnormality	None	Birth
Corpus callosum agenesis	Abnormality	N/A	–
Corpus callosum agenesis	Abnormality	N/A	–
Corpus callosum agenesis	None	None	Birth
Corpus callosum agenesis	None	None	Birth
Corpus callosum agenesis	None	None	Birth
Corpus callosum agenesis	None	N/A	–
Corpus callosum agenesis	None	N/A	–
Corpus callosum anomaly	Abnormality	N/A	–
Ventriculomegaly	Abnormality	Abnormality	Birth
Ventriculomegaly	Abnormality	Abnormality	Birth
Ventriculomegaly	Abnormality	Abnormality	Birth
Ventriculomegaly	Abnormality	None	Birth
Ventriculomegaly	Abnormality	None	Birth
Ventriculomegaly	Abnormality	None	Birth
Ventriculomegaly	None	None	Birth
Dandy-Walker syndrome	Abnormality	Abnormality	Birth
Dandy-Walker syndrome	Abnormality	N/A	–
Dandy-Walker syndrome	None	None	Birth
NTD: Meningomyelocoele	Abnormality	Abnormality	Birth
NTD	Abnormality	Abnormality	Termination
NTD	Abnormality	Abnormality	Termination
NTD: Lipomeningocele	Abnormality	Abnormality	Birth
NTD: Lipomeningocele	None	Abnormality	Birth
NTD: Encephalocele in twin	Abnormality	Abnormality	Termination
Arachnoid cyst	Abnormality	Abnormality	Birth
Arachnoid cyst	Abnormality	N/A	–
Choroid plexus cyst	Abnormality	None	Birth
Choroid plexus cyst	None	None	Birth
Urinary tract abnormality			
Multi-cystic dysplastic kidney	Abnormality	Abnormality	Birth
Multi-cystic dysplastic kidney	Abnormality	Abnormality	Birth
Multi-cystic dysplastic kidney	Abnormality	Abnormality	Birth
Multi-cystic dysplastic kidney	Abnormality	Abnormality	Birth
Multi-cystic dysplastic kidney	Abnormality	Abnormality	Termination
Duplex kidney, hydronephrosis	Abnormality	Abnormality	Birth
Duplex kidney, hydronephrosis	Abnormality	Abnormality	Birth
Duplex kidney, hydronephrosis	Abnormality	Abnormality	Birth
Duplex kidney, hydronephrosis	Abnormality	Abnormality	Birth
Posterior urethral valve stenosis	Abnormality	Abnormality	Birth
Posterior urethral valve stenosis	Abnormality	Abnormality	Birth
Posterior urethral valve stenosis	Abnormality	Abnormality	Birth
Kidney cysts	Abnormality	Abnormality	Birth
Kidney cysts	Abnormality	Abnormality	Birth
Kidney agenesis	Abnormality	Abnormality	Termination
Bladder extrophy	None	Abnormality	Termination

Table S1. *(Continued)*

Anomaly	MRI	Outcome	Source of outcome
Thoracic			
Diaphragmatic hernia	Abnormality	Abnormality	Birth
Diaphragmatic hernia	Abnormality	Abnormality	Termination
Diaphragmatic hernia	None	Abnormality	Termination
CCAM	Abnormality	Abnormality	Birth
CCAM	Abnormality	Abnormality	Birth
CCAM in twin	Abnormality	Abnormality	Selective feticide
Lung sequestration	Abnormality	Abnormality	Birth
Lung sequestration	Abnormality	None	Birth
Situs inversus	None	Abnormality	Birth
Situs inversus	None	Abnormality	Birth
Heart defect	Abnormality	None	Birth
Facial			
Cleft lip/palate	Abnormality	Abnormality	Birth
Cleft lip/palate	Abnormality	Abnormality	Birth
Cleft lip/palate	Abnormality	Abnormality	Birth
Cleft lip/palate	Abnormality	Abnormality	Termination
Cleft lip/palate	Abnormality	Abnormality	Termination
Cleft lip/palate	Abnormality	Abnormality	Termination
Cleft lip/palate	Abnormality	Abnormality	Termination
Cleft lip/palate	Abnormality	Abnormality	Termination
Gastro-intestinal			
Agastria	Abnormality	Abnormality	Birth
Duodenal stenosis	Abnormality	Abnormality	Birth
Esophageal atresia	Failed	None	Birth
Pelvic cyst	Abnormality	None	Birth
Rectal stenosis	None	Abnormality	Birth
Other			
More than one system	Abnormality	Abnormality	Termination
More than one system	Abnormality	Abnormality	Termination
More than one system	Abnormality	Abnormality	Termination

N/A, not available; NTD, neural tube defect; CCAM, Congenital cystic adenomatoid malformation.