

## Evaluation of fetal MRI in a South African referral centre

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**Background.** The Department of Radiology at Groote Schuur Hospital, Cape Town, South Africa, has been performing fetal magnetic resonance imaging (MRI) since 2007. Fetal MRI findings have not previously been analysed to correlate them with antenatal and postnatal findings.

**Objectives.** To determine the most common indication for fetal MRI, and to correlate antenatal MRI with antenatal ultrasound (US), postnatal imaging and postmortem findings.

**Methods.** This was a retrospective study of imaging carried out between January 2006 and December 2011. Seventy fetal MRI cases with complete antenatal and postnatal medical records were included. Antenatal US and antenatal MRI were compared, and also compared with the postnatal imaging findings. Stata 12 was used to analyse the data, and Spearman's test to test the agreement between the results.

**Results.** Intracranial pathology was the most common indication for fetal MRI, with ventriculomegaly being the commonest indication determined from prenatal US. There was 72% agreement between antenatal US and fetal MRI. Postnatal findings showed 28% agreement with antenatal US and 39% agreement with fetal MRI.

**Conclusions.** Intracranial pathology was the major indication for fetal MRI. There was good agreement between prenatal US and fetal MRI but poor agreement between antenatal and postnatal findings, largely as a result of resolution of ventriculomegaly.

*S Afr Med J* 2015;105(11):930-933. DOI:10.7196/SAMJ.2015.v105i11.9415



A number of studies have shown the supremacy of magnetic resonance imaging (MRI) over ultrasound (US) in fetal imaging.<sup>[1-3]</sup> Use of this technique has yet to be reported from developing countries, where prenatal care and resources may be limited. Locally the accuracy of prenatal US has yet to be determined against MRI, and the success of limited-sequence fetal MRI in predicting fetal pathology has not yet been reported from a South African (SA) or sub-Saharan African institution. No substantial fetal MRI series has been reported from Africa, and only a few cases<sup>[4]</sup> have been reported from other institutions in SA.

This study reviews prenatal and postnatal MRI performed at Groote Schuur Hospital (GSH), Cape Town, SA, over the 6-year period 2006 - 2011.

### Objective

To determine the current indications for fetal MRI, and the degree of agreement between antenatal MRI and antenatal US, postnatal imaging and postmortem findings in one SA referral centre.

### Methods

This was a longitudinal retrospective observational study of fetal MRI performed at GSH. All fetal MRI scans done from 1 January 2006 to 31 December 2011 were included. Those without prenatal US or postnatal information pertinent to the imaging findings and final diagnosis were excluded.

Patient records were accessed after approval from the Human Research Ethics Committee of the University of Cape (approval number: 507/2009). Records included patient clinical notes, antenatal US reports, fetal and postnatal MRI images and reports and, where applicable, postmortem reports.

All prenatal fetal MRI scans were performed on a Siemens Symphony 1.5 Tesla MRI scanner with a 'short protocol' using the fast imaging with steady-state precession (FISP) sequence (TR = 4.3 and TE = 2.2). Where there was a neurological indication, scans were obtained routinely in three planes centred on the fetal head and/or spinal column. In the event of a non-neurological indication, imaging was centred in three planes over the relevant anatomical region.

Maternal demographic data, including HIV and VDRL status, were obtained from the clinical records.

Antenatal US reports accessed from the fetal and maternal unit database formed the basis for referral for MRI, which may have resulted in positive or negative bias in fetal MRI reporting.

Any diagnostic discrepancies between the US and MRI reports prompted review of the MRI scans, in particular with regard to measurement of the ventricles in cases of suspected hydrocephalus.

Abnormalities were broadly categorised into neurological and non-neurological. Ventriculomegaly was defined as a lateral atrial (trigonal) diameter of  $\geq 10$  mm and was categorised as mild (10 - 12 mm), moderate (13 - 15 mm) and severe ( $>16$  mm).

Spearman's correlation test was used to test the agreement between the antenatal US and fetal MRI, and the postnatal findings (clinical, imaging (CT or MRI) or postmortem).

### Results

Seventy-three patients who had undergone fetal MRI were identified. Documentation was not available in three patients, and these were excluded from the study. A total of 70 patients met the inclusion and exclusion criteria. The mean maternal age of the study population was 27.6 years (range 17 - 43), and the mean gestational age was 29.3 weeks (range 16 - 38) at the time of first antenatal US examination.

The mean gestational age at time of fetal MRI was 34 weeks (range 31 - 37). The mean interval between antenatal US and MRI was 4.7 weeks.

One patient had cytomegalovirus (CMV) infection, and two patients were VDRL-positive. Two fetuses had chromosomal abnormalities confirmed on genetic karyotyping, one Klinefelter syndrome and the other Patau syndrome.

There were 12 (17.1%) fetal/neonatal deaths, including three (4.2%) in which the pregnancy was terminated. In five (7.1%) of these cases, a postmortem examination was conducted.

**Prenatal ultrasound findings**

The majority of referrals (54/70, 77.1%) for fetal MRI were for intracranial pathology detected at US. Of these, 32/54 (59.2%) were for hydrocephalus/ventriculomegaly and 9/54 (16.6%) for suspected Dandy-Walker malformation. Other neurological indications included 'cysts', 'corpus callosus agenesis' and 'holoprosencephaly'.

**Fetal MRI findings (n=70)**

Ten (14.3) of the antenatal MRI scans were normal. Hydrocephalus/ventriculomegaly was confirmed on fetal MRI in 25 cases. This represents 35.7% of the total number of fetal MRI scans and 78.1% of those referred for suspected ventriculomegaly on antenatal US. The fetal MRI findings are summarised in Fig. 1.

**Additional information on fetal MRI**

Of the 70 cases reviewed, seven (10.0%) had additional findings on MRI (Fig. 2). Six of these (8.6%) were found to have corpus callosus agenesis (Fig. 3), and one had a Chiari II malformation associated with a myelomeningocele. All seven had been referred for MRI with ventriculomegaly diagnosed on US.

**Ventriculomegaly**

Of the 32 cases referred with an US diagnosis of ventriculomegaly, 25 were confirmed on MRI. Twenty-two (68.7%) involved both lateral ventricles, nine (28.1%) were unilateral and one involved the third ventricle and both lateral ventricles.

Seven cases of ventriculomegaly (21.8%) had resolved spontaneously at follow-up antenatal US. In these patients the mean gestational age at antenatal US was 31 weeks (range 20 - 33). The mean ventricular size was 11 mm (mild ventriculomegaly). Six cases had a ventricular size of 11 mm and one 12 mm. None of the cases that resolved spontaneously had associated fetal anomalies.

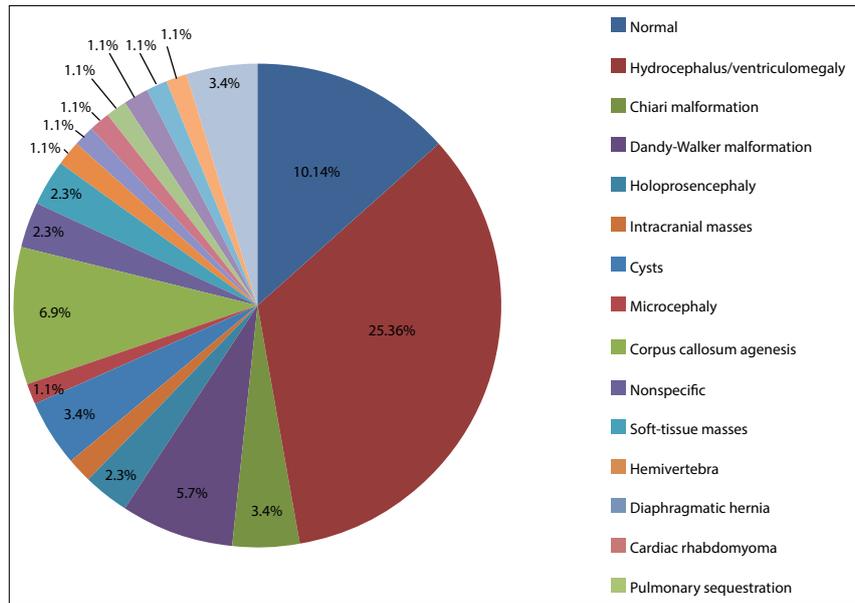


Fig. 1. Fetal MRI findings overall.

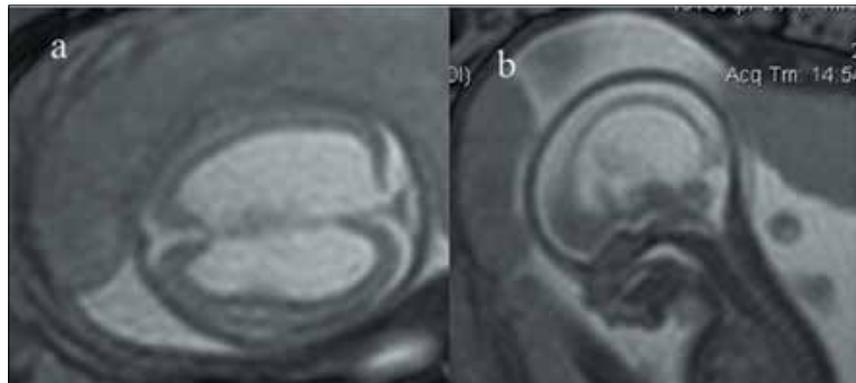


Fig. 2, a and b. FFE T2-weighted fetal MRI scans in (a) axial and (b) sagittal planes, demonstrating severe ventriculomegaly at 26 weeks' gestation. Corpus callosus agenesis was difficult to identify in this case, but was diagnosed on postnatal imaging.

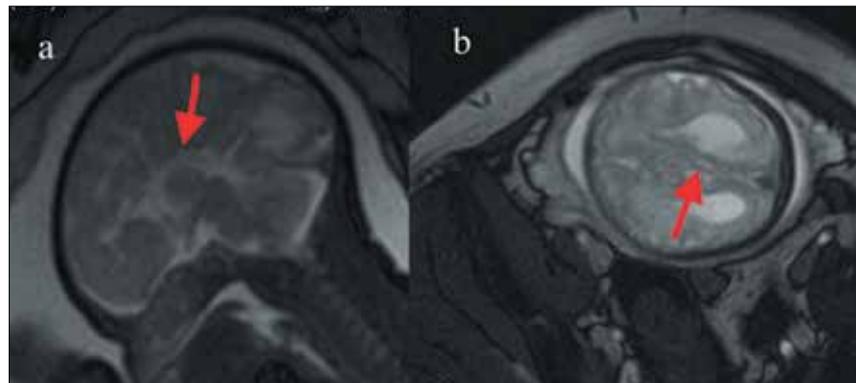


Fig. 3, a and b. FFE T2-weighted fetal MRI scan of corpus callosus agenesis (arrows) at 32 weeks' gestation, referred due to ventriculomegaly at antenatal US.

Of the twenty-two cases (68.7%) with persistent antenatal ventriculomegaly, 25.0% (8/32) had unexplained ventriculomegaly, 18.7% (6/32) had corpus callosus agenesis and 9.3% (3/32) had Chiari malformations. Two of these were

of the Chiari II variety with lumbosacral cutaneous defect, meningocele, ventriculomegaly and small posterior fossa with vermian descent. One had a Chiari III malformation with an occipital encephalocele, a small crowded posterior fossa and

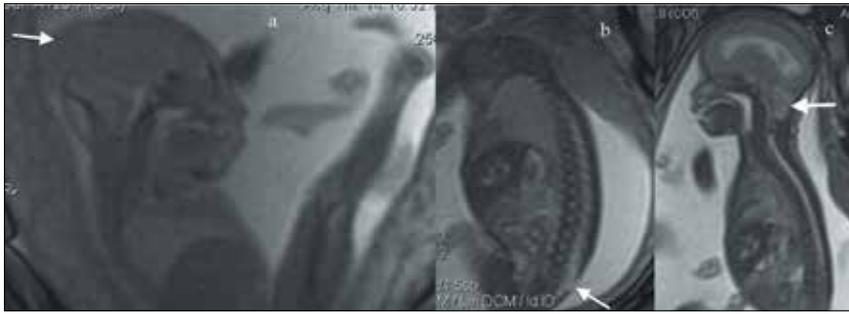


Fig. 4, a - c. Chiari malformations demonstrated with fetal MRI. (a) FFE T2-weighted fetal MRI (sagittal images) demonstrating a Chiari III malformation with occipital encephalocele (arrow) at 24 weeks' gestation. (b and c) FFE T2-weighted fetal MRI scan at 23 weeks' gestation – sagittal images demonstrating Chiari II malformation (note spinal defect, arrow) and crowding of the posterior fossa structures.

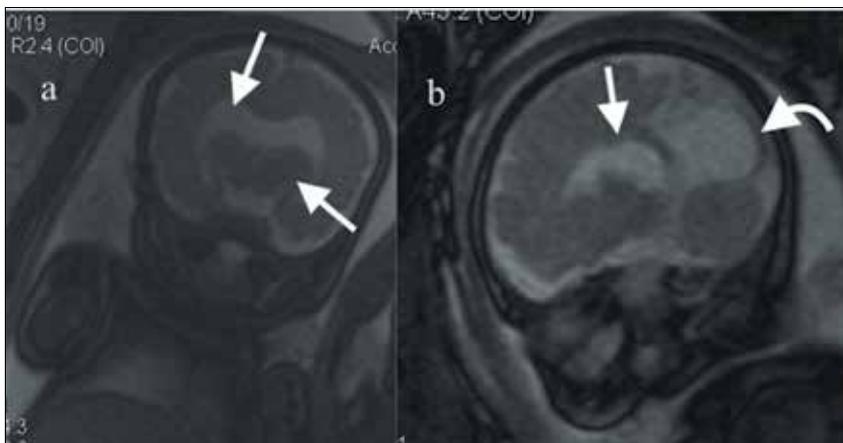


Fig. 5, a and b. FFE T2-weighted fetal MRI scan at 32 weeks' gestation demonstrating semilobar holoprosencephaly in a patient with Patau syndrome. (a) coronal image demonstrates that the thalami are partially fused and a monoventricle (arrows). The anterior horns of both lateral ventricles are absent. There is absence of the rostrum and genu of the corpus callosum, with only the posterior aspect of body and splenium present. (b) Sagittal scan demonstrates a characteristic large posterior cyst (curved arrow).

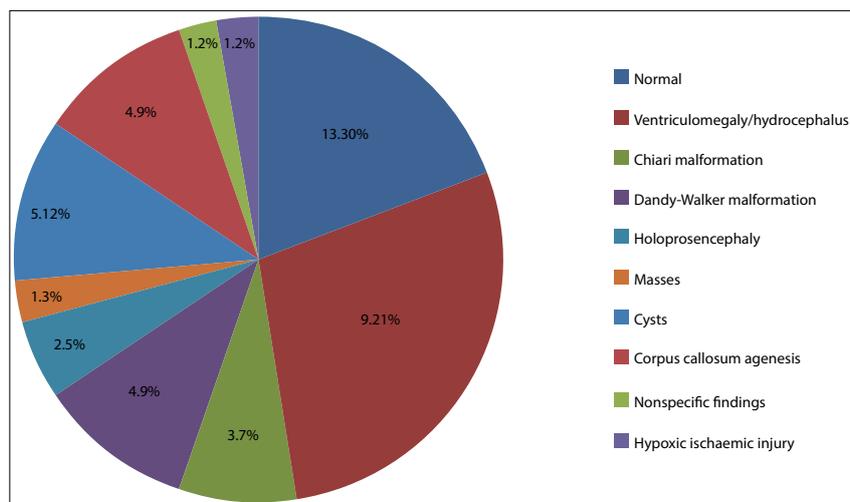


Fig. 6. Neurological postnatal findings.

ventriculomegaly (Fig. 4). This abnormality had not been detected on antenatal US. Two cases of semilobar holoprosencephaly (Fig. 5) were confirmed among those with ventriculomegaly.

**Non-neurological fetal MRI indications and findings**

Non-neurological indications for MRI were identified in 16 cases. Four fetuses had congenital diaphragmatic hernias (one right sided and three

left sided). Two cases had soft-tissue masses, of which one had Klippel-Trenaunay-Weber syndrome and the other a facial teratoma, both diagnosed antenatally. Other abnormalities were pulmonary sequestrations ( $n=2$ ), hemivertebra ( $n=2$ ), bronchogenic cyst ( $n=1$ ), haemangioma ( $n=1$ ), duodenal atresia ( $n=1$ ) and ventricular rhabdomyoma ( $n=1$ ).

**Postnatal findings: Clinical, imaging and postmortem**

Hydrocephalus/ventriculomegaly was the most common finding on postnatal CT or MRI. The neurological postnatal imaging findings are graphically presented in Fig. 6.

Postmortem examinations demonstrated an arachnoid cyst, corpus callosum agenesis and left diaphragmatic hernia. No post-mortem confirmation was possible in two fetuses that died *in utero*. One of these had a severe Dandy-Walker malformation, and the pregnancy was terminated medically.

**Maternal diagnosis and imaging findings**

Two mothers had positive serological tests for syphilis. The fetal anomalies found in these cases were Chiari II malformation and Klippel-Trenaunay-Weber syndrome.

Fetal chromosome testing confirmed trisomy 13 (Patau syndrome) in one of the cases of holoprosencephaly and a 47,XXY karyotype (Klinefelter's syndrome) in one of the cases referred for ventriculomegaly.

**Statistical analysis**

Our study demonstrated significant agreement between antenatal US and fetal MRI, with a Spearman's correlation coefficient of 0.7246 ( $p<0.0001$ ). However, correlation between antenatal US and postnatal findings was lower, with a ratio of 0.2817 ( $p=0.02$ ) and a correlation coefficient of 0.3879 ( $p<0.001$ ) between the fetal MRI and postnatal findings. These findings are summarised in Table 1.

**Discussion**

GSH is fortunate in having a team of dedicated and experienced fetal ultrasonographers. Maternal size, the presence of polyhydramnios and fetal position may reduce the reliability of US examination. Furthermore, limited access to MRI in our resource-restricted environment may have resulted in delay between antenatal US and MRI, which could have affected correlation either positively or negatively.

**Agreement between fetal MRI and antenatal US**

Our results demonstrate a reasonably high agreement (72%; Spearman's  $\rho=0.7246$ )

**Table 1. Statistical correlation between antenatal imaging findings and postnatal findings**

Agreement categories	Spearman's correlation coefficient
Antenatal ultrasound/fetal MRI	0.7246; $p < 0.0001$
Antenatal ultrasound/postnatal findings	0.2817; $p < 0.02$
Fetal MRI/postnatal findings	0.3879; $p < 0.01$

between fetal MRI and antenatal US, although this is lower than the agreement of 83% reported by Griffiths *et al.*<sup>[5]</sup> MRI revealed additional brain anomalies not seen on US more commonly in our study than did the Griffiths study (29% v. 17%). We speculate that these discrepancies may be attributable to reduced US sensitivity associated with late antenatal booking in our setting, the mean gestational age at first US being 29.3 weeks. Resolution of mild ventriculomegaly without associated major anatomical brain abnormality, a well-described phenomenon,<sup>[6]</sup> occurred in just under a third of cases in our study.

Gaglioti *et al.*<sup>[7]</sup> demonstrated a positive correlation between degree of ventriculomegaly and rate of morbidity and mortality. These authors recommended fetal MRI on all suspected cases of ventriculomegaly to exclude other anomalies, especially in those with moderate to severe ventriculomegaly.

### Agreement between antenatal imaging and postnatal findings

There was a low agreement of 28% (Spearman's  $\rho = 0.2817$ ) between antenatal US and postnatal findings, with 14% of studies reported as normal postnatally. A somewhat higher agreement of 39% (Spearman's  $\rho = 0.3879$ ) was found between fetal antenatal MRI and postnatal findings. In a study of 100 patients, Dhoubib *et al.*<sup>[8]</sup> showed an 85% agreement when they compared antenatal and postnatal MRI brain findings. Objective measures of the degree of hydrocephalus necessitate close follow-up with trigonal measurements in the identical plane. Late gestation, maternal obesity and technical challenges may pose challenges to attaining good diagnostic imaging and could explain our lack of correlation.

Few centres in Africa, even where MRI is available, appear to perform fetal MRI. The reasons for this may reflect lack of

skills and resources. They may also include a fatalistic attitude on the parts of both patient and clinician, combined with the belief that late termination is not possible even in the setting of a very severe/lethal fetal condition.

One patient in our population with ventriculomegaly was diagnosed with CMV infection postnatally. The typical findings of periventricular calcification, migrational disorder, cerebral volume loss and white matter abnormalities seen in congenital CMV infection<sup>[9]</sup> may be impossible to diagnose on the fast T2 images acquired in antenatal MRI.

Chiari II malformation and Klippel-Trenaunay-Weber syndrome, found in the fetuses of two VDRL-positive patients, are not known to be associated with congenital syphilis and were therefore considered unrelated. Ventriculomegaly found in a fetus with Klinefelter syndrome (47,XXY) was also considered to be coincidental.

Holoprosencephaly was an expected finding in the fetus diagnosed with Patau syndrome (trisomy 13), although the other associated anomalies (such as polydactyly, flexion of the fingers, heart defects, facial clefting and neural tube defects<sup>[10]</sup>) were not identified.

### Conclusions

The most common indications for fetal MRI in this SA referral centre were for intracranial pathology. In the majority of cases, these scans followed detection of ventriculomegaly at prenatal US. Our study confirms the value of antenatal US as a screening tool for the assessment of ventricular size. It further confirms the complementary role of fetal MRI in assessing callosal integrity and size and anatomical detail of the contents of the posterior fossa, particularly in the setting of more readily diagnosable ventriculomegaly. Confirmation of these abnormalities allows

refinement of genetic counselling with respect to fetal outcome.

Agreement between antenatal US and fetal MRI in our setting is comparable to that reported in other centres. The poor correlation between the prenatal and postnatal findings largely results from resolution of ventriculomegaly. However, issues such as achieving earlier booking of patients and capacitation of US services to permit routine scans for all pregnant women need to be addressed. We recommend interdisciplinary review of all imaging with discussion in every case. Further prospective research with neurological and developmental follow-up of these cases would be helpful in determining the implications of the antenatal findings, particularly in the setting of late gestational presentation. 3 Tesla MRI and double reading may also improve sensitivity and specificity of future interpretation of both antenatal modalities.

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Accepted 5 October 2015.