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**A Review Of Antenatal MR Imaging And Correlation With Antenatal Ultrasound,  
Postnatal Imaging And Post Mortem Findings**

**A Thesis Submitted to the Faculty of Health Sciences, University of Cape Town in  
Fulfilment of the Requirements for the degree of Master of Medicine in Radiology**

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## **Dedication**

This work is dedicated to my late mother, Rexa Nkhambule Kumwenda. She passed away while I was about to write my final fellowship exams.

'I love you mum and will always do'.

I further dedicate this work to my family (my wife Judith, daughter Michelle and my son Ian) for tolerating my busy schedule.

University of Cape Town

## DECLARATION

I, *Arthur Daire* hereby declare that the work on which this dissertation/thesis is based is my original work (except where acknowledgements indicate otherwise) and that neither the whole work nor any part of it has been, is being, or is to be submitted for another degree in this or any other university.

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## **ABSTRACT:**

### **OBJECTIVES:**

To determine the most common indication for foetal MRI, and to correlate ante-natal MRI with ante-natal ultrasound, post-natal imaging and post mortem findings

### **METHODS:**

This was a retrospective study of imaging between January 2006 and December 2011. Seventy foetal MRI cases with complete medical records (antenatal and postnatal) were included in the study. Antenatal ultrasound and antenatal MR imaging was compared and also compared with the postnatal imaging findings. Stata 12 was used to analyse the Data. Spearman's test was used to test the agreement between the results.

### **RESULTS:**

Intracranial pathology was the most common indication for foetal MRI, with ventriculomegaly being the commonest indication determined from prenatal ultrasound. There was 72% agreement between antenatal ultrasound and foetal MRI. Post-natal findings showed 28% agreement with antenatal ultrasound and 39% agreement with foetal MRI.

### **CONCLUSION:**

Intracranial pathology was the major indication for foetal MRI. The study found good agreement between prenatal ultrasound and foetal MRI but poor agreement between antenatal and postnatal findings.

## 1. INTRODUCTION AND LITERATURE REVIEW

Ultrasonography has been the primary imaging modality for foetal imaging since the late 50's and early 60's<sup>1</sup>. Prior to modern ultrasound, other imaging modalities included plain radiography of the maternal abdomen and amniography, both using ionising radiation and the latter being invasive in nature<sup>2</sup>. Ultrasound technique became the primary modality because it is free of ionising radiation (and therefore safe for the foetus), relatively cheap, widely available and has proven utility. However it is limited by the small field of view, limited visualisation of the posterior fossa in late gestation (after 33 weeks) because of ossification of calvarium, attenuation of the beam by maternal adipose tissue, limited soft-tissue contrast and because it is user dependent<sup>3</sup>.

Foetal magnetic resonance imaging (MRI) has come to play a role as an adjunct to sonography. MRI does not use ionising radiation, has high spatial resolution with excellent tissue contrast, allows multiplanar views, and has a wide field of view which allows analysis of complex multi-organ, foetal pathologies. Assessment of foetal position, anatomy of umbilical cord, amount of amniotic fluid, maternal uterus, ovaries and birth canal can also be performed at the same sitting<sup>4</sup>.

The safety of MR imaging in pregnancy has not been proven, however there are no known biological risks<sup>5,6</sup>. Despite this, it is recommended by the International Society of Magnetic Resonance in Medicine that foetal MRI should not be performed before the second trimester of gestation<sup>7</sup>. Where there is suspicion of a significant or life-threatening abnormality the potential diagnostic benefit of foetal MRI outweighs the negligible hazards<sup>8</sup>.

The initial challenge in foetal MRI using long acquisition techniques was intrauterine foetal motion requiring maternal sedation. However the development of fast MR imaging techniques has made the process of data acquisition short, and this has eliminated the need for sedation<sup>9</sup>. Steady-state sequences are used to achieve this with the advantage of shorter imaging times, achieved due to the short repetition times in these<sup>10</sup>.

A number of studies have shown the supremacy of MRI over ultrasound in foetal imaging: Hubbart et al<sup>11</sup> demonstrated that one can make incorrect diagnoses with ultrasound on assessment of chest masses. Danzer et al<sup>12</sup> demonstrated that MRI is better than ultrasound in assessment of intrapelvic and abdominal extent of sacrococcygeal teratoma and the mass effect of the tumour on adjacent organs. MR has also been shown to be superior to ultrasound for the assessment of corpus callosum agenesis. In a study by Mirza et al<sup>13</sup> about a third of suspected cases of complete or partial agenesis of corpus callosum on prenatal ultrasound showed a normal brain anatomy on foetal MRI. Moreover, MRI is better in depicting the posterior fossa than ultrasound, late in gestational age,<sup>14</sup> because the calvarium is more ossified at that stage, obstructing the ultrasound beam. Pistorius et al<sup>15</sup> have drawn up a list of recommendations for foetal imaging reproduced as Appendix 1.

In our Tertiary Academic centre at Groote Schuur Hospital, in the Western Cape of South Africa, a dedicated program is in place including the surrounding Maternity and Obstetric Units (MOUs), whereby patients with foetal anomalies are identified during routine antenatal ultrasound scans and referred to our Foetal and Maternity unit (FMU) for further assessment (sonography, genetic counselling and amniocentesis). In the FMU, patients are rescanned by dedicated specialist

obstetricians to confirm the suspected foetal anomaly and upon their recommendation, a referral is made to radiology for foetal MRI. All patients that are admitted to the Foetal and Maternal Unit undergo routine counselling for amniocentesis. Other patients are counselled regarding fetocide depending on the foetal anomaly that may be identified.

This study, reviews pre-natal and post-natal MR imaging performed at Groote Schuur Hospital (GSH) for the period spanning January 2006 till December 2011 (a 72-month-period).

## 2. Aim and Specific Objectives of the Study

### 2.1 Aim

To determine the most common indication for foetal MRI, and to determine agreement between ante-natal MRI and ante-natal ultrasound, post-natal imaging and post mortem findings

### 2.2 Specific Objectives

To determine the range of and commonest indications for foetal MRI based on request cards

To describe the range of foetal abnormalities detected on antenatal ultrasound and MRI

To determine agreement between the foetal MRI findings and the antenatal ultrasound findings

To determine agreement between antenatal imaging findings and post natal clinical, imaging or post-mortem findings.

## 3 Materials and Methods

This study is a longitudinal **retrospective observational study**.

Database: Foetal MRI performed at GSH

Inclusion criteria: all foetal MRI from Jan 2006 till December 2011

Exclusion criteria: Those without prenatal ultrasound or postnatal information e.g. request cards, reports or other documents pertinent to the imaging findings and final diagnosis.

Patient's records were accessed after permission from the Groote Schuur Hospital Superintendent, Red Cross Children's Hospital and University of Cape Town ethical committee [Approval number: 507/2009]. These records included patient folders, antenatal ultrasound reports, foetal MRI images and reports and post natal imaging and/or clinical findings. Where applicable, post-mortem reports were reviewed. The study period spanned 6 years from January 2006 till December 2011 (a 72-month-period)

All Prenatal foetal MRI cases were scanned on a Siemens Symphony 1.5 Tesla MRI scanner at Groote Schuur Hospital, Division of Radiology. Fast Imaging with Steady State Precession (FISP) sequence, (TR=4.3 and TE=2.2) images were acquired in 3 planes routinely.

Patient information was retrieved from the maternal folders and included HIV status, VDRL status, CMV infection and any recorded syndromes.

All the antenatal ultrasound reports were accessed from the foetal and maternal unit ultrasound database. Ultrasound images are not stored on this database and only the reports could be evaluated. Because these ultrasound reports formed the basis for referral to MRI, the MRI readings were not blinded and in fact may have been biased positively or negatively as the indication for foetal MRI was read off from the request forms.

The foetal MRI reports were reviewed by the primary investigator, in conjunction with a neuroradiologist, who was also not blinded to the antenatal ultrasound findings. Any discrepancies between the reports of the two modalities prompted review of the MRI scans in particular with regard to measurement of the ventricles in suspected hydrocephalus. Ventriculomegaly was defined as lateral atria (trigone) diameter of 10mm or more on ultrasound, and is categorised as mild (10-12mm), moderate (13-15mm) and severe (>16mm).

Abnormalities were broadly categorised into neurological and non-neurological.

Data was entered into Microsoft Excel 2010. Stata 12 was used to analyse the data. An arbitrary diagnosis code was created for each diagnosis to facilitate analysis in Stata 12.

Spearman's correlation test was used to test the agreement between the antenatal ultrasound and foetal MRI, and the post-natal findings (Clinical, imaging or post-mortem).

### **3.1 Consent**

The UCT research ethics committee approved the study. [Approval number: 507/2009].

## **4 Results**

73 patients had foetal MRIs. Documentation was not available in 3 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 (range =17-43, standard deviation =6.242), with a mean gestation age of 29.25 weeks, range =16-38, at the time of 1<sup>st</sup> antenatal ultrasound.

The prevalence rate of HIV in the study population was 20%. One patient had Cytomegalovirus (CMV) infection. 2 patients were VDRL positive. Two patients had diagnosed syndromes, one with Klinefelter and the other with Patau syndrome.

### **4.1 Deaths**

There were 12 (17%) foetal / neonatal deaths. Of these, 9 (13%) were neonatal deaths and 3 (4%) were fetocide. 6 (8%) cases underwent post-mortem and 1 case had post-surgical histological confirmation of the diagnosis post-natally.

## 4.2 Foetal MRI Indications / Pre-natal Ultrasound findings

The most common indications for foetal MRI were: intracranial pathology (78%), with hydrocephalus/ventriculomegaly (44%) being the most common, followed by Dandy-Walker malformation (13%). Other conditions included cysts, corpus callosum agenesis and holoprosencephaly. These are summarised in tables 1a and 1b.

**Table 3a: neurological prenatal Ultrasound findings**

Neurological prenatal US findings	N	%
Hydrocephalus/ventriculomegaly	32	46
Dandy walker malformation	9	13
Cysts	4	5
Corpus callosum agenesis	3	4
Holoprosencephaly	2	3
Chiari malformation	1	1.4
Intracranial Masses	1	1.4
Encephalocele	1	1.4
Microcephaly	1	1.4
Total	54	76.6

**Table 1b: Non-neurological Pre-natal Ultrasound findings**

Non-neurological Pre-natal Ultrasound findings	n	%
Diaphragmatic hernia	4	6
Cardiac anomalies	1	1.4
Pulmonary sequestration	2	3
Soft tissue masses	2	3
Non specific	2	3
Hemi-vertebra	1	1.4
duodenal atresia	1	1.4

bronchogenic cyst	1	1.4
Teratoma	1	1.4
multiple anomalies	1	1.4
Total	16	23.4

### 4.3 Foetal MRI Findings

14% (n=10) of the foetal MRI scans were normal. Hydrocephalus/ ventriculomegaly was again the commonest finding at 36% (n=25). Figure 1 below summarises these findings

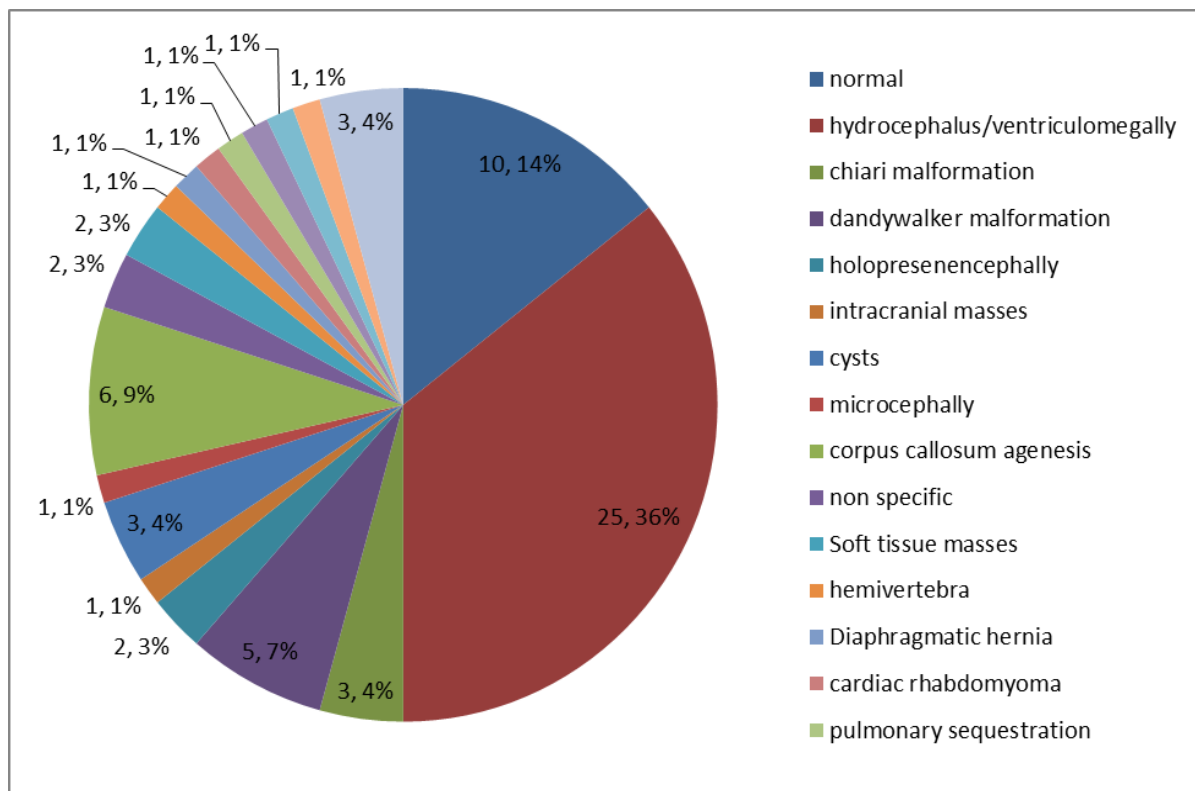
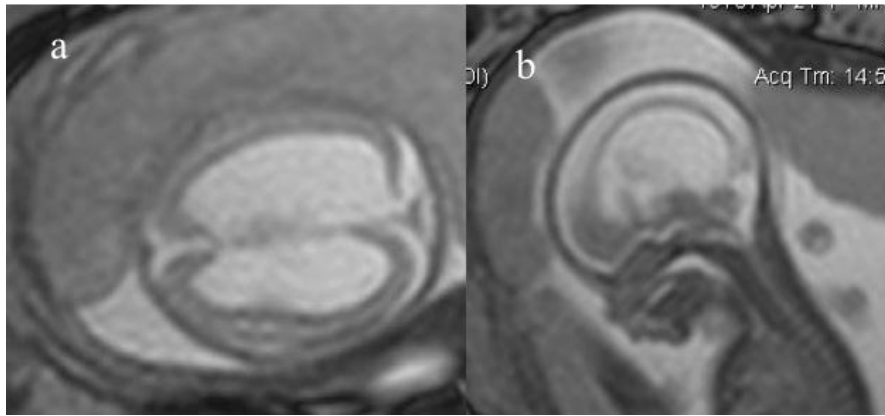


Figure 1: Foetal MRI findings - Overall

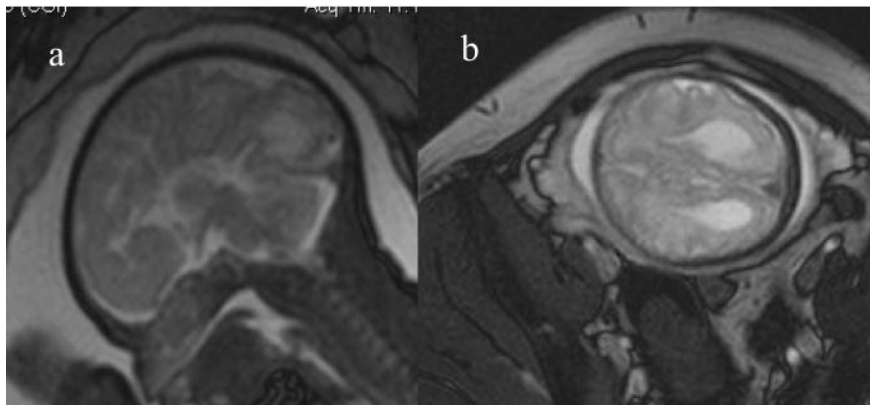
### 4.4 Neurological Findings:

#### 4.4.1 Cases Where Additional Information Was Obtained On Foetal MRI

There were 7 cases in which additional findings were found on MRI. These cases all had ventriculomegaly as the indication for MRI (figure 2 a and b). Six of these cases (8%) were found to have corpus callosum agenesis (figure 3 a and b) in addition to the ventriculomegaly and 1 case had a Chiari II malformation associated with a spinal myelomeningocele.



**Figure 2a and b** FFE T2 weighted foetal MRI in (a) axial and (b) sagittal planes demonstrating severe ventriculomegaly at 26 weeks gestation. Corpus callosum agenesis was difficult to identify in this case, but was diagnosed on postnatal imaging.



**Figure 3a and b:** FFE T2 weighted foetal MRI of Corpus callosum (CC) agenesis at 32 weeks gestation and referred due to ventriculomegaly at antenatal ultrasound.

Sagittal image demonstrates vertically radiating gyri in keeping with absence of inversion of the cingulate gyrus - a sign of CC agenesis

Axial image demonstrates colpocephaly and widely separated ventricles.

#### **4.4.2 Ventriculomegaly**

Of the 32 cases referred with ventriculomegaly from antenatal ultrasound, all were confirmed on foetal MRI. The average gestation age at time of foetal MRI was 34 weeks (range 31-37 weeks).

69% (n=22) were bilateral.

28% (n=9) were unilateral

3% (n=1) were trilateral (3<sup>rd</sup> and lateral ventricles)

Ten of these cases (31%) resolved spontaneously on follow up antenatal ultrasound. Of these:

The average gestation age at time of antenatal ultrasound was 31weeks (range 20-33 weeks). The average ventricular size was 12mm (mild ventriculomegaly).

Six cases had a ventricular size of 11mm, two had a ventricular size of 12 mm, one case had a ventricular size of 13 mm and 1 case had a ventricular size of 16 mm. None of the cases that resolved spontaneously had associated foetal anomalies.

Of the twenty-two cases (69%) with persistent ventriculomegaly:

25% (8/32) had unexplained ventriculomegaly

18% (6/32) had corpus callosum agenesis

9% (3/32) had Chiari malformations. Two of these were Chiari II malformation (both cases with lumbo-sacral cutaneous defect with a small overlying meningocele, ventriculomegaly and a small posterior fossa with vermian decent) and one was Chiari III malformation (with occipital encephalocele, small crowded posterior fossa, ventriculomegaly) (figure 4 a and b). (2 of these were missed on antenatal ultrasound)

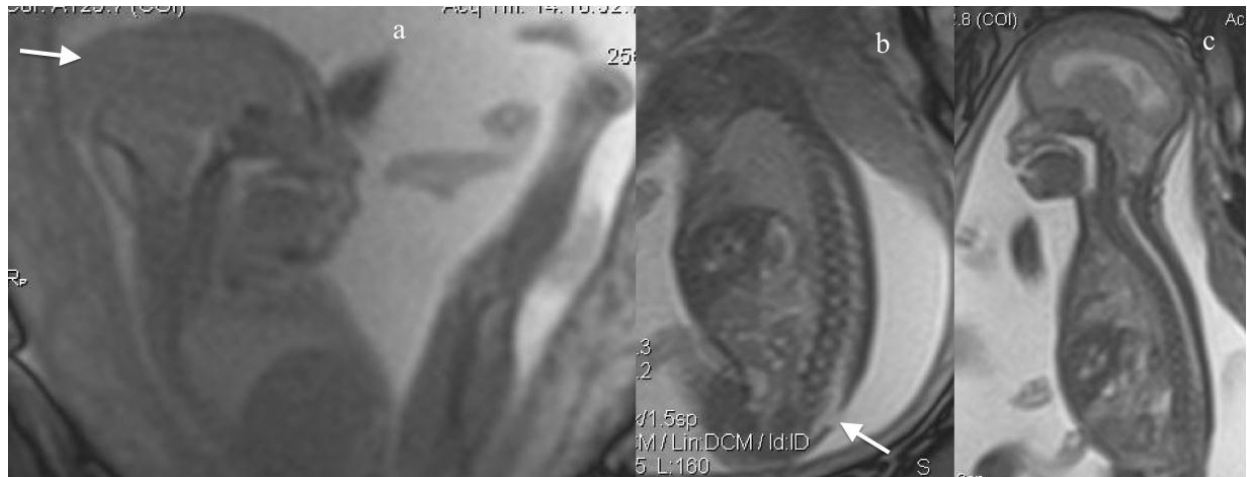
6% ( 2/32) had semi-lobar holoprosencephaly (figure 5 a and b below)

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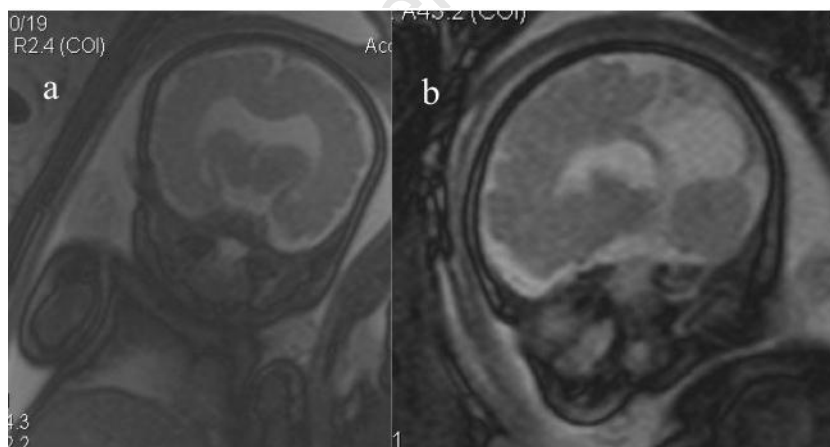
**Figure 4a-c: Chiari Malformation demonstrated with foetal MRI**

FFE T2 weighted Foetal MRI (sagittal images) demonstrating a Chiari III malformation with occipital encephalocele (arrow) at 24 weeks gestation. Chiari III

**(b and c):** FFE T2 weighted Foetal MRI (at 23 weeks gestation) sagittal images demonstrating Chiari II malformation (note spinal defect; arrow) and crowding of the posterior fossa structures.



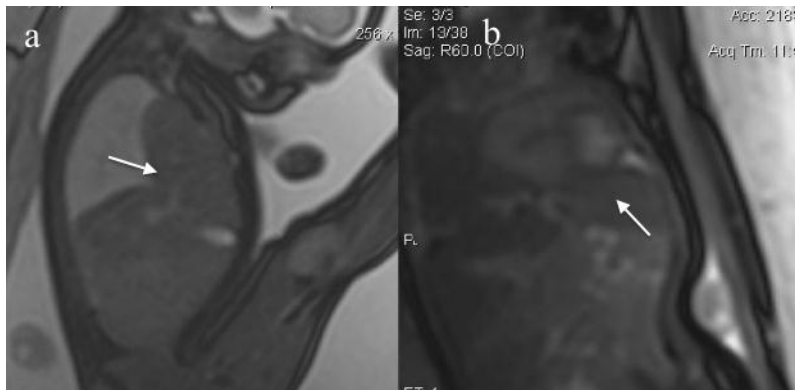
**Figure 5a and b:** FFE T2 weighted foetal MRI at 32 weeks gestation demonstrating semilobar holoprosencephaly in a patient with Patau syndrome. (a) Coronal image demonstrates that the Thalami are partially fused. The anterior horns of both lateral ventricles were absent. There was absence of the rostrum and genu of the corpus callosum with only posterior aspect of body and splenium present. (b) Sagittal demonstrates a characteristic large posterior cyst.



#### 4.5 Non-neurological Foetal MRI findings.

The 2 most common non-neurological findings on MRI were congenital diaphragmatic hernia (n = 4; 27%) (one was right sided and three were left sided)(Figure 6 a and b), and soft tissue masses (n=2; 13%) such as Klippel Trenaunay-Weber (figure 7).Others included pulmonary sequestration (figure 8 a and b), hemivertebra, teratoma and bronchogenic cyst and these are summarised in Figure 9 below.

**Figure 6 a and b: FFE T2 weighted foetal MRI at 32 weeks demonstrating a right-sided congenital diaphragmatic hernia (Morgagni type): (a) Sagittal and (b) coronal images demonstrate liver herniating (mushroom sign) into right hemi-thorax (arrows)**



**Figure 7: Coronal FFE T2 weighted foetal MRI at 32 weeks gestation Klippel-Trenaunay Weber syndrome with a hypertrophied right leg (arrow). No flow voids were evident**

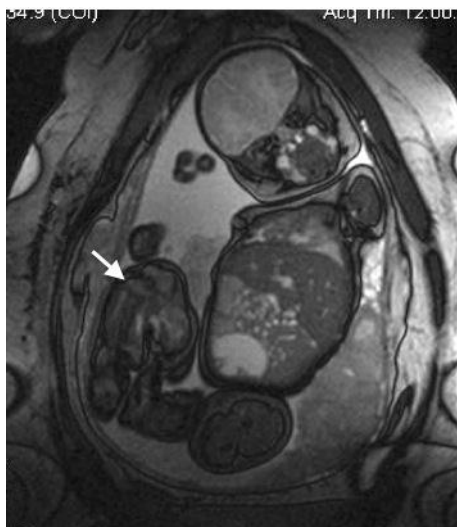


Figure 8 a and b: FFE T2W foetal MRI at 31 weeks gestation demonstrating a right paraspinal sequestration. (a) Oblique coronal and (b) axial imaging of the chest demonstrate high-signal foci (arrows). This was confirmed on histology postnatally after surgery.

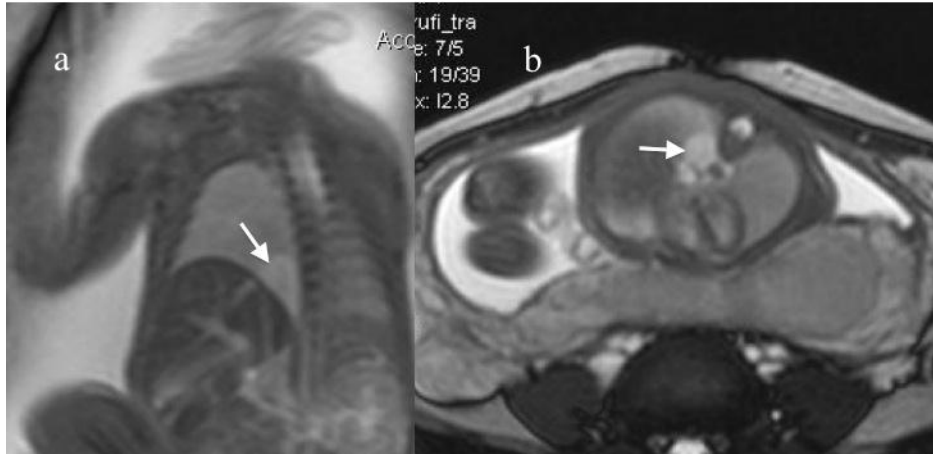
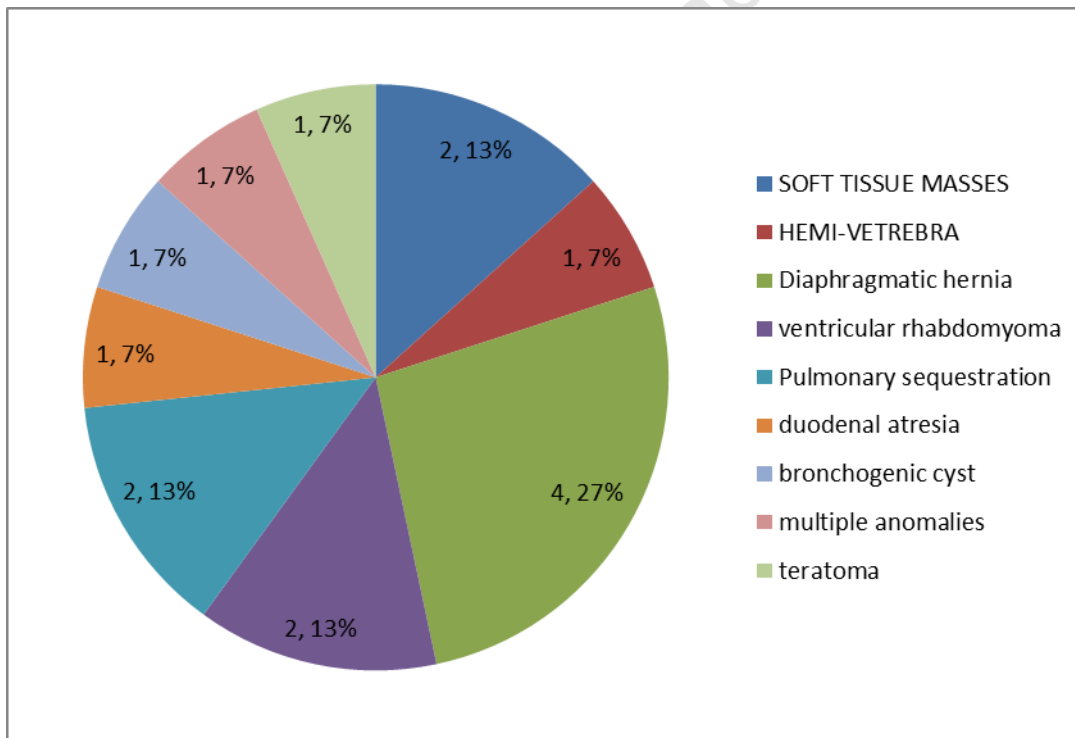


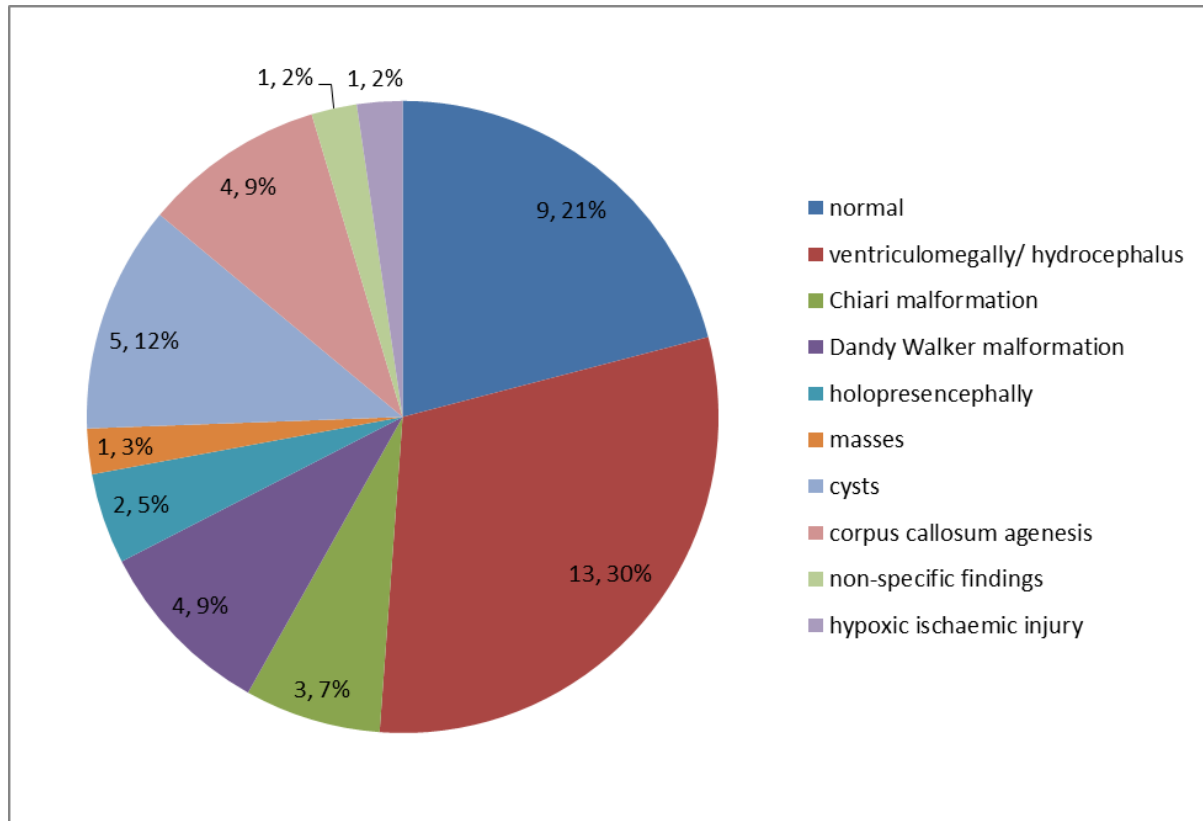
Figure 9: Non neurological indications for foetal MRI



#### 4.6 Post Natal Imaging Findings, Clinical Findings or Post-Mortem Findings

Again, hydrocephalus/ ventriculomegaly was the most common finding on post natal CT or MR imaging. The neurological post natal imaging findings are graphically presented in figure 10.

Figure 10: Neurological post-natal findings



#### Postmortem Findings;

There were 5 postmortem that were done with the following findings documented: Arachnoid cyst, Corpus callosum agenesis, Left diaphragmatic hernia. One case, who underwent fetocide (antenatal diagnosis of Dandy-Walker malformation) was severely macerated with severe autolysis and only found adrenal and renal hypoplasia. No postmortem results were found for the last case.

#### 4.7 Maternal diagnosis and Imaging Findings:

VDRL was positive in two mothers, and the foetal anomalies found in these were Chiari II malformation and Klippel Trenaunay-Weber syndrome. Holoprosencephaly was identified in our case with Patau syndrome. Ventriculomegaly was found in the foetus with Klinefelter syndrome on genetic screening.

#### 4.8 Statistical analysis

Table 2 demonstrates agreement values between pre-natal US, foetal MRI and post-natal findings:

Agreement Categories	Spearman's Correlation coefficient
Antenatal ultrasound /Foetal MRI	0.7246, p<0.0001
Antenatal ultrasound/ Post natal findings	0.2817, p=0.02
Foetal MRI/Post natal findings	0.3879, p<0.001

**Table 4: Agreement values between antenatal imaging findings and post-natal findings**

## 5 DISCUSSION

Our study population reflects the geographical location of the study as well as the institutional population. The prevalence rate of HIV in the study population of 20% was slightly higher than seen in published data of antenatal mothers (18.5% in 2010)<sup>16</sup>. This was thought to be a result of the small sample size since the population is the same and a similar prevalence is expected.

Only one patient in our population had documented CMV infection. Congenital CMV infection can result in periventricular calcifications, migrational disorders, cerebral volume loss, and ventriculomegaly and white matter abnormalities<sup>17</sup>. In our patient, the imaging yielded only ventriculomegaly.

VDRL was positive in two patients, and anomalies found were Chiari 2 malformation and Klippel Trenaunay syndrome. These conditions are not known to be associated with congenital syphilis, therefore were considered unrelated.

The chromosomal abnormalities included in the study were Patau and Klinefelter syndromes. In Patau syndrome, the foetus may have holoprosencephaly, polydactyly, flexion of the fingers, heart defects, facial clefting and neural tube defects<sup>18</sup>. Holoprosencephaly was identified in our case with Patau syndrome. Ventriculomegaly was found in the patient with Klinefelter syndrome. As this is not a known association, this was thought to be a coincidence occurrence.

### **5.1 Agreement between antenatal ultrasound and Foetal MRI**

The results demonstrate a high agreement of 72% (Spearman's  $\rho=0.7246$ ) between US and foetal MRI. The number of cases (14% overall) reported as normal on MRI may have brought this agreement down.

Griffiths et al<sup>19</sup> also demonstrated that a high agreement (83%) but not all of their cases with suspected ventriculomegaly were confirmed on foetal MRI. Their study looked at ventriculomegaly only and had no postnatal imaging or post-mortem confirmation. They demonstrated additional brain anomalies in 17% of their cases compared to 29% who had additional brain anomalies diagnosed on foetal MRI in our study.

31% (10 / 32) of the cases with suspected ventriculomegaly were normal on follow up ultrasound. Levine et al<sup>20</sup> showed almost a similar proportion (32%) of normal ventricles on confirmatory ultrasound just before foetal MRI. A higher degree of ventriculomegaly is reported to be associated with higher rate of mortality and morbidity as demonstrated by Gaglioti et al<sup>21</sup>, who recommends that all suspected cases of ventriculomegaly on antenatal ultrasound need foetal MRI for further evaluation and to exclude other anomalies, especially in those with moderate to severe ventriculomegaly.

In our study, there was no quantification of the degree of ventriculomegaly at foetal MRI in the reports. As a result all cases that were reported as having resolution of ventriculomegaly were reviewed and the ventricles were measured to confirm this. Objective measures of the degree of hydrocephalus need to be introduced into our practice and those with moderate or severe ventriculomegaly should be carefully reviewed and flagged to the clinicians due to high risk of associated morbidity and mortality.

### **5.2 Agreement between antenatal ultrasound and postnatal findings**

There was a low agreement of 28% (Spearman's  $\rho=0.2817$ ) between antenatal ultrasound and postnatal findings with 14% of studies reported normal post-natally.

A diagnosis specific or system specific follow up study, may demonstrate an improved relationship by having a larger pool of cases for analysis instead of a mix of conditions as was in this study design.

### **5.3 Agreement between foetal MRI and postnatal findings**

A low agreement of 39% was found (Spearman's  $\rho=0.3879$ ) between foetal MRI findings and postnatal findings, but this was better than the relationship between ultrasound and postnatal findings.

The study by Dhouib A et al<sup>22</sup>, showed an 85 % agreement when they compared antenatal and postnatal MRI findings. However, in their case they considered one system only (cerebral findings) and compared one imaging modality. In addition, their sample was larger (100 cases) than ours.

From the above, it may help to consider comparing body systems (neurological, cardiopulmonary, GIT and musculoskeletal) and calculate how much agreement there is between the system with a larger study population,

As such a follow up study is recommended with the above mentioned suggestions taken into consideration.

Generally, ventriculomegaly is reported with a high frequency, and this turns out to be advantageous because a number of these cases have additional abnormalities detected only on foetal MRI. This reaffirms that foetal MRI compliments US and can be used a second-line imaging modality to demonstrate abnormalities not visible with ultrasound but which are flagged through the identification of moderate and severe hydrocephalus.

## **6 Conclusion:**

Intracranial pathology is the major indication for foetal MRI, with ventriculomegaly being the commonest indication determined from prenatal ultrasound.

A high agreement was achieved between antenatal ultrasound and foetal MRI. However, very low correlation was demonstrated between prenatal and the postnatal findings. A follow up study with standardised postnatal evaluations and routine post-mortem evaluation in cases of fetocide as well as a narrower scope in the system examined would help to further evaluate this relationship.

All cases of suspected ventriculomegaly on prenatal ultrasound should undergo foetal MRI, despite the significant proportion of normal cases, because of possible associated brain anomalies and foetal MRI studies need to be thoroughly evaluated for these. Correlation of studies pre and postnatally is complicated by what may represent resolution of positive findings. Overcalling hydrocephalus on ultrasound may represent an excellent screening test as we have shown additional findings in hydrocephalus patients that have significant impact on management and prognosis.



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