The impact of adding fetal MRI to sonographically diagnosed intrauterine ventriculomegaly: a prospective cohort study

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Keywords: Ventriculomegaly, ultrasonography, magnetic resonance imaging

Abstract

Objective: *Intrauterine fetal ventriculomegaly (IVM) is one of the most commonly detected fetal anomalies. Prenatal diagnosis in IVM is considered a challenge with a significant impact on management. The current study aims to evaluate the added value of performing fetal MRI to sonographically diagnosed IVM.*

Methods: *A prospective cohort study was conducted at a tertiary University Hospital in the period between January 2017 and March 2019. We included pregnant women with a single fetus sonographically diagnosed IVM (symmetrical or asymmetrical). First, a basic obstetric sonographic examination was done, followed by a detailed (2D/3D) fetal CNS anomaly scan for the detection of other associated anomalies. A fetal MRI brain scan was performed for all cases.*

Results: *Sixty women were included in the study. Of the 60 fetuses with IVM, additional findings were seen on MRI in 14 cases (23%), and most of these findings were identified in fetuses with severe IVM (about 50%). No additional abnormalities were identified in fetuses of less than 24 weeks gestation. Callosal and septum pellucidum lesions (29%), along with posterior fossa abnormalities (28%) and cortical malformations (21%) accounted for the most common additional significant fetal MRI findings. Fetal MRI sensitivity, specificity, and positive and negative predictive values in correlation with those of prenatal ultrasound turned out to be notably higher, approaching nearly 100 %.*

Conclusions: *Fetal MRI for sonographically diagnosed moderate or severe IVM is recommended to guide clinical management.*

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Introduction

Cerebral ventriculomegaly (VM) is one of the most commonly detected fetal anomalies found at the mid-trimester ultrasound.[1] Congenital VM is a heterogeneous disease for which genetic, infectious, ischemic and neoplastic causes have been implicated.[2] The classification of VM has varied in published studies; mild (10–12 mm), moderate (>12–15 mm), or severe (>15 mm) is a commonly accepted categorization.[3,4]

Ultrasound (US) is a popular screening modality for fetal CNS abnormalities. However, with US usage, some limitations may hinder proper diagnosis, including maternal obesity, oligohydramnios and fetal head engagement in late pregnancy, or acoustic shadowing by surrounding bony structures.[5]

Fetal magnetic resonance imaging (MRI) is being used increasingly as a complementary tool to US in fetal CNS abnormalities assessment. This is because MRI is displayed in multiple planes, has better soft-tissue contrast and better depiction of subtle parenchymal abnormalities, and shows maturational stages of gray and white matter development, at a level that is beyond the US capability.[6] In addition, MRI, just like US, causes no exposure to ionizing radiation and appears to have no teratogenic effect on the fetus.[7]

Fetal MRI is performed in cases of IVM (intrauterine ventriculomegaly) to detect any additional abnormalities that might give insight into the etiology of the VM as well as the neurodevelopmental outcome for the fetus.[8,9] These include corpus callosum agenesis, cortical malformations, cerebellar malformations, hemimegalencephaly, periventricular white matter injury, and heterotopia, porencephaly, multicystic encephalomalacia, intraventricular hemorrhage and germinal matrix hemorrhage.[8,10]

Therefore, the current study aims to determine the impact of adding a fetal MRI to support the management plan for sonographically diagnosed IVM.

Materials and methods

Study type, setting, and duration

The current study was a prospective cohort study conducted at a tertiary University Hospital between January 2017 and March 2019. The Institutional Ethical Review Board approved the study protocol. All women who participated in the study signed a written informed consent before inclusion.

Study participants

All eligible women attending the outpatient clinic for antenatal care were approached to participate in the study. We included pregnant women with a single fetus at 20-32 weeks of gestation calculated based on sure reliable dates, with sonographically diagnosed IVM (symmetrical or asymmetrical). We excluded women with multiple pregnancies, any contraindication to

perform MRI, and those who declined participation in the study.

Recruitment

The recruited women were assessed through detailed history taking and clinical examination. Fetal MRI followed detailed sonographic fetal CNS anomaly scan ultrasound on the brain. Additionally, postnatal MRI brain to non-terminated and live birth cases was done for confirmation of the initial diagnosis made by fetal MRI.

US technique

The sonographic examination was done in the supine position with her head slightly raised, using (Voluson E, GE industrial CO., USA) with the trans-abdominal transducer of a bandwidth 3.5 MHz associated with color Doppler added property. First, a basic obstetric sonographic examination was done, followed by a detailed (2D/3D) fetal CNS anomaly scan to detect other anomalies associated. All cases were evaluated by a single level II sonographer to avoid any interobserver bias.

MRI technique

MRI examination was performed on a 1.5-Tesla MR scanner (Ingenia 1.5 Tesla, Philips, Netherland) using a multi-channel phased-array coil to allow increased coverage of the fetal head and increased signal-to-noise ratio. The mother was made to lie supine or on her left side (if more comfortable) during the exam (typically 45–60 min). The mother was made as comfortable as possible to minimize fetal motion, and she fasted four hours before the MR exam. All MRI readings were interpreted by a single experienced radiologist.

Image interpretation parameters

- VM was considered when atrial width equal to or greater than 10 mm, measured at the posterior margin of the choroid plexus's glomus on an axial image through the thalami.

- VM was classified as mild (10–12 mm), moderate (>12–15 mm) and severe (>15 mm)

Statistical analysis

The data were collected and entered into a Microsoft Access database then analyzed using the Statistical Package for Social Science (SPSS Inc., Chicago, version 22). Qualitative variables were presented as frequency and percentage. A Chi-square test was used for comparison between groups. The sensitivity and specificity of ultrasound and MRI were calculated. For analysis, $p < 0.05$ was significant.

Results

Out of 68 evaluated pregnant women, sixty women were enrolled in our study. Eight women were excluded due to multiple pregnancy (n=3) and declined to participate (n=5). The mean age was 31.5±8.3 years. Table 1 shows the difference between MRI and US in the degree of VM.

There was a nonsignificant statistical difference between the VM grades in US and MRI ($p = 0.105$). Also, Table1 clarifies the classification of VM cases

into mild, moderate, and severe grades, with the most common one noted to be the mild VM degree.

Table 1. Assessment of degree of ventriculomegaly by US versus MRI in the study cases.

VM Degree US	VM degree MRI			*P* -value
	Mild	Moderate	Severe	
Mild	26	7	0	0.105
Moderate	0	15	3	
Severe	0	2	7	

VM; ventriculomegaly, US; ultrasound, MRI; magnetic resonance imaging

The gestational age (GA) of the involved fetuses ranged from (20-32) weeks with a mean value of 26±4.5 weeks. Fetal MRI additional abnormalities (about 23 %) and changing diagnosis (1.6%) were more pronounced after 24 weeks. (Table 2)

Before 24 weeks, fetal MRI confirmed the diagnosis with no additional abnormalities addressed (Table 2).

Table 2. Range and mean value of GA with relation to the additional findings by fetal MRI

Gestational age			MRI over US			*P*- value
Range	Mean		Add	Change diagnosis	Confirm	
20-32 weeks	26±4.5 weeks	>24 weeks	14 (23%)	1 (1.6 %)	12	0.016
		<24 weeks	0	0	33	

GA; gestational age, US; ultrasound, MRI; magnetic resonance imaging

Table 3 shows a comparison between Fetal MRI and the prenatal US with confirmatory postnatal MRI to non-terminated and live birth cases (25%). It shows the percent of each of the fetal MRI additional findings (23%), changed

sonographic diagnosis (1.6%), and confirmed the sonographic diagnosis (75%). The Table shows the significance of adding fetal MRI modality to the prenatal US (p= 0.045).

Table 3. Comparison of fetal MRI and US with significance of adding fetal MRI modality to prenatal ultrasound

VM degree	US Diagnosis	Fetal MRI			Postnatal MRI to non-terminated & live birth cases	*P*–value
		Confirm diagnosis	Additional Findings	Change US diagnosis		
Mild	Isolated VM or incomplete imaging findings		4		As fetal MRI	0.045
Moderate			2			
Severe			8			
Mild	IV hemorrhage			Mild VM, No IV hemorrhage	Just mild VM	
Mild	Isolated VM or with US additional findings	27			As Fetal MRI	
Moderate		16				
Severe		2				
Percent		75%	23 %	1.6%	25%	

VM; ventriculomegaly, US; ultrasound, MRI; magnetic resonance imaging

The fetal MRI additional abnormalities in our study are illustrated in Table 4, which shows that the most commonly detected additional abnormalities were corpus callosal and septum pellucidum dysgenesis (about 29%) followed by posterior fossa abnormalities (28%) and cortical malformations (21%). (Figures 1-2)

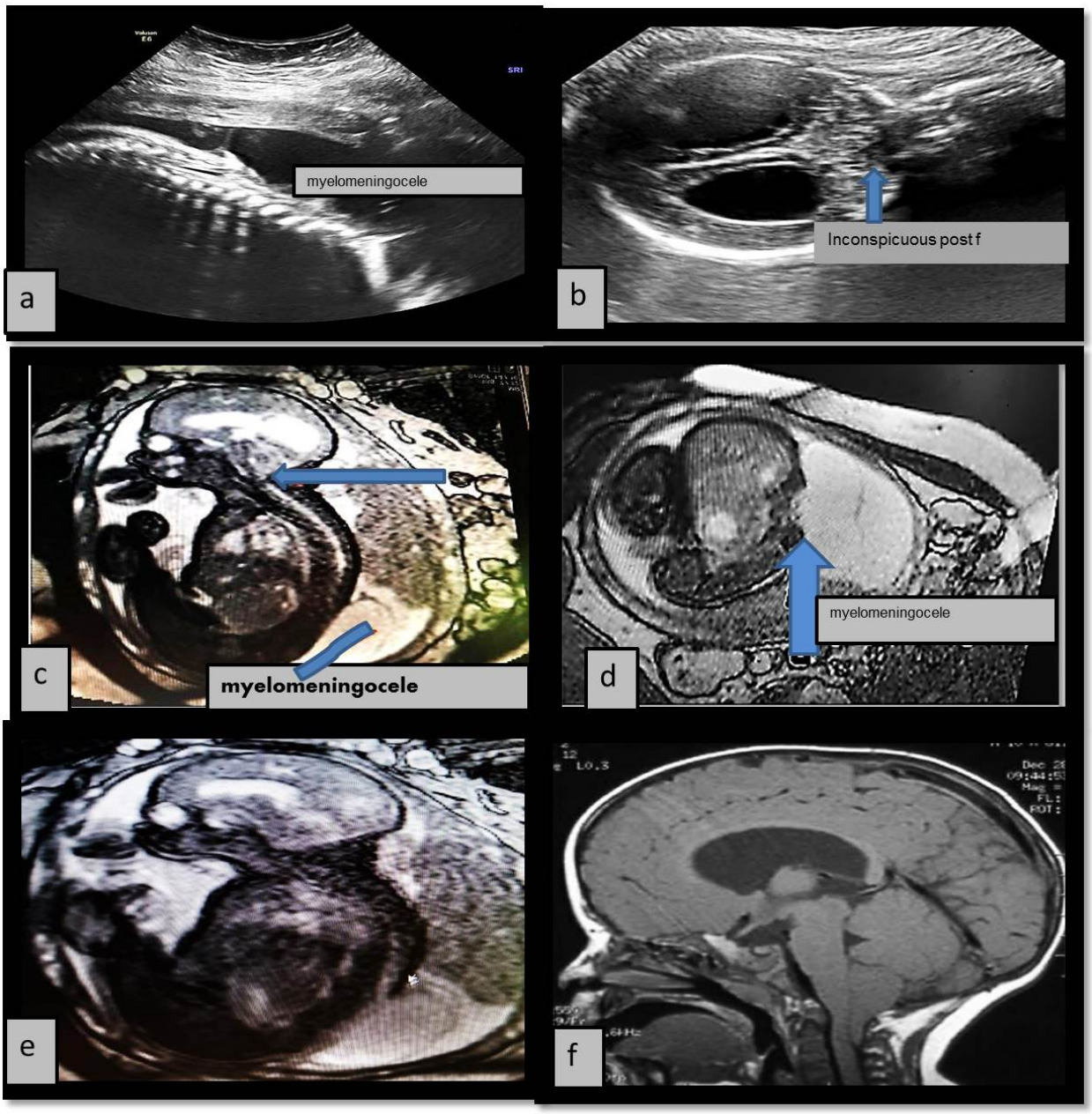

Figure 1. Fetus 32 weeks GA (a) Sagittal U.S image shows myelomeningocele at the distal spine.(b) Coronal U.S image shows moderately dilated ventricles with inconspicuous posterior fossa suggesting Chiari II. (c),(d) and (e) MRI T2WI in sagittal and axial planes confirmed U.S findings with adding the degree of cerebellar tonsil herniation and the corpus callosal dysgenesis (d) is a postnatal MRI, showing the same findings as the fetal MRI.

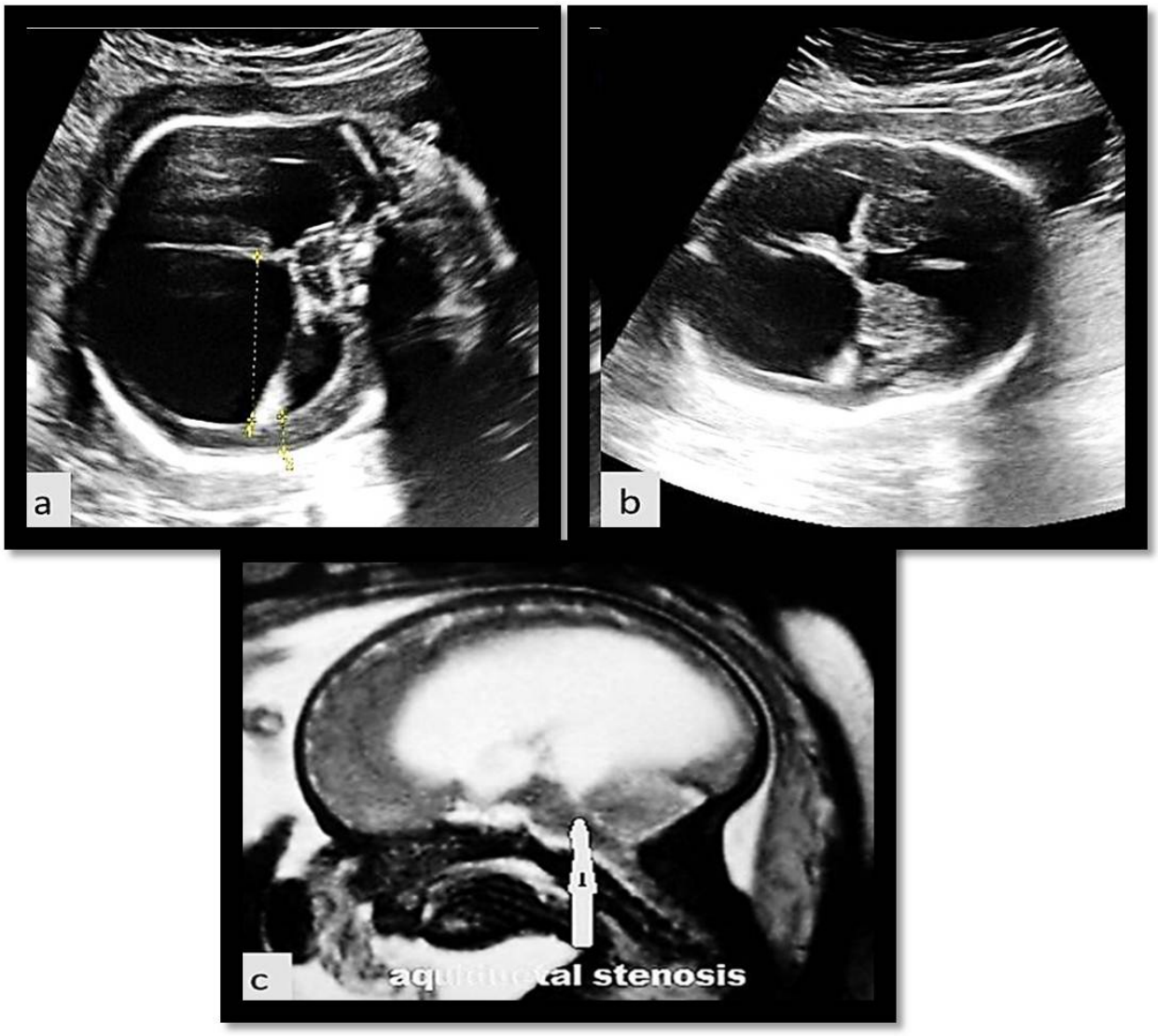

Figure 2. Fetus of 24 weeks GA, (a, b) is U.S (axial & coronal images) showing moderate dilatation of supratentorial ventricular system.(c) Fetal MRI in sagittal plane shows non-communicating hydrocephalus with aquiductal stenosis.

Table 4 shows how the management strategy changed when no additional abnormalities were present in isolated VM cases in our study.

Table 4. The change in the management strategy in isolated VM cases with no additional abnormalities

Cases with no additional findings (with VM degree)	Clinician recommendation	Postnatal MRI (to non-terminated & live birth cases)
Isolated mild VM	Follow up…if no change or regress. continue pregnancy	As fetal MRI
Isolated moderate VM	Follow up…if regress…. continue pregnancy	As fetal MRI
Isolated severe VM	Termination	----------

Lastly, Table 5 shows the difference between US and fetal MRI regarding sensitivity, specificity, positive & negative predictive values in our study, where they were about 100%, 98%, 95%,and 100% respectively for the MRI, while about 74%, 86%, 84.5%, 76% respectively for the US, revealing superiority of MRI upon US regarding those items in fetal VM assessment.

Table 5. The sensitivity, specificity, negative and positive predictive value (NPV, PPV) of fetal MRI and prenatal US in fetal VM assessment

	Sensitivity	Specificity	PPV	NPV
Ultrasound	74%	86%	84.5%	77%
Fetal MRI	100%	98%	95%	100%

Discussion

There is no doubt that VM is one of the most common abnormalities found on prenatal ultrasound, and it is a marker for increased risk of underlying malformations, chromosomal abnormalities, and infection.[11] Fetal MRI is a useful adjunct to ultrasound in suspected fetal anatomic abnormalities and is increasingly used for fetal brain imaging.[12,13] Our study found that maternal age was of significance as 80% of the pregnant females in our cases were more than 34 years old, which suggested that advanced maternal age may be associated with higher risk of congenital anomalies, including those of the CNS. Our findings were similar to those in a study conducted by Hollier et al., 2000[14], which reported that advanced maternal

age beyond 35 years old was associated with significantly increased risk of congenital fetal malformations. Nevertheless, these data contradict a study conducted by Goetzinger et al., 2014[15] indicating that maternal age was associated with a lower risk for major fetal anomalies. This contradiction can probably be attributed to racial differences.

Much like previous studies, our results revealed that MRI measurements of lateral ventricle size were, on average, 1-2 mm greater than US measurements. However, no notable changes were detected in VM grading of mild, moderate and severe relative to ultrasound. These results matched those of Nicholas Behrendt et al., 2016[16], who stated that fetal MRI measurements of the brain ventricles were about 1 mm larger than measurements of the same ventricles by ultrasound. However, this size difference was not sufficient to change the grading of anomalies from the values assigned after US. Moreover, findings in a study by Levine et al., 2008[17] also agreed with our findings in that they noted measurements of the lateral ventricles on MRI that were about 0.6 mm larger than the same ventricles measured by the US.

We found additional fetal MRI abnormalities in 14 of 60 fetuses (23%), and a change from the sonographic diagnosis in one case (1.6%), which resulted from misinterpretation of the US image as showing IV hemorrhage when, in fact, fetal MRI proved that it was merely choroid plexus. This result was in contrast to the study addressed by Kandula et al., 2015[1], where additional fetal MRI abnormalities were found in 10 out of 59 cases (about 17 %). Similarly, Parazzini et al., 2012[18], identified additional MRI abnormalities in 19.5% of fetuses.

For our cases, additional fetal MRI findings were more pronounced after 24 weeks GA, which, as anticipated, agreed with the 2010 claim by ACR[19] that fetal MRI study might give limited diagnostic information in early gestational age due to the small size of the fetus and fetal movement.

Something to be considered in our results is that additional fetal MRI findings were more notably detected in severe VM (about 50%), which is in agreement with data from studies conducted by Morris et al., 2007[20] and Griffiths et al., 2010.[21] These authors found, respectively, that 57% and 58% of fetuses with severe VM had additional findings on MRI. Likewise, Kandula et al., 2015[1] found in their study that a large proportion of their cases that demonstrated severe IVM under US had additional findings on MRI. Furthermore, these findings agreed with Gaglioti et al., 2009[22], who stated that the rate of associated malformations is higher (=60%) in severe VM (15 mm) and lower (10-50%) in cases of borderline VM (10-15 mm).

One clear finding in this research is the demonstration of why performing fetal MRI on all fetuses with severe IVM (VM 15 mm) is useful and highly recommended. Fetal MRI usually processes many additional findings that are far beyond the capability of prenatal ultrasound, such as agenesis of the corpus callosum, absent septum

pellucidum, subependymal heterotopia and hemimegalencephaly with better differentiation of severe IVM from cases that image similarly, such as hydranencephaly, porencephalic cyst and alobar holoprosencephaly.[5]

In our study, additional abnormalities detected by fetal MRI included callosal and septum pellucidum lesions (29%), followed by posterior fossa abnormalities (28%) and cortical malformation (21%), which accounted for the majority of significant fetal MRI additional findings. Our findings confirmed, to a great extent, the findings of many previous studies, including Kandula et al., 2015[1], which claimed that all significant additional fetal MRI abnormalities were callosal and septum pellucidum lesions, malformations of cortical development and periventricular abnormalities.

The results of our study show, furthermore, that the presence of structural CNS abnormalities with VM correlates more closely with the decision to terminate pregnancy than does the degree of VM dilation, suggesting that the associations between abnormalities and VM may serve as better predictors of pregnancy outcomes than the severity of VM itself. This study agrees with Li et al., 2011[23], which states that termination of pregnancy occurred at a much higher rate when fetuses had additional CNS anomalies (40%, compared to 7% for fetuses with isolated VM <12mm, 16% for fetuses with isolated VM >12mm and 0% for fetuses categorized as normal). In addition, our results corroborate Gupta et al., 1994[24], which found that the presence of CNS anomalies associated with mild VM rendered the outcome much worse than the presence of isolated mild VM alone.

We performed confirmatory postnatal MRI for non-terminated and live birth cases (25%), which revealed findings that were nearly identical to those found with fetal MRI, that contained almost nil additional findings and that changed a diagnosis in only a single case, where postnatal confirmation of simple Dandy-Walker (DW) variant was mistaken on fetal MRI for DW variant with cortical dysplasia. As such, the high positive and negative predictive values shown in these findings demonstrate that fetal MRI renders images with a sensitivity and specificity far beyond that of ultrasound evaluation. Furthermore, our findings agree with those in research by Trompoukis et al., 2012[25], which concluded that fetal MRI provides more accurate diagnosis as compared to ultrasound examination, with fetal MRI sensitivity, specificity and positive predictive value as a screening tool approaching 100%. Moreover, our findings were, to a great extent, identical to the findings of Hamisa et al., 2013[26], where the author claims that fetal MRI is useful as a complementary modality to 2D/4D ultrasound in the diagnosis of fetal CNS anomalies because it can provide specificity as well as positive and negative predictive values of about 100%.

Limitations in our study included the relatively low frequency with which postnatal MRI was actually performed owing to the high rate at which termination became the ultimate outcome for many participants' pregnancies. Our recommendation for

the future is to add fetal MRI to prenatal ultrasound when assessing cases of fetal VM as it provides greater sensitivity and specificity and because it provides additional information that can play an important role in identifying best practices when determining fetal outcomes. In conclusion, prenatal ultrasound is an unquestionably useful modality for fetal screening. Fetal MRI has proven to be an ideal complementary tool to ultrasound with higher sensitivity and specificity, especially in assessing fetuses with moderate and severe IVM at more than 24 weeks gestation, where it depicts additional CNS abnormalities far beyond the range of ultrasound that can affect prognosis and clinical management.

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