

*Research Article***Fetal MRI Value in Fetal CNS Anomalies****Mohamed A. Mourad, MD***; **Soha T. Hamed, MD**** and **Sara M. Ragae***

* Department of Radiology, Faculty of Medicine, Minia University, Minia, Egypt.

** Department of Radiology, Faculty of Medicine, Cairo University, Cairo, Egypt.

Abstract

Background: Antenatal evaluation of the fetal central nervous system (CNS) plays an important role in the field of perinatology. **Objectives:** to elaborate on sonographic & MRI prenatal diagnosis of various fetal central nervous system malformations. **Patients & method:** Data were gathered prospectively from 70 pregnant women with ultrasound-diagnosed or suspected CNS anomalies referred for MRI between April, 2016 and July, 2019; followed by postpartum neonatal MRI brain examination to non-terminated, live birth cases. **Results:** Of the seventy fetuses with CNS anomalies, Fetal MRI added findings to prenatal U/S imaging in 17 cases (24%) and most of these findings were identified in fetuses with severe IVM (about 50%). No additional abnormalities were identified by fetal MRI in fetuses less than 24 weeks gestation. Callosal and septum pellucidum lesions accounted for most common significant fetal MRI additional findings with percent of (53%). Management was changed according to the additional findings where Increased rate of termination was more associated with cases with additional abnormalities rather than the isolated VM cases. **Conclusion:** This study recommend fetal MRI for sonographically diagnosed or suspected fetal CNS anomalies to guide the clinical management.

Key words: Fetal MRI, Fetal CNS anomalies, prenatal ultrasound, Intrauterine ventriculomegaly.

Abbreviations

GA(gestational age), IV (intraventricular), ,NO.(number),IUF(Intrauterine fetal death).

Introduction

Antenatal evaluation of the fetal central nervous system (CNS) plays an important role in the field of perinatology⁽¹⁾.

Ultrasound is the primary modality used to assess the fetus. The quality of ultrasound however, is adversely affected by factors such as maternal obesity, unfavorable fetal position, multiple gestations, decreased amniotic fluid or the near-field reverberation artifact⁽²⁾. The abnormalities detected on Ultrasound may at times be very subtle or inconclusive. In such cases, several studies have shown that MRI is a helpful modality^(3,4,5). The aim of the study was to elaborate on sonographic & MRI prenatal diagnosis of various fetal central nervous

Patients and Methods

This prospective study was approved by the ethics committee of our institution during the period between April, 2016 and July, 2019. It included 70 pregnant women with their age ranging from 18 to 45 years & of gestational age ranging from 20 to 32 weeks at time of examination (sonographically and by MRI). This study was conducted in our radiology department for patients referred from the obstetrics and gynecology department. We performed fetal MRI to sonographically diagnosed fetal VM at the same setting with no time lag between the two modalities; followed by postnatal MRI brain to 20 (29 %) of our 70 cases, who weren't terminated & were live birth.

- **Inclusion criteria** (2D/3D)
Sonographically diagnosed IVM (symmetrical or asymmetrical).

- **Exclusion criteria** were; MRI contraindication (as cardiac pace maker), Mother's refusal to do fetal MRI and twin pregnancy
- **U/S technique:**

Sonographic examination was done in supine position using (Voluson E, Toshiba, Japan) with trans-abdominal transducer of a bandwidth 3.5 MHz associated with color Doppler added property. First Basic obstetric sonographic examination will be done, followed by a detailed (2D/3D) fetal CNS anomaly scan with detection of other associated body anomalies as spinal dysraphism and others.

- **Fetal MRI technique:**

MRI examination was performed on 1.5-Tesla MR scanner ((Ingenia 1.5 Tesla, Philips, Netherland) without maternal sedation. Mothers fasted 4 h before the examination. They were made to lie supine during the examination or on their left side (if more comfortable).

Fetuses were imaged with a total scan time about 10-15 minutes in the following sequences: Single Shot Fast Spin Echo T2WI (SSFSE T2), Gradient echo-planar T2-W images, Fast multi-planar spoiled gradient-recalled acquisition in the steady state (FMPSGR)

- **Postnatal MRI technique of the brain:** MRI examination was performed on 1.5-Tesla MR scanner ((Ingenia 1.5 Tesla, Philips, Netherland) with infantile sedation. It was made in different pulse sequences and planes

- **Image interpretation parameters:**
 - Brain volume estimation was performed using the fronto-occipital, cerebral biparietal and bone biparietal diameters.
 - Ventriculomegaly was considered when atrial width equal to or greater than 10 mm.
 - VM was classified in to mild (10–12 mm), moderate (>12–15 mm) & severe (>15 mm) in both U/S and MRI modalities which was based on Gaglioti P et al., 2005 and Yu-Han Huang et al., 2013 classification.

Statistical analysis

Statistic Package for Social Sciences (SPSS v 17.0 for Windows, Chicago, IL) software was used for data entry and analysis.

Qualitative data were presented by numbers and Statistical significance was assessed using the chi square χ^2 test to compare differences between the two independent groups. Significance was interpreted as $p < 0.05$.

Results

Seventy pregnant females were enrolled in the study; More than 1 CNS abnormality finding could be associated in the same case.

Maternal age was ranging from 18 to 45 years of mean value about 27.5+/- 8.3 years. In addition our results revealed that about 80% of our pregnant females were above 35 years old Regarding the gestational age (GA) of the involved fetuses, it ranged from 20 to 32 weeks with mean value of 26 +/-4.5 weeks. Fetal MRI additional abnormalities (about 24 %) & changing diagnosis (6%) were more pronounced after 24 weeks GA.

Hydrocephalus was considered as the most commonly detected abnormalities in the study accounting for 70% of the cases, followed by posterior fossa anomalies (24.2%) and then midline anomalies about 17 % of the cases of the study (subdivided in to corpus callosal dysgenesis (14%) and holo-prosencephaly cases (2.9%)).

Degree of VM were compared in fetal MRI and prenatal U.S in hydrocephalus cases, there was no statistical significance in difference between the VM grades in U.S and MRI (of p -value about 0.105). (**Table I**)

The fetal MRI additional abnormalities in our study are illustrated at (**Table II**) which shows that the most commonly detected additional abnormalities were corpus callosal & septum pellucidum dysgenesis (53%) followed by posterior fossa abnormalities (29.4%) & cortical malformations

(17.7%). In addition, table IV shows how that the additional abnormalities addressed by fetal MRI changed the management, with higher rate of recommended termination by clinicians. It also shows postnatal MRI in cases who were not terminated & were live births.

Isolated VM cases in the study with no additional abnormalities, had different management strategy compared to those with additional abnormalities

Comparison was done between our two main modalities , the fetal MRI & the prenatal ultrasound regarding the confirmed sonographic diagnosis cases (49), the cases with fetal MRI additional abnormalities (17 cases) and lastly the cases with changes sonographic diagnosis (4 cases) (**Table III**). In addition, Table III also shows the postnatal MRI to some cases, with clarifying significance of adding fetal MRI modality to prenatal U.S. (*p*-value about 0.045).

Figure legends:

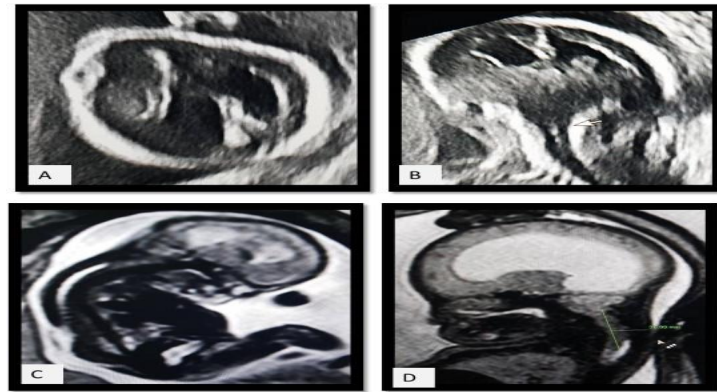


Fig. (1): Fetus of 27 weeks GA. (a,b) axial and coronal U/S images of the fetal brain showing lemon shaped fetal skull with inconspicuous posterior fossa with moderate hydrocephalic changes....suggesting Chiari II (c,d) sagittal fetal MRI images confirming diagnosis with estimation of the length of downwards cerebellar herniation through the spinal canal.

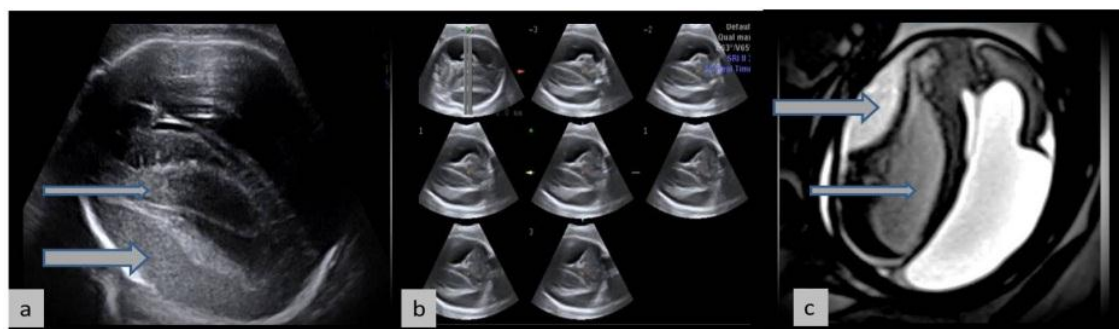


Fig. (2): Fetus of 36 weeks GA, (a , b) Axial & TUI U.S images revealing asymmetrical VM with suspicion of extra-axial (thick arrow) and I.V. (thin arrow) hemorrhage. (c) Fetal MRI confirm the diagnosis with marked compression of the ipsilateral lateral ventricle ,along with midline shift to the left side ;however no IV hemorrhage noted.

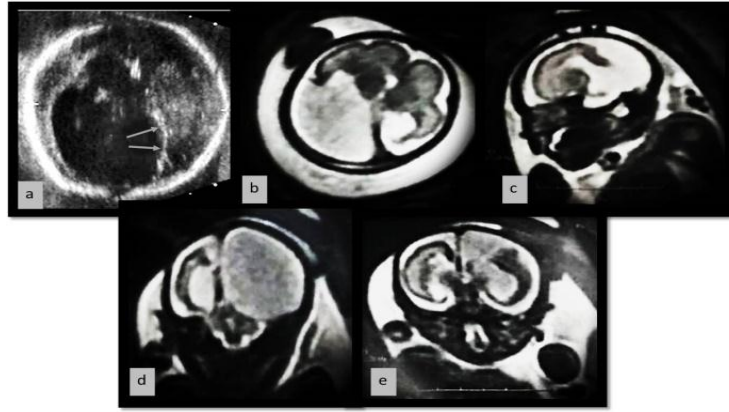


Fig. (3): Fetus of 26 weeks GA (a) axial U.S. image revealing asymmetrical ventricular dilatation, with bowed falx cerebri. (b ,c, d, e) axial, sagittal & coronal cuts of the fetal MRI revealing mild to moderate VM with inter-hemispheric cyst type I connected to one of the lateral ventricles associated with Corpus callosal dysgenesis.

Table I: VM degree by US versus VM degree by MRI & its significance, with VM grading in our cases.

VM. Degree U.S	VM degree MRI			P -value	Significance
	Mild	Mod	Severe		
Mild	26	7	0	0.105	Not Significant
Moderate	0	15	3		
Severe	0		7		

Table (II): showing Fetal MRI additional abnormalities , their percent & their management with postnatal MRI to non-terminated & live birth cases.

Cases with MRI additional findings	NO.	VM degree by U/S	Clinician Recommendation	Parents' decision	Postnatal MRI
I)Dysgenesis of corpus callosum	4	Severe	Termination	Continued pregnancy
		Mild		Stillbirth
		Moderate		Terminated
		Slit shaped		Terminated	As fetal MRI
II)Absent septum pellucidum	1	Mild	Termination	Continued	As fetal MRI
Pontocerebellar dysplasia	1	Severe	Termination	Terminated
Aquiductal stenosis (isolated and associated with interhemispheric cyst	2	Severe	Termination	Continued pregnancy	As fetal MRI(1)
D-M J dysplasia with aquiductal stenosis	1	Severe	Termination	Terminated
rhomben-cephalosynapsis with z-shape brainstem & aquiductal stenosis (HARDE \$)	1	Mild	Termination	IUFD
Hemimegalencephaly with schizencephaly	1	Severe	Termination	terminated
periventricular heterotopia with cortical dysplasia.	1	Severe	Termination	Continued pregnancy	As fetal MRI, without cortical dysplasia
Pachygyria with microcephaly	1	normal	Termination	Continued	As fetal MRI
Interhemispheric cyst type I	1	Moderate	Termination	Continued pregnancy	As fetal MRI
Arachnoid cyst	1	Normal	Follow up	Continued pregnancy	As fetal MRI
Hydranencephaly	1	Severe	Termination	Terminated
Sacroccygeal teratoma extension & component.	1	Normal	Termination if was diagnosed earlier.	Continue pregnancy	As fetal MRI
Total	17				8

Table (III): Comparison of fetal MRI with prenatal ultrasound regarding the cases in the study with significance of adding fetal MRI modality to prenatal ultrasound.

U.S. versus MRI	Ultrasound Diagnosis	Fetal MRI			Postnatal MRI to traceable, non-terminated & live birth cases.	P value	significance
		Confirm diagnosis	Additional abnormalities	Changed U.S. diagnosis			
	Isolated VM /Incomplete Imaging findings		17 cases		Almost As fetal MRI	0.045	Significant
	DW variant			Only mild VM	As fetal MRI		
	Aquiductal stenosis			hydranencephaly	-----		
	Porencephaly			Inter-hemispheric cyst	As fetal MRI		
	IV hemorrhage			Mild VM only	As fetal MRI		
	Rest of U.S. diagnosed cases	49			As fetal MRI		
Percent and no.		(49) 70%	(17) 24 %	(4) 6%	(20) 29%		

Discussion

Central nervous system (CNS) anomalies are the most common abnormalities of all malformations⁽⁶⁾. They are increasingly being recognized prenatally due to advances in fetal neuroimaging. Prenatal counseling aims at critical prognostication for the future neurodevelopmental outcomes⁽⁷⁾.

In the study, the maternal age was figured out to be of significance; where 80% of the pregnant females in the study were older than 34 years old. That made an allusion that advanced maternal age could participate to the role of increased risk of congenital anomalies including CNS anomalies which was equivalent to the study conducted by Simerpal K. Gill et al., 2012⁽⁸⁾ who reported that advanced maternal age beyond 35 years old was associated with increased risk of fetal CNS anomalies especially NTDs & cranio-synostosis.

In addition, the results revealed that MRI measurements of the lateral ventricular size in cases of VM were on average about 1-2 mm greater than US measurements. However, no notable changes were noted in VM grading to mild, moderate and severe relative to ultrasound. These results perfectly matched those of Nicholas Behrendt et al., 2016⁽⁹⁾

Fetal MRI additional abnormalities were yielded in 17 cases which constituted about 24% of our cases. This result was in rapprochement to the study addressed by Tejaswi Kandula 2015 et al.,⁽¹⁰⁾ who found fetal MRI additional findings in 10 out of 59 cases (about 17%).

As for the gestational age of the cases in the study, fetal MRI additional findings were more pronounced after 24 weeks GA which was in coherence with and based on what was postulated by ACR, 2010⁽¹¹⁾ that fetal

MRI study may give limited diagnostic information in early gestational age due to the small size of the fetus and fetal movement.

A conclusion was approached in the study regarding the incidence of the additional abnormalities processed by fetal MRI, where callosal and septum pellucidum lesions were found out to be the most commonly detected additional abnormality accounting 53% of the additional findings, followed by posterior fossa abnormalities (29.4%) & then cortical malformation (17.7%) accounted for major percent of the significant fetal MRI additional findings. That was to a high degree affirmed by many previous studies as that of Tejaswi Kandula et al., 2015⁽¹⁰⁾.

Something to be considered in the results that cases with severe ventriculomegaly represented about 47% of fetal MRI additional abnormalities & 25% of the changed sono-graphic diagnosis by MRI. That was in accordance with the study conducted by Griffiths et al., 2010⁽¹²⁾.

A conclusion was approached in the study concerning how presence of structural CNS abnormalities in hydrocephalic cases manipulate management rather than the degree of VM dilatation. Where additional abnormalities in VM cases were noted to have high association with termination of pregnancy compared to isolated VM cases. This conclusion proved the fact that associated CNS abnormalities act as a better predictor of outcome rather than degree of ventricular dilatation, which coped with many other studies as that conducted by Y Li et al., 2011⁽¹³⁾.

In addition to aiding in management and prediction of the neurodevelopmental outcome, fetal MRI additional abnormalities were noted to give a clue about the possibility of recurrence & the need for genetic testing in the diagnosed fetal brain malformations as well. An example for this; is two cases in our study which were formerly diagnosed by U/S as hydranencephaly and lissencephaly ;On the other hand fetal MRI additional findings rendered

the diagnoses as Fowler and Walker Warburg (HARDE) syndrome respectively which were proved to be autosomal recessive syndromes with the imminent need for genetic testing. That was in agreement with what was postulated by Tejaswi Kandula et al., 2015⁽¹⁰⁾ in his study.

Other than the additional findings (24%) addressed by fetal MRI upon prenatal ultrasound, Fetal MRI also changed sonographic diagnosis in about 4 cases (5.7%) in the study; where sonographic diagnosis of those cases were Dandy walker variant, porencephaly, IV hemorrhage and aqueductal stenosis; turned out to be isolated mild Ventriculomegaly, Inter-hemispheric cyst, just asymmetrical mild ventriculomegaly (with the choroid plexus misinterpreted by U.S as being IV hemorrhage) and hydranencephaly respectively. The first three cases were confirmed by post natal MRI, while the last one was terminated.

Fetal MRI confirmed 70% of prenatal sonographically diagnosed cases & helped to terminate pregnancy in 42 cases.

In the study confirmatory postnatal MRI was applied to traceable, non-terminated & live birth cases (about 29%). It confirmed the fetal MRI findings with almost nil additional findings and only modified prenatal MRI diagnosis in one case. That was coping with the study conducted by Trompoukis P et al., 2012⁽¹⁴⁾ which stated that fetal MRI provided more accurate diagnosis compared to ultrasound examination with fetal MRI sensitivity, specificity and positive predictive value as a screening tool approaches 100%.

A controversy exists whether ultrasound or MRI is more practical and effective in prenatal assessment of fetal CNS abnormalities. Although the study revealed that fetal MRI is superior to ultrasound in many aspects, On the other hand, It also revealed that prenatal ultrasound proved better in detection of intracranial calcifications, intra-tumoral vascularity fetal face with detection of cleft lips & bony abnormalities as in cranio-synostosis by means of surface

rendering (skeletal mode) and associated extra-CNS bony dysplasias. That was in agreement with the study conducted by Pooh 2011⁽¹⁵⁾.

However that was against the study conducted by Malinger et al., 2002⁽¹⁶⁾ as well who rightfully criticized that the past reports describing superiority of MRI over ultrasound may have been biased because a comparison was made with routine trans-abdominal sonography without confirmatory tertiary level ultrasound examination, especially by trans-vaginal sonography.

Limitations in our study included the relatively narrowed number of cases which performed postnatal MRI, owing to the high ratio of termination decision, the IUFD, the still birth cases, as well as the non-traceable cases.

Our recommendations in the future is adding fetal MRI to prenatal ultrasound in fetal CNS anomalies; where it is of great value concerning accuracy in complete diagnosis compared to the prenatal ultrasound & it greatly manipulates the fetal neurodevelopmental outcome and management.

Conclusion

Prenatal ultrasound is unquestionably favorable modality for fetal screening. Fetal MRI depicted additional CNS abnormalities -far beyond ultrasound- and changed sonographic diagnosis in some cases; that aid in prediction of the neurodevelopmental outcome, affecting the prognosis and the clinical management with giving a clue about the possibility of recurrence & the need for genetic testing.

So as to conclude, we can safely say that fetal MRI in the study proved to be a perfect crucial complementary tool to prenatal ultrasound in fetal CNS anomalies whether diagnosed or suspected by U/S.

References

1. Manju Nair, Bidyut Kumar; Embryology for fetal medicine; 2016; chapter 4:53-66.

2. Ganesh Rao B, Ramamurthy BS. MRI of the fetal brain. *Indian J Radiol Imaging* 2009;19(1):69-74.
3. L. F. Gonçalves, W. Lee, Diagnostic accuracy of ultrasonography and magnetic resonance imaging for the detection of fetal anomalies: a blinded case-control study, *Ultrasound Obstet Gynecol*, 2018; Jun 5, 48(2):185 - 192.
4. Coakley FV, Glenn OA, Qayyum A, Barkovich AJ, Golstein R, Filly RA, et al., Fetal MRI: a developing technique for the developing patient. *AJR Am J Roentgenol* 2004; 182; 55: 242-53.
5. Twickler DM, Magee KP, Caire J, Zaretsky M, Fleckenstein JL, Ramus RM. Second-opinion magnetic resonance imaging for suspected fetal central nervous system abnormalities. *Am J Obstet Gynecol* 2003;188:492-6.
6. Sadan Tutus, Sezin Ozyurt, Evaluation and prevalence of major central nervous system malformations: a retrospective study, *North Clin Istanbul*. 2014; 1(2): 78-83.
7. Agarwal S, Jake Keller, Fetal central nervous system malformations: a ten year review of prenatal consultations at a tertiary care center, April 18, 2017; 88: 150.
8. Simerpal K, Cheryl Broussard, Association between Maternal Age and Birth Defects of Unknown Etiology, *Birth Defects Res A Clin Mol Teratol.*, Dec 2012; 94(12): 1010-1018.
9. Nicholas J. Behrendt MD, Michael V Zaretsky, Ultrasound versus MRI: Is there a difference in measurements of the fetal lateral ventricles?, 5 April 2016; 30(3):298-301.
10. Tejaswi K, Michael F, Isolated ventriculomegaly on prenatal ultrasound: What does fetal MRI add? *Journal of Medical Imaging and Radiation Oncology* 59, 2015; 154-162.
11. Practice guideline for the safe and optimal performance of fetal magnetic resonance imaging (MRI), ACR-SPR (American College of Radiology - Society for Pediatric Radiology), 2010: 10.
12. Griffiths PD, Reeves MJ, Morris JE, Mason G, Russell SA, Paley MNJ,

- Whitby EH. A prospective study of fetuses with isolated ventriculomegaly investigated by antenatal sonography and in utero MR imaging. *AJNR* 2010; 31: 106–11.
13. Y Li, JA Estroff, Ultrasound and MRI in fetuses with ventriculomegaly: Can cortical development be used to predict postnatal outcome? *AJR Am J Roentgenol.*, Jun 2011; 196(6): 1457–1467.
 14. Trompoukis P, Papantoniou N, Fetal MRI: is it really helpful? *J Matern Fetal Neonatal Med.*, Nov 2012; 25(11):2363-8.
 15. Pooh RK, 3D and 4D sonography and magnetic resonance in the assessment of normal and abnormal CNS development: alternative or complementary, *J. Perinat. Med.* 39, 2011; 3–13.
 16. Malinger G, D Lev, T Lerman- Sagie: Is fetal magnetic resonance imaging superior to neurosonography for detection of brain anomalies? *Ultrasound Obstet Gynecol*, 2002; 317: ;20(4):317-21.