# Prenatal Ultrasonography in the Diagnosis of Neurological Fetal Anomalies with Postnatal Confirmation

**Ahmed T.Galal[a], Sayed A. Sayed[a], Hazem M.M .Abd-El-Gaffar[b], Abd-El-Raheem Abd Rabo Sadk[c], Bothyna Z. Elsayed[d*]**

[a]Department of Human Anatomy and Embryology, Faculty of Medicine, Assiut University, Assiut, Egypt.
[b]Department of Obstetrics and Genecology, Faculty of Medicine, Sohag University, Sohag, Egypt.
[c]Department of Pediatrics and Neonatology, Faculty of Medicine, Sohag University, Sohag, Egypt.
[d]Department of Human Anatomy and Embryology, Faculty of Medicine, Sohag University, Sohag, Egypt.

**Abstract**

**Background:** Congenital anomalies affecting the central nervous system are among the most prevalent. The most common central nervous system anomalies are neural tube defects, which affect roughly 1-2 of every 1000 newborns.

**Objectives:** We detect the accuracy of ultrasound to diagnose CNS abnormalities**.**

**Patients and methods:** Descriptive cross-sectional study on 567 patients coming for antenatal care at Sohag Governorate undergoing mid anatomical scan between September 2021 and December 2022. After getting approval from the ethical committee at Sohag University and written consent from each woman. Clinical or post-natal neuroimaging using computed tomography or magnetic resonance imaging validated the prenatal diagnosis in situations where pregnancy progressed and the fetus survived. The total number of miscarriages, stillbirths, and infant deaths was recorded.

**Results:** Diagnostic accuracy of ultrasound in diagnosis of congenital neurological Anomalies: 2D&3D US had 100% sensitivity and100% specificity with positive predictive value 100% and negative predictive value 100% in all parameters.

**Conclusions:** Based on these findings, we can say that ultrasonography is useful for detecting and diagnosing some defects of the fetal central nervous system.

**Keywords:** Ultrasonography; Neurological; Anomalies .

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***Correspondence**: bothina.zakria@med.sohag.edu.eg

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## Introduction

The central nervous system (CNS) is composed of the brain and the spinal cord. They both develop from the embryonic ectoderm alongside other structures like the skin. Their development begins as early as the 3rd and 4th weeks of embryonic life, starting with the process of neurulation, which is the development of the neural tube. The neural tube closes spontaneously rostrally and caudally. In the fifth to sixth week, the first appearance of the brain, the prosencephalic development ensues. The primitive brain is comprised of prosencephalon, mesencephalon, and rhombencephalon. The prosencephalon divides further into telencephalon and diencephalon through a series of developmental stages, namely: formation, cleavage, and development of the midline **.(Gaitanis and Tarui, 2018; Dias and Partington, 2015; Petryk et al., 2015)**.

Any form of developmental alteration in these leads to the malformation of the developing brain **(Marin-Valencia et al., 2014)**.

Fetal central nervous system (CNS) abnormalities are second only to cardiac malformations in their frequency of occurrence. Early and accurate diagnosis at prenatal US is therefore essential, allowing improved prenatal counseling and facilitating appropriate referral **(Cater et al., 2020)**.

Central nervous system (CNS) malformations are some of the most common of all congenital abnormalities. Neural tube defects are the most frequent CNS malformations to about 1–2 cases per 1000 births **(Malinger, 2007)**.

Prenatal detection and accurate definition of CNS malformations are important because these anomalies frequently have a severe prognosis and are often associated with genetic syndromes **(Rizzo et al., 2011)** .The development of the brain and spinal cord is an extremely complicated process which continues into the second decade before final maturity is achieved. Abnormality in the development of CNS is common, up to 75% of fetal deaths and 40% of deaths in infancy are due to CNS malformations **(Rizzo et al., 2011)**

Fetal neurological abnormalities are six main categories at prenatal US. Developmental anomalies include neural tube defects and neuronal migration disorders. Posterior fossa disorders include Dandy-Walker malformation variants and Chiari II malformation. Ventricular anomalies include aqueductal stenosis. Midline disorders include those on the spectrum of holoprosencephaly, agenesis of the corpus callosum, and septo-optic dysplasia. Vascular anomalies include veins of Galen malformations. Miscellaneous disorders include hydranencephaly, porencephaly, tumors, and intracranial hemorrhage **(Cater et al., 2020)**.

The study is to detect the accuracy of ultrasound to diagnose CNS abnormalities with postnatal conformation.

## Patients and Methods

This descriptive cross-sectional study was carried out on 567 patients coming for antenatal care at Sohag Governorate undergoing mid anatomical scan from September 2021 to December 2022 after approval from the ethical committee at Sohag University and obtaining a written consent from each woman.

**Inclusion criteria:** Pregnant women have mid-anatomical scan at 20-22 weeks.

**Methods:** All patients were subjected to the followings:

- Complete history was taken from patients: age, body mass index

(BMI), consanguinity, maternal history, and family history.
- General examination.
- Radiological investigations:
- Two-dimensional Ultrasound (US) were performed to detect the presence of antenatal anomalies.

***Two-dimensional ultrasound technique***

Antenatal examination of the anomalies was done for all pregnant women using two-dimensional US (The Voluson E8 color Doppler US diagnostic instrument) during the second trimester. First, the abdominal convex array probe C1-5-D was adopted, and the probe frequency was set to 2.0 MHz. The lower abdomen was scanned for the presence of any anomalies **(Pang et al., 2021).**

Four standard recommended views-trans ventricular, falx, cavum, and posterior fossa or trans cerebellar views-provide an overview of fetal intracranial anatomy during the second trimester anatomy scan.

***Fetal outcome and follow up***

All of the newborns in the research had a postnatal checkup and confirmation of the defects by a pediatric expert to ascertain their individual health.

Clinical or post-natal neuroimaging using computed tomography or magnetic resonance imaging validated the prenatal diagnosis in situations where pregnancy progressed and the fetus survived. The total number of miscarriages, stillbirths, and infant deaths was recorded.

**Statistical analysis**

SPSS v26 was used for the statistical analysis (IBM Inc., Chicago, IL, USA). The average and standard deviation of numerical variables were provided (SD). Percentages and frequencies were used to illustrate qualitative factors ( percent ).

**Results**

This study was a descriptive cross-sectional study conducted on 567 pregnant women coming for antenatal care at sohag governorate undergo mid anatomical scan. The age ranged from 16 to 48 years with a mean value (± SD) of 29.72 (±5.97) years. BMI ranged from 19 to 41 kg/m2 with a mean value (± SD) of 28.92 (±4.06) kg/$m^2$. Consanguinity was present in44 (7.76%) patients and not in 523 (92.24%) patients. **(Table.1 & Fig.1).**

**Table1. Demographic data of the studied mothers**

| **Variables** | | **N=567** |
|---|---|---|
| **Age (years)** | **Mean ± SD** | 29.7 ± 5.97 |
| | **Range** | 16 - 48 |
| **BMI (kg/$m^2$)** | **Mean ± SD** | 28.9 ± 4.06 |
| | **Range** | 19 - 41 |
| **Consanguinity** | **Yes** | 44 (7.76%) |
| | **No** | 523 (92.24%) |

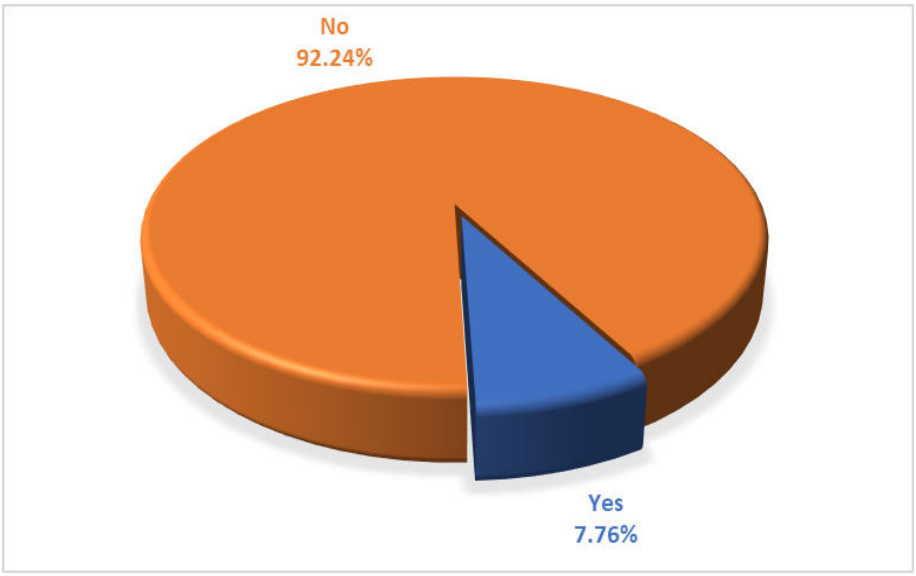



**Fig.1. Consanguinity of the studied mothers**

Maternal medical history was negative in 50 (87.72%) patients and positive 7(12.28%) patients. Positive maternal medical history was Positive TOURCH infection in 5 (8.77%) patients, teratogenic drugs in 1 (1.75%) patient and brain atrophy in1 (1.75%) patient. **(Table.2 & Fig.2)**

**Table2.Maternal medical history of the studied patients with neurological anomalies**

| Variables | | N=57 |
|---|---|---|
| Maternal medical history | Negative | 50 (87.72%) |
| | Positive | 7(12.28%) |
| | Positive TOURCH infection | 5 (8.77%) |
| | Positive teratogenic drugs | 1 (1.75%) |
| | Brain atrophy | 1 (1.75%) |

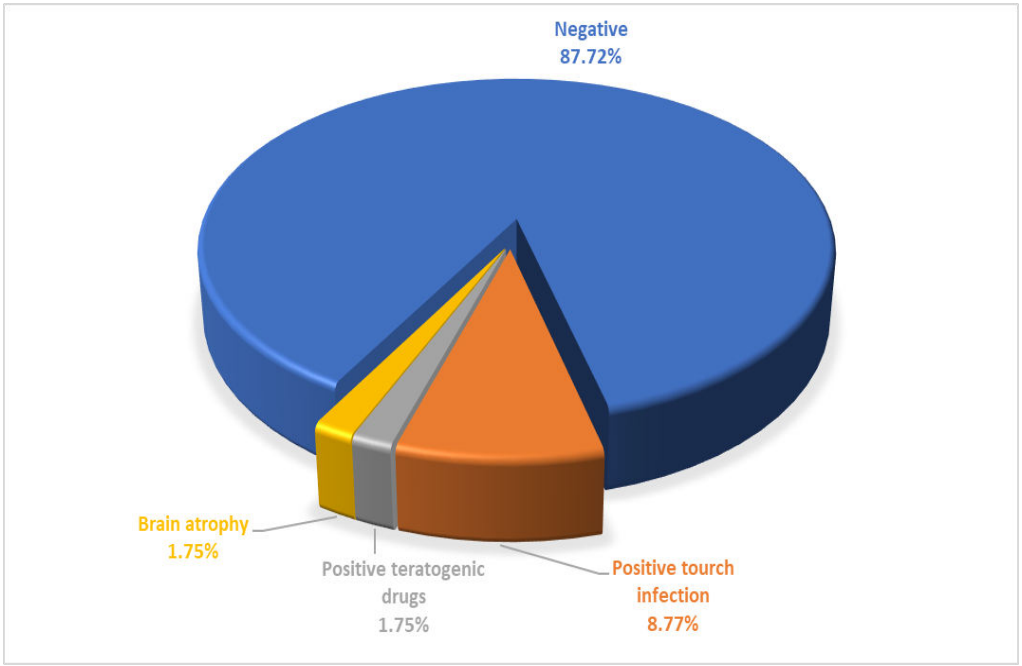



**Fig.2. Maternal medical history of the studied**

Family history was negative in 37 (64.91%) patients and positive in 20(35.09%) patients. Positive congenital in other siblings in 9 (15.79%) patients, microcephaly, epilepsy, hydrocephalus, Deafness, CHD and hydrocephalus in 1 (1.75%) patient and Brain atrophy in 6 (10.53%) patients. **(Table.3 & Fig.3).**

**Table 3. Family history of the studied patients**

| Variables | | N=57 |
|---|---|---|
| Family history | **Negative** | 37 (64.91%) |
| | **Positive** | 20(35.09%) |
| | **Positive congenital in other siblings** | 9 (15.79%) |
| | **Microcephaly** | 1 (1.75%) |
| | **Brain atrophy** | 6 (10.53%) |
| | **Epilepsy** | 1 (1.75%) |
| | **Hydrocephalus** | 1 (1.75%) |
| | **Deafness, CHD** | 1 (1.75%) |
| | **Hydrocephalus** | 1 (1.75%) |

CHD: Congenital heart disease

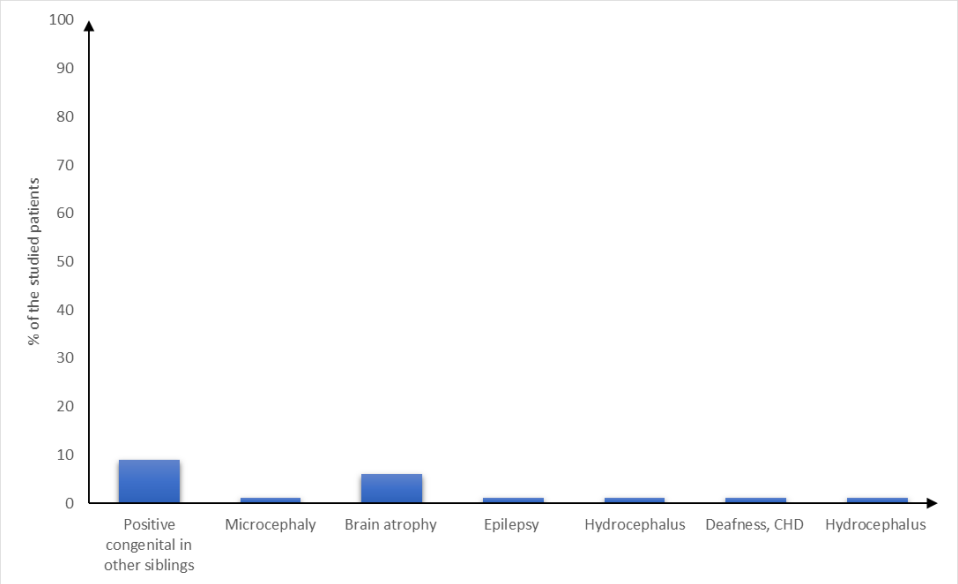



**Fig. 3. Family history (Positive) of the studied**

***Prevalence of neurological congenial anomalies in Sohag governorate***

Mid anatomical scans were performed on 567 pregnant women neurlogicl who presented for antenatal scan in the Sohag governorate. It was noticed that (90% n=510) females in the current study had not congenital anomalies in her baby and (10% n=57) had neurlogicl congenital anomalies in her baby findings as shown in (**Fig.4),** so the prevalence of neurological congenital anomalies detected by ultrasound in Sohag governorate was 10%.

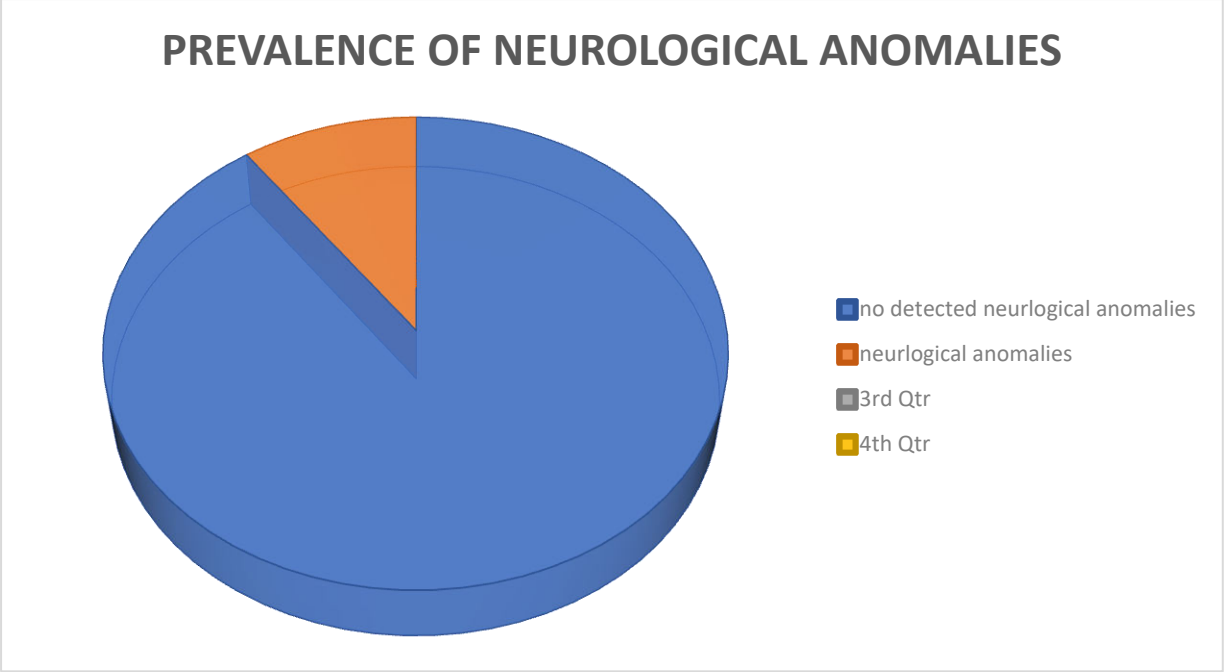



**Fig. 4. Prevalence of neurological congenital anomalies**

Antenatal diagnosis showed microcephaly in 8 (14.04%) patients, Microcephaly, hepatosplenomegaly in2 (3.51%) patients, Dandy-walker syndrome in 7 (12.28%) patients, Joubert syndrome in 2 (3.51%) patients, Hydrocephalus in 16 (28.07%) patients( **Fig.5**), Hydrocephalous, CHD, Biventricular dilation hydrocephalus, Holoprosencephaly, hydrocephalus, Hydrocephalus aqueductal stenosis, Holoprosencephaly, cleft lip and palate, Intracranial calcification IUGR, Occipital encephalocele meningomyelocele, Left cerebral hemisphere atrophy, Left ventriculomegaly agenesis of corpus callosum, Retrocerebellar dermoid cyst, Spina bifida, middle cerebral artery aneurysm**(Fig.6)** and intracranial hemorrhage in 1 (1.75%) patient **(Fig.7)**, corpus callosum agenesis in 4 (7.02%) patients, anencephaly in 3 (5.26%) patients( **Fig.8,9,10** ) and vein of Galen aneurysm in 2 (3.51%) patients( **Table.4).**

**Table 4. Antenatal diagnosis of the studied patients**

| Variables | | N=57 |
|---|---|---|
| **Antenatal diagnosis** | **Microcephaly** | 8 (14.04%) |
| | **Microcephaly, hepatosplenomegaly** | 2 (3.51%) |
| | **Dandy-walker syndrome** | 7 (12.28%) |
| | **Joubert syndrome** | 2 (3.51%) |
| | **Hydrocephalus** | 16 (28.07%) |
| | **Hydrocephalous, CHD** | 1 (1.75%) |
| | **Biventricular dilation hydrocephalus** | 1 (1.75%) |
| | **Holoprosencephaly, hydrocephalus** | 1 (1.75%) |
| | **Hydrocephalus aqueductal stenosis** | 1 (1.75%) |
| | **Holoprosencephaly, cleft lip and palate** | 1 (1.75%) |
| | **Intracranial calcification IUGR** | 1 (1.75%) |

| | | |
|---|---|---|
| | **Occipital encephalocele meningomyelocele** | 1 (1.75%) |
| | **Left cerebral hemisphere atrophy** | 1 (1.75%) |
| | **Left ventriculomegaly agenesis of corpus callosum** | 1 (1.75%) |
| | **Retrocerebellar dermoid cyst** | 1 (1.75%) |
| | **Corpus callosum agenesis** | 4 (7.02%) |
| | **Spina bifida** | 1 (1.75%) |
| | **Anencephaly** | 3 (5.26%) |
| | **Vein of Galen aneurysm** | 2 (3.51%) |
| | **Middle cerebral artery aneurysm** | 1 (1.75%) |
| | **Intracranial hemorrhage** | 1 (1.75%) |

CHD: Congenital heart disease

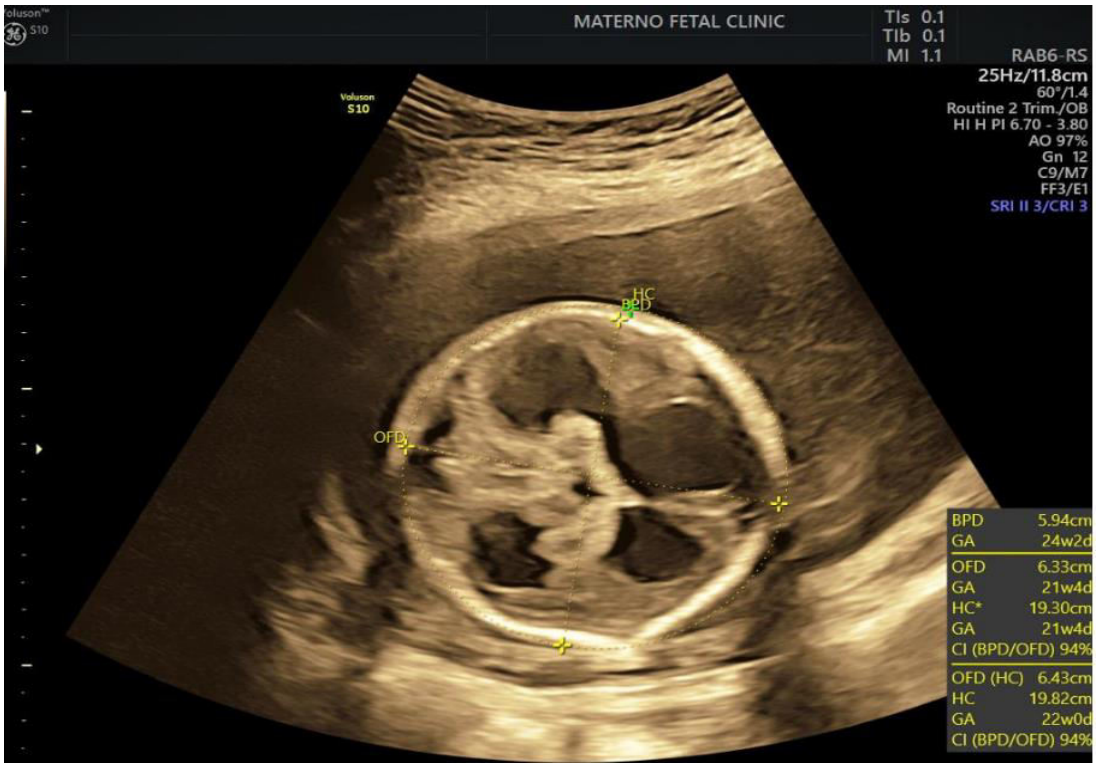
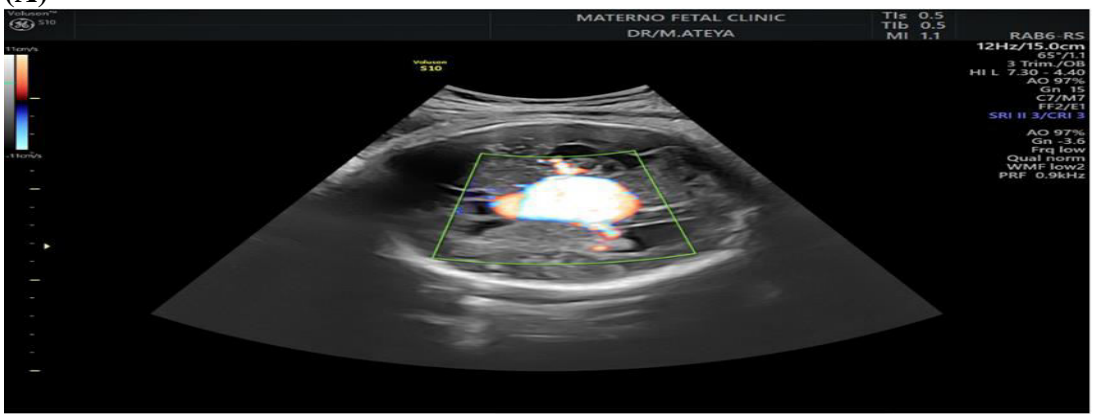
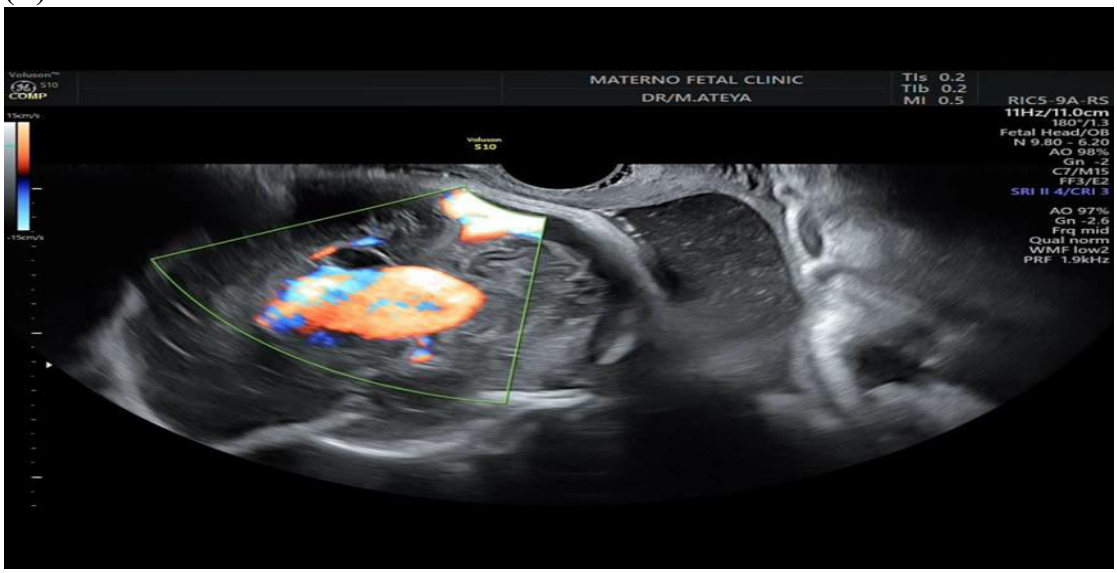



**Fig.5. Two-dimensional ultrasound showing hydrocephallus of the studied patients.**

(A)




(B)




(C)

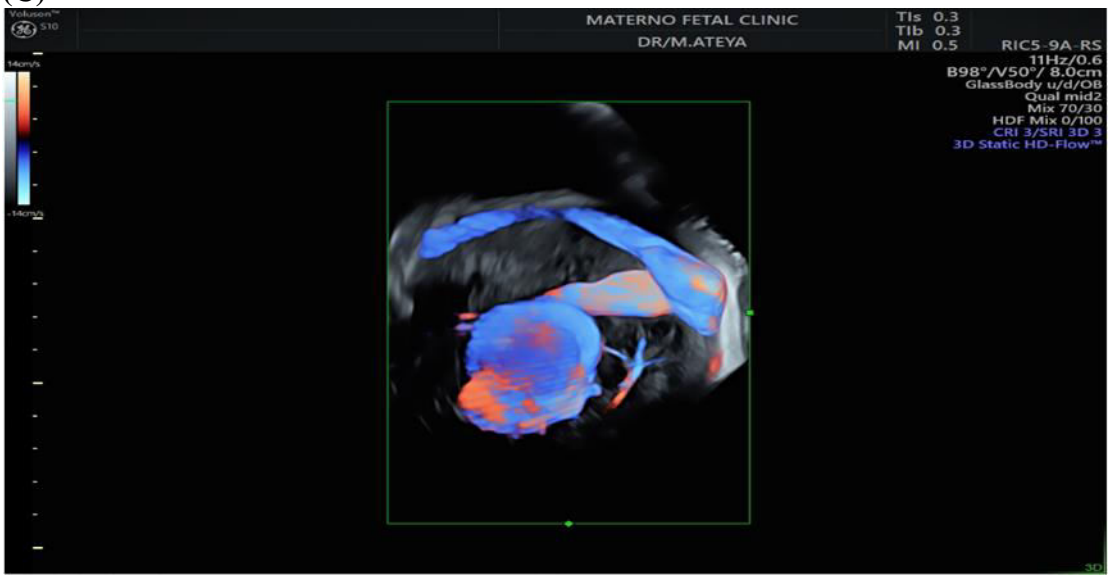



**Fig. 6. Two-dimensional ultrasound showing aneurysm in (A,B,C), all are Doppler colored .**

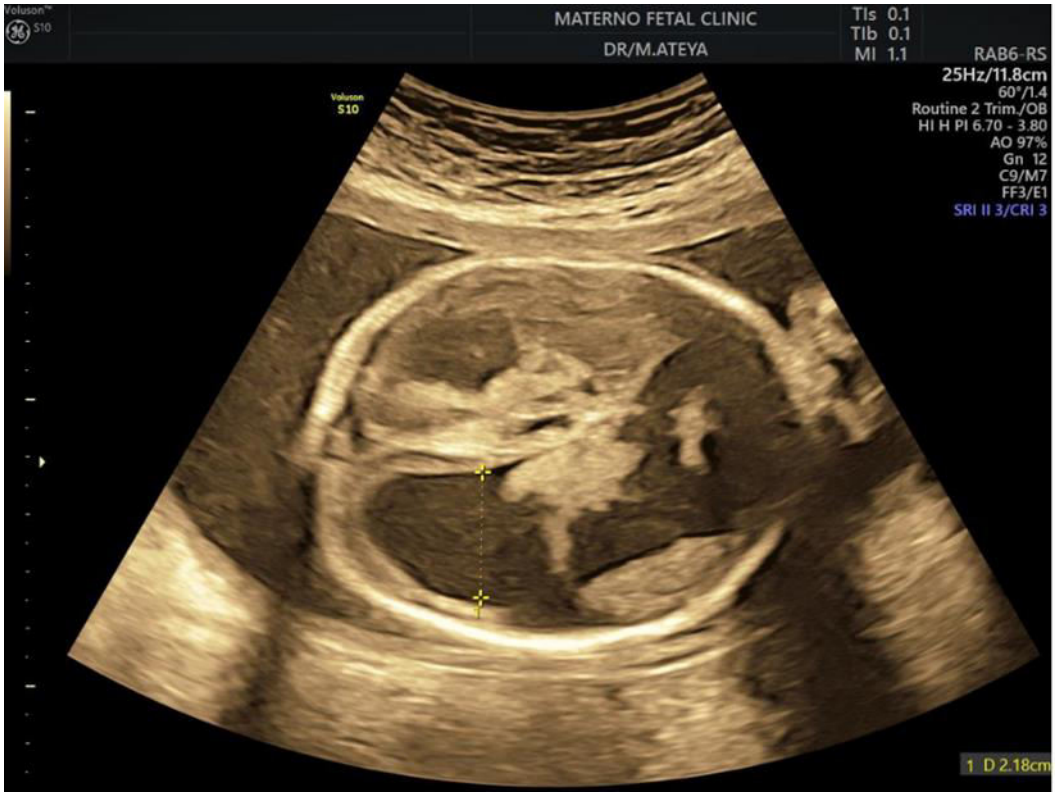



**Fig.7. Two-dimensional ultrasound showing intracranial hemorrhage of the studied patients.**

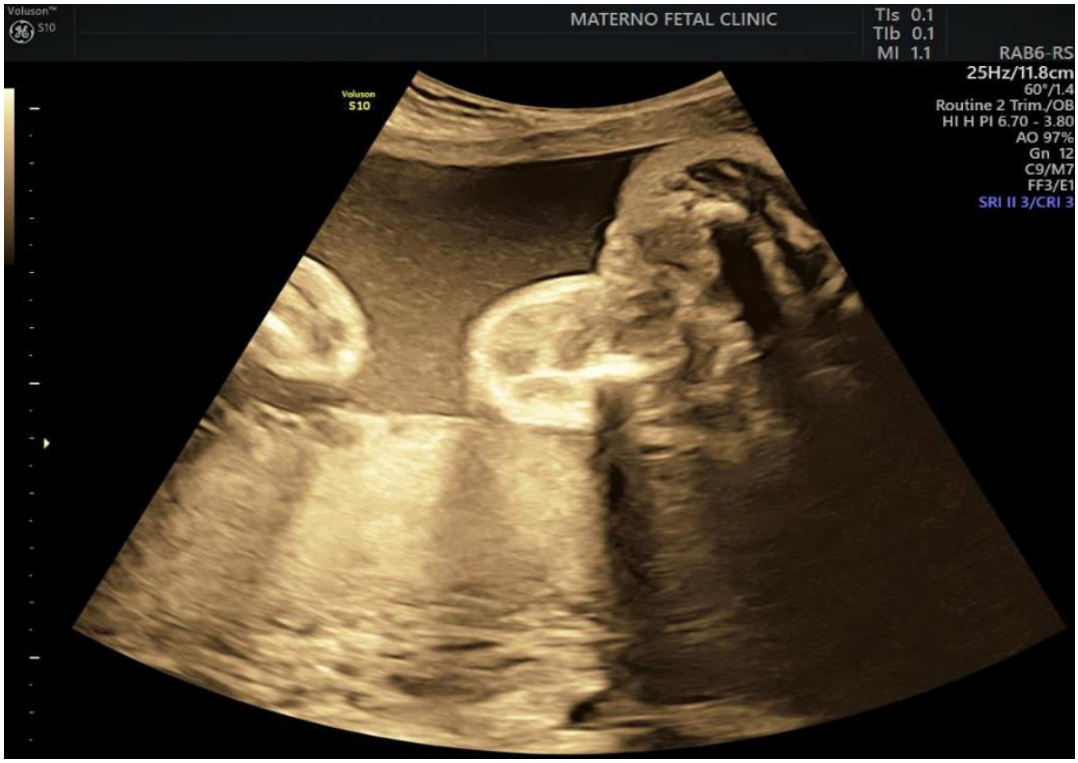



**Fig. 8. Two-dimensional ultrasound showing acrania of the studied patients.**

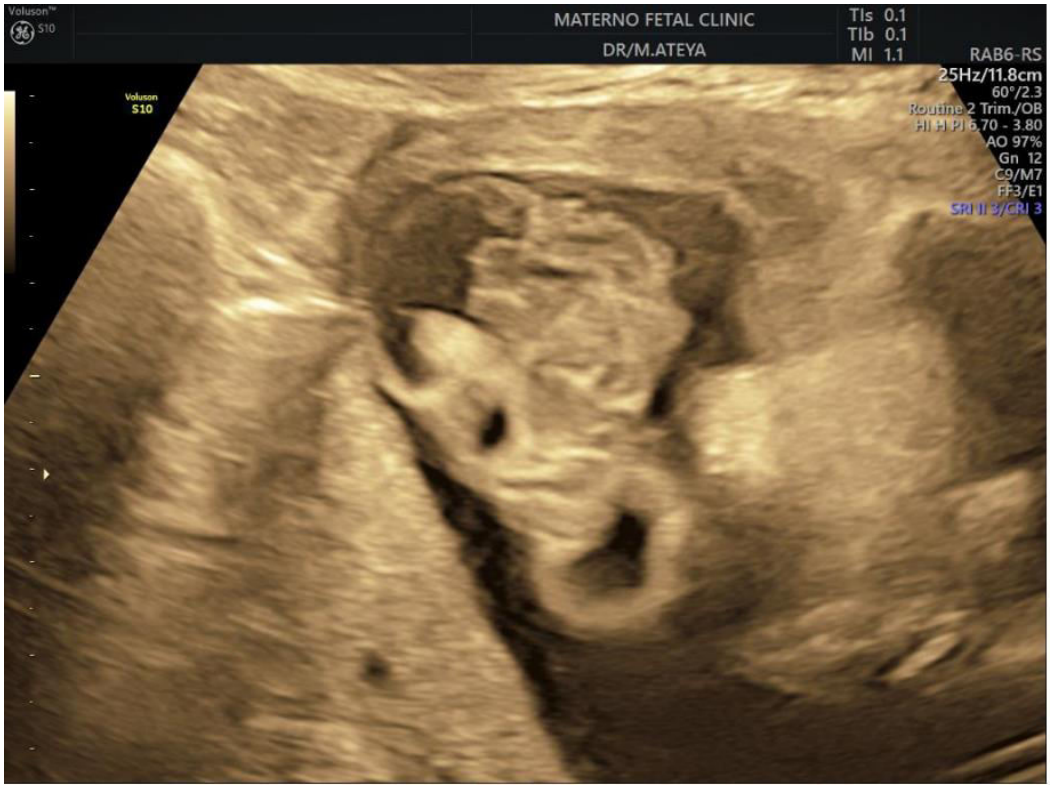



**Fig. 9. Two-dimensional ultrasound showing exencephaly of the studied patients.**

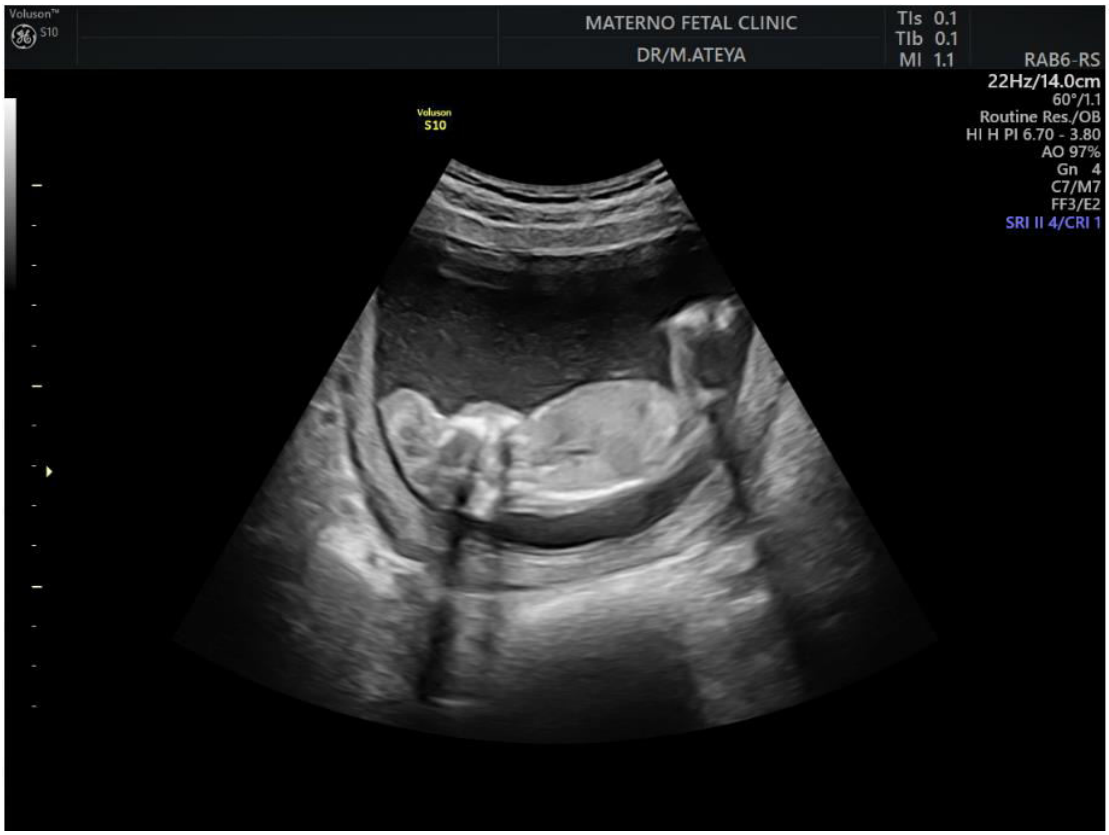



**Fig.10. Two-dimensional ultrasound showing excencephaly of the studied patient.**

Postnatal confirmation was Clinically in 19 (33.33%) patients, Hydrocephalus markedly dilated ventricles ambiguous genitalia in1 (1.75%) patient, Clinically meningitis 1st day, hydrocephalus in1 (1.75%) patient(**Fig.11**), CT confirmation in 6 (10.53%) patients, - Brain atrophy, Dandy-walker syndrome (hydrocephalus CT), Hydrocephalus, HIE, CT non communicating hydrocephalus(**Fig.12,13**), CT communicating hydrocephalus ,hypogenesis corpus callosum VSD, CT molar tooth, mild brain atrophy, CT semilobar holoprosencephaly, Butterfly vertebra and Clinically, CT markedly dilated ventricular system decreased brain volume in 1 (1.75%) patient, MRI Confirmation in 11 (19.3%) patients , MRI brain atrophy, Biventricular dilation hydrocephalus MRI diffuse brain atrophy(**Fig.14**), MRI multi cystic brain encephalomalacia at 5th month of age, MRI mild hypoplastic corpus callosum, dilated ventricles PVL, MRI Left MRI Left open-lip schizencephally abscent septum pellucidum (**Fig.15**), MRI confirmation, inter hemisphere cyst and MRI, squent in 1 (1.75%) patient.(**Table.5**).

**Table 5. Postnatal confirmation of the studied patients**

| Variables | N=57 |
|---|---|
| **Clinically** | 19 (33.33%) |
| **Hydrocephalus markedly dilated ventricles ambiguous genitalia** | 1 (1.75%) |
| **Clinically meningitis 1st day, hydrocephalus** | 1 (1.75%) |
| **CT confirmation** | 6 (10.53%) |
| ○ **Brain atrophy** | 1 (1.75%) |
| ○ **Dandy-walker syndrome (hydrocephalus CT)** | 1 (1.75%) |
| ○ **Hydrocephalus, HIE** | 1 (1.75%) |
| ○ **CT non communicating hydrocephalus.** | 1 (1.75%) |
| ○ **CT communicating hydrocephalus, hypogenesis corpus callosum VSD.** | 1 (1.75%) |
| ○ **CT molar tooth, mild brain atrophy** | 1 (1.75%) |
| ○ **CT semilobar holoprosencephaly** | 1 (1.75%) |
| ○ **Butterfly vertebra** | 1 (1.75%) |
| **Clinically, CT markedly dilated ventricular system decreased brain volume** | 1 (1.75%) |
| **MRI Confirmation** | 11 (19.3%) |
| ○ **MRI brain atrophy** | 1 (1.75%) |
| ○ **Biventricular dilation hydrocephalus MRI diffuse brain atrophy** | 1 (1.75%) |
| ○ **MRI multi cystic brain encephalomalacia at 5th month of age** | 1 (1.75%) |
| ○ **MRI mild hypoplastic corpus callosum, dilated ventricles PVL** | 1 (1.75 %) |
| ○ **MRI Left open-lip schizencephally abscent septum pellucidum .** | 1 (1.75%) |
| ○ **MRI confirmation, inter hemisphere cyst.** | 1 (1.75%) |
| ○ **MRI, squent** | 1 (1.75%) |

CT: computed tomography, MRI: magnetic resonance imaging, HIE: hypoxic-ischemic encephalopathy, VSD: ventricular septal defect.

**Fig.11. A case of hydrocephalus before intervention.**

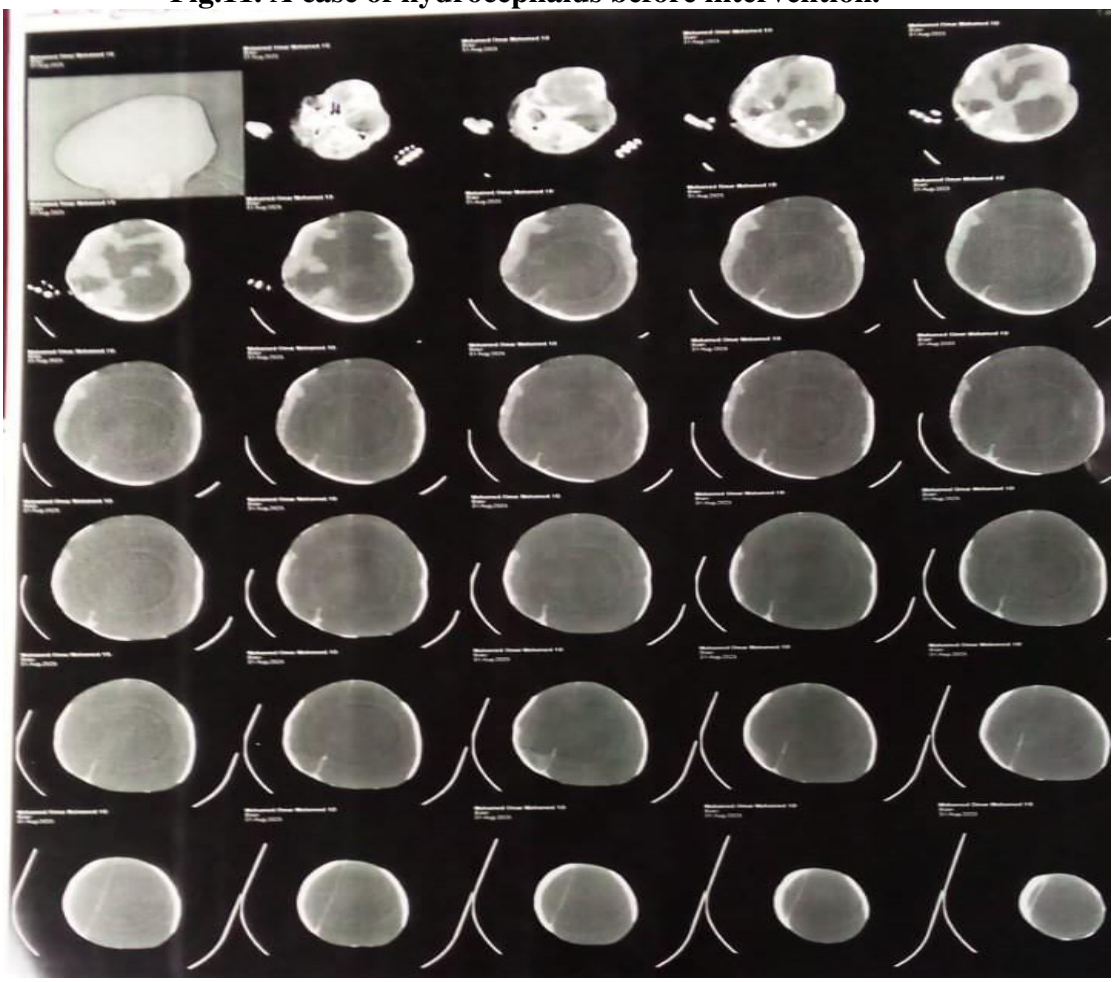


**Fig.12: CT of the newborn (of Fig,11) showing supratentorial hydrocephalus.**

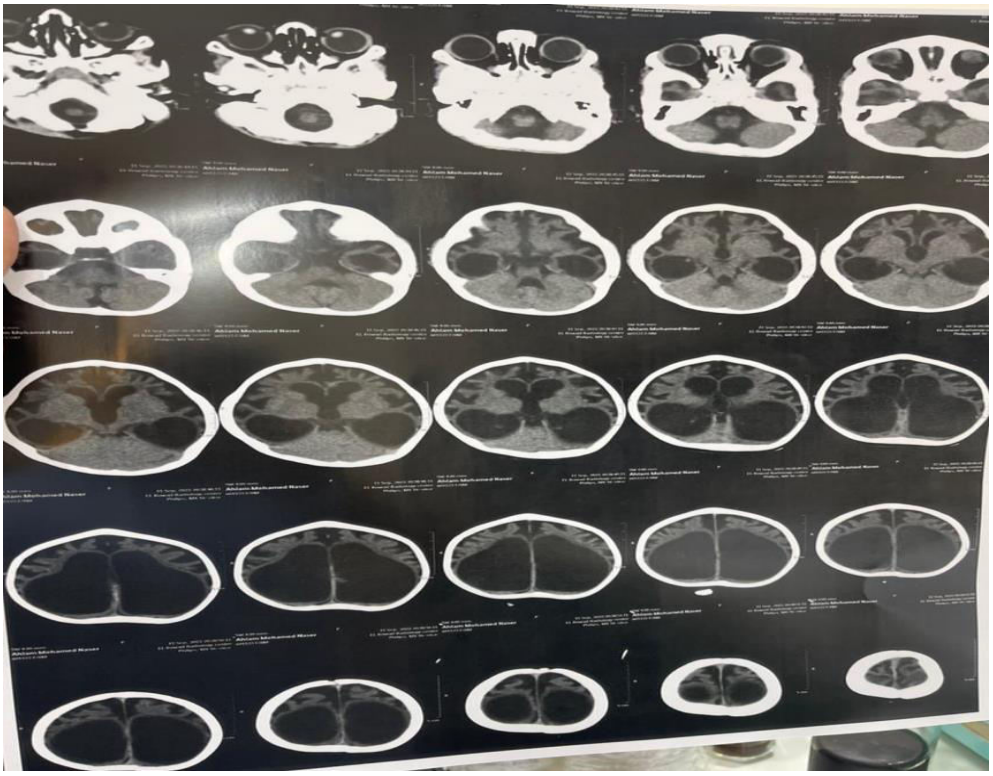
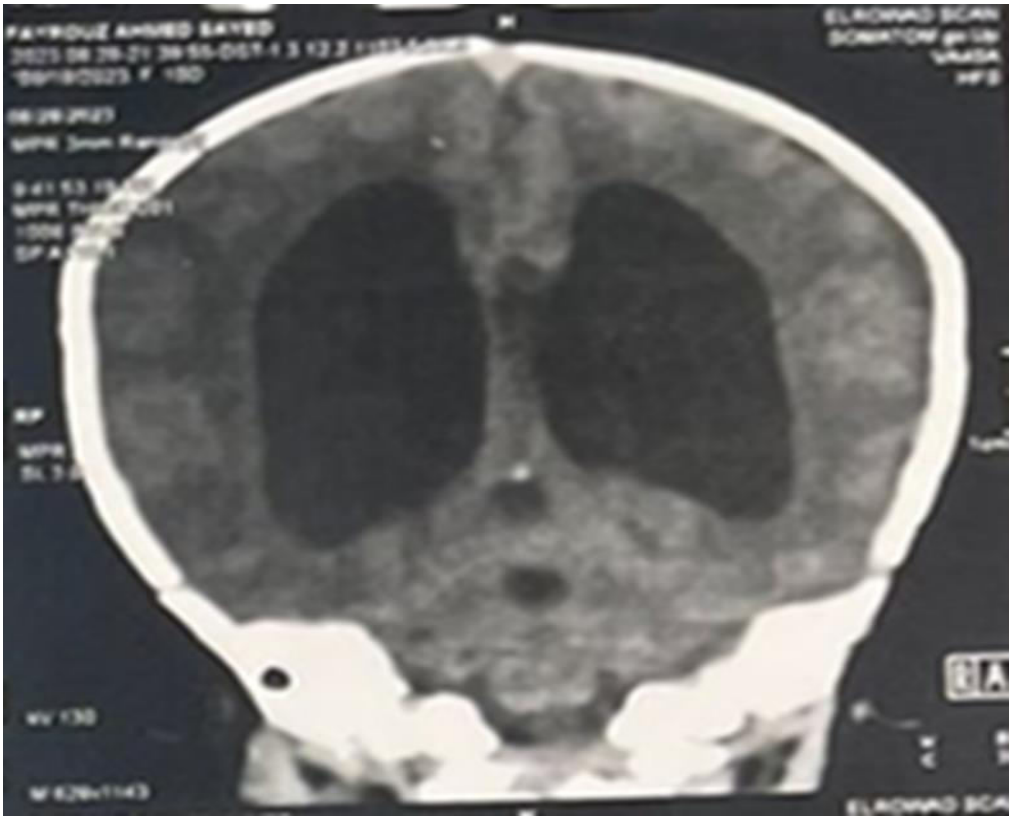


**Fig.13.MsCTof the brain showing obstructive non communicating hydrocephalic changes mostly secondary to aqueduct stenosis.**



**. Fig.14 .MRI showing biventricular hydrocephalus.**

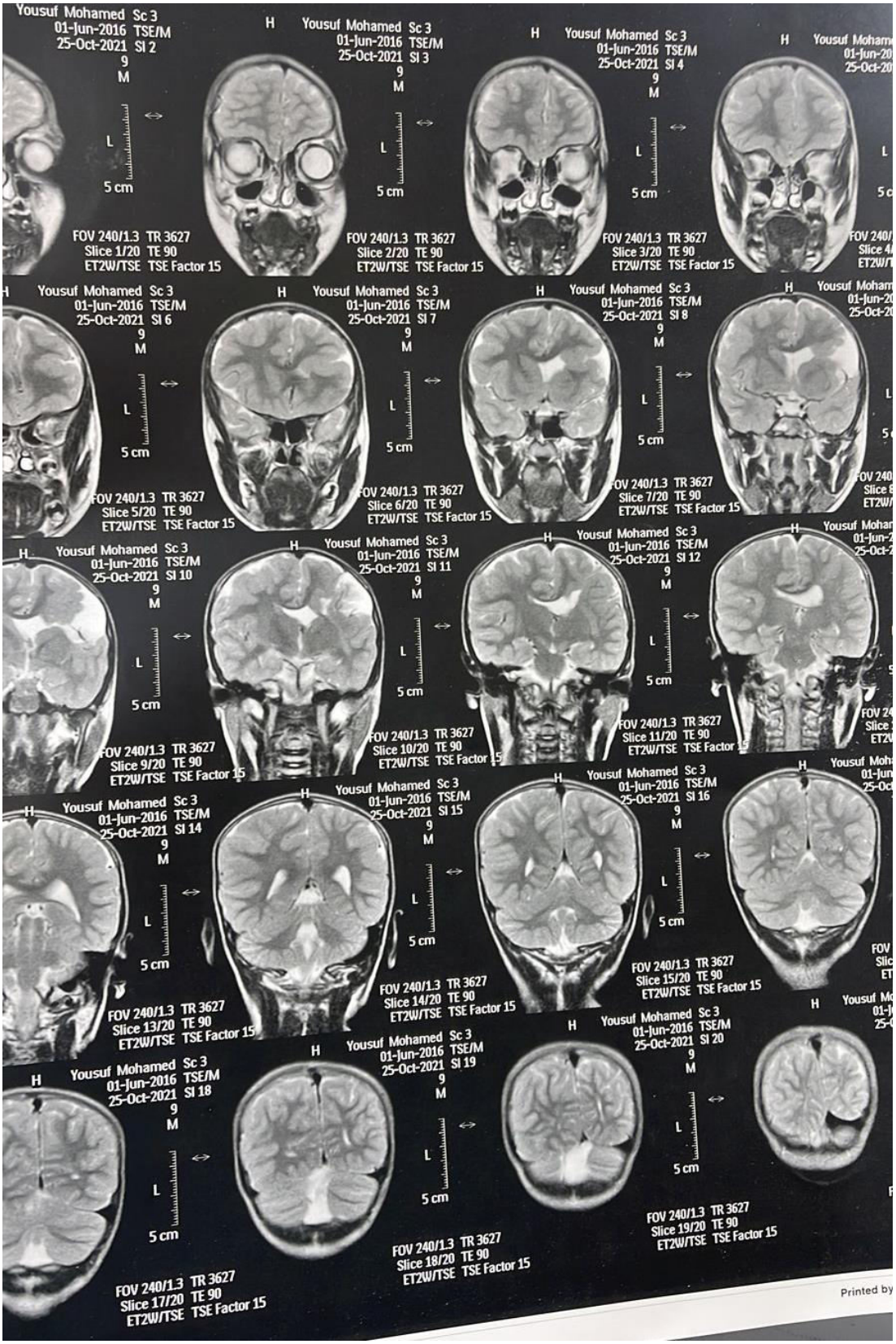



**Fig.15 . MRI showing open lip schizencephally (left tempro-parital cleft and absent septum pellucidum.**

In our study 57 cases of neurological Mal formation detected by ultrasound and all were confirmed postnatally either clinically or by radiological imaging CT or MRI. Diagnostic accuracy of ultrasound in diagnosis of congenital neurological anomalies: 2D&3D US had 100% sensitivity and100% specificity with positive predictive value 100% and negative predictive value 100% in all parameters, **(Table. 6).**

**Table 6: Diagnostic accuracy of ultrasound in diagnosis of congenital neurological anomalies**

| Variables | | Postnatal confirmation | |
|---|---|---|---|
| **Prenatal diagnosis by 2D & 3D US** | | Positive | Negative |
| | Positive | 57 | 0 |
| | Negative | 0 | 510 |

**Discussion**

The United States is able to evaluate and diagnose central nervous system malformations in the foetus at any stage of pregnancy. The ultrasound examination also covers the spinal cord and brain. Since the majority of brain development occurs during pregnancy, understanding whether the elements of the central nervous system exhibit complex embryology and architecture is crucial. During pregnancy, there are alterations in the CNS that are correlated with alterations in the US parts of the CNS **(Hassan et al., 2022)**.The embryology and architecture of the CNS, as well as its ultrasonography properties at different gestational ages, must be understood by all professionals engaged in prenatal examination to prevent misdiagnosis. In addition, knowing the following about the congenital defects that might impact the central nervous system is crucial **(Hassan et al., 2022) .** Evaluation of the foetal central nervous system during ultrasonography is typically done in the axial, sagittal, and coronal planes using abdominal and vaginal methods in the first trimester. Examination of foetal morphology during 20–24 weeks of gestation is when most attempts to identify CNS abnormalities are made **(ISUOG, 2007)** . Since the brain is a three-dimensional organ with a complex anatomy, the midline structures such as the corpus callosum, brain stem, cerebellar vermis, and cerebral cortex are probably not evaluated if the scan of the foetal skull is performed just in the axial planes **(Malinger G et al.,2006).** Multiplaner study of the embryonic brain regions using sagittal and coronal images of the foetal skull was reported by **Timor Tritsch et al., (1996)** (Timor-Tritsch and Monteagudo, 1996). The ultrasonographic examination of the brain and spine in foetuses is governed by two sets of recommendations produced by ISUOG, titled "basic CNS assessment" and "neurosonographic evaluation"**(ISUOG 2007)**.

The aim of our work was to detect the accuracy of ultrasound to diagnose CNS abnormalities with postnatal confirmation.

This was a descriptive cross-sectional study conducted on 567 pregnant women coming for antenatal care at Sohag governorate undergo mid anatomical scan.

In our study, the age ranged from 16 to 48 years with a mean value (± SD) of 29.72 (±5.97) years. BMI ranged from 19 to 41 kg/m$^2$ with a mean value (± SD) of 28.92 (±4.06) kg/m$^2$.

In our study, maternal medical history was negative in 50 (87.72%)

patients and positive 7(12.28%) patients. Positive maternal medical history was Positive TOURCH infection in 5 (8.77%) patients, teratogenic drugs in 1 (1.75%) patient and brain atrophy in1 (1.75%) patient.

According to **Munim et al. (2006)** who aimed to describe the trends of congenital abnormalities seen at a tertiary care facility in Karachi. They reported that the mean age of the women in this study was 27.3 years with SD ± 5.3. Among the study subjects 11.6% were women above the age of 35 years. Only 8.8% of them had a previous history of congenital malformations.

Patients visiting the fetomaternal centre at Minia University were surveyed to determine the prevalence of central nervous system abnormalities (**Hassan et al., 2022**). It was shown that 25% of patients had a history of other congenital fetal abnormalities and 6% had a history of other central nervous system .In our study, antenatal diagnosis showed microcephaly in 8 (14.04%) patients, , hepatosplenomegaly in 2 (3.51%) patients, Dandy-walker syndrome in 7 (12.28%) patients, Joubert syndrome in 2 (3.51%) patients, Hydrocephalus in16 (28.07%) patients, Hydrocephalous, CHD, Biventricular dilation hydrocephalus, Holoprosencephaly, hydrocephalus, Hydrocephalus aqueductal stenosis, Holoprosencephaly, cleft lip and palate, Intracranial calcification IUGR, Occipital encephalocele meningomyelocele, Left cerebral hemisphere atrophy, Left ventriculomegaly agenesis of corpus callosum, Retrocerebellar dermoid cyst, Spina bifida, middle cerebral artery aneurysm and intracranial hemorrhage in 1 (1.75%) patient, corpus callosum agenesis in 4 (7.02%) patients, anencephaly in 3 (5.26%) patients and vein of Galen aneurysm in 2 (3.51%) patients.

**Hassan et al. (2022**) we learn that ultrasonography may identify CNS defects in 79 fetuses. Ventriculomegaly was the most often seen abnormality (22%). Due to the continuous process of brain development, modest ventriculomegaly may still be considered a normal variant. The high rate of Ventriculomegaly in our sample (42% of cases) may be explained by the fact that enlargement of the lateral ventricle has been documented in fetuses with aneuploidy during the first trimester. Ultrasound examination is operator dependant and requires thorough and skilled examination since it sometimes involves trial and error. Sixty-four percent of the instances in which a diagnosis of CNS abnormalities was verified after birth, compared with 19 percent of the cases in which therapeutic termination of pregnancy was used. According to a study conducted by Fatma et al. (**Fatma Salah El-Dein Mohammed et al., 2019**), the identification rate of CNS abnormalities using ultrasonography was 90%. They found that prenatal detection of CNS abnormalities occurred in 90% of patients.

When considering whether or not to terminate a pregnancy, ultrasound diagnosis of prenatal brain anatomic abnormalities is crucial. Patients are more likely to agree to this approach since it is non-invasive. Multiple studies have shown that the United States is able to identify brain abnormalities with a sensitivity of 92% to 99.7%.(**Abozaid et al., 2022**).

In our study Diagnostic accuracy of ultrasound in diagnosis of congenital neurological anomalies :2D&3D US had 100% sensitivity and100% specificity with positive

predictive value 100% and negative predictive value 100% in all parameters.

Ultrasound has been shown to have a 90% detection rate for neural tube abnormalities in a case-control study (**Gupta et al.,2001**)For the diagnosis of congenital anomalies, the research team at **Gonçalves et al. (2016)** found that MRI was more sensitive than 3D -US (MRI, 88.9 percent (16/18) vs. 3DUS, 66.7 percent (12/18) vs. 2D-US, 72.2 percent (13/18)), and that it also provided additional information affecting prognosis. The diagnostic accuracy of 2D-US, 3D-US, and MRI for non-CNS abnormalities was comparable. The sensitivity of MRI was 85.6 percent (77/90) whereas the sensitivity of 3D-US was 94.4 percent (85/90) and the sensitivity of 2D-US was 92.2 percent (83/90). While 2D-US and 3D-US were more reliable than MRI for ruling out CNS disorders before birth, confirmation of these findings after delivery was not possible for MRI.

**Conclusion**

Based on these findings, we can say that Diagnostic accuracy of ultrasound in diagnosis of congenital neurological anomalies :2D&3D US had 100% sensitivity and100% specificity. Our results also imply that imaging tools like CT and MRI scans are effective for confirming diagnoses of neurological and developmental abnormalities in babies, even if clinical assessment is a crucial tool in making the initial diagnosis.

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