ROLE OF CRANIAL ULTRASOUND IN DIAGNOSIS OF CONGENITAL BRAIN ANOMALIES

By

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ABSTRACT

Introduction: *Central nervous system (CNS) anomalies are the second most frequent serious congenital anomaly, after congenital heart disease. There is significant variation in incidences of congenital CNS anomalies in different regions of world including Europe. In the neonatal period cranial US can be used as the initial modality to exclude a major structural malformation.*

Aim of the study: *To study the role of cranial ultrasound in early detection of congenital brain anomalies in high risk neonates.*

Patients and Methods: *this descriptive study was conducted on 100 neonates from Al Azhar university hospitals. During the period from November 2019 to May 2020, by simple random method then strictly evaluated clinically and laboratory and subjected to cranial ultrasound.*

Results: *The incidence of cranial ultrasound abnormalities in high-risk neonates is 9% in the present study. There were 57% of male and 43% of female neonates, 34% preterm and 66% term high-risk neonates enrolled in the study, The abnormalities included the following: Complete agenesis of corpus callosum (2neonates), Partial agenesis of corpus callosum (2 neonate), Hydrocephalus (2neonates), Ventriculomegaly (1neonate), Dandy walker malformation (1neonate), Cerebellar hypoplasia (1 neonate), There was no significant correlation of incidence of abnormal cranial ultrasound findings in male and female, days of life, mode of delivery, maternal age or consanguinity, Correlation of dysmorphic features, abnormal neurological signs, non-gestational DM and lack of intake of folic acid in the 1st trimester with cranial ultrasound findings were statistically significant.*

Conclusion: *Tran's anterior fontanelle Sonography is useful, safe, simple bedside method of diagnosis of congenital brain malformations and does not need to transfer a patient who may be critically ill. Dysmorphic features, non-gestational DM and neonatal convulsion are associated with increased risk of congenital brain anomalies.*

Keywords: *Brain, Congenital malformations, cranial ultrasound.*

INTRODUCTION

Congenital brain anomalies, whether they are isolated (single) or part of syndromes, are a common cause of medical intervention, long-term illness, and death. The neonatologist often is the first person to identify necessary evaluations and management and to explain the cause of the anomalies and the prognosis for the child to the parents. Different anomalies may be classified as malformations, deformations and disruptions **(Usami t al., 2016)**.

Central nervous system (CNS) anomalies are the second most frequent serious congenital anomaly, after congenital heart disease. There is significant variation in incidences of congenital CNS anomalies in different regions of world including Europe **(Barkovich, 2011)**.

In the neonatal period cranial US can be used as the initial modality to exclude a major structural malformation **(Fawer, 2010)**.

Cranial US are correlated with anatomical and pathological findings and clinical outcomes. Appropriate correlation of the US features with clinical history can assist in improving the diagnostic yield. Familiarity with the US features of congenital brain anomalies is therefore an extremely valuable tool, as it facilitates an accurate diagnosis and treatment these anomalies. **(Barkovich et al., 2011)**.

Aims of the Work

To study the role of cranial ultrasound in early detection of congenital brain anomalies in high risk neonates.

PATIENTS AND METHODS

This descriptive study was conducted on 100 neonates admitted to the Neonatal Intensive Care Unit (NICU), in Al Azhar university hospitals. During the period from November 2019 to May 2020, by simple random method then strictly evaluated clinically and laboratory and subjected to cranial ultrasound.

I. Patients:

Inclusion criteria:

- Prematurity (gestational age 27-38 weeks).
- Neonatal Respiratory distress with DOWN score ≥4 irrespective to the underlying etiology.
- Evidence of neonatal Sepsis (clinically and laboratory).
- Evidence of hypoxic ischemic insult.
- Neonatal hyperbilirubinemia.

- Infants of diabetic mothers whether gestational or non-gestational diabetes.
- Dysmorphism.

Exclusion criteria:

- Craniosynostosis with closed AF.
- Healthy full term.

II. Methods:

All the studied cases were subjected to the following:

A. Complete history taking.

B. Complete general and systemic examination.

C. Laboratory evaluation when needed.

D. Imaging study:

Imaging including Transcranial ultrasound through the anterior fontanels by using general electric and Toshiba apparatus equipped with 5 MHZ. micro convex transducer.

Statistical analysis of the data:

Data were fed to the computer and analyzed using IBM SPSS software package version 20.0. (Armonk, NY: IBM Corp).

Ethical considerations:

A. Written Parent consent for the study was obtained before the study.

B. Approval of the local ethical committee was obtained.

C. The authors declared no potential conflict of interest with respect to the research & publication.

D. All the data of the patient & results of the study are confidential & the caregiver has the right to keep it.

E. The authors received no financial support for the research & publications of the article.

F. The caregiver has the right to withdraw from the study.

RESULTS

Table (1): Demographic Data and Some Clinical Characters of the Studied Neonates

	No. **(n= 100)**	%
Age (days)		
≤ 3days	64	64.0
>3days	36	36.0
Sex		
Male	57	57.0
Female	43	43.0
Gestational age by weeks		
≥ 37 weeks	66	66.0
<37 weeks	34	34.0
Weight		
<10th percentile	7	7.0
>90th percentile	5	5.0
Between 10th and 90th percentile	88	88.0
Length		
<10th percentile	4	4.0
Between 10th and 90th percentile	96	96.0
Head circumference		
<10th percentile	6	6.0
>90th percentile	5	5.0
Between 10th and 90th percentile	89	89.0
Dysmorphic features		
Absent	91	91.0
Present	9	9.0
Neurological signs		
Absent	90	90.0
Present **e.g.** convulsion	10	10.0

This table shows that 64% of the studied neonates' ≤ 3 days post-natal age, 57% were male and 66% of them were full term.

It shows also that most of the studied neonates were appropriate for gestational age regarding to Weight, length & Head circumference and most of them had no dysmorphic features.

Table (2): Different Causes of Admission in the Studied Neonates

Cause of admission	No. (n= 100)	%
Sepsis	19	19.0%
IUGR	6	6.0%
Hypoxic ischemic encephalopathy	4	4.0%
Infant of diabetic mother	10	10.0%
Neonatal convulsion	8	8.0%
Neonatal hyperbilirunemia	17	17.0%
Respiratory distress syndrome	36	36.0%

This table show that the most common cause of admission was Respiratory distress syndrome (36 %), followed by neonatal sepsis (19%) and the least common cause of admission was HIE (4%).

Table (3): Abnormal Cranial Ultrasound Findings in the Studied Neonates

Finding	No. (n=100)	%
Complete agenesis of corpus callosum	2	2.0
Partial agenesis of corpus callosum	2	2.0
Hydrocephalus	2	2.0
Ventriculomegaly	1	1.0
Dandy walker malformation	1	1.0
Cerebellar hypoplasia	1	1.0
Total of Finding	**9**	**9.0**

This table shows that complete and partial agenesis of corpus callosum (4%), Hydrocephalus (2%), ventriculomegaly (1%), Dandy walker malformation (1%), and Cerebellar hypoplasia (1%).

Table (4): Maternal Risk Factors in the Studied Neonates

	No.	%
Maternal Risk Factors	24	24.0
Antepartum hyperthermia	4	4.0
Drugs intake e.g. Valporic acid	2	2.0
Malnutrition	1	1.0
Chronic DM	5	5.0
Gestational DM	4	4.0
Maternal Obesity	6	9.0
Exposure to radiation	2	2.0
Folic acid intake in 1st trimester		
Yes	92	92.0
No	8	8.0
Consanguinity		
Yes	19	19.0
No	81	81.0

This table shows that the most common risk factor was maternal obesity (6 %), then Gestational & non-Gestational DM (9%) and the least risk factor was malnutrition (1%).

Table (5): Correlation between cranial ultrasound findings regarding clinical manifestations in both groups

	Finding				Test of Sig.	P
	Group A (n = 91)		Group B (n = 9)			
	No.	%	No.	%		
Age (days)						
≤ 3 days	61	67	3	33.3	χ^2= 5.003	^{FE}p= 0.057
>3 days	30	32.9	6	66.6		
Mean ± SD.	2.49 ± 1.80		3.55 ± 2.42			
Gestational age by weeks					χ^2= 2.325	^{FE}p= 0.177
≤37	28	30.7	4	44.4		
>37	63	69.2	5	55.5		
Sex						
Male	51	56	6	66.6	χ^2= 0.3771	^{FE}p= 0.5391
Female	40	43.9	3	33.3		
Weight						
<10th percentile	6	6.5	1	11.1	χ^2= 1.0949	^{FE}p= 0.5784
>90th percentile	4	4.3	1	11.1		
Between 10th and 90th percentile	81	89	7	77.7		
Head circumference						
<10th percentile	3	3.2	3	33.3	χ^2= 31.637*	^{FE}p= 0.0001*
>90th percentile	2	2.1	3	33.3		
Between 10th and 90th percentile	86	94.5	3	33.3		
Dysmorphic features						
No	86	94.5	5	55.5	χ^2= 15.171*	^{FE}p= 0.00098*
Yes	5	5.4	4	44.4		
Neurological signs						
Absent	84	92.3	6	66.6	χ^2= 5.9829*	^{FE}p= 0.01445*
Present e.g. convulsion	7	7.6	3	33.3		

χ2: Chi square test FE: Fisher Exact t: Student t-test.
p: p value for association between different categories *: Statistically significant at p ≤ 0.05.

This table shows that there are significant differences between group A & B, regarding head circumference & dysmorphic features. Otherwise no statistical significance between group A & B.

Table (6): Correlation between cranial ultrasound findings regarding maternal risk factors in both groups

	Finding				Test of Sig.	P
	Group A (n = 91)		Group B (n = 9)			
	No.	%	No.	%		
Maternal condition						
No	62	68.1	5	55.5	χ^2= 1.3266	^{FE}p= 0.2494
Hyperthermia	4	4.3	0	0.0		
Drugs intake	2	2.1	0	0.0		
Malnutrition	1	1.09	0	0.0		
Gestational DM	4	4.3	0	0.0		
Exposure to radiation	2	2.1	0	0.0		
Maternal Obesity	5	5.4	1	11.1	χ^2= 0.256	^{FE}p= 0.6123
Chronic DM	2	2.1	3	33.3	χ^2= 7.1502*	^{FE}p= 0.074*
Folic acid intake in 1st trimester						
Yes	86	94.5	6	66.6	χ^2= 8.624*	^{FE}p= 0.003*
No	5	5.4	3	33.3		
Consanguinity						
No	73	80.2	8	88.8	χ^2= 0.550	^{FE}p= 0.433
Yes	18	19.7	1	11.1		

χ2: Chi square test FE: Fisher Exact MC: Monte Carlo U: Mann Whitney test.
p: p value for association between different categories.

This table shows that there is significant correlation between maternal chronic D.M. & Folic acid intake in 1st trimester and cranial ultrasound findings in our studied groups.

DISCUSSION

The present study included (100) high risk neonates, 57 were females and the remaining were males, The majority were less than 3 days old (64%), while those ≥ 3 days old were (36%), the majority of cases were ≥37weeks (66%), while the remaining were < 37 weeks, the majority of cases admitted with Respiratory distress syndrome (34%) followed by neonatal Sepsis (19%) then neonatal hyperbilirubinemia (17%) lastly Infant of Diabetic mother (10 %) of the total cases.

Our results showed that cranial ultrasonographic findings in the studied cases were abnormal in (9%) and normal in (91%), in

comparison with **Nagaraj et al. (2016)**, who showed that The CUS was normal in (62%) and abnormal in (38%) of their study cases. while in study done by **Gover et al., (2011)**, who showed that the abnormal CUS was found in 10.2% of high-risk neonate's and this findings is in agreement with our results.

The low ratio of abnormal ultrasound findings in our results may be explained that we looked for congenital brain anomalies only, while in other studies they looked for all brain malformations.

Our results showed that cranial ultrasonographic abnormalities included the following: Complete agenesis of corpus callosum (2 neonates), Partial agenesis of corpus callosum (2 neonate), Hydrocephalus (2 neonates), Ventriculomegaly (1 neonate), Dandy walker malformation (1 neonate), Cerebellar hypoplasia (1 neonate), this findings are in agreement with study done by **Chang et al., (2012)** who found that Minor anomalies were found in 318 cases (10%) neonates with tiny cysts, and major anomalies were found in 637 (20%) neonates, including obstructive hydrocephalus, agenesis of the corpus callosum and Dandy walker malformation.

The common congenital brain malformations can be detected by ultrasound: hydrocephalus, holoprosencephaly, agenesis of corpus callosum, schizencephaly and hydranencephaly **(Maller et al., 2019)**.

In our study, there was no significant statically difference between the abnormal CUS findings and sex of the patients, post-natal age, birth weight or length, mode of delivery, maternal age or consanguinity; this is in concordance with a study done by **Gover et al. (2011)**, who found that There was no association between non-structural CUS findings (hemorrhage, echogenicity or anomalies) and mode of delivery, birth weight, maternal age and consanguinity.

In our study, there was significant relation between the abnormal CUS findings and abnormal head circumference (microcephaly & macrocephaly), and this is contrary with study done by **Gover et al. (2011)**, who found that There was no relationship between any CUS abnormality and head circumference.

Regarding abnormal neurological signs and dysmorphic features which detected by clinical examination there was significant

relation between these dysmorphic features and the CUS findings in our study, This is in agreement with a study done by **Puvabanditsin et al. (2018)** who found similar results significantly-observed among high risk neonates with dysmorphic features, Also there was significant relation between abnormal neurological signs and the CUS findings in our study, This is in agreement with a study done by **Nagaraj et al. (2016)**, who found similar results since there was statistically significant correlation with neonates having seizures and abnormal cranial ultrasound.

Regarding the maternal risk factors, there was significant relation between Chronic DM and the CUS findings in our study. This finding is in agreement with study done by **Cloherty et al., (2008)** who showed that the central nervous system anomalies e.g., (anencephaly, meningocele syndrome, holoprosencephaly) and cardiac anomalies make up two-thirds of the malformations seen in IDMs. Although there is a general increase in the anomaly rate in IDMs, no anomaly is specific for IDMs, although half of all cases of caudal regression syndrome (sacral agenesis) are seen in IDMs. There have been several studies correlating metabolic control of diabetes in early pregnancy with malformations in IDMs. Among the more recent studies, that performed by the Joslin Clinic that showed a relation between elevated HbA1 in the first trimester and major anomalies in IDMs. The data are consistent with the hypothesis that poor metabolic control of maternal diabetes in the first trimester is associated with an increased risk of major congenital malformations.

Also, there was significant relation between lack of intake of folic acid in 1st trimester and the CUS findings in our study, and this is in agreement with study done by **Salerno et al., (2008)**, who found that at least 3% of babies are born with some congenital malformation in his study. The intake of folic acid prior to conception and during the early stages of pregnancy plays an important role in preventing neural tube defects, severe anomalies of brain embryogenesis, and other malformations such as cardiac and urinary tract anomalies, oro-facial clefts and limb reduction defects.

CONCLUSION

1. Trans-fontanellar Sonography is useful, safe, simple bedside method for diagnosis of congenital brain malformations.
2. Dysmorphic features, non-gestational DM and neonatal convulsion are associated with increased risk of congenital brain anomalies.

RECOMMENDATIONS

1. Neonatal screening of high-risk neonates with cranial ultrasound for early detection of congenital brain malformation.
2. Confirmation of the diagnosis of congenital brain anomalie can be done using more advanced technique with high resolution like CT scan & MRI.
3. The avoidance of teratogenic drugs during pregnancy, smoking, avoidance of X-ray radiation and adequate nutrition contribute in part to lessening the risk of brain anomalies. This can be achieved by proper health education and antenatal care.
4. Folic acid administration to pregnant mothers in the 1st trimester to avoid congenital brain anomalies.
5. Well control of maternal diabetes during pregnancy.

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دور الموجات فوق الصوتية علي الرأس في تشخيص العيوب الخلقية بالمخ

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المقدمة: تشوهات الجهاز العصبي المركزي هي ثاني أكثر العيوب الخلقية خطورة بعد أمراض القلب الخلقية. هناك تباين كبير في حالات التشوهات الخلقية في الجهاز العصبي المركزي في مناطق مختلفة من العالم بما في ذلك أوروبا. في فترة حديثي الولادة يمكن استخدام الموجات فوق الصوتية علي الرأس كطريقة أولية لاستبعاد التشوهات الخلقية.

الهدف من البحث: دراسة دور الموجات فوق الصوتية علي الرأس في الكشف المبكر عن تشوهات الدماغ الخلقية في الأطفال حديثي الولادة ذوي الخطورة العالية.

مادة البحث وخطوات العمل: أجريت هذه الدراسة الوصفية على 100 طفل حديثي الولادة الذين تم حجزهم في وحدة العناية المركزة لحديثي الولادة، بمستشفيات جامعة الأزهر (الحسين وباب الشعرية)، في الفترة ما بين نوفمبر 2019 إلى مايو 2020، حيث تم اختيارهم بطريقة عشوائية بسيطة وإجراء الموجات فوق الصوتية علي الرأس.

وقد أظهرت هذة الدراسة النتائج الآتية:

نسبة حدوث العيوب الخلقية بالمخ والتي تم تشخيصها عند الأطفال حديثي الولادة ذوي الخطورة العالية هي 9 ٪ في هذه الدراسة. كان هناك 57٪ من الذكور و43٪ من الإناث حديثي الولادة، و 34٪ الخدج و 66٪ من حديثي الولادة ذوي الخطورة العالية المسجلين في الدراسة، وشملت العيوب ما يلي:عدم التخلق الكامل للجسم الثفني (2 %)، التكوّن الجزئي للجسم الثفني (2 %)، استسقاء الرأس (2 %)، تضخم البطين (1 %)، تشوه دانـدي ووكر (1 %)، نقص تنسج المخيخ (1%)، ولم يكن هناك ارتباط بحدوث نتائج غير طبيعية في الموجات فوق الصوتية في الجمجمة في الذكور والإناث، العمر بالأيام، وطريقة الولادة، وعمر الأم أو صلة القرابة، وترابط سمات التشوه، وعلامات عصبية غير طبيعية، داء السكري المزمن لدي الأم، وعدم تناول حمض الفوليك في الثلث الأول من الحمل مع نتائج الموجات فوق الصوتية في الجمجمة ذات دلالة إحصائية.

خلاصة البحث:

1. يعد التصوير بالموجات فوق الصوتية عبر اليافوخ أداة مفيدة وآمنة وبسيطة لتشخيص تشوهات الدماغ الخلقية ولا يحتاج إلى نقل المريض الذي قد يكون في حالة صحية حرجة.

2. ترتبط الملامح المشوهة، داء السكري المزمن لدي الأم وتشنجات حديثي الولادة بزيادة خطر حدوث تشوهات الدماغ الخلقية.

التوصيات:

1. فحص حديثي الولادة ذوي الخطورة العالية باستخدام الموجات فوق الصوتية علي الرأس للكشف المبكر عن العيوب الخلقية بالمخ.
2. تأكيد تشخيص العيوب الخلقية بالمخ يمكن أن يتم باستخدام تقنية أكثر تقدما مع دقة عالية مثل الأشعة المقطعية والتصوير بالرنين المغناطيسي.
3. تجنب العقاقير التي تسبب تشوه الأجنه أثناء الحمل، والتدخين، وتجنب الأشعة السينية تساهم جزئياً في تقليل مخاطر العيوب الخلقية بالمخ. يمكن تحقيق ذلك من خلال التثقيف الصحي المناسب والرعاية قبل الولادة.
4. إعطاء حمض الفوليك للأمهات الحوامل في الأشهر الثلاثة الأولى لتجنب العيوب الخلقية بالمخ.
5. التحكم الجيد لمرض السكر المزمن لدي الأم اثناء الحمل.