Types ,Frequency,Clinical Presentation of Congenital Central Nervous System Anomalies in Al- Kadmayhia Teaching Hospital

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ABSTRACT:

BACKGROUND:

The central nervous system (CNS)anomalies are the most severe, difficult to detect its etiology, and predict its clinical presentation and course.

OBJECTIVE:

To find out the common types of congenital malformations in central nervous system.,determine the frequency and the clinical features of these malformations.

And to study the risk factors associated with congenital central nervous system malformations.

PATIENTS AND METHODS:

This cross-sectional study was performed at Al-Kadhimiyia Teaching Hospital (Neonatal care unit) from the 1st of January to the 1st of July, 2011.

One hundred newborn infants were proved to have congenital abnormalities by physical examination alone. Fifty five neonates were diagnosed as having CNS congenital anomalies.

neonatal evaluation include: gestational age, sex, body weight, type of CNS congenital anomaly.

Maternal age, parity, antenatal care, any history of abortion, previous baby with CNS congenital abnormality, still births, or drug intake during pregnancy.

the residency of the family and consanguinity .

RESULTS:

The number of neonates delivered alive was 2700 neonates, one hundred of them (3.7% of total deliveries) were delivered with congenital anomalies, and 55 cases from those (2% from total deliveries / 55% from congenitally abnormal deliveries) have had CNS congenital anomalies,the most frequent anomalies aremeningocele 25(45.5%),the second and third in frequency were hydrocephaly 12 (21.8%), and myelomeningocele 10 (18.2%) respectively.

There were 34(61.8%) male and 21 (38.2%) female. There were 30(54.5%) full term and 25(45.5%) preterm.

Thirty cases out of the total 55 cases (54.5%) with body weight 3-3.5 kg.

Most of the affected neonates to mothers with an age range of 20-40 years where 34 mothers (61.8%) aged between 20-30 years .

Most of the mothers were multipara (45 cases / 81.8%) .The majority of the neonates were the product of a consanguineous marriage 39 (70.9%).

Maternal peri-conceptional folic acid supplementation was not taken in the vast majority of cases (43 cases / 78.2%).

Positive family history of CNS congenital anomalies was reported in 4 cases only (7.3%) .

Familial residence was documented as urban in 30 cases (54.5%), and rural in 25 cases (45.5%).

CONCLUSION:

The most common type of CNS anomalies is meningocele with relatively higher male to female ratio.These anomalies occur in full term multipara mothers. Occur more frequent in infants with larger body weight and to younger multipara mothers. Consanguinity is a major risk. There was a low utilization of maternal peri-conceptional folic acid supplementation

KEY WORDS: central nervous system, neonates, folic acid, consanguinity.

INTRODUCTION:

Congenital malformations affect approximately 2-3% of all live births every year. Congenital brain anomalies, whether they are isolated (single) or part of syndromes, are a common cause of medical intervention, long-term illness, and death.

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There is significant variation in incidences of congenital CNS anomalies in different regions of world. [1].

Congenital CNS anomalies are a heterogeneous disease for which genetic, infectious, teratogenic and neoplastic causes have been implicated.

Ultrasound (US) examination is an effective modality for the diagnosis of these anomalies in experienced hands. Cranial US correlate well with anatomical and pathological findings and clinical outcomes. Cranial US detection of congenital brain anomalies is useful for diagnostic purposes, and it also may allow for more appropriate management and more accurate neurological prognostication. [2].

The importance of disordered nervous system maturation in causing chronic abnormalities of brain function has become fully apparent. Among all the congenital anomalies, disorders of the central nervous system (CNS) are the most severe, difficult to detect its etiology, and predict its clinical presentation and course. Seventy five percent of fetal deaths and 40% of deaths within the first year of life are secondary to CNS malformations. Furthermore, 5% to 15% of pediatric neurology hospital admissions appear to be primarily related to cerebral and spinal cord anomalies [3].

Genetic and non-genetic interactions are responsible for 20% of CNS malformations; monogenic malformations, account for 7.5% of malformations; chromosomal factors account for 6%; and environmental factors including maternal infections, maternal diabetes, irradiation, and drugs account for at least another 3.5%. In the remainder, more than 60% of cases, the cause of the CNS malformation are uncertain. [4].

Developmental CNS malformations are a complex group of congenital malformations often presenting with variable neuro-developmental dysfunctions [5].

Congenital abnormalities of the CNS can be divided into developmental malformations and disruptions.

Developmental malformations result from flawed development of the brain. This may be caused by chromosomal abnormalities and single gene defects that alter the blueprint of the brain, or by imbalances of factors that control gene expression during development. Gene defects may be in the germline or may develop after conception by spontaneous somatic mutation or from the action of harmful physical or chemical agents. Some malformations are caused by multiple genetic and environmental factors acting in concert (multifactorial etiology).

Disruptions result from destruction of the normally developed (or developing) brain and are caused by environmental or intrinsic factors such as fetal infection, exposure of the fetus to harmful chemicals, radiation, and fetal hypoxia. The line between malformation and disruption is sometimes blurred because an extrinsic factor (e.g. radiation) may cause direct physical injury but also damage genes that are important for development.

Developmental malformations are usually either midline or bilateral and symmetric and do not show gliosis. On the other hand, most disruptions are focal and asymmetric and are associated with gliosis and other reactive changes. However, these reactions may not be present if the disruption occurs in the first trimester, when the brain is immature. For these reasons, it is hard, to distinguish malformation from disruption. This distinction carries important implications. Malformations carry a recurrence risk that can be calculated. Disruptions do not recur, unless the exposure recurs or continues.

The timing of exposure is critical for both, malformations and disruptions. The earlier the exposure, the more severe the defect. The most critical period for malformations and disruptions is the third to eighth week of gestation, during which the brain and most organs take form [6].

AIMS OF THE STUDY:

To find out the common types of congenital malformations of central nervous system.To determine the frequency and the clinical features of these malformations.To study the risk factors that associated with congenital central nervous system malformations.

PATIENTS AND METHODS:

This cross-sectional study was performed at Al-Kadhimiyia Teaching Hospital (Neonatal care unit) from the 1st of January to the 1st of July, 2011.

A total of 2700 neonates were admitted to NCU during the period of study. One hundred newborn infants were proved to have congenital abnormalities by physical examination alone in the nursery care unit. Fifty five neonates were diagnosed as having CNS congenital anomalies after birth in the NCU.

The questionnaire for neonatal evaluation include: gestational age, sex, body weight, type of CNS congenital anomaly.

A detailed maternal history which include: age, parity, antenatal care, previous baby with CNS

congenital abnormality, medical illness, or drug intake during pregnancy.

Moreover, the residency of the family and consanguinity between father and mother had been recorded.

The data was collected, organized and tabulated by using the computer software Statistics Package for Social Science (SPSS) version 17. The results are expressed in the form of numbers, percentages and Chi-square Pearson correlation which was statistically significant at p.value less than 0.05 .

RESULTS:

The number of neonates delivered alive during the six months period of study in Al-Kadhimiyia teaching hospital was 2700 neonates, one hundred of them (3.7% of total deliveries) were delivered with congenital anomalies, and 55 cases from those (2% from total deliveries / 55% from congenitally abnormal deliveries) have had CNS congenital anomalies. Table [1].

Nearly half of the cases had meningocele (25 cases / 45.5%). The second and third in frequency were hydrocephaly (12 cases / 21.8%), and myelomeningocele (10 cases / 18.2%) respectively. Table [2].

The 55 cases with the CNS congenital anomalies were divided into 34 cases (61.8%) as males and 21 cases (38.2%) as females. With the male: female ratio being 1.6 : 1.Table [3].

The reported cases with CNS congenital anomalies were 30 full term neonates (54.5%) and 25 preterm neonates (45.5%). Table [4].

Thirty cases out of the total 55 cases (54.5%) were delivered with body weight ranging from 3-3.5 kg, and only 8 cases (14.5%) were weighting ≤ 2, kgP<0.05. Table [5].

Most of the affected neonates were delivered to mothers with an age range of 20-40 years where 34 mothers (61.8%) aged between 20-30 years and 14 mothers (25.5%) aged between 31-40 years,P<0.05. Table [6].

Most of the mothers were multipara (45 cases / 81.8%) and only 10 mothers (18.2%) were primigravida,P<0.05. Table [7].

The majority of the neonates who had encountered CNS congenital anomalies were the product of a consanguineous marriage as indicated by 39 cases out of the total 55 cases giving a percentage of 70.9%, P<0.05.Table [8].

Maternal peri-conceptional folic acid supplementation was an important question in this study and the answer was NO in the vast majority of cases (43 cases / 78.2%) and only few mothers had taken folic acid although not in a regular basis or only after they knew about their pregnancy,P<0.05. Table [9].

Positive family history of CNS congenital anomalies was reported in 4 cases only (7.3%) and many mothers had delivered neonates with CNS anomalies for the first time (51 cases / 92.7%). Table [10].

Familial residence was documented as urban in 30 cases (54.5%), and rural in 25 cases (45.5%). Table [11].

Table 1: The numbers of normal neonates and those who were delivered with CNS and other congenital anomalies and their percentages from total deliveries:

	Neonates with congenital anomalies (% from congenital anomalies)	Neonates with congenital anomalies {% from total deliveries}	Normal neonates {% from total deliveries}
CNS anomalies	55 (55%)	{2%}	2600 {96.3%}
Other anomalies	45 (45%)	{1.7%}	
Total	100 (100%)	{3.7%}	

Table 2: Type and frequency of CNS anomalies.

Types of CNS anomalies	Frequency (% from total)
Meningocele	25 (45.5)
Hydrocephaly	12 (21.8)
Myelomeningocele	10 (18.2)
Microcephaly	7 (12.7)
Spina bifida occulta	1 (1.8)
Total	55 (100)

Table 3:The relation between sex and CNS anomalies.

Sex	CNS anomalies (% from total CNS anomalies)	
Males	34 (61.8)	P value > 0.05
Females	21 (38.2)	
Total	55 (100%)	

Table 4: The relation between gestational age and CNS anomalies.

Gestational age	CNS anomalies (% from total)	
Full term	30 (54.5)	P value > 0.05
Preterm	25 (45.5)	
Total	55 (100)	

Table 5:The relation between body weight and CNS anomalies.

Body weight	CNS anomalies (% from total)	
≤ 1 kg	2 (3.6)	P value < 0.05
> 1-2 kg	6 (10.9)	
> 2-2.5 kg	17 (30.9)	
> 2.5-3.5 kg	30 (54.6)	
Total	55 (100)	

Table 6: Maternal age in relation to the incidence of CNS congenital anomalies in their neonates.

Maternal age	CNS anomalies (% from total)	
≤ 20 yr	2 (3.6)	P value < 0.05
21-30 yr	34 (61.8)	
31-40 yr	14 (25.5)	
> 41 yr	5 (9.1)	
Total	55 (100)	

Table 7:The relation between parity and CNS anomalies.

Parity	CNS anomalies (% from total)	
Primigravida	10 (18.2)	P value < 0.05
Multigravida	45 (81.8)	
Total	55 (100)	

Table 8:The relation between consanguinity and CNS anomalies.

Consanguinity	CNS anomalies (% from total)	
Yes	39 (70.9)	P value < 0.05
No	16 (29.1)	
Total	55 (100)	

Table 9:The relation between maternal folic acid supplementation and CNS anomalies.

Folic acid	CNS anomalies (% from total)	
Yes	12 (21.8)	P value < 0.05
No	43 (78.2)	
Total	55 (100)	

Table 10: The relation between family history and CNS anomalies.

Family history of CNS anomalies	CNS anomalies (% from total)	
Positive	4(7.3)	P value > 0.05
Negative	51(92.7)	

Table 11:The relation between residency and CNS anomalies.

Residency	CNS anomalies (% from total)	
Urban	30 (54.5)	P value > 0.05
Rural area	25 (45.5)	
Total	55 (100)	

DISCUSSION:

One hundred patients were noted to have congenital anomalies (3.7% from total deliveries), from those 55 cases (55%) have had congenital CNS anomalies. Nearly the same results were reported by :

Gillani S; Kazmi ,et al, study (in Pakistan 2011) where 100 cases (4.2%) had congenital anomalies and from those 31% had CNS anomalies [7].

Adeleye AO; study reported 54 cases delivered with CNS congenital anomalies which gave an incidence of 3.5% of total deliveries and 61% of deliveries with congenital anomalies[8,9].

Guardiola A; et al, study (in Brazil 2009) indicated an incidence of 3.67% of congenital anomalies, of which 36% were presented with CNS anomalies [10].

Meningocele, hydrocephaly, and meningomyelocele were the most frequently presented congenital CNS anomalies in this study with the documentation of 25 cases (45.5%), 12 cases (21.8%), and 10 cases (18.2%) respectively.

By Gillani S; et al, study (in Pakistan 2011) meningomyelocele was the commonest with an incidence of 71% [17], and by Komolafe EO; et al study (in Nigeria 2008) hydrocephaly accounted for about half of the cases (48.3%) and spina bifida came the next in frequency with an incidence of (18.5%) [11].

In Himmetoglu O; et al, study (in Ankara, Turkey 1996) spina bifida reported to be the first with an incidence of 45% followed by anencephaly as 40% [12]. This may be related to different in sample size studied or may be there is certain genetic or environmental risk factors lead to this differences.

Although the statistical relationship between the sex of neonates and the incidence of CNS congenital anomalies was not significant in this study (P value > 0.05) the incidence in males was 61.8% leaving the remaining 38.2% for females with the male : female ratio being 1.6 : 1.

The male : female ratio was 1 : 1.1 by Idowu OE; et al study (in Lagos, Nigeria 2012) [13], 2 : 1 by Adeleye AO; et al study (in Ibadan, Nigeria 2009) [18] , and 1.3 : 1 by Sobaniec-Lotowska M; et al, study (in Poland 1996) [14].

Being a full term or preterm neonate was not a significant risk factor for having a CNS congenital anomaly (P value > 0.05) as 54.5% of the cases were full term and 45.5% of cases were preterm. This may be explained be the early development of the CNS in the first trimester of pregnancy.

Such type of relationship between the gestational age and the incidence of CNS congenital anomalies was also reported to be non-significant by Al-Gazali LI; et al, study (in United Arab Emirates 1999) [15].

The relation between neonatal body weight and the incidence of CNS congenital anomalies was significant in this study as indicated statically (P value < 0.05) with the incidence being more with increasing body weight to be 54.6% in neonates weighting > 2.5-3.5 kg and 30.9% in patients weighting > 2-2.5 kg.

Pinar H;et al study (in USA 1998) claimed that most of the CNS congenital anomalies were reported in neonates weighting 2.4-6.4 kg simulating the results indicated in our study [16].

Statistically significant relationship was indicated in this study (P value < 0.05) between the maternal age and the incidence of CNS congenital anomalies in their neonates where most of the cases had born to mothers aged from 21-30 years (34 cases / 61.8%) and 31-40 years (14 cases / 25.5%) indicating a more incidence in middle aged mothers. This may be due to interplay between environmental &genetic factors that play role in the etiology of CNS anomalies during child bearing maternal age.

Guardiola A;et al, study (in Brazil 2009) stated that young maternal age was associated with more incidence of CNS congenital anomalies in their neonates without indicating the specific maternal ages [10].

Parity was also significant (P value < 0.05) in relation to congenital CNS anomalies where the

majority of others were multipara (81.8%). This may be explained in part by increasing maternal age with increasing number of pregnancies.

Nielsen LA;et al, study (in Denmark 2006) assumed that the incidence of CNS congenital anomalies increase with increase parity and put the explanation as due to increasing maternal age and decreasing maternal health with increase parity [17].

Truly the effect of consanguinity was significant on increasing the incidence of CNS congenital anomalies (P value < 0.05) as 70.9% of neonates delivered with CNS anomalies were the product of consanguineous marriage. It is well known that the risk of a child having a recessively inherited condition is higher if the parents are related, and the more closely related the parents are, the higher the risk.Since the majority of the anomalies caused by recessive genes &is probably related to high level of consanguinity in our population.

In a study (in UAE 1999) by Al-Gazali LI;et al, the reports had indicated that consanguinity was documented in around 42% of cases and nearly similar percentages were reported in some other Arabic countries where consanguinity is considered to be an important part of their cultures [15].

There is no doubt about the increasing incidence of CNS anomalies in neonates born to mothers who did not had a peri-conceptional folic acid supplementation (P value < 0.05). This is indicated in this study by the 78.2% of cases with no folic acid supplementation and only 21.8% of cases had born to mothers who had taken folic acid although not on a regular basis. This is because the closure of the neural tube is usually consideredcomplete by the fourth week of pregnancy so that if

folic acid is to have a prophylactic effect against neural tube defects it is clearly necessary for it tohave been taken before and immediately after conception.

Adeleye AO; et alstudy (in Ibadan, Nigeria 2010) claimed that all the mothers had no folic acid supplementation [9], which is the same reported by Idowu OE; et al study (in Lagos, Nigeria 2012) [13]. Pinar H; et al study (in USA 1998) put the incidence of 80% of CNS anomalies in neonates born to mothers with no peri-conceptional folic acid supplementation [16].

Family history of CNS congenital anomalies was detected in only 7.3% of cases in this study revealing a non-significant relation (P value > 0.05) between family history and the increasing incidence of CNS anomalies.

Himmetoglu O; et al, study (in Ankara, Turkey 1996) was one of the few studies to look for such relationship which was also non-significant [12], as also reported by Mishra PC; et al study (in India 1989) [18].

No significant relationship (P value > 0.05) detected between the residency of the family and the incidence of CNS anomalies where about half of the cases were from urban areas and the other half were from rural areas.

By Adeleye AO; et al study (in Ibadan, Nigeria 2010) the incidence was more in rural areas with a 65% [9].Since there is no clear criteria between rural and urban areas in our society so the result may not reflect the true frequency of CNS anomalies in both groups.

CONCLUSION:

The most common type of CNS anomalies is meningocele, with relatively higher male to female ratio.CNS anomalies occur in full term infants ,with larger body weight and more frequent in multipara mothers and younger mothers.

Consanguinity is a major risk for delivery of infants with CNS anomalies.Maternal peri-conceptional folic acid supplementation is very important factor in prevention of CNS anomalies.

RECOMMENDATIONS:

Provide good antenatal care (ANC) for all mothers and advice about the importance of peri-conceptional folic acid supplementation.

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