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ORIGINAL ARTICLE

Risk Factors and Types of Congenital Anomalies among Newborn Admitted to NICU in Children Welfare Teaching Hospital / Baghdad City 2019

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ABSTRACT

***Background:** A congenital anomaly defined as any abnormality of physical structure found at birth or during the first few weeks of life, Structural anomalies are considered to be major when are visible to inspection, the rest of them are considered occult.*

***Objective:** To assess the common associated risk factors of congenital anomalies, and to study the types of congenital anomalies among neonates admitted to the tertiary care unit.*

***Patients and methods**: A case control study was carried out in Children Welfare Teaching Hospital in Medical city complex during four months from 2nd of January to 30th of April 2019; collect certain data from 500 cases admitted to the NICU. Analysis of data was carried out using the available statistical package of SPSS-25.*

***Results:** The most common congenital anomalies is in the C.V.S which was on the top of the list (70.67%), followed by anomalies of the C.N.S. (31.33%), and anomalies of the G.I.T. (16%). Congenital anomalies are more common among full term neonates (72.7%).The most common maternal associated risk factor are consanguineous marriage (p value=0.0001), mothers`age (>35) years old (p value=0.001), gravida four and above (p value=0.001).*

***Conclusions:** congenital anomalies are more common among full term neonates, with the same occurrence in both genders. The commonest associated maternal factors are mothers` age (>35), multigravida, consanguineous marriage. Polyhydramnios is an associated factor with congenital anomalies. TORCH infection especially CMV carry a risk for congenital anomalies.*

***Keywords:** Risk Factors, Congenital anomalies, Newborn, Neonatal Intensive Care Unit (NICU)*

1. INTRODUCTION

The WHO defined Congenital Anomalies as structural, functional, or metabolic anomalies that originate during intrauterine life and can interfere with the body functions (1). They result from defective embryogenesis or intrinsic abnormalities in the development process (2). Congenital anomalies are classified according to severity into major and minor anomalies (3). They can also be classified into three groups of severity: minor, severe, and lethal anomalies. Severe and lethal anomalies together are considered as major anomalies (4). On the other hand, the international classification of diseases classified Congenital anomalies according to the affected body system (5). Identifying the causes of congenital anomalies is an important target for prevention and genetic counseling but their determination is difficult because a congenital anomaly may have different causes(6).Causative factors in 60% of cases will be unexplained but well recognized are genetic conditions, environmental pollutants, teratogens, infectious agents, drugs and uncontrolled medical disorders like diabetes and epilepsy in antenatal period, and multifactorial inheritance was responsible in most of the anomalies.(7,8). According to WHO (2015), about three million babies are born yearly with major CAs constituting about 3% of all newborns (1). The global report of birth defects (2006) showed that the prevalence of CAs varied between high-, middle-, and low-income countries with 94% of all CAs occur in middle- and low-income countries. CAs were as high as 82/1000 live births in Sudan and as low as 39.7/1000 live births in France (9). In 2006, the prevalence of CAs in the USA, UK, Germany, and Canada was between 45 and 50/1000 live births (9,10). In Africa and the Middle East, the reported prevalence was much lower. It ranged between 20 and 30/1000 live births in Kenya, Uganda, Nigeria, Saudi Arabia, and Pakistan (11,12). In Egypt, the prevalence of CAs was 65.3/1000 live births. (9). While in Iraq, the prevalence of CAs was 21.7/1000 births according to the last registration of Iraqi ministry of health in 2012 (13). Congenital anomalies are a worldwide problem. They are important causes of childhood deaths, chronic illness, and disability. The WHO estimated that annually, 303,000 newborns die within 4 weeks of birth worldwide due to CAs. In 2006, worldwide, out of 2.68 million neonatal deaths, the WHO estimated that 11.3% of them died from CAs (2). Approximately 95% of the children who died from CAs were from middle- and low-income countries (9).

Congenital anomalies can also result in long-term physical, mental, visual, and auditory disabilities if not managed appropriately and have significant negative impacts on individuals, families, health care system, and societies (1, 14).

2. METHODOLOGY

A case-control study conducted in neonatal intensive care unit in The Children Welfare Teaching Hospital in Medical-City Complex and Al-Khadimya children Hospital in Baghdad, which is a tertiary center that receives patients and referral cases from every part in the country during the period from the 2nd of January to the first of May 2019 looking for management A convenient sample of (500) neonate(age less than one month) whom were admitted to the NICU during the studied period were studied in a case control study, the case group is 150 neonates with Congenital anomalies which have been studied a comparison to a randomly selected 350 neonates without Congenital anomalies.

Inclusion criteria:

All neonates of both sex whom aged less than one month and are admitted to the NICU and are present during the time of data collection were included in this study.

Exclusion criteria:

A- Any baby whose age is more than 30 days is excluded from the study.

B- Mothers or caregivers of neonates who refuse to participate in the study (only one mother refuse).

Ethical consideration:

Official agreement was obtained from the Arabic board of family medicine. Agreement of Children Welfare Teaching Hospital- Medical City Health Directorate was obtained

Prior to data collection, the purpose of the study was explained to the parents and /or caregiver of the neonate and their consents were obtained. All ethical issues were approved by the author in accordance with the Declaration of Helsinki of World Medical Association , 2013 for the ethical principles of researches involving human. Confidentiality of data and privacy were assured.

Statistical analysis: Analysis of data was carried out using the available statistical package of SPSS-25 (Statistical Packages for Social Sciences- version 25). Data were presented in simple

measures of frequency, percentage, mean, standard deviation, and range (minimum-maximum values). The significance of difference in qualitative data was tested using Pearson Chi-square test with application of Yate's correction or Fisher Exact test whenever applicable. Statistical significance was considered whenever the P value was equal or less than 0.05.

3. RESULTS

The demographic data of the studied groups showed no statistically signifciant difference in the neonatal birth weight and gender , (P>0.05). A significant association was found between term neonates (≥37) and congenital anomalies (p. value = 0.01). About 72.7% of cases with congenetal anomalies were full term neonates compared to 64.3% of the control group(**Table 1**). Congenital anomalies were signifciantly associated with older maternal age (>35) (p value=0.001). Consanguinity, especially in first degree shows highly association of having Congenital anomalies(p value=0.0001) consanguinity where 64.7% of Congenital anomalies group in comparison to 43.1% of the control group; while Blood group and Rh. incompatibility didn`t show any association with Congenital anomalies (p value=0.648). Higher proportion of mothers in cases group were multigravida of ≥ 4 compared to control group, (56.7%) and (38.6%), respectively, (p value=0.001). Gestational DM, pre-eclampsia and exposure to radiation during pregnancy were found to be signifciant risk factors for congenital anomalies, (P.value <0.05). Maternal TORCH infection was signifciantly associated with congenital anomalies in the siblings especially CMV where the percentage of congenital anomalies is 3.3% compared to none in control group (p value<0.001). A signifciant association was found between maternal thyroid disease and getting abnormal baby ,10% of congenital anomalies group versus 2.6% of control group (p value<0.001). Similarly, mothers of 14% of congenital anomalies babies had polyhydramnios during the pregnancy compared to 5.1% in control group, (P.value=0.003). Smoking was signifciantly associated with congenitally anomalies (P.value = 0.013). Additionally, having a previous infant with congenital anomalies was signifciant risk factor to get a new baby with congenital anomalies (P.value <0.001). Regarding folic acid intake, a signifciant association was found between not taking folic acid and congenital anomalies, 30% in cases group and 4.6% in control group, (P.value<0.001),(**Table 2**).

Distribution of congenital anomalies by systems, revealed that some cases had more than one anomaly. However, 19 cases with musculoskeletal system anomalies conytibutted for (12.6%) of all congenital anomalies cases, cleft lip and palate are the most frequent one (11 cases). Genitourinary system anomalies reported in 18 cases (12%), hypospadias is the most frequent one (6 cases), CNS anomalies found in 47 cases (31.33%) and the hydrocephalus cases were the more frequent (19 cases). There were 106 cases with cardiovascular anomalies (70.67%); ASD anomalies were the more frequent (58 cases). In Gastro-intestinal system there were 24 cases (16%) and TEF was the more frequent (11 cases). In respiratory system only 3 cases had diaphragmatic hernia (2%). Endocrine system anomalies reported in 9 cases about 6% whereas inborn error of metabolism was the commonest one (4 cases). There were 14 cases with miscellaneous/ Syndromes about (9.33%) and Down syndrome cases were the more frequent cases (6 cases), all these findins are demonstrated in (**Table 3**), moreover, the overall distribution of different types of congenital anomalies according to the affected systems, are shown in (**Figure 1**); Cardiovascular anomalies had the higher proportion followed by C.N.S., G.I.T., Musculoskeletal system Genitourinary system, Miscellaneous/syndromes, Endocrine system, , and the lowest proportion in respiratory system.

Table 1. Comparison of birth weight, gender and gestational age at delivery of the studied groups

Variable		Case group (N=150)		Control group (N=350)		P. value
		No	%	No	%	
Birth weight (Kg)	<2.5	51	34	130	37	0.246 ns
	2.5-4	93	62	195	55.7	
	>4	6	4	25	7.1	
Gender	Male	76	50.7	192	54.9	0.389 ns
	Female	74	49.3	158	45.1	
Gestational age at delivery (weeks)	Preterm <37	41	27.3	125	35.7	0.010*
	Term (37-42)	109	72.7	225	64.3	

*Significant, ns: not significant

Table 2. Comparison of demographic characteristics, obstetrical and medical history of mothers in both studied groups

Factors		Case group (N=150)		Control group (N=350)		P.value*
		No	%	No	%	
Mother age (year)	<20	15	10	32	9.1	0.001
	20-35	56	37.3	179	51.1	
	>35	79	52.6	139	39.7	
Consanguinity	1st degree	97	64.7	151	43.1	<0.001
	2nd degree	10	6.7	24	6.9	
	Not	43	28.7	175	50	
Blood group and Rh incompatibility	Yes	34	22.7	86	24.6	0.648
	No	116	77.3	264	75.4	
Gravidity	1	31	20.7	69	19.7	0.001
	2	16	10.7	81	23.1	
	3	18	12	65	18.6	
	≥4	85	56.7	135	38.6	
Gestational Diabetes	Yes	13	8.7	8	2.3	0.001
	No	137	91.3	342	97.7	
Preeclampsia	Yes	29	19.3	17	4.9	<0.001
	No	121	80.7	333	95.1	
Exposure to radiation during pregnancy	Yes	5	3.3	1	0.3	0.004
	No	145	96.7	349	99.7	
TORCH infection	Rubella	2	1.3	0	0	<0.001
	Toxoplasmosis	2	1.3	6	1.7	
	CMV	5	3.3	0	0	
Thyroid disease	Yes	15	10	9	2.6	0.001
	No	135	90	341	97.4	
Amniotic fluid abnormality	Polyhydramnious	21	14	18	5.1	0.003
	Oligohydramnios	13	8.7	2.7	7.7	
	Normal	116	77.3	305	87.1	
Passive smoking	Yes	95	63.3	200	57.1	0.013
	No	55	36.7	150	42.9	
Previous infant with Congenital anomalies	Yes	26	17.3	15	4.3	<0.001
	No	124	82.7	335	95.7	
Folic acid intake	Yes	105	70	334	95.4	<0.001
	No	45	30	16	4.6	

*All associations were significant except with Blood group and Rh incompatibility

Table 3. Distribution of types of congenital anomalies according to body systems

System	Congenital anomaly	No	Total	%
Cardiovascular system	ASD	58	106	70.7
	PDA	22		
	MR	2		
	TR	2		
	TOF	1		
	PS	3		
	VSD	18		
Central nervous system	Anencephaly	2	47	31.3
	Hydrocephalus	19		
	Meningomyelocele	16		
	Microcephaly	9		
	Werding Hoffman Syndrome	1		
Gastro-intestinal system	Hirschsprung disease	3	24	16.0
	TEF	11		
	Omphalocele	1		
	Imperforated anus	9		
Musculoskeletal	Ectrodactyly	2	19	12.6
	Osteopetrosis	3		
	Cleft lipandpalate	11		
	Choanal atresia	3		
Genitourinary system	Ureteral Duplication	2	18	12.0
	Dilated PCS	3		
	Bilateral hydronephrosis	3		
	Unilateral hypolastic kidney	2		
	Bilateral hypoplastic kidney	3		
	Hypospadias	6		
	Micropenis	2		
	Single kidney	1		
Miscellaneous / Syndromes	Prun belly Disease	2	14	9.3
	Down syndrome	6		
	Congenital leukemia	1		
	Trisomy 18 Edward Syndrome	1		
	Pierre robin syndrome	2		
	Corneal opacity	2		
Endocrine system	Congenital Adrenal gland hyperplasia	3	9	6.0
	Hypothyrodism	2		
	Inborn error of metabolism	4		
Respiratory system	Diaphragmatic hernia	3	3	2.0

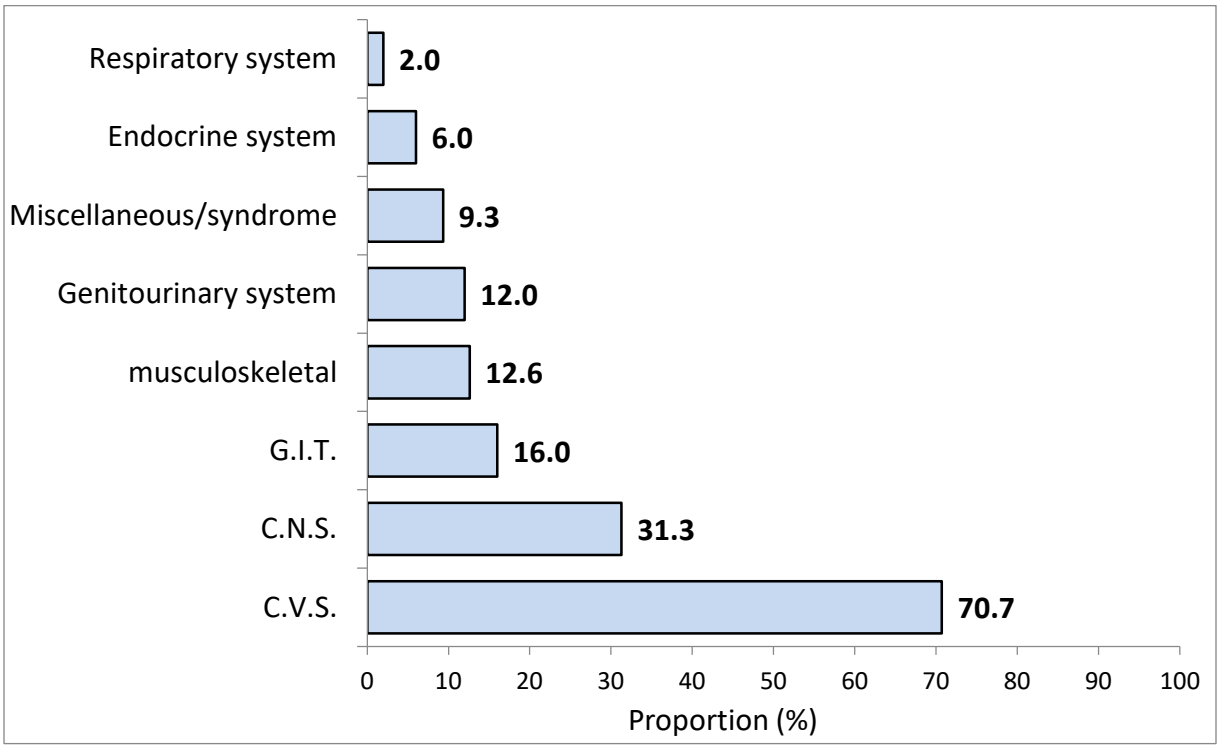

Figure 1. Proportional distribution of congenital anomalies among the studied group

4. DISCUSSION

This study shows that Maternal age (>35) had high percentage of Congenital anomalies (p value=0.001) which is near the result found in study in Egypt in 2007 by Osman MA, Mostafa MM, Essa AE (15) who observed direct relation between the maternal age and incidence of congenital anomalies showing low incidence with age <20 years old and high with age between 20-35 years old. Advanced maternal age (> 35 years) reported to be the most frequent risk factor for birth defects in Brazil in 2007 by Costa CM, da Gama SG, Leal MC (16). While that is totally disagreed by a study in Nepal 2017 by Bastola R et al (17) which found the highest no. of Congenital anomalies in mothers<20 years. Consanguinity was the most common cause for most of the malformation especially of 1st degree 64.7%(p value=0.0001), That is agreed in a study conducted in Oman in 2010 by Tayebi N, Yazdani K, Naghshin N.(18), which showed the prevalence of congenital anomalies were mostly observed in consanguineous marriages compared to non-consanguineous marriage (p value=0.018). This

is totally disagreed by the study in Nepal in 2017 by Bastola R et al (17) which found only 8.33% of neonates with Congenital anomalies. had consanguinity history. Blood group andRh incompatibility had no association with the appearance of Congenital anomalies in this study that is agreed with the study in al-Mousel city in Iraq 2012 by Taboo ZA (19) which find that Rh incompatibility are not independent risk factor for Congenital anomalies.

Regarding gravidity there was significant association between multigravida=>4 and the appearance of Congenital anomalies in the offspring in this study (p value=0.001). This is agreed by the study in Pakistan in 2009 by Jehangir W et al (12), which found that the total no. of malformed neonates from multigravida is eight times more than that from primigravida. While the study in al-Mousel city in Iraq done in 2012 by Taboo Z. report that the percentage of Congenital anomalies reached the peak with primigravida (19) which disagreed with this study. Gestational diabetes mellitus (p value=0.001), pre-eclampsia(p value=0.0001), and thyroid disease (p value=0.001) of the mother show a positive association with congenital malformation in the current birth sample, This is agreed by Ordóñez MP et al in Santiago 2003 (20). And according to Nazer J in Chile 2004 (21), diabetes accounts for the induction of diabetic embryopathy, resulting in malformations. In the study of Gupta S, Gupta P, Soni JS in 2012 in India (22) state that the pre eclamptic mothers gave birth to anomalous babies which are similar to the finding in this study. The maternal exposure to radiation during pregnancy shows association with Congenital anomalies (p value=0.004) with a percentage of 3.3% in this study, which is quite similar to the finding in Indian study in 2010 by Gupta S, Gupta P and Soni JS(22) where their findings were 12.5%. It is difficult to find a study that disagrees with the current findings. In the current study we found that TORCH infection had association with having baby with Congenital anomalies(p value=0.0001) especially in CMV infection 3.3% (inspite of very small no. recoded), while a study in Al-Mousel city 2012 by Taboo Z. (19) found that history of toxoplasmosis infection was reported as risk factor for congenital anomaly(4.64%) while other virus infections of the mother are not independent risk factor for Congenital anomalies, while a study in al-Brazil 2006 by Costa CM, Gama SG and Leal MD (23) reported that the association between Toxoplasmosis and Congenital anomalies is not statistically significant. The abnormality in Amniotic fluid shows association with Congenital anomalies(p value=0.003).The percentage

of anomalous babies of mothers with oligohydromnios was 8.7%, While polyhydromnios was 14% , which is quite similar to the finding in Indian study in 2010 by Gupta S, Gupta P and Soni JS(22) where their findings were 5.12% and 11.7% respectively. In this study we found that passive smoking in mothers had an association with having Congenital anomalies in their babies (p value=0.013), this is disagreed with the studies in Mousel city 2012 by Taboo Z. (19) and in Lebanon 2014 by Francine R, Pascale S and Aline1a H (2) which report active smoking(not passive) as not an independent risk factor for Congenital anomalies (p value=0.433). It is difficult to find a study that agrees with the current finding. The same condition regarding having a previous infant with Congenital anomalies the current study found an association with having a new baby with Congenital anomalies (p value=0.0001), that is disagreed by the study in Lebanon 2014 by Francine R, Pascale S and Aline1a H (2) which found that the association between them is not statistically significant (p value=1.000). Also in the study of al-Mousel city 2012 by Taboo Z. (19) found that only 2.78% 0f babies with Congenital anomalies their mothers had a previous infant with Congenital anomalies. Regarding folic acid intake, in this study we found that 95.4% of neonate without Congenital anomalies. their mothers were taking folic acid during pregnancy (p value=0.0001). This is similar to finding in the study in Lebanon 2014 by Francine R, Pascale S and Aline1a H (2) which found that 97.3% of babies without Congenital anomalies. their mothers were taking multivitamins during their pregnancy. The most common Congenital anomalies found was in the C.V.S. 70.67% of all C.A.s. and ASD was the most common one, while in previous study in Iraq 2013 by Naoom MB (24) found C.V.S. anomaly the most common anomalies but to much less extent (21.8%) also in study in Lebanon 2014 by Francine R, Pascale S and Aline1a H et al(2) but to a lesser extent (16.66%).While in Pakistan 2011 Gillani S et al (25) reported the highest frequency in C.N.S.(31%) , While in Indian study in 2009 by Singh A and Gupta RK (26) musculoskeletal is the highest (30.6%) and the lowest is C.V.S. . These variations between different studies could be explained by the effect of diverse racial, ethnic and social factors in various parts of the world or in different geographical area. Other explanations are the type of sample and the criteria for diagnosis that is to say differences in study design and methodology.

5. CONCLUSIONS

Congenital anomalies are more common among full term neonates, with the same occurrence in both genders. The commonest associated maternal factors are mothers` age (>35), multigravida, consanguineous marriage. Polyhydramnios is an associated factor with congenital anomalies. TORCH infection especially CMV carry a risk for congenital anomalies.

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