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Incidence, Types and Main Risk Factors of Congenital Anomalies of Newborns in Al-Najaf Al-Ashraf

Nadia Abdulmunem Sahib Alhamami[1]*, Nisreen Hussein Abdulsada[1], Masar Raheem Abbas[1]

1.MBChB, DOG, Al-Forat Al-Awsat Teaching Hospital, Najaf, Iraq

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Summary:

Congenital anomalies, or malformations, are the second leading cause of death in children under 28 days and under 5 years of age. Globally, they affect 1 in 33 babies and cause 3.2 million disabilities a year. Different risk factors could contribute to the development of these anomalies such as genetic, infectious or environmental but in most cases it is difficult to identify their cause. This study aimed to assess the incidence, rates, types and main risk factors of congenital anomalies in our hospital during the period 2016-2020. We found an average incidence of 4.38/1000 live births among 38165 live births reported for the same period. Osteoarticular system, cardiovascular system and head and neck were the more affected systems. The main risk factors reported in our study were consanguinity and extreme maternal age of less than 18 and older than 35 years. The more frequent type was Hydrocephaly followed by Anencephaly while the least type was Omphalocele. Therefore, for better monitoring of high-risk pregnancies, there is a need for specialized health services, with prenatal examinations for morphological assessment and genetic studies also we recommend further studies including other centers in our province.

Keywords: *Congenital Anomalies, Newborns, Incidence, Etiology, Types, Risk factor*

***Corresponding Author**, Dr.Nadia Abdulmunem Sahib Alhamami, alhamami_nas_dog@gmail.com*

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1. INTRODUCTION

Congenital malformations have worried humanity for centuries, they represent a public health problem that affects the family nucleus and society. Classically, genetic, environmental and multifactorial causes of congenital anomalies have been identified; becoming the genetic factors in the most frequent (1). Its repercussions can be the aesthetic aspect, functional alterations with temporary , permanent sequelae or death. These defects can occur in one or more segments, organs, or systems. When a pregnant woman is exposed to a teratogenic agent, an infectious process or suffers from a chronic degenerative disease, the frequency increases to 14.9 per 1 000 and mortality up to 15.1% (2–4). Congenital malformations represented an important cause of fetal death with high morbidity and mortality in infants, ranking first in causes of infant mortality in many countries of the world. They cause 3.2 million disabilities per year. An estimated 276,000 children die each year from birth defects worldwide. About 94% of severe birth defects occur in low- and middle-income countries, where women often do not have access to enough nutritious food and where exposure to agents or factors such as infection and other risk factors are high (5–10). In Iraq, according to the annual reports of Ministry of Health for the year 2016-2020 (11) and previous Iraqi studies, incidence of congenital malformation was 2.5 per 1000 live birth and varied across the Iraqi Provinces; the incidence rate ranged between 0.5/1000 live birth in Al-Muthanna province to 5.6/1000 in Kirkuk, however, in our province , Al-Najaf , the rate is 4.1/1000 live birth which is higher than the average national rate (2,12–15).

Congenital malformations defined as any structural lesion of an organ or part of it, due to an alteration that occurs during the morphogenesis process and that may correspond to minor or major, single, multiple or isolated defects (10). The World Health Organization (WHO) defines them as any abnormality of morphological, structural, functional or molecular development, which can occur internally or externally, familial or sporadic, hereditary or not transmitted, single or multiple, resulting from an imperfect embryogenesis (10,12,13). Etiology. Among the causes of malformations , environmental factors represents 15%, genetic factors almost 30% and those due to the interaction of the environment with the genetic susceptibility of the individual that constitute the majority of cases with 55%. . However, despite great technological advances, the primary cause remains unknown in most cases and many appear without any antecedent family or known risk factors and therefore, each fetus

has a risk of suffering a significant structural defect at the time of birth and for this reason the timely detection of congenital malformations is of radical importance (1,3).

Types of congenital malformations.

Depending on their severity, they are classified into major and minor anomalies, and depending on the number they are classified as single or multiple and also classified according to the systems they are affected. Such as skull and nervous system, cardiovascular , respiratory System , digestive, GIT malformations , Defects of the abdominal wall, genito-urinary system, upper and lower limb malformations and chromosomal abnormalities such as Down syndrome, Turner syndrome and Klinefelter syndrome (10).

Risk factors associated with congenital malformations: Congenital anomalies can be caused by various factors , these can summarized as followed. Genetic factors, environmental factors (chemical, physical and biological such as intrauterine viral or bacterial infection). Among Chemical agents are drugs and chemical substances. Physical Agents like high temperature, hypoxic conditions and ionizing radiation(14,15)

Maternal risk factors: Maternal age less than 18 years and older than 35 years, are related to congenital malformations, increasing the risk in ages older than 45 years, at these ages there is a greater risk of malformations such as Down syndrome and other anomalies In general, the risk of neural tube defects such as anencephaly and spina bifida also increases after 40 years of age (16). Alcohol consumption in pregnancy may cause microcephaly, microphthalmia and isolated cleft lip or cleft palate (17). Tobacco use carries an increased risk of cardiovascular, limb, cleft palate, and genitourinary abnormalities. Cocaine can cause congenital genitourinary, cardiac, and central nervous system abnormalities (18). Other maternal factors include Obesity, gestational diabetes mellitus and pre-gestational diabetes are associated with skeletal malformations, neural tube defects, agenesis, kidney cysts, and gastrointestinal malformations such as atresia of the duodenum and rectum. Chronic arterial hypertension were associated with a significant increase in the risk of cardiac malformations. Epilepsy and antiepileptic drugs are proven teratogens (19–21).

Perinatal infections: Maternal infections during the first weeks of pregnancy are associated with different malformations. TORCHS (toxoplasmosis, rubella, cytomegalovirus, herpes, syphilis) can cause microcephaly, chorioretinitis, encephalopathies, intracranial calcifications, microphthalmia, and cataracts (1,22,23).

Family history of congenital malformations: The presence of a family history of congenital anomalies increases their incidence as follows: mother with abnormalities 5-18%, father 9%, previous child 2-5%, two previous children 10% (24,25).

Non-consumption of supplements during pregnancy: A diet deficient in micronutrients is related to pre-eclampsia, premature birth, delayed intrauterine growth , low birth weight (LBW) and congenital malformations, if the diet is low in protein, calcium, fruit and cereals, even when the energy intake appropriate, there is a higher incidence of abortions and perinatal deaths; The relationship between folic acid deficiency and the increase in neural tube defects (NTD) is also well known, therefore nutritional supplementation with iron, folic acid, iodine, vitamins and minerals are necessary during gestation (25,26).

Polyhydramnios: The congenital malformations most frequently associated with polyhydramnios are those of the gastrointestinal and central nervous systems (27)

2. PATIENTS AND METHODS

A retrospective mixed design Cross-sectional/Case-control observational correlational study was carried out during the period January to July 2021, at Al-Furat Al-Awsat Teaching Hospital, Obstetrics And Gynecology Department, Bio-statistics department in addition to the neonatology department.

Study Population and Sample

It was integrated by the newborns cared for in the neonatology area of our hospital, file records of registered live birth with congenital anomalies for the last complete 5 years; 2016-2020 were reviewed. We estimated the total live births during the specified period and they were 38165 among them a total of 167 medical records for live newborns with congenital anomalies for different etiologies were reported.

Inclusion criteria

Iraqi women who give birth in our hospital during the studied period 2016-2020 .

Live newborns diagnosed with congenital malformations treated in the neonatology unit of our hospital.

Exclusion criteria

Healthy newborns

Newborns diagnosed with other pathologies.

Medical records with missed or unavailable information

Pre-analytical Phase: After reviewing the literature, the research project was proposed, which was approved by the Ethical committee of Najaf Health Directorate and Hospital administration office

Analytical phase: To fulfill the objective of the study, the malformations were grouped according to the affected system or organ. Clinical history of newborns with a diagnosis of congenital malformation, the risk factors to which the mothers were exposed were reviewed, for this study the risk factors that were considered were maternal age , the non-consumption of supplements during pregnancy, the presence of acute infectious diseases during pregnancy, chronic maternal diseases, exposure to chemical agents, radiation, teratogenic drugs, maternal toxic habits, family history of congenital malformation and the presence of oligohydramnios or polyhydramnios during pregnancy, in this way it was possible to establish the most frequent risk factors in these pathologies, it should be noted that some cases were related to more than one risk factors. After establishing the frequency of the risk factors associated with each congenital malformation, a table was designed for each gender, in this way it was possible to relate the three study variables, which are the most frequent risk factors, the type of malformation and gender, thus achieving this objective.

3. RESULTS

During the period 2016-2020 a total of 38165 live births had been occurred in our hospital among them 167 babies with congenital malformation were reported, giving an incidence rate of 4.38 per 1000 live birth . Among the total deliveries, 24611 were normal vaginal deliveries (NVD) and 13554 were cesarean sections (CS) giving a rate of 65.5 and 35.5, respectively , (Table 1 & Figure 1). According to the affected system, Osteoarticular system 1.28 /1000, Cardiovascular system 1.07/1000, Head and neck 0.55/1000, Genital system 0.34/1000, , Nervous system 0.26/1000, Digestive system 0.16/1000, Urinary system 0.13/1000, Chromosomopathies 0.08/1000, Respiratory system 0.05/1000 and all other systems with 0.45/1000 live births (**Table 2**). When the data of the 167 cases (mothers of babies with congenital malformation) compared to 200 mothers who give normal newborns as (Control group), the demographic characteristics of the studied groups revealed significantly that age < 18 years and older than 35 years, housewives and those with low socioeconomic status were significant risk factors of congenital malformation , (**Table 3**). Obstetrical history of the studied groups indicated that history of abortion was significant risk

factor for congenital malformation, (P. value = 0.020) while gravidity , parity or previous cesarean section were not significantly different between both groups, (P. value > 0.05), (**Table 4**). Medications use and febrile illness during pregnancy, pre-gestational diabetes mellitus, gestational diabetes mellitus, pre-gestational hypertension, gestational hypertension, other maternal diseases, consanguinity, history of congenital anomalies in offspring were significant risk factors for congenital malformation, (in all comparisons, P. value < 0.05), however, consanguinity was the more frequent one, (**Table 5**). Regarding the 167 Congenital anomalies reported during the study period, Hydrocephaly was the more frequent one, contributed for 32.9% , followed by Anencephaly 19.8%, Spina-Bifida 7.2% ,Polycystic kidney 6.6% and Encephalocele 6.0%. Other Congenital anomalies were less frequent and the least one was Omphalocele reported in only one case, however, all reported anomalies are summarized in (**Table 6**).

Table 1. Total live births and cumulative incidence rate of congenital anomalies for the period 2016-2020 in Al-Furat Al-Awsat Teaching Hospital

Parameter	No.	%	Incidence/1000 live birth
Normal newborns	37998	99.56	995.6
Newborns with congenital anomalies	167	0.44	4.38
Total live births	38165	100.0	

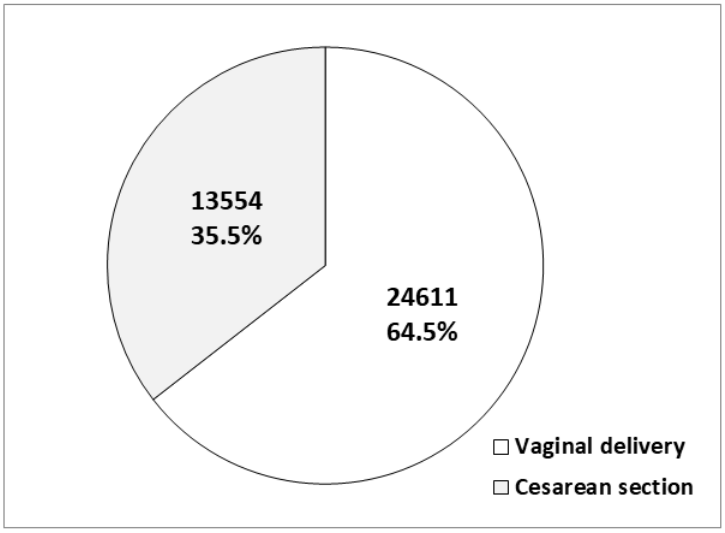


Figure 1. Mode of delivery during the studied period 2016-2020

Table 2. Congenital anomalies reported among 167 babies during the period 2016-2020 according to the affected body system

Congenital anomalies	Frequency	Proportion/167	Incidence/1000 Live birth
Osteoarticular system	49	29.3%	1.28
Cardiovascular system	41	24.6%	1.07
Head and neck	21	12.6%	0.55
Genital system	13	7.8%	0.45
Nervous system	10	6.0%	0.34
Digestive system	6	3.6%	0.26
Urinary system	5	3.0%	0.16
Chromosomopathies	3	1.8%	0.13
Respiratory system	2	1.2%	0.08
Others	17	10.2%	0.05
Total	167	100.0%	4.38

Table 3. Demographic characteristics of the studied groups

Variable		Cases		Controls		P. value
		No.	%	No.	%	
Maternal age	< 18	39	23.4	27	13.5	0.001 sig
	18 - 25	31	18.6	42	21.0	
	26-30	23	13.8	54	27.0	
	31-35	28	16.8	46	23.0	
	> 35	46	27.5	31	15.5	
Residence	Urban	109	65.3	134	67.0	0.811 ns
	Rural	58	34.7	66	33.0	
Occupation	Housewife	118	70.7	123	61.5	0.019 sig
	Employed	35	21	67	33.5	
	Student	14	8.4	10	5.0	
Economic status	Low	76	45.50	113	56.5	0.035 sig
	Good	91	55.50	87	43.5	
Total		167	100	200	100.0	

sig: significant, ns: not significant

Cases: mothers of babies with Congenital anomalies

Table 4. Comparison of obstetrical history of the studied groups

Variable		Cases		Controls		P. value
		No.	%	No.	%	
Gravidity	Multigravida	121	72.5	147	73.5	0.915 ns
	Primigravida	46	27.5	53	26.5	
Parity	Nulliparous	65	38.9	74	37.0	0.787 ns
	Multiparous	102	61.1	126	63.0	
History Abortion	Yes	24	14.4	13	6.5	0.020 sig
	No	143	85.6	187	93.5	
Previous cesarean section	Yes	64	38.3	71	35.5	0.652 ns
	No	103	61.7	129	64.5	
Total		167	100	200	100.0	

sig: significant, ns: not significant
Cases: mothers of babies with Congenital anomalies

Table 5. Comparison of medical history of the studied before and after gestation

Variable	Cases		Controls		P. value
	No	%	No	%	
Use medications during pregnancy	22	13.2	9	4.5	0.005 sig
Febrile illness during pregnancy	18	10.8	11	5.5	0.046 sig
Pre-gestational Diabetes Mellitus	27	16.2	16	8.0	0.011 sig
Gestational Diabetes Mellitus	29	17.4	20	10.0	0.027 sig
Pre-gestational hypertension	19	11.4	12	6.0	0.048 sig
Gestational hypertension	31	18.6	17	8.5	0.003 sig
Other Maternal diseases	25	15.0	11	5.5	0.002 sig
Consanguinity	63	37.7	38	19.0	0.001 sig
History of congenital anomalies in siblings	11	6.6	1	0.5	0.003 sig

Cases: Mothers of babies with congenital anomalies
None of the cases or controls had history of Chemotherapy, irradiation or smoking
sig: significant, ns: not significant

Table 6. Congenital anomalies reported among 167 babies during the period 2016-2020

Congenital anomalies	Frequency	Proportion
Hydrocephaly	55	32.9
Anencephaly	33	19.8
Spina-Bifida	12	7.2
Polycystic kidney	11	6.6
Encephalocele	10	6.0
Achondroplasia	9	5.4
Microcephaly	8	4.8
Imperforated anus	7	4.2
Fetal ascitis	5	3.0
Meningomyelocele	5	3.0
Cleft lip / palate	5	3.0
Congenital Heart disease	3	1.8
Hydropes fetalis	2	1.2
Duodenal atresia	2	1.2
Omphalocele	1	0.6

4. DISCUSSION

During intrauterine life human embryos are protected by embryonic membrane and other protective measures, however, during early gestation weeks exposure of mothers to some teratogenic factors may lead to developmental disorders and anomalies. In majority of congenital anomalies , however, almost 60% of congenital anomalies have an unknown origin. Genetic congenital anomalies have the largest number of studies, such as chromosomopathies, and those of environmental etiology, caused by teratogens, are the least investigated . Among the causal factors of congenital anomalies, infectious agents, environmental agents such as radiation, mechanical factors and chemical compounds, as well as maternal diseases, stand out. Some maternal factors such as age, lifestyle, type of pregnancy and maternal health, among others, have been researched and related to the occurrence of congenital anomalies (1). Hence we aimed in this to assess the possible risk

factors among Iraqi population in AlNajaf , therefore , a mixed design study was performed, at initial phase we used cross-sectional design to assess the total deliveries in our hospital for the specified period of 5 years (2016-2020). In Iraq , an average of 1021482 births a year , of them almost an average 2900 with congenital anomalies (11). In the present study we found that during this period the incidence of congenital anomalies was 4.38 per 1000 live birth , these finding relatively higher than that reported in Najaf province according to the annual statistical reports of ministry of health in Iraq for the same period, also the reported incidence rate in our study was higher than the national rate in Iraq where the incidence rate is 2.8 per 1000 live birth. Nonetheless , our incidence rate was lower than some other provinces in Iraq, and there is wide variation in the incidence rates across all Iraqi Provinces (11). The characterization of these congenital anomalies is important information for the planning and implementation of programs that assist people with these conditions and their families , however, underreporting of congenital anomalies could not be excluded, particularly in 2020 due to COVID-19 pandemic and its effect on the health centers in our province. During the study period, there was a predominance of newborns with Hydrocephaly (32.9%), followed by Anencephaly 19.8%, Spina-Bifida 7.2% ,Polycystic kidney 6.6% and Encephalocele 6.0%. Other Congenital anomalies were less frequent and the least one was Omphalocele reported in only one case. In earlier Iraqi studies, findings similar to those found in other national studies , where the incidence /1000 live births was 3.63 in Erbil (2), 3.3 in Sulaimaniyah (28), and 1.73 in Karbala (29). However, the rate much higher and reach 40/1000 among newborns admitted to NICU , as it was reported in Al-Ramadi , western of Iraq Furthermore, studies in other countries reported variant incidence rates, in Brazil it was 17.9/1000 live births, in Iran incidence of congenital anomalies ranged between 0.5 to 6.2/ 1000 live births across the Iranian provinces(30), In Europe the incidence ranged between 1.5-4.1 per 1000 live births(3) with some variation in the cumulative incidence in and type specific rates.

Regarding the affected systems Osteoarticular system was the more frequent contributed for 29.3% of the 167 congenital anomalies with a rate of 1.28/1000 live births, followed by 24.6% for cardiovascular system, 12.6% for head and neck, other systems were affected in less proportions ranged 1.2% to 10.2%. these findings almost similar to the findings of Ameen et al. study (2) and kamal et al. study (28).

The main risk factors reported in our study included consanguinity as the more frequent one, extreme maternal age , < 18 and > 35 years age , being housewife , low socioeconomic status,

history of abortion, also medications use and febrile illness during pregnancy, pre-gestational diabetes mellitus, gestational diabetes mellitus, pre-gestational hypertension, gestational hypertension, other maternal diseases, consanguinity, history of congenital anomalies in offspring were significant risk factors for congenital malformation. Congenital anomalies can lead to preterm birth, implying high rates of morbidity and mortality. The extremes of reproductive age are related to a greater number of perinatal complications. It is widely postulated that many risk factors could lead to these anomalies, therefore, our finding were not unexpected and supported by other studies (23,31,32), nonetheless other studies reported other risk factors that were not reported in our study such as exposure to irradiation and chemotherapy (33–36). Diseases such as diabetes and hypertension tend to appear more frequently in older individuals. Therefore, pregnancies of older women have a higher incidence of diabetes, high blood pressure and, consequently, a higher probability of perinatal complications, such as abortion, congenital anomalies, pre-eclampsia, eclampsia and premature births, among others(4,37–41). Therefore, for better monitoring of these high-risk pregnancies, there is a need for specialized health services, with prenatal examinations for morphological assessment and genetic studies (42–46). Regarding the distribution of congenital anomalies reported in our study, Hydrocephaly was the more frequent one, contributed for 32.9% , followed by Anencephaly 19.8%, Spina-Bifida 7.2% ,Polycystic kidney 6.6% and Encephalocele 6.0%. Other Congenital anomalies were less frequent and the least one was Omphalocele reported in only one case. These findings similar to other studies and literature with some variation in the proportions of these types (2,38,47–52).

As a limitation of the study, it was difficult to identify cases of multiple anomalies, which are important cause of death in the neonatal period.

5. CONCLUSION

The incidence of congenital anomalies among Iraqi newborns in Al-Najaf, Al-Furat Al-Awsat Teaching Hospital for the period 2016-2020 was 4.38 per 1000 live births.

Main risk factor for congenital anomalies reported for the study period were consanguinity marriage, extreme maternal age, less than 18 and above 35 years, being housewife , low socioeconomic status , history of abortion, also medications use and febrile illness during pregnancy, pre-gestational diabetes mellitus, gestational diabetes mellitus, pre-gestational hypertension, gestational hypertension, other maternal diseases, consanguinity, history of congenital anomalies in offspring were significant risk factors for congenital malformation.

Therefore, for better monitoring of high-risk pregnancies, there is a need for specialized health services, with prenatal examinations for morphological assessment and genetic studies. The Ministry of Health should continue to promote controls in pregnant women, which allows the detection of risk factors as well as their timely treatment for the prevention of congenital malformations in newborns. Both public and private hospitals must timely and adequately report the presence of congenital malformations to the competent health agencies, in order to have a real and updated database of what happens with this problem in our environment. On the other hand, the identification of cases would make it more feasible, the follow-up, assistance and comprehensive support by governmental and non-governmental organizations for the patient and his family. We recommend further studies including other centers in our province.

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Conflict of interest: None

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