

Original Article

# Congenital anomalies and early neonatal mortality: A tertiary hospital study

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#### Abstract:

JFac Med Baghdad 2022; Vol.64, No . 1 Received: Jan., 2022 Accepted: Mar.. 2022 Published: April. 2022 **Background:** The prevalence of congenital anomalies at birth is underestimated in developing countries due to the unavailability of perinatal diagnostic tests or accurate medical records. The prevalence of congenital defects may help to establish a baseline, track changes over time, and uncover etiological clues. **Objectives:** This study aims to explore the prevalence and types of major congenital anomalies in one of the main referral tertiary centers in Baghdad, highlighting the parents' and neonatal characteristics and assessing the mortality rate in this group of patients.

**Patients and Methods:** A case series study was conducted in Baghdad Teaching Hospital during the period between May 2017 and May 2018. Total deliveries were 6553, all live neonates with congenital anomalies were included regardless of their gestational age or birth weight. The patient's hospital notes were reviewed for the patient's characteristics, parentage, maternal chronic disease, drug history, and other study parameters. The early neonatal outcome was assessed within 7 days of the delivery.

**Results:** The prevalence of congenital malformations was 21.5 per 1000 birth with the most frequent anomaly affecting the nervous system (41.8%) followed by multiple syndromic malformations (12.8%) and digestive system (12.1%). The mean maternal age was  $27.8 (\pm 7.8)$  ranging from 14-47. The rate of diseased mothers was 18.4%, only half of them were on regular medications. Out of a total of 399 early neonatal death during the study period, death due to congenital malformations constituted 19.8%. Congenitally deformed patients died at a rate of 56%, which was significantly associated with low gestational age and birth weight.

**Conclusion:** The mortality rate for patients with congenital anomalies was high and associated with low gestational age and low birth weight. It is critical to test for congenital malformations early in pregnancy, particularly for high-risk parents with advanced age, consanguinity, and history of congenital anomalies. **Keywords:** congenital malformations, prevalence, neonatal mortality rate, Baghdad

#### Introduction:

The prevalence of congenital anomalies at birth varies greatly worldwide; such a high variation in prevalence could be related to social, racial, ecological, and economic influences (1, 2). In developing countries, the prevalence rates of congenital anomalies are underestimated due to the unavailability of diagnostic capabilities or accurate medical records as well as underreporting (2). The term congenital malformation (CM) was initially defined by the WHO document in 1972 as structural

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defects at birth (3). In October 2012, the WHO released a fact sheet updating the definition of the congenital anomalies as structural or functional anomalies including metabolic disorders which are present at birth (4). The congenital anomalies are divided into two broad categories; the major uncorrectable anomalies associate impaired normal body functions or reduced life expectancy. Minor congenital anomalies, on the other hand, do not associate with significant disability or functional effects (5). The etiology of the congenital anomalies remains unclear but is thought to be multifactorial. These factors may be genetic (10-30%), environmental factors (5-10%), or multifactorial inheritance (20-35%) while (30-40%) are unknown (6). Implicated maternal factors include age, lifestyle, illnesses during pregnancy, antenatal care, medication use, and non-use of peri-conceptual folic acid (7).

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Parental consanguinity, previous miscarriage and stillbirths, and inheritable congenital disease are other important factors in the etiology of congenital anomalies (7).

Fetal anomaly scanning is the most effective method of reducing the prevalence of serious congenital abnormalities and increasing the survival rate of those born with these issues (8). The finding of a correctable abnormality can serve to indicate that delivery should take place in a center with pediatric surgery facilities and the discovery of a severe uncorrectable abnormality might result in offering pregnancy termination (8). Parental emotional responses such as denial, the feeling of guilt, worry, grief, and shame occur after the birth of an infant with major congenital anomalies, highlighting the significance of proper counseling (9). Knowledge about the prevalence of congenital anomalies is useful to obtain baseline rates, document changes over time, and identify clues to the etiology of the conditions. This knowledge is also helpful to plan and assess antenatal screening for congenital anomalies, especially for highrisk populations (10). This study aims to evaluate the prevalence and types of major congenital anomalies in one of the main referral tertiary centers in Baghdad, highlighting the parent and neonatal characteristics and assessing the mortality rate in this group of patients.

#### Methods:

This is a case series study conducted in Baghdad Teaching Hospital during the period between May 2017 and May 2018. All neonates with congenital anomalies were included regardless of their gestational age or birth weight. Only live births were included. The patient's hospital notes were reviewed for the patient's characteristics, parentage, maternal chronic disease, and drug history, and other study parameters. The early neonatal outcome was assessed after 7 days of the delivery.

Collected data was tabulated then analyzed using the SPSS statistical package version 25 (SPSS, Inc., Chicago, IL). Frequencies and percentages, mean and standard deviation (SD), and range were used for descriptive data. Chi-square tests were used to assess the associations between demographic characteristics of cases and the outcomes. The level of statistical significance (P-value) was set at < 0.05.

# Results

During the period of the study, we have recorded 141 congenital anomalies out of 6553 total live deliveries. The prevalence of congenital malformations was 21.5 per 1000 birth with the most frequent anomaly affecting the central nervous system (CNS) (41.8%) followed by multiple syndromic malformations (12.8%) and the gastrointestinal tract (GIT) (12.1%) as detailed in Table 1. In addition to the well-known syndromes, multiple malformations included 8.5% of the cases with a

combination of malformations involving the CNS, musculoskeletal, GIT, renal, chromosomal or cardiac.

Table 1: The types and rate of congenital anomalies
with prevalence per 1000 live births

Congenital malformation	Number	(%)	Prevalence/100 0 live birth
Nervous system	59	41.8	9.0
Meningocele	29	20.6	4.4
Hydrocephalous	12	8.5	1.8
Anencephaly	12	8.5	1.8
Encephalocele	11	7.8	1.8
Spinal tail	1	0.7	0.2
Digestive system	17	12.1	2.6
Diaphragmatic	7	5.0	1.1
hernia	5	3.5	0.8
Duodenal atresia	3	2.1	0.5
Esophageal atresia	2	1.4	0.3
Cloacal dystrophy	1	0.7	0.2
Imperforated anus	1	0.7	0.2
Multiple	18	12.8	2.7
malformations	1	0.7	0.2
Corazon syndrome	1	0.7	0.2
Pfeiffer syndrome	1	0.7	0.2
Mermaid syndrome	1	0.7	0.2
Charge syndrome	1	0.7	0.2
Holt-oram syndrome	1	0.7	0.2
Potter syndrome Others	12	8.5	1.8
Skeletal	13	9.2	2.0
Clubfoot	4	2.8	0.6
Coccygeal teratoma	3	2.1	0.5
Geno recuvatum	2	1.4	0.3
Thanatophoric	2	1.4	0.3
Hypochondroplasia	1	0.7	0.2
Osteogenesis	1	0.7	0.2
imperfect	1	0.7	0.2
Abdominal wall	13	9.2	2.0
defect	8	5.7	1.2
Omphalocele	3	2.1	0.5
Gastroschisis	2	1.4	0.3
Prune belly	2	1.4	0.5
Chromosomal	9	6.3	1.6
Down (monosomy	5	3.5	0.8
21)	3	2.1	0.5
Edward (Trisomy 18)	1	0.7	0.2
Patau (Trisomy 13)	1	0.7	0.2
Urinary	5	3.5	0.8
Polycystic kidney	3	2.1	0.5
Multicystic	2	1.4	0.3
dysplastic	=		
Cardiac	4	2.8	0.7
	•	1.4	0.3
Others	2	1.4	0.3
Others Ambiguous genitalia Conjoined twin	2	0.7 0.7	0.2

Parents' characteristics are summarized in table 2. The mean maternal age was 27.8 years  $(\pm 7.8)$  ranging from 14-47 years. Only 3 (2%) were 40 years or older, whereas mothers younger than 20 years constituted 19 (13.5%). Two thirds of the mothers with gastroschisis newborns were younger than 20 years old. As for

paternal age, Ten (7%) were 45 years or older and three (2.1%) were younger than 20 years, with a mean of 32.6  $(\pm 8.26)$  ranging between 19-74 years. It is worth noting that all mothers 40 years or older have their husbands older than 45 years with an overall consanguinity rate of 50%. The rate of diseased mothers was 18.4%, only half of them were on regular medical therapy. The mean number of siblings for patients in the cohort was four ranging between 1-12; 13/141 (9.2%) of the cases had a sibling with congenital anomaly, 10/13 (77%) were with a similar condition.

#### **Table 2: Parent's characteristics**

Parent's characteristics	Value
Paternal age (years): No (%)	
<20	3 (2.1)
20-44	128 (90.1)
≥45	10 (7.0)
Maternal age: (years): No (%)	
<20	19 (13.3)
20-39	119 (83.8)
≥40	3 (2.1)
Gravida: mean (±SD) Range	4.08 (±2.5)1-12
History of abortion: mean (±SD) Range	0.55 (±1.11) 0-7
Maternal disease: No (%)	26 (18.4)
Hypertension	16 (11.5)
Infertility	3 (2.2)
Thyroid	2 (1.4)
Diabetes	1 (0.7)
Epilepsy	1 (0.7)
Cardiac	1 (0.7)
Hepatitis	1 (0.7)
Stroke	1 (0.7)
Drug history: No (%)	13 (9.2)
Consanguinity: No (%)	73 (51.8)
Previous congenital anomaly No (%)	13 (9.2)

The mean gestational age of the patients was  $35.5 (\pm 2.9)$  weeks with a mean neonatal weight of  $2.55 (\pm 0.7)$  Kg.

Seventy-seven out of 141 (54.6%) were preterm who did not complete 37 weeks of gestation, and 2/141 (1%) were extremely preterm who did not complete 28 weeks. There was a slight female predominance with a male to female ratio of 1: 1.5 (Table 3). The antenatal diagnosis was completely absent in a third of the cases, the other third was diagnosed late (predelivery) whereas only one-third of the cases were diagnosed at 20-24 weeks (Table 3).

#### Table 3: Neonatal characteristics and outcome

Neonatal characteristics	Value	
Gestational age: mean (±SD)	35.7 (±2.92)	
Range	26-41 week	
Birth weight: mean (±SD)	2.55 (±0.75)	
Range	0.7-5.20 Kg	
Gender: No (%)		
Male	57 (40.4)	
Female	84 (59.6)	
Antenatal diagnosis: No (%)		
No antenatal diagnosis	42 (29.8)	
At 20 weeks	19 (13.5)	
At 24 weeks	32 (22.7)	
At the third trimester	48 (34.0)	
Neonatal outcome: No (%)		
Early neonatal death	79 (56.0)	
Alive (at 7 days after birth)	62 (44.0)	

Out of a total of 399 early neonatal deaths during the study period, death due to congenital malformations constituted 19.8%. The death rate of congenitally malformed patients was 56% that was significantly associated with low gestational age and low birth weight (Figure 1A and B).

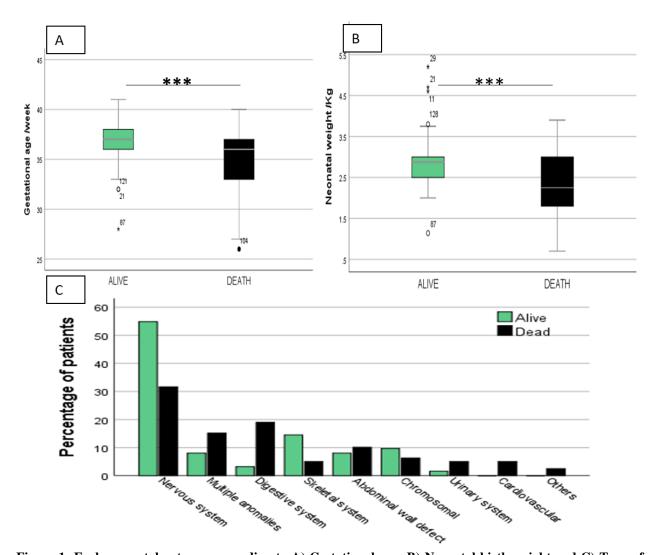


Figure 1: Early neonatal outcome according to A) Gestational age; B) Neonatal birth weight and C) Type of congenital anomaly. \*\*\* P<0.0001.

Although the highest death rate was seen in neonates with CNS anomalies, the survival rate in these patients was higher (Figure 1C). By contrast, survival of patients with digestive, urinary, cardiac, and multiple malformations was significantly lower (P=0.02). No significant association was seen between early neonatal death rate and type of delivery, maternal disease, history of a previous condition, or consanguinity (Table 4).

Parameters		Alive	Dead	P value
Type of the delivery	Normal Caesarian	12 (19.4) 50 (80.6)	15 (19.0) 64 (81.0)	0.95
Maternal disease	No Yes	45 (87.1) 8 (12.9)	59 (74.7) 20 (25.3)	0.067
Previous condition	No Yes	58 (95.1) 3 (4.9)	69 (87.3) 10 (12.7)	0.118
Consanguinity	No Yes	32 (51.6) 30 (48.4)	36 (45.6) 43 (54.4)	0.476

#### **Discussion:**

Congenital malformations are a global health issue that considerably impacts the patients' and their families' quality of life in addition to the financial burden it incurs on the family and health care providers. The estimated number of children born with severe congenital anomalies is 7.9 million annually. 295,000 of them die within the first few weeks of their life (11). The prevalence of CM widely varies across countries. One of the highest prevalence rates was reported in Pakistan at 4.2% (12) followed by Egypt at 2.5% (13) and Ethiopia at 2.0% (14) while India (15) and Hong Kong reported lower prevalence rates at 1.9% and 0.6% respectively. In Iraq, studies reported that the prevalence of CM in different regions varied greatly with a trend of increased rate over the last decade. In Baghdad, Hameed et al in 2007 found that the overall prevalence of CM in four main hospitals was 1.2% of live births (16). In our cohort, the prevalence was (2.1%) which is about 1.8 times higher than what has been reported before 10 years (1.1%) in the same hospital. In Al Anbar province, the prevalence reported in 2012 was 4.04% (17) which is more than four-folds the prevalence reported by Al Janabi in 2007 (0.85%) (18). In Basra, the prevalence increased from 0.81% in 1994 to 1.3 in 2013. The lowest prevalence was reported in the North, where recent studies found that the prevalence of CM in Erbil province was 0.363% (19) and in Sulaymaniyah was 0.33% (20). All of these studies were conducted in one or a limited number of public hospitals which may underestimate the actual prevalence since they missed a considerable number of deliveries that took place at home or in private hospitals. Although the overall prevalence in Iraq is close to that of Egypt, it is higher than in the neighboring countries. The prevalence of CM in Saudi Arabia was 0.4% (21) and 1.2 in Kuwait (22). CM of the nervous system is the most frequent congenital malformation reported by the majority of local and regional studies whereas circulatory system malformations are the most frequent anomaly that required hospital admission in Iraq and the western countries (11, 23). This could be related to improvement in the diagnostic ability related to these specific abnormalities, which facilitate pregnancy termination (11) which is not accepted in our culture. Some local studies reported higher cardiovascular malformations (24), however, they included patients who required hospital or neonatal intensive care units (NICU) admission rather than any patients delivered with a congenital anomaly. The anomalies of the nervous system remained to be the highest in the records of Baghdad teaching hospital since 2007 (16). However, there was a 4% increase in the prevalence of digestive system malformations when comparing recent findings with those of 2007.

Many factors influence the prevalence of congenital anomalies in the general population. Parents' age, particularly that of the mother, is associated with specific congenital malformations. The association between mother's age older than 40 years at delivery and Down syndrome is well established (11). In our cohort, 80% of Down syndrome newborns were born to mothers older than 35 years with only one older than 40. Other anomalies such as gastroschisis are more frequently associated with mothers younger than 20 years old (25). We found that 66% of the mothers with gastroschisis newborns were younger than 20 years old. The association of paternal age at childbearing with offspring birth defects has been proposed by many studies (26, 27). Several mechanisms were suggested for this association such as paternal mutations and aneuploidy (26). A population-based Norwegian study indicated that the incidence of malformations was 3.5% in the paternal age category 45-49 compared to 2.8% category 30-34 (26). In agreement with these findings, we found that 7% of patients with congenital anomalies had their fathers older than 45 years. Consanguinity is another risk factor that was flagged in half of our patients. The risk of Mendelian recessive inheritance was reported to be particularly higher in consanguineous parents (28). In the UK, studies reported a growing risk factor in some Muslim immigrants (29). Maternal health conditions and drug history during pregnancy are important risk factors. The mothers of 18% of our patients had health issues during the studied pregnancy such as hypertension, DM, and epilepsy, however only half of them were on regular medications. Nervous system anomalies were observed in two-thirds of these patients; although previous studies reported that antihypertensive and antiepileptic therapies are associated with different types of cardiovascular congenital anomalies (11). Early antenatal diagnosis in the second trimester was relatively low in our cohort; 29% of the cases were diagnosed at delivery without prior radiological or sonographic confirmation. This is probably due to poor antenatal visit compliance and missing the 20th-week fetal anomaly scan by an experienced radiologist. Second-trimester sonography generally targets low-risk population while mother's who have had a prior pregnancy with congenital abnormality need focused intensive screening to avoid the late diagnosis of some fetal malformations such as an encephaly, omphalocele, and limb anomalies that can be detected earlier at 10-14 weeks of pregnancy (30). Detection of these anomalies earlier using other diagnostic procedures such as Magnetic Resonance Imaging (MRI), genetic testing, molecular testing of the chorionic villus sample (CVS) or amniocytes, fetal blood sample, a direct biopsy of fetal tissue provides a better chance for early intervention (31). Diagnosis of the anomalies also leads

to clinical decision-making on the method of delivery hence preventing birth-associated stress to the mother and the infant. In the case of deadly congenital defects, early diagnosis assists in clinical decision making on the care of the pregnancy (32). Congenital anomalies continue to be the leading cause of death in neonates. According to the WHO, 17%–42% of infant mortality was attributed to a congenital anomaly in Euro countries (33). This is significantly underestimated in low/middle-income countries because the actual cause of death is not reported in a well-formed database (34). We have shown that the CM-related death rate was 19.8% which is within the range reported by the Euro countries. There was an increasing trend in the CMrelated mortality in the same hospital over the period between 2007 and 2009 with an overall rate of 17% (35). As expected, the rate of death was significantly associated with gestational age and birth weight (36). In our cohort, the death rate observed in cardiac and conjoined twins was (100%), followed by digestive anomalies (88%) and urinary anomalies (80%) while the lowest death rate was in patients with skeletal anomalies (30.8%). In England, it was reported that the highest CM-related mortality rates were due to congenital heart defect (51%), chromosomal anomalies (28%), and digestive system anomalies (27%) (37). There were several limitations in this study. Starting with the design of the study which targeted congenital anomalies in live births and excluded those with stillbirth and abortion. There were also difficulties in collecting data about the maternal characteristics of all the 6553 births, hence we could not calculate the odds ratio and predictors of congenital anomalies. Other limitations include a lack of information about parental residency, educational and socioeconomic status. Besides, difficulties in a longer follow up of the patients restricted the ability to calculate the mortality rate in children under 5 years.

# Conclusion

The mortality rate for patients with congenital anomalies was high and associated with low gestational age and low birth weight Screening for such anomalies pre and peri-conception as well as medical genetic screening are vital for the early detection and management of congenital anomalies especially for high-risk parents with extreme age, consanguinity, and previous history of congenital anomaly.

#### Author contributions:

H.Talab, A.Kamal and K.Naama conceived study concept. H.Talab and A.Kamal designed the study. K.Naama, A.Kamal and H.Talab collected the data, H.Talab and A.Kamal interpreted the data and drafted the first manuscript. K.Naama reviewed the manuscript critically.

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# التشوهات الخلقية والوفيات المبكرة للأطفال حديثي الولادة: دراسة مستشفى مرجعي

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**الخلفية**: يتم التقليل من شأن انتشار التشوهات الخلقية عند الولادة في البلدان النامية بسبب عدم توفر الإختبارات التشخيصية في الفترة المحيطة بالولادة أو السجلات الطبية الدقيقة. قد تساعد دراسة إنتشار العيوب الخلقية على وضع خط أساس، وتتبع التغيرات بمرور الوقت، والكشف عن القرائن المسببة. **الهدف**: تهدف هذه الدراسة إلى تقييم إنتشار وأنواع التشوهات الخلقية الرئيسية في أحدى المستشفيات المرجعية الرئيسية في بغداد، وتسليط الضوء على خصائص الوالدين وحديثي الولادة وتقييم معدل الوفيات في هذه الفئة من المرضي.

**المرضى والمنهجيةً:** أجريّت دراسةً في مستشفى بغداد التّعليمي خلال الفترة بين أيار 2017 وأيار 2018. وبلغ مجموع الولادات 6553 حالة، وأدرجت جميع الولادات الحية المصابة بتشوهات خلقية بغض النظر عن عمر الحمل أو وزن الولادة. تمت مراجعة ملاحظات المستشفى للمريض، والنسب، والأمراض المزمنة الأمومية، وتاريخ الدواء، وغيرها من معابير الدراسة. تم تقييم النتيجة المبكرة لحديثي الولادة في غضون سبعة أيام من الولادة.

النتائج: كان إنتشار التشوهات الخلقية 2.15 لكل 1000 ولادة مع أعلى تشوه متكرر يؤثّر على الجهاز العصبي (4.1%) يليه تشوهات متعددة (1.21%) والجهاز الهضمي (12.8%). وكان متوسط سن الأم 27.8 (±7.8) ويتراوح بين 14 و47 عاما. وكان معدل الأمهات المريضات 18.4%، وكان نصفهن فقط يتناولن أدوية بإنتظام. ومن بين ما مجموعه 399 حالة وفاة مبكرة لحديثي الولادة خلال فترة الدراسة، شكلت الوفاة الناجمة عن التشوهات الخلقية 19.8%، وتوفى المرضى المشوهون خلقيا بمعدل 56%، وهو ما ارتبط ارتباط كبيرا بعمر الحمل ووزن الوليد.

الخلاصة: إن معدل وفيات مرضى التشوهات الخلقية مرتفع ويرتبط بعمر الحمل ووزن الولادة. من المهم إختبار التشوهات الخلقية في وقت مبكر من الحمل، خاصة بالنسبة للأباء المعرضين لخطر كبير مع التقدم في العمر، والإصابة بالتشوهات الخلقية وتاريخها.

مفتاح الكلمات: الشوهات الخلقية، انتشار، معدل وفيات الاطفال، بغداد