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PATTERNS AND PREVALENCE OF CONGENITAL ANOMALIES AMONG NEONATES AND ASSOCIATED RISK FACTORS IN MISURATA CENTRAL HOSPITAL –LIBYA / 2015

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ABSTRACT

Background: Congenital anomalies are defined as structural or functional abnormalities that present at birth. They are a major cause of neonatal stillbirths and neonatal morbidity and mortality. **Objective**: to determine the prevalence and patterns of congenital anomalies among newborns in Misurata central hospital; to estimate the subsequent mortality among these babies; and to identify the maternal and perinatal risk factors associated with these congenital malformations. **Methods**: a cross sectional study was conducted on 73 neonates with congenital anomalies in neonatal ICU of Misurata Teaching Hospital, Libya. We retrospectively analyzed the hospital records from January 2015 to December 2015. The collected data include maternal characteristics and risk factors; neonatal characteristics, diagnosis and complication; patterns of congenital anomalies; and imaging study. **Results:** The studied neonates are (56.2 %) boys, (42.4%) girls and (1.4%) ambiguous. About (71.2%) of them were survived, while only (28.8%) of them died. Majority of CA neonates are borne to multi-gravid mothers (86.3%), aged 30-40 years (59%), delivered by CS (67.1 %) and cephalic presentation represents (83.5 %). Neonates are mainly preterm (76.7%) and of normal birth weight (41.1%). The prevalence of CAs in this study was 1.17%. The main patterns founded were Cleft lip & palate, CHD, Syndromatic baby, undescended testis and hypospadius (50.3%, 35.6%, 9.6%, 8.2% and 6.8%) respectively, The main maternal risk factors are DM, drugs, HTN and oligohydramnios (37%, 31.5%, 11% and 9.6%) respectively. The main neonatal complications are RDS, sepsis and TTN (37%, 6.8% and 5.5%) respectively. **Conclusion:** cleft palate and lip, CHD, Syndromatic baby, undescended testis and hypospadius are the most common congenital anomalies in Misurata. Maternal age above 30 years, multiparity, prematurity, CS, DM, drugs, HTN and oligohydramnios are the main risk factors. There is need of increasing pre-pregnancy screening, proper antenatal care and the establishment of an ongoing surveillance system for CA.

KEYWORDS: Congenital anomalies, Prevalence, Pattern, Risk Factors, Mortality

INTRODUCTION

Congenital anomalies (CA) refers to any abnormality, whether genetic or not, which is present at birth.[1] They can be defined as structural or functional abnormalities including metabolic disorders, present at birth or few weeks after birth.[2]

Primary malformations are caused by endogenous disturbances of primordial tissues. Secondary malformations (disruption) arise when organs develop abnormally from a normal primordium.[3] These defects of prenatal origin result from defective embryogenesis or intrinsic abnormalities in the development process. Birth defects can be isolated abnormalities or part of a syndrome.[4] Structural defects of prenatal origin are classified into three groups, according to the cause, timing and extent of the developmental disturbance: Malformations (defective organogenesis); Dysplasia (abnormal cell or tissue structure); and Deformation (mechanically induced changes of normal structure).[1]

Prevalence of major malformation has been variously reported as 3-4% to 6-8%, about one fifth of all such malformations are severe and life threatening.[1] Based on the World Health Organization (WHO) report, about 3 million fetuses and infants are born each year with major CA. They are found in approximately 3% of newborns.[5] Worldwide surveys have shown that birth prevalence of congenital anomalies varies greatly from country to country. The most common serious congenital disorders are congenital heart defects, neural tube defects and Down syndrome.[6]

Approximately 40% to 60% of CA is of unknown origin. The etiology of Congenital Malformation is genetic (30-40%) and environmental (5 to 10%). Among the genetic etiology, chromosomal abnormality constitutes 6%,

single gene disorders 25% and multifactorial 20- 30%; however, for nearly 50% of CA, the cause is yet to be known.[7]

Congenital anomalies are an important cause of neonatal mortality both in developed and developing countries. It accounts for 8-15% 13-16% of neonatal deaths.[8] more than 70% die in the first month of life.3 Due to high cost of treatment and rehabilitation of these anomalies, early identification of causative and risk factors and early prevention is necessary where possible.[1]

Additional efforts must be put to increase knowledge and better understand the epidemiology of children with birth defects and that will help improve the health of our children. Thus the present study was conducted aiming to determine the prevalence and patterns of congenital anomalies among the newborns in Misurata central hospital; to estimate the subsequent mortality among these babies; and to identify the maternal and perinatal risk factors associated with these congenital malformations.

METHODS

Study setting: This study was conducted as a descriptive cross sectional study at the neonatal intensive care unit of Misurata teaching hospital in Libya, based on hospital files records. We retrospectively analyzed the hospital records over a period of one year from January 2015 to December 2015.

Study subjects: Our study included 73 babies with congenital anomaly admitted to the neonatal ICU of Misurata teaching hospital.

Ethical issue: Approval was granted from the hospital administration prior to the collection of data from the hospital records.

Data collection: The collected data includes

A) Maternal characteristics: (i) age, (ii) parity, (iii) mode of delivery, (iv) maternal risk factors, (v) used drugs.
B) Neonatal characteristics: (i) sex, (ii) gestational age, (iii) birth weight, (iv) presentation (v) antenatal diagnosis, (vi) neonatal complication.
C) Patterns of congenital anomalies.
D) Imaging study: Echo, C-x-ray with NGT, Uss and CT scan.

Statistical analysis: Date was analyzed by SPSS software version 18 and the results was summarized, presented and displayed as frequencies and percentage in suitable tables. Statistical analysis of qualitative data was performed using Chi-square test, while fisher exact test was used if there is an expected value in a cell < 5. Results were accepted as significant when ($p < 0.05$).

RESULTS

Table 1: Admissions and mortality of studied babies according to gender.

Gender	Live babies 52 (71.2 %)				Deaths 21 (28.8 %)		Total N. (73)	
	D (48)		T (4)					
	N.	%	N.	%	N.	%	N.	%
Boy	27	51.9	2	3.8	12	57.1	41	56.2
Girl	21	40.4	2	3.8	8	38.1	31	42.4
Ambiguous	0	0	0	0	1	4.8	1	1.4

Chi Square = 0.45 p = 0.25 (Non-Significant)

There is no statistical significant difference in studied babies and subsequent deaths regarding to sex. (Table, 1).

Table 2: Admissions and mortality of studied babies according to birth weight.

Birth Weight	Live babies 52 (71.2 %)				Deaths 21 (28.8 %)		Total N. (73)	
	D (48)		T (4)					
	N.	%	N.	%	N.	%	N.	%
Macrosomia (> 4 Kg)	15	28.8	0	0	1	4.8	16	21.9
Normal Weight (2.5 - 4 Kg)	18	34.6	3	5.7	9	42.9	30	41.1
LBW (1.501 - ≤ 2.5 Kg)	13	25	1	1.9	9	42.9	23	31.5
VLBW (1.001 - ≤ 1.5 Kg)	2	3.8	0	0	1	4.8	3	4.1
ELBW (≤ 1 Kg)	0	0	0	0	1	4.8	1	1.4

Chi Square = 2.2 p = 0.32 (Non- Significant)

Most neonates are of normal birth weight (41.1%), while LBW and macrosomia represent only 31.5% and 21.9% respectively. And there is no significant difference in subsequent death according to birth weight ($p > 0.05$). (Table, 2).

Table 3: Admissions and mortality of studied babies according to gestational age.

Gestational age		Live babies 52 (71.2 %)				Deaths 21 (28.8 %)		Total N. (73)	
		D (48)		T (4)					
		N.	%	N.	%	N.	%	N.	%
Preterm birth	< 37 Wks	35	67.3	4	7.7	17	81	56	76.7
Full-term birth	37 – 40 Wks	9	17.3	0	0	3	14.2	12	16.4
Post-term birth	> 40 Wks	1	1.9	0	0	0	0	1	1.4
FT		3	5.7	0	0	1	4.8	4	5.5

Chi Square = 56.5 p < 0.001 (Highly Significant)

Regarding gestational age, the majority of low birth weight neonates are preterm < 37 Wks (76.7%) and that is highly statistically significant. Also, there is a significant increase in subsequent death among premature babies from those full term (p < 0.05). (Table, 3).

Table 4: Admissions and mortality of studied babies according to maternal age.

Maternal age	Live babies 52 (71.2 %)				Deaths 21 (28.8 %)		Total N. (73)	
	D (48)		T (4)					
	N.	%	N.	%	N.	%	N.	%
≤ 20	0	0	0	0	2	9.5	2	2.7
- 25	6	11.5	1	1.9	2	9.5	9	12.3
- 30	7	13.4	2	3.8	6	28.6	15	20.5
- 35	17	32.7	0	0	6	28.6	23	31.5
- 40	15	28.8	1	1.9	4	19	20	27.5
> 40	3	5.8	0	0	1	4.8	4	5.5

Chi Square = 16.7 p = 0.005 (Highly Significant)

Majority of studied babies are borne to mothers aged 30-40 years (59%) and that is statistically significant. While, there are no significant increase in subsequent death (p > 0.05). (Table, 4).

Table 5: Admissions and mortality of studied babies according to mothers' parity.

Parity	Live babies 52 (71.2 %)				Deaths 21 (28.8 %)		Total N. (73)	
	D (48)		T (4)					
	N.	%	N.	%	N.	%	N.	%
Primi-gravida	6	11.5	0	0	4	19	10	13.7
1 - 5	31	59.6	4	7.7	15	71.5	50	68.5
> 5	11	21.2	0	0	2	9.5	13	17.8

Chi Square = 19.8 p < 0.001 (Highly Significant)

Most of cases are borne to multi-gravid mothers (86.3%) and that is statistically significant. and that is statistically significant. While, there are no significant increase in subsequent death (p > 0.05). (Table, 5).

Table 6: Admissions and mortality of studied babies according to mode of delivery.

Mode of Delivery	Live babies 52 (71.2 %)				Deaths 21 (28.8 %)		Total N. (73)	
	D (48)		T (4)					
	N.	%	N.	%	N.	%	N.	%
N.V.D	16	30.7	1	1.9	7	33.3	24	32.9
Elective C\S	14	26.9	2	3.8	9	42.9	25	34.2
Urgent C\S	18	34.6	1	1.9	5	23.8	24	32.9

Chi Square = 3.4 p = 0.032 (Significant)

Most studied babies are delivered by CS (67.1 %) with a significant increase in subsequent neonatal death among those borne by NVD (Table, 6).

Table 7: Admissions and mortality of studied babies according to presentation.

Presentation	Live babies 52 (71.2 %)				Deaths 21 (28.8 %)		Total N. (73)	
	D (48)		T (4)					
	N.	%	N.	%	N.	%	N.	%
Cephalic	46	88.5	1	1.9	14	66.7	61	83.5
Breech	2	3.8	3	5.7	6	28.5	11	15.1
Face	0	0	0	0	1	4.8	1	1.4

Chi Square = 17.9 $p < 0.001$ (Highly Significant)

Majority of studied babies are of cephalic presentation (83.5 %) with a significant increase in subsequent death among those borne by malprentation (Table, 7).

Table 8: Admissions and mortality of studied babies according to maternal risks.

Maternal risks	Live babies 52 (71.2 %)				Deaths 21 (28.8 %)		Total N. (73)	
	D (48)		T (4)					
	N.	%	N.	%	N.	%	N.	%
DM	26	50	0	0	1	4.8	27	37
HTN	7	13.5	0	0	1	4.8	8	11
Drugs	20	38.5	1	1.9	2	9.5	23	31.5
Polyhydramnios	1	1.9	1	1.9	0	0	2	2.7
UTI	1	1.9	0	0	0	0	1	1.4
APH	0	0	0	0	2	9.5	2	2.7
Oligohydramnios	3	5.7	0	0	4	19	7	9.6

Chi Square = 31.7 $p < 0.001$ (Highly Significant)

The main maternal risk factors among mothers of the studied babies are DM, drugs, HTN and oligohydramnios (37%, 31.5%, 11% and 9.6%) respectively, and that is highly statistically significant. While, there is no significant difference in neonatal deaths due to any of these maternal risk factors. (Table, 8).

Table 9: Admissions and mortality of studied babies according to used drugs.

Drugs	Live babies 52 (71.2 %)		Deaths 21 (28.8 %)		Total N. (73)	
	N.	%	N.	%	N.	%
Insulin	15	28.8	1	4.8	16	21.9
Oral hypoglycemic	2	3.8	1	4.8	3	4.1
Antihypertensive	3	5.7	0	0	3	4.1
Thyroxine	1	1.9	0	0	1	1.4

Chi Square = 9.2 $p = 0.026$ (Highly Significant)

21.9% of mothers of the studied cases used insulin, and that is highly statistically significant. **(Table, 9).**

Table 10: Admissions and mortality of studied babies according to Neonatal complication.

Neonatal complication	Live babies 52 (71.2 %)				Deaths 21 (28.8 %)		Total N. (73)	
	D (48)		T (4)					
	N.	%	N.	%	N.	%	N.	%
RDS	15	28.8	2	3.8	10	48	27	37*
Sepsis	1	1.9	0	0	4	19	5	6.8
TTN	4	7.7	0	0	0	0	4	5.5
Birth asphyxia	0	0	0	0	1	4.8	1	1.4
Complication Pneumothorax	0	0	0	0	1	4.8	1	1.4

Chi Square = 21.3 $p < 0.001$ (Highly Significant)

The main neonatal complications among the studied babies are RDS, sepsis and TTN (37%, 6.8% and 5.5%) respectively, and only RDS is statistically significant. (Table, 10).

Table 11: Admissions and mortality of studied babies according to imaging study.

Imaging study	Live babies 52 (71.2 %)				Deaths 21 (28.8 %)		Total N. (73)	
	D (48)		T (4)					
	N.	%	N.	%	N.	%	N.	%
Echo	18	34.6	2	3.8	3	14.2	23	31.5
C-x-ray with NGT	0	0	2	3.8	1	4.8	3	4.1
Uss	4	7.7	0	0	0	0	4	5.5
CT scan	1	1.9	0	0	2	9.5	3	4.1

The imaging studies done to the studied babies as follow Echo (31.5%), C-x-ray with NGT (4.1%), Uss (5.5%) and CT scan (4.1%). (Table, 11).

Table 12: Pattern of congenital anomalies among studied babies.

Pattern of congenital anomaly	Live babies 52 (71.2 %)				Deaths 21 (28.8 %)		Total N. (73)	
	D (48)		T (4)					
	N.	%	N.	%	N.	%	N.	%
CHD	19	36.5	1	1.9	6	28.5	26	35.6**
Cleft lip & palate	1	1.9	0	0	1	44.4	2	50.3**
Esophageal atresia	0	0	2	3.8	0	0	2	2.7
Diaphragmatic hernia	0	0	0	0	1	4.8	1	1.4
Ambiguous genitalia	0	0	0	0	1	4.8	1	1.4
Edward syndrome	0	0	0	0	3	14.2	3	4.1
Down syndrome	1	1.9	0	0	0	0	1	1.4
Potter syndrome	0	0	0	0	1	4.8	1	1.4
Hydrocephalus	1	1.9	0	0	1	4.8	2	2.7
Genorecurvatum	1	1.9	0	0	0	0	1	1.4
Hypospadius	5	9.6	0	0	0	0	5	6.8*
Undescended testis	2	3.8	0	0	4	19	6	8.2*
Syndromatic baby	0	0	0	0	7	33.3	7	9.6*
Hydronephrosis	2	3.8	0	0	0	0	2	2.7
Choanal atresia	1	1.9	0	0	0	0	1	1.4
Congenital lung emphysema	0	0	0	0	1	4.8	1	1.4
Anencephaly	0	0	0	0	2	9.5	2	2.7
Colloiden baby (ecthyosis)	1	1.9	0	0	1	4.8	2	2.7
Arthrogryposis	1	1.9	0	0	1	4.8	2	2.7
Encephalocele	0	0	0	0	2	9.5	2	2.7
Epidermolysisballosa	1	1.9	0	0	0	0	1	1.4
Polycystic kidney	0	0	0	0	1	4.8	1	1.4
Meningocele	0	0	0	0	1	4.8	1	1.4
Poldactaly	0	0	0	0	2	9.5	2	2.7

** $p < 0.001$ (Highly Significant) * $p < 0.05$ (Significant)

The main patterns of congenital anomalies founded among the studied babies were Cleft lip & palate, CHD, Syndromatic baby, undescended testis and hypospadius (50.3%, 35.6%, 9.6%, 8.2% and 6.8%) respectively, and these congenital anomalies are statistically significant. Also, there is a statistically significant death among syndromatic babies. (Table, 13).

DISCUSSION

The pattern and prevalence of congenital anomalies may vary over time or with geographical location. This may reflect a complex interaction of known and unknown genetic and environmental factors which including socio-cultural, racial and ethnic variables.[2] Congenital malformations have become important causes of perinatal mortality in developing countries.[8] Most children, born with major congenital anomalies and survive, are affected physically, mentally, or socially and can be at increased risk of morbidity due to various health disorders.[9]

Our study involved 73 newborns with congenital anomalies in Misurata centeral hospital between January and December 2015. It aims to determine the pattern and proportion of congenital anomalies among newborns and

the associated maternal and perinatal risk factors. Our data was based on the hospital's medical records.

The prevalence of congenital malformation in the present study was 1.17% which is comparable with other similar studies recorded from brazil (1.07%)[10] and Gorgan (1.01),[11] higher than that in United Arab Emarat (0.79%),[12] and is lower than that of Saudi Arabia (2.94%),[13] Bahrain (2.7%),[14] Lebanon (2.4%),[5] Iraq (3.5%),[9] Tehran (3.5%),[11] India (2.22% and 3.6%)[2,15] and West Bengal (2.03%).[1] This higher prevalence of documented birth defects in other studies may be due to advanced diagnostic technology, especially USG and echocardiography. These variations between different studies could be explained by the effect of diverse racial, social factors, environmental pollution, socioeconomic, percent of consanguinity marriage, nutritional status and habits in various parts of the world or in different geographical area. Furthermore the type of sample, study design, methodology and the criteria for diagnosis have differences.[16]

With regard to pattern of congenital anomalies, our study revealed that the commonest congenital malformations are gastrointestinal and congenital heart diseases (50.3% and 35.6%,) respectively. These findings are comparable to that of Sagunabai et al[17] who reported gastrointestinal malformations to rank the highest and that of Charan et al[1] who find that CHD was the commonest CA followed by musculoskeletal and genitourinary system in a descending order of frequency. While, Shama et al[18] reported that the CNS defects have the highest prevalence where as Sarkar et al[8] reported that musculoskeletal abnormalities were the commonest.

In this study, among the studied 73 neonates with congenital anomalies, (56.2%) are boys, (42.4%) are girls and (1.4%) are ambiguous. There is no statistical significant difference in CA regarding to sex, which concurs with the findings of Francine et al.[5] and Biri et al.[19] where both genders are equally distributed. While, many studies have demonstrated male predominance amongst congenital malformed babies.[1,8,9] They attributed the more male babies with congenital anomalies because of the fact that the females were affected with more lethal congenital malformations and could not survive to be born with signs of life.[8]

In the present study, no association of low birth weight with increased risk of congenital malformation was noted. The majority of studied neonates are of normal birth weight (41.1%). These findings are in disagreement with many previous studies, in which association of LBW with increased risk of congenital malformations is very well- documented.[1,8,20]

The majority of studied neonates are preterm < 37 Wks (76.7%) and that is highly statistically significant. Strong association of prematurity with increased risk of congenital malformation was noted in this study. This is in concordance with previous studies, that stated that the prevalence of congenital malformations was significantly higher in preterm babies as compared to full term neonates.[1,8]

Mode of delivery also showed a significant association with congenital anomalies in this study with cesarean section being more commonly associated than normal delivery. In this study, cesarean deliveries were present in 67.1% of CA babies. This outcome was similar to the observations of Sarkar et al.[8] and Taboo.[16] On contrary to our study, findings reported by Hindryckx et al[21] who found 80% of patients were delivered with vaginal delivery while 20% with Caesarean section. The possible explanation for this difference is that vaginal route could traumatize and expose the neural tissue to bacteria normally present in the birth canal.[16] However; this association should be interpreted with caution as most of the CA cases are complicated with threatened maternal condition and still in premature gestation and mothers are needed to be delivered by CS.

Maternal age is an important parameter in the birth of a congenitally malformed fetus.[5] This study has statistically shown that mothers above 30 years of age stand at a higher risk of producing malformed babies. This finding was similar to the observations of Charan et al.[1] Also, Sagunabai et al[17] reported that mothers' age more than 35 years have a higher risk of giving birth to malformed babies. Grag and colleague also noted a high occurrence of congenital abnormality among women who are between 33 and 39 years of age.[22] However in the study of Francine et al [5] where this correlation was not evident and that of Datta et al[20] who documented statistically insignificant association of increased maternal age and congenital malformation.

Previous studies have reported significantly higher prevalence of malformation among the mothers of gravida 4 or more.[1,2,23] our results are consistent with that finding as most of cases are borne to multi-gravid mothers (86.3%). This indicates that as the birth order increases there is an increased risk of congenital malformations. Khanna and Prasad Mittal reported maximum number of malformations in third gravid mothers.[2] The result was incomparable to observations made by Taboo in her study, as the maximum number of congenital anomalies was seen in primigravida.[16]

The main prenatal and maternal risk factors among mothers of the studied babies are DM, drugs, HTN and oligohydramnios (37%, 31.5%, 11% and 9.6%) respectively. This is comparable to the findings of Ordonez et al who founded that diabetes mellitus, arterial hypertension and hypothyroidism show a positive association with congenital malformation.[24] While Deshpande et al[2] stated that toxemia of pregnancy, VDRL positivity, unstable lie and urinary tract infections were seen as some of the pre-natal factors in their study. The previous studies evaluated the factors that

significantly increase the risk of congenital malformations in newborn included the presence of hydramnios, diabetic mothers, eclampsia, previous abortions and history of malformed babies in previous child.[1]

In this study, the main neonatal complications among the studied babies are RDS, sepsis and TTN (37%, 6.8% and 5.5%) respectively. About (71.2%) of studied babies were survived, while only (28.8%) of them died with a statistical significant difference in CA subsequent neonatal deaths among premature babies, with malprentation who were borne by NVD. These findings are in agreement with that of Kurinczuk et al.[25]

CONCLUSION

In conclusion, the most common congenital anomalies in Misurata are cleft palate and lip, CHD, Syndromatic baby, undescended testis and hypospadius. Strong association of prematurity, CS, maternal age above 30 years and multi-gravid with increased risk of congenital malformation was noted in this study. DM, drugs, HTN and oligohydramnios are the main prenatal and maternal risk factors in our study. We thus recommend that all neonates should be thoroughly examined and screened for congenital anomalies. In addition, registry of CA is very important and the establishment of an ongoing surveillance system for CA is highly recommended.

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