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Epidemiological and clinical profile of congenital malformations in Benghazi Pediatric Hospital

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Highlights

- **This study was conducted in Benghazi pediatric hospital among patients with dysmorphic features who had multiple congenital malformations.**
- **Screening tools were X-ray, ultrasonography, ECHO, MRI and CT.**
- **Congenital malformation is a significant cause of morbidity and mortality among infants and children.**
- **The most common malformation was cardiac and the most common syndrome was Trisomy 21.**

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ABSTRACT

Objectives: The objectives were to assess the nature and the frequency of congenital malformations among infants and children who were admitted to Benghazi pediatric hospital and to study the associated maternal and neonatal risk factors.

Patients and methods: A cross-sectional study design was used for this study. It included infants and children aged (0-16 yrs.) who were admitted to Benghazi Children Hospital and who were following the genetic clinic, during the period of March 2016 to March 2017. These cases had dysmorphic features and multiple congenital malformations. A record sheet was used to collect the required data from cases.

Results: The total number of patients was 81 children, 51.85% were females, 48.15% were males and infants represented 62%. Cases with a history of consanguineous marriage represented 28.40%. Equal proportions of mothers (1.23%) had a history of diabetes, epilepsy and cardiomyopathy. Nearly a quarter of cases, (24.69%) were low birth weight. Prevalence of congenital malformations (CMs) according to organs were; CVS (50.62%), musculoskeletal (44.44%), eye (24.7%), limb defect (17.3%), GIT (14.8%), ear (14.8%), CNS (11.11%), urogenital (external & internal)(11%), cleft lip & palate (9.9%) and Trisomy 21 syndrome (48.1%). Trisomy 21 syndrome have a high frequency of CHD compared to other syndromes; 67.9% had CHD, P=.01. Most cases (90%) died within the first year of life, p=.002. Twenty-six percent of the studied population died during the study period.

Conclusion: Most children with CMs and chromosomal abnormalities died within the first year of life. There is a limitation of screening tools, which could lead to imprecise genetic counseling. CM is a significant cause of morbidity and admission. The highest prevalence of CMs was CVS. Trisomy 21 syndrome was the most prevalent chromosomal abnormalities; these cases were at more risk to have CHD compared to other syndromes. There is a shortage of medical services, which applied as segmental services.

1. Introduction

According to WHO, the term congenital malformations can be defined as structural or functional anomalies that occur during intrauterine life and can be identified prenatally, at birth, or sometimes may only be detected later in infancy, such as hearing defects (WHO, 2016). Congenital malformations may be minor or major. The minor malformation is defined as structural abnormality present at birth, which has minimal effect on clinical function but has a cosmetic effect e.g. preauricular tag. Major malformation has significant effects on function or social acceptability e.g. CHD, CNS anomalies (NTD, hydrocephalus), digestive anomalies (abdominal wall defect and diaphragmatic hernia), (American College of Medical Genetics, 2013). The pattern and prevalence of congenital malformations vary over time and geographical location. This could be related to different detection and recording methods. The true difference in frequency may be caused by a complex interaction of known and unknown genetic and environmental factors including sociocultural, racial variables (Singh *et al.*, 2009, Sekhobo, 2001). European Surveillance of Congenital Anomalies (EUROCAT, 2014) is a WHO collaborating center for the surveillance of congenital malformations. It is concerned with the detection of prevalence and risk factors of congenital malformations over the countries. Congenital malformations have been reported to be a major cause of mortality and morbidity in children (Singh, 2014). It also causes psychological trauma to their parents since it puts the entire life of children with congenital malformations into jeopardy. The economic effect on the parents especially mothers is significant in the family has a malformed child. A ray of hope has come in the form of

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prenatal diagnosis of congenital anomalies preconception counseling is the rule of the day (Gupta, 2012).

In Benghazi pediatric Hospital, we face many children with congenital malformation quite frequently. Therefore, we would like to dedicate a study to assess their defects and their health problems; we can say this study will be the first one concerning this category in the Hospital.

2. Patients and Methods

2.1 Samples

This was a cross-sectional study that included infants and children aged (0-16 years) with dysmorphic features and multiple congenital malformations). These cases were admitted to Children Hospital and were following the genetic clinic in Benghazi during the period of March 2016 to March 2017. Isolated congenital malformations were not involved in this study e.g.; isolated CHD, isolated CNS anomalies (hydrocephalus and NTD). The Benghazi pediatric Hospital has three hundred bed capacity. It is considered as a secondary referral hospital for cases coming from the eastern region of Libya. There are nine specialized clinics such as a genetic clinic.

2.2 Data collection

Face to face interviews with parents and caretakers of young infants were carried out to collect socio-demographic and clinical information such as maternal age, parity history of parent`s illness, paternal age, drug intake during pregnancy, exposure to X-ray, history of congenital malformation in the family, parental consanguinity, maternal exposure to pollutants, antenatal health caring, and birth weight. All young infants had to go through physical examination (general & systematic), to register dysmorphic features. Radiological examinations performed using; Echo, X-ray imaging, cranial and abdominal ultrasonography, CT & MRI. Patients with multiple congenital anomalies were grouped according to the specific anomalies of the syndrome. If they were qualified as a specific syndrome, they were then categorized into that syndrome. If no syndrome could be classified by those anomalies and more than two systems were involved, it was recorded as multiple congenital anomalies. Written approval from the administration office of the hospital was taken before starting the study. Also, the parent`s verbal consent was taken after explaining the aim and importance of the study.

2.3 Statistical analysis

All data are collected and checked for any missing and fed to PC, the analysis was done using SPSS program version 22 descriptive statistics and analytical statistics were applied when needed.

3. Results

Eighty-one patients were found eligible for this study. Their age ranged (one day to 16 years). Fig. 1 shows that 51/81(63%) of congenital anomaly cases were less than one year and 30/ 81 (37%) aged one year and more. There were 39/81(48.15%) males and 42/81(51.85%) females (Fig. 2). Patients who had a family history of CMs or syndromes in other family members were 17.28%. Nearly one-third (28.40%) of parents had consanguineous marriage (Table 1).

Equal number & proportions of mothers {one mother (1.23%) had a history of diabetes, epilepsy and cardiomyopathy) (Table 2). Concerning the birth weight of cases: 24.69% had low birth weight (<2.500kg) and 62.96% of patients had normal weight. Chart for normal children have been used in this study, 35.8% of patients had normal head circumferences, 64.2% had microcephaly (head circumference below 3rd centile) and no macrocephaly cases have been detected (Table 3).

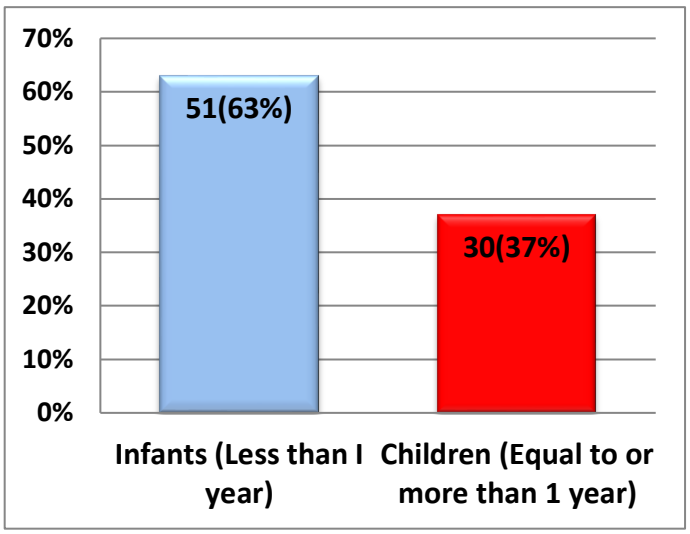

Fig. 1. Distribution of multiple congenital malformation patients according to the age.

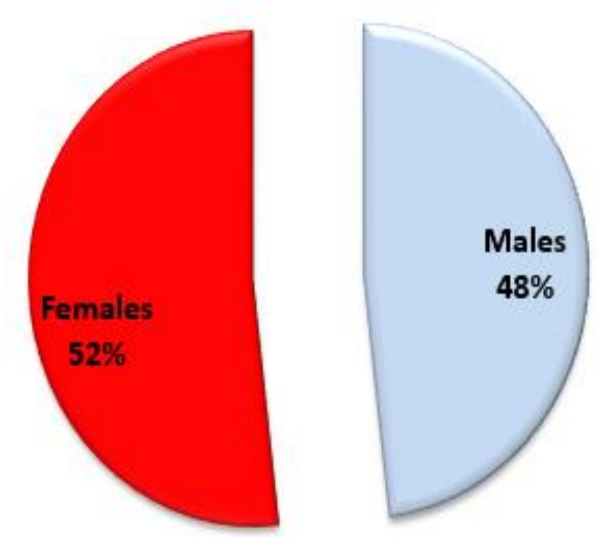

Fig. 2. Gender of multiple congenital malformation patients, Benghazi pediatric Hospital

Table1

History of consanguinity among parents of Congenital Anomaly cases– Benghazi pediatric Hospital

History of Consanguinity	№	%
Positive history of Consanguinity	23	28.4
No History of Consanguinity	58	71.6
Total	**18**	**100.0**

Table 2

Health status of Congenital Anomaly cases' Mothers during Pregnancy – Benghazi pediatric Hospital

Health status of mothers	№	%
Epileptic	1	1.2
Diabetic	1	1.2
Cardiomyopathy	1	1.2
No illnesses	78	96.3
Total	**81**	**100.0**

Table 3

Head Circumference of Congenital Anomaly Cases – Benghazi pediatric Hospital

Head Circumference of cases	№	%
Microcephaly	52	64.2
Normal Head Circumferences	29	35.8
Total	**81**	**100.0**

Brain imaging revealed that: 62/81(76.5%) of cases were normal, 4/81(5%) had partial or complete absence of corpus callosum. Equal proportions of cases (1.2%) had; Left Lip Schizenecephaly, Very Large Ventricles and Incomplete separation of the cerebral hemisphere, Dandy-Walker and Hydrocephaly (Table 4). USS abdomen showed that: 60/81 (74.1%) of cases had normal findings, 11(13.6%) their USS was not available, 2/81 (2.5%) had poor differentiation between cortex and medulla of the kidney. Equal proportions of cases (1.2%) had; diaphragmatic hernia, unilateral renal agenesis, left kidney hydronephrosis, horseshoe kidney and bilateral mild PCS dilatation (Table 5).

Table 4

Brain imaging of Congenital Anomaly Cases–Benghazi pediatric Hospital

Brain imaging of Congenital Anomaly Cases	№	%
Complete Absence of Corpus Callosum	2	2.5
Partial Absence of Corpus Callosum	2	2.5
Left Lip Schizenecephaly	1	1.2
Very Large Ventricles and Incomplete separation of cerebral hemisphere	1	1.2
Dandy-Walker and Hydrocephaly	1	1.2
Normal	62	76.5
Combined anomalies	12	14.8
Total	**81**	**100.0**

Table 5

Ultrasound Scan Abdomen of Congenital Anomaly Cases – Benghazi pediatric Hospital

USS Abdomen of Congenital Anomaly Cases	№	%
Normal	60	74.1
Not available	11	13.6
Poor Differentiation Between Cortex and Medulla of Kidney	2	2.5
Atrophic Kidney	1	1.2
Left Diaphragmatic Hernia	1	1.2
Horse Shoe Kidney	1	1.2
Mild Dilatation of PCS and Ureter Dilatation	1	1.2
Right and Left Small Kidney	1	1.2
Left Kidney Hydronephrosis	1	1.2
Unilateral renal agenesis	1	1.2
Bilateral Mild PCS Dilatation	1	1.2
Total	**81**	**100.0**

Most of the patients had ECHO screening 73/81 (90.1%), normal echo findings were prevalent among 28/81 (34.6%) of cases, CHD was found in 45/81. Equal proportions of patients (13.6%) had wither ASD or mixed CHD. Similarly, 9.9% of patients had atrial ventricular canal and a similar proportion of their ECHO was not available. Patients diagnosed to have ventricular septal defect represented 7.4% and Patent Ductus Arteriosus 4.9%. Equal proportions (1.2%) of patients had; dilated P A, TOF, Truncus Arteriosus, Left Pulmonary Artery Branch Stenosis and Dilated chamber (Table 6).

Table 6

ECHO screening of Congenital Anomaly Cases–Children Hospital Benghazi

ECHO screening of Congenital Anomaly Cases	№	%
Normal	28	34.6
Atrial Septal Defect	11	13.6
Mixed types of CHD	11	13.6
Atrial Ventricular Canal	8	9.9
Not available	8	9.9
Ventricular Septal Defect	6	7.4
Patent Ductus Arteriosus	4	4.9
Dilated P A	1	1.2
T O F	1	1.2
Truncus Arteriosus	1	1.2
Left Pulmonary Artery Branch Stenosis	1	1.2
Dilated Chamber	1	1.2
Total	**81**	**100.0**

The frequency of congenital anomalies was cardiac anomaly (50.62%), CNS anomaly 11.1%, musculoskeletal anomaly 44.44%, patients had limb defect (17.3%), internal urogenital anomalies (6.2%), external urogenital anomaly (4.9%), (24.7%) of patients had eye anomalies, Ear anomalies were observed in (14.8%) of patients, GIT anomalies 14.8%, cleft palate, lip or both 9.9%(Fig. 3).

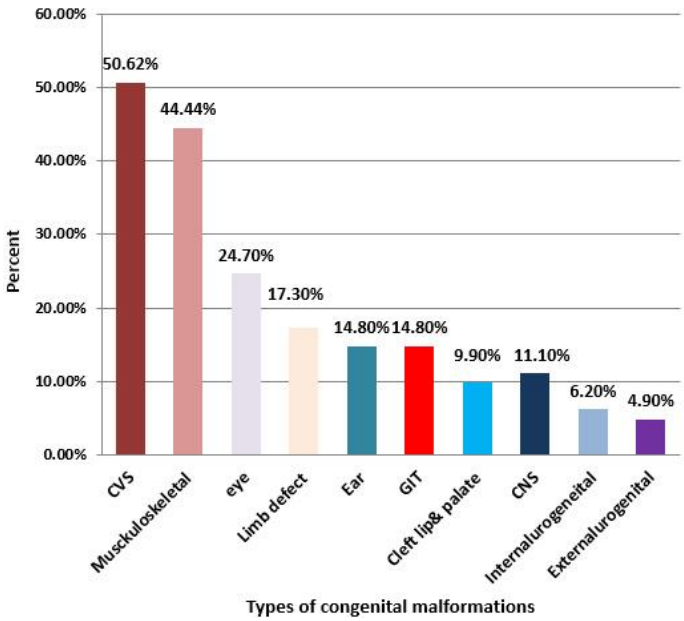

Fig. 3. Major congenital anomalies in the study cases- Benghazi pediatrics hospital.

Trisomy 21 syndrome was the highest prevalence nearly half of the cases (48%). Down syndrome has a higher prevalence of CHD in comparison to other syndrome P=0.01 (Table 7). About 1/4 of patients died during the study period (25.93%). Infants (<1 year) had a higher prevalence of death compared to older children, P=0.002 (Table 8).

Table 7

Cardiac Anomalies among Trisomy 21 compared to other syndromes– Benghazi pediatric Hospital

Type of anomaly	Cardiac Anomalies				Total		P.value
	Anomaly		No anomaly				
	№	%	№	%	№	%	
Trisomy 21	25	61.0	14	35.0	39	48.1	0.01
Other syndromes	16	39.0	26	65.0	42	51.9	
Total	41	100.0	40	100.0	81	100.0	

Table 8

Proportion of deaths among infants(<1yr) compared to other patients(>1yr)– Benghazi pediatric Hospital

Age category	Deaths				Total		P value
	Died		Alive				
	№	%	№	%	№	%	
Infants (< 1 year)	19	90.5	31	51.7	50	61.7	0.002
Children (> 1 year)	2	9.5	29	48.3	31	38.3	
Total	21	100.0	60	100.0	81	100.0	

4. Discussion

The total number of patients included in the present study was 81, they were examined and screened for multiple congenital malformations and dysmorphic features. The most important clinically relevant finding was the highest prevalence of death in the first year of life **P**=.002, the birth defect was the first leading cause of death in infants as mentioned in the literature review (WHO, 2015; March of Dimes, 2017). According to WHO, more than 8 million babies worldwide are born each year with a serious birth defect. Birth defects are the leading cause of death in the first year of life, and babies who survive may be physically or mentally disabled, taking a costly toll on their families, communities, and nation. The eldest patient in this study was 16 years old; they were diagnosed in early childhood but still are following a pediatrics Hospital.

The current study found that 51.85% were females and 48.15% were males, the ratio was nearly 1:1 no significant difference between both genders. Mohammed *et al.* (2011) had noticed a higher male to female ratio (1:1.7) compared to the present study. Family history of a syndrome or CMs was positive in 17.28%, this finding is in agreement with Shawky *et al.* (2011), and family history of CMs was reported to occur in 16.69%". About one-third of the parents of our study population had a consanguineous marriage (28.4%). Consanguinity is an important factor, which was found to increase the risk of CMs in a study conducted by Francine *et al.* (2014). Previous studies by Fida *et al.* (2007) have demonstrated that the incidence of congenital anomalies in consanguineous parents were higher in Saudi compared to non-Saudi, this is probably related to the high rate of consanguineous marriages in Saudi Arabia. Also, mothers' health before and during pregnancies were considered in this study, 96.30% were healthy with no chronic illnesses, 1.23% were diabetic mothers this low prevalence could be due to the small size of a sample. Many studies support those diabetic mothers have a higher prevalence of getting children with CMs as in the study conducted by Gupta *et al* (2012) 28.5% of the diabetic mothers had anomalous babies. Another study conducted by Agha *et al.* (2016) the adjusted birth prevalence of congenital abnormalities was 1.6 times higher among mothers with pre-gestational diabetes than those without. The prevalence of epileptic mothers in our study was 1.23%, in a study conducted by Razaz *et al.* (2017) confirmed the relation between maternal epilepsy and higher risks of preterm birth, SGA live birth, low Apgar score, and major malformation. In our study birth weight was low (<2.500 kg) in 24.69%, it can thus be suggested that low birth is associated with CMs, higher prevalence of low birth weight in patients with CMs in study conducted by Hussain *et al.* (2014) which observed the association of LBW with increased incidence of anomalies. Microcephaly (head circumference <3rd) was 64.20%, the chart for normal children has been used not a specific chart, plus Trisomy 21 syndrome cases were the predominant in this study. The screening tools which was available in Benghazi pediatrics Hospital are USS, MRI, ECHO, X-ray which done in postnatal period, chromosomal analysis is not available in our Hospital, so the family worriment of recurrence will not be mitigated, by the available tools anatomical defect of internal organs detected, demonstrate kidney anomalies in our population in this study were poor differentiation between cortex and medulla of kidney 2.5%, PCS dilatation 2.5%, hydronephrosis 1.2%, horseshoe kidney 1.2%, unilateral renal agenesis 1.2% and 60/81 (74.1) was normal kidney in comparing to study conducted by Bondagji (2014) showed that the most common abnormalities detected were hydronephrosis, polycystic kidney disease, multicystic dysplastic kidney, and renal agenesis, in descending order of frequency The importance of this study is to determine the type and prevalence of congenital malformation. Prevalence studies of congenital anomalies are useful to establish baseline rates, to document changes over time, and to identify clues to etiology. They are also important for planning and evaluating antenatal screening for congenital anomalies, particularly in high-risk populations, the current study found that cardiovascular system anomaly has the highest prevalence (50.62%), (67.9%) of Down syndrome in this study had CHD compared to study conducted by Colvin *et al* (2017). Trisomy 21 syndrome is associated with high incidence (45–50%) of CHD, in our study we have compared the prevalence of CHD in Trisomy 21 syndrome and other syndromes, the result is Down syndrome at more risk for CHD in comparing to other syndromes (P=0.01). In this study cardiovascular anomaly is followed in descending order by musculoskeletal anomaly (44.44%), eye anomaly (24.7%), limb defect (17.3%), GIT anomaly (14.8%), ear anomaly (14.8%), CNS anomaly (11.11%), urogenital anomaly (external& internal) (11%), and cleft lip & palate (9.9%). In comparison to other studies and surveillance, a study conducted by Dastgiri *et al.* (2002) showed the categories of defects with the highest prevalence were congenital heart disease, anomalies of limbs, and digestive system anomalies. EUROCAT registries from 2011-2015 highest anomalies were CVS, followed by urinary system, CNS, digestive system and cleft lip& palate and eye anomalies. In Saudi Arabia, a study conducted by Fida *et al.* (2007) showed the most observed congenital anomalies were CVS, followed by musculoskeletal/limb, external genitalia, urinary system, chromosomal, orofacial, CNS, skin, eyes. In Egypt study conducted by Mohammed *et al.* (2011) demonstrated that the skeletal system anomalies had the highest frequency, followed in descending order by chromosomal abnormalities, circulatory system anomalies, central nervous

system (CNS) anomalies, genital organs anomalies, gastrointestinal tract (GIT) anomalies, eye and ear anomalies, and lastly urinary system and others anomalies. In this study, Trisomy 21 syndrome was the most common syndrome (48.1%), followed by Patau and Edward (6.2%), confirmed that these syndrome diagnosed only by dysmorphic features, this prevalence is supported by a previous study (Pierce *et al*., 2017). They showed that Trisomy 21 is the most common autosomal aneuploidy with a national birth prevalence of 14.57 per 10,000 or 1 in 691 live births, Edward syndrome is the second most common multiple malformation syndromes 0.3 per 1000, while Patau syndrome 1 in 5000 (Jones *et al.*, 2013). The prognosis of study population as ending by death provides some support for the conceptual premise that the birth defect is an important cause of death in pediatrics, as mentioned in the literature review, in current study 25.93% died during the study periods, the highest prevalence of death happened in the first year of life (90.5%) (P=.002). Medical services that are applied to these patients in Benghazi Children Hospital are segmental services, as admission and following for their current health problems. Genetic clinics apply to counsel for postnatal screening and referring to subspecialty e.g. audiometry, phonetics, visual assessment, and behavioral therapy.

When the child is disabled and may not be a productive individual in the future, this will have a great impact on the parent's time and money, in addition to that, the economic cost would be overwhelming on the health services and society. The study of Stabile *et al.* (2012) assessed the economic cost of childhood disability. In this study, it was shown that the direct costs to families, indirect costs through reduced family labor supply, direct costs to disabled children as they age into the labor force, and the costs of safety net programs for children with disabilities average $30,500 a year per family with a disabled child. They note that the cost estimates on which they base their calculation vary widely depending on the methodology, jurisdiction, and data used. Because their calculations do not include all costs, notably medical costs covered through health insurance, they represent a lower bound.

5. Conclusion

Most of the children with CMs and chromosomal abnormalities died within the first year of life. There is a limitation of screening tools, which make genetic counseling imprecise. CMs is a significant cause of morbidity and admission, the prevalent health problem was a respiratory system so passive prophylaxis should be considered, then followed by cardiac system, digestive system, musculoskeletal problems, CNS, others, hematology problems, endocrine problems, renal and behavioral abnormalities. Prevalence of CM in descending order the highest was CVS, musculoskeletal, Eyes, limb defects, GIT, Ear, CNS, urogenital and cleft lip& palate. Down syndrome is the most chromosomal abnormalities; Down syndrome at more risk has CHD in comparison to other syndromes. There is a shortage of medical services, which applied as segmental services.

Recommendation

- *Originate a center for congenital malformation.*
- *Further study to detect the risk factors.*
- *Further study to assist the prevalence and incidence of CMs among children.*
- *If I have another chance and facility, I would like to assess the risk factor and the causes of CMs.*
- *Develop advanced genetic counselling e.g. karyotype.*

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