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Original Article

Associated Cardiac Anomalies Detected by Echocardiography in Infants and Children with Congenital Malformations. A Prospective-Analytical Study

Alaa Mamdouh Abdelfatah*[1], Mostafa Abdelazim Hassan[2], Ahmed Hagag Ismail[2]
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***Correspondence:** Pediatric department, Minia insurance hospital & faculty of Medicine, Al-Azhar University, Egypt
Email: alaaabdelfattah2@gmail.com
Full list of author information is available at the end of the article.

Abstract

Background: Infants with congenital malformations are more common to have cardiac malformations.

Aim: To detect the frequency of associated congenital heart diseases and other congenital malformation of different systems.

Subjects and methods: sixty patients who were admitted at pediatric and neonatology department at Minia health insurance hospital & Al-Azhar University- Assuit hospital aging from 1 day to 48 months (4 years) old will be included in the study between first of January 2022 and the end of November 2022.

Results: A total number of 60 patients with known congenital malformations, 10 patients with Genitourinary congenital malformations (16.6%), 9 patients with renal malformations (15%), 8 patients with digestive malformations (13.3%) , 9 patients with biliary atresia (15%), 10 patients with genetic malformations (16.6%), 14 facial congenital malformations (23.3 %). The echocardiography showed in seventy patients mild ASD (28.3%) while 5 patients showed moderate ASD (8.3%), 5 patients showed mild TR (8.3%), 17 patients showed PDA (28.3%), 6 patients showed PFO (10%), 2 patients showed mild MR (represent 3.3%), 18 patients showed VSD (represent 30%) . 29 patients showed normal PASP (48.3%), 4 patients had severe PASP (6.7%), 10 patients with moderate PASP (16.7%), 17 patients with mild PASP (28.3 %) with mean 40.3±13.

Conclusions: Regarding the correlation between cardiac anomalies and other congenital malformations, there were significant correlation between cardiac anomalies and renal system, biliary system, genetic abnormalities and facial malformations, so more attention and careful cardiac examination using echocardiography in those patients is advised.

Key words: Cardiac; malformations; congenital anomalies; echocardiography

Introduction

Congenital malformations are the leading cause of infant mortality in developed countries, with critical congenital heart disease being the major contributor to death and morbidity despite the development of specialized pediatric cardiac centers. Congenital heart disease (CHD) is defined as congenital heart disease requiring surgery or catheter intervention in the first year of life and constitutes ~25% of CHD. Although CHD is the most common form of congenital malformation and occurs in 9 of every 1,000 live births, it is not always identified early and referred to a pediatric cardiologist. There is, therefore, a need for all cardiac sonographers, regardless of their pediatric experience, to be able to detect CHD and recognize those cases that are critical in nature [1].

A maternal history of medication, drug, or alcohol use or excessive smoking may contribute to cardiac and other systemic findings. The prenatal history may reveal a maternal infection early in pregnancy (possibly teratogenic) or later in pregnancy (causing myocarditis or myocardial dysfunction in infants) [2].

Congenital cardiac anomalies may co-exist with non-cardiac congenital anomalies and, for those requiring surgical correction, there can be an anesthetic risk. Records of children aged between 1day and 10 years undergoing corrective surgery for non-cardiac congenital malformations were examined and results of clinical cardiac examinations and surgical and echo findings were analyzed [3].

Patients requiring non-cardiac surgery with suspected or symptomatic structural cardiac anomalies may have peri-operative risk. A pre-anaesthetic echo is requested for most non-cardiac surgeries to identify possible cardiac structural anomalies [4].

The use of medications in pregnancy is almost inevitable, especially for underlying physiological disorders of the

mother and the physiological changes that are brought about in gestation. More than 85% of pregnant women take medications during pregnancy [5]. Amongst all these medications, the ones commonly used in pregnancy are antidepressants, antihypertensive, anesthetic, analgesic, medications for heartburn, antiemetic, anti-diabetic, antibiotics and statin drugs [6].

The administration of a drug in a pregnant woman is challenging owing to the pharmacokinetic changes that occur with pregnancy and the risk of harm to the developing fetus [7]. The need for medication cannot be completely ruled out since certain medical conditions (e.g., elevated blood pressure, asthma) can exacerbate the mother's health and consequently harm the fetus. On the other hand, some drugs can pose substantial risk to the fetus for their ability to cross the placental barrier and the fetal blood brain barrier. This is a matter of concern since most drugs cross the placenta and reaches the fetal systemic circulation. Moreover, more than 10% of the congenital anomalies occur due to the maternal exposure to drugs during pregnancy [8]. An appropriate volume of amniotic fluid is one of the most important components of a healthy pregnancy, as it acts as a protective cushion for the fetus, prevents compression of the umbilical cord, and promotes fetal lung development. While the average volume of amniotic fluid varies with gestational age, abnormally low amniotic fluid volume has been associated with adverse pregnancy outcomes. Oligohydramnios, in which the volume of amniotic fluid is abnormally low (< 500 ml) between the 32nd and 36th weeks of pregnancy, is a serious condition for the fetus and the mother. Oligohydramnios can be diagnosed with ultrasound performed during the late second trimester or the third trimester and is defined by an Amniotic Fluid Index (AFI) below 5 cms or below the 5th percentile to

approximate the amniotic fluid volume [9].

There is a well-described association between maternal diabetes mellitus and risk of congenital heart disease (CHD) in offspring. Although the clinical diagnoses of type 2 diabetes or gestational diabetes are strong risk factors for CHD, subclinical abnormalities of glucose and insulin metabolism are common within the general population and could also confer risk for CHD as tetralogy of Fallot (TOF) and dextro-transposition of the great arteries (dTGA)[10].

Aim of the Work: To detect the frequency of associated congenital heart diseases and other congenital malformation of different systems.

Methods

This study included a considerable number of patients (60 patients) who were admitted in pediatric and neonatology department at Minia health insurance hospital & Al Azhar university of Assuit hospital aging from 1 day to 4 years old. The studied groups were subjected to: Complete history taking including the cause of patient admission and physical examination. Laboratory investigations: CBC, Electrolytes, Renal Functions, Liver Functions Karyotyping for selected cases. Radiology included echocardiography, x-ray and ultrasound.

Echocardiography: Examination was performed by a pediatric cardiologist having experience in echocardiography. The examination was consisted of M-mode, 2-D, pulsed, continuous wave and color Doppler blood flow velocity measurements of the heart valves. Echocardiographic assessment was to document presence of cardiac malformations as patent foramen oval (PFO) and/or patent ductus arteriosus (PDA),Ventricular septal defect (VSD), Atrial Septal defect (ASD) , Atrio-ventricular Septal defect (AVSD) and fallot's tetralogy as well as to detect other congenital heart diseases, to evaluate chamber enlargement and

pulmonary artery dilation and to evaluate ventricular function as well.

Inclusion characteristics: All age groups (60 cases) from 1day to 4 years admitted at Minia Health Insurance hospital & Al-Azhar University Assuit hospital with both sex male & females equally included.

Exclusion criteria: All normal children are excluded.

Ethical considerations

This study was carried out after being approved by the local ethics committee of the faculty of Medicine, Al-Azhar university, Assuit, Egypt and written informed consents were obtained from the parents and they informed about the nature and steps of the study and privacy of collected data were assured.

Statistical analysis

Data were checked, entered and analyzed using SPSS version 23 for data processing. The following statistical methods were used for analysis of results of the present study. Data were expressed as number and percentage for qualitative variables and mean + standard deviation (SD) for quantitative one. Comparing groups was done using: *Chi square-test (X^2):* for comparison of qualitative data. *Student's "t"- test* for comparison of quantitative data of 2 independent samples.

Results

Our data demonstrated according to the following tables: Table 1: A total of 60 patients (age ranges between 3 days - 120 months; mean age, 22.2 ± 27.9). All patients were identified as 41 males (represent 68.3%) and 19 females (represent 31.7 %), 50 patients out of 60 received antenatal care (83.3%), 49 patients were admitted to NICU (81.7%) and 15 patients (25%) had positive family history.

Table 2 and figure 1: A total number of 60 patients with known congenital malformations, 10 patients with Genitourinary congenital malformations (represent 16.6%) ,9 patients with renal congenital malformations (represent 15%), 8 patients with digestive

congenital malformations(represent 13.3%), 9 patients with biliary congenital malformations (represent 15%), 10 patients with genetic malformations (represent 16.6%), 14 facial congenital malformations (represent 23.3 %).

Table 3: Echocardiography revealed for 60 patients were done, 17 patients showed mild ASD (represent 28.3%) while 5 patients showed moderate ASD (represent 8.3%).5 patients showed mild TR (represent 8.3%). 17 patients showed PDA (represent 28.3%), 6 patients showed PFO (represent 10%), 2 patients showed mild MR (represent 3.3%), 18 patients showed VSD (represent 30%) . 29 patients showed normal PASP (represent 48.3%), 4 patients had severe PASP (represent 6.7%), 10 patients with moderate PASP (represent 16.7%) , 17 patients with mild PASP (represent 28.3 %) with mean 40.3±13. EF for 60 patients were done, showed range of (51-78) and mean 63.4± 6.7. Table 4 and figure (2) showed the relation between cardiac affection and other congenital malformations.

Discussion

Several studies have been conducted to show the relation between cardiac and non-cardiac malformations based on associated echo findings in children with congenital malformations.

The number of patients in this study is 60 patients, 41 were males and 19 were females which are less than that in the study done by Ekure et al., with total number of 101 children with congenital malformations that had echocardiography studies done as part of their clinical evaluation [11].

In our study, the age of patients range from 3 days to 10 years old with mean 22.2±27.9, this range is similar to the study done by Ludorf et al., in which the range of age is from 1 day to above five years [12].

Congenital heart defects accounted for more than half of the most frequent defects co-occurring with hypospadias, ASD (390 [18.7%] of 2084 cases of non-

isolated hypospadias) and VSD (290 [13.9%] of 2084 cases of non-isolated hypospadias) while according to our study to the genitourinary system 2 cases of hypospadias were detected out of 10 patients and echo revealed ASD associated with VSD in one case while the other showed ASD only [12, 13].

Regarding undescended testis as a part of genitourinary malformations 252 patients at the time of presentation with age ranged from neonate to 12 years. There were 28 % with bilateral undescended testes while unilateral ones accounted for 72 %. The incidence of left undescended testes (38%) was roughly equal to that of the right (35 %).

Fifty-one (20%) patients were found to have at least one associated anomaly, 7 patients showed cardiovascular anomalies: VSD (2 cases), VSD and overriding aorta (1 case), Pulmonary stenosis (3 cases) and dextrocardia (1 case). According to this study 7 patients with undescended testis out of 10 patients with genitourinary malformations, 2 patients with bilateral undescended testis (28.5%), 5 patients with unilateral undescended testis (71.5%) which is compatible with the above study. 3 patients with unilateral Right undescended testis (42.8%) and 2 patients with unilateral left undescended testis (28.5%) 2 patients out of 7 (showing VSD as an isolated cardiac anomaly) & 1 patient showing VSD with PDA [14].

Resuming our study, A case of 2-days old infant with ambiguous genitalia was detected, chromosomal analysis revealed (46 XX) and echo revealed NAD, which is unlike the case report done by Shaffer et al., [14] that showed a 1-day old infant that had symptoms of CHD. Echocardiographic examinations revealed a ventricular septal defect (VSD) along with atrial septal defect (ASD) as CHD while chromosomal analysis revealed the normal female complement = 46 (44, XX).

A study for Orün UA et al., [15] showed that 242 patients with gastrointestinal

system malformations were included in the study. Of 242 patients, 135 (55.8%) were male and 107 (44.2%) were female, and their age range was 0-15 years. The most frequent GISM were ano-rectal malformations (43.2%), atresia involving stomach, ileum or colon (21%) and esophageal atresia/trachea-esophageal fistula (18.3%). Congenital heart defects were observed in 28.5% of the participants. The most frequent defects were as follows; ASD (31 patients, 44.9%), VSD (17 patients, 24.6%) and PDA (5 patients, 7.2%) [16].

According to our study 8 patients were included among GIT malformations, 4 males (50 %) and 4 females (50%) with age from 3 days to 10 years. The most frequent GISM were tracheo-esophageal fistulas (50 %), ano-rectal malformations (25 %) and Hirschsprung disease (25%). Congenital heart defects were observed in 75% of patients. The most frequent were VSD (5 patients 62.5 %), ASD (4 patients, 50 %) and PDA (3 patients 37.5%).

A total of fifty-two publications reported data on infants with Hirschsprung disease associated with CHD.

Septation defects were recorded in 57% (atrial septal defects in 29%, ventricular septal defects in 32%), a patent ductus arteriosus in 39%, vascular abnormalities in 16%, valvular heart defects in 4% and Tetralogy of Fallot in 7%, while in our study 2 patients out of 8 patients with GIT malformations showed Hirschsprung disease (25%) showing ASD in the 2 detected a case which is compatible with the above study with these results in accordance with other studies[17,18].

Guttman et al., [17] made a study including 328 patients with biliary atresia, 44 (13%) had associated cardiac congenital abnormalities, VSD (10 patients represent 38.4 %), ASD (7 patients represent 26.9%), PS (11 patients represent 42%).

According to our study there a significant relationship between biliary affection and cardiac affection as 9 patients were included , 7 patients out of 9 showed

cardiac anomalies (87.5%) , ASD was the most common (6 patients represent 85.7%) and VSD (1 patient 14.2%) which is against the above study as ASD is more common.

Down syndrome co-occurs with other birth defects and medical problems, most commonly structural heart and digestive abnormalities and more rarely musculoskeletal, urinary, or respiratory anomalies [19].

According to this study among the cases with genetic abnormalities (10 cases out of 60 represent 16 %), 9 patients were karyotyped as down syndrome (represent 90%) 5 females (represent 50%) and 4 males (represent 40%) and 1 male case was Cornelia de Lange syndrome (represent 10%) with age ranges from 3 days to 48 months. The number of cases included in our study is less than that in the study done by Vida VL et al., as 349 patients were reviewed, 189 (54.1 %) also had an associated congenital cardiac malformation, with a range from 2 to 13 months [19].

In a study [19] included 152 patients with Down syndrome (80.4 %) the cardiac lesion was isolated while 37 patients (19.6 %) had multiple defects .The most common single defect was PDA (28.6 %), followed by VSD (27.5%), ASD in (12.7%) and AVSD defect (9.5%).The most frequent concomitant malformation found co-existing with other congenital cardiac lesions was PDA found in 17.5% the results in agreement with other reports [20].

In this study karyotyping - for selected cases- was done, 8 patients were karyotyped as trisomy 21 and only one case was karyotyped as mosaic type.

2 patients out of 9 patients with Down syndrome (22.2%) the cardiac lesion was isolated while in 77.7% multiple defects were found. The most common single defect was PDA (22.2%) and no other single lesions were detected. The most frequent concomitant malformation found co-existing with other cardiac lesions was PDA (4 patients out of 9 which represent 44.4%) which is

concomitant with the above study followed by AVSD (3 patients out of 9 represent 33.3%) and Tetralogy of Fallot (1 patient out of 9 represents 11.1%). Consequently, there is a significant relationship between genetic malformations and cardiac malformations.

According to Akash et al., [19] study, Out of 200 patients of cleft lip and palate, 30 patients (15%) were associated with congenital cardiac anomalies with male to female ratio of 1:1. Associated congenital cardiac anomalies were most frequently seen in unilateral cleft palate patients (21.05%) The most common cardiac anomaly was VSD (36.6%).

While according to our study out of 14 patients with cleft lip and palate anomalies, 13 patients (92.9%) were associated with congenital cardiac anomalies with male to female ratio 1.4:1 which means a significant relationship between cardiac affection and facial anomalies which is against the mentioned study. Associated anomalies were most seen in unilateral cleft palate patients who are compatible with the above study but unlike the above study the most common cardiac anomaly was ASD (21.4%) followed by PDA (14.3%).

The results of this study are in agreement with another study included thirty cases of congenital solitary functioning kidneys seen at the pediatric renal service at the Jordan University Hospital [21]. There were 20 males and 10 females, whose ages ranged from 5 days to 14 years. In 20 patients (67%), the left kidney was absent. Associated anomalies were detected in 23 (77%) of the 30 patients; cardiovascular anomalies were present in 4/30 (13%), while in our study 9 patients with solitary kidneys were detected, 7 males and 2 female whose age ranged from 3 days to 7 years.

In 5 cases the left kidney was absent (55.5%), 3 cases with Right absent kidney (33.3%) and 1 case with congenital absence of both kidneys (Potter syndrome) (11.1%). Cardiovascular anomalies were detected

in 8 patients out of 9 (88.9 %) with PDA common cardiac anomaly (33.3%) followed by VSD (22.2%) and consequently there is a significant relationship between cardiac and renal anomalies which is against the above mentioned study. The results are in agreement with others [22,23].

Conclusions

Regarding the correlation between cardiac anomalies and other congenital malformations, there were significant correlation between cardiac anomalies and renal system, biliary system, genetic abnormalities and facial malformations, so more attention and careful cardiac examination using echocardiography in those patients is advised. However there is no significant correlation between cardiac anomalies and digestive or genital tract anomalies. Further studies with larger sample size are needed to confirm the current results

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Author's contributions

All authors contributed equally in this work and approved the manuscript for publication

Conflict of interest

The authors have no conflict of interests to declare.

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Author's details

[1]Pediatric department, Minia insurance hospital & faculty of Medicine, Al-Azhar university, Egypt

[2]Pediatric department, faculty of Medicine, Al-Azhar university, Assuit, Egypt.

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Table 1: Demographic data and clinical characteristics of studied patients with congenital malformations:

Item		**Descriptive statistics (N=60)**
Age (Months)	Range	(0.1- 48)
	Mean ± SD	12.2±17.9
	Median/(IQR)	9.5/(2-35.8)
Sex	Male	41(68.3%)
	Female	19(31.7%)
Residence	Rural	27(45%)
	Urban	33(55%)
Family history	-Ve	45(75%)
	+Ve	15(25%)
Antenatal care	No	10(16.7%)
	Yes	50(83.3%)
NICU admission	No	11(18.3%)
	Yes	49(81.7%)
Mode of delivery	SVD	45(75%)
	CS	15(25%)
Antenatal care	No	10(16.7%)
	Yes	50(83.3%)

Table 2: Types of congenital anomalies of studied patients

Item	Descriptive statistics (N=60)
Genitourinary malformations	10(16.7%)
• Hypospadias	2(20%)
• Undescended testis	7(70%)
• Ambiguous genitalia	1(10%)
Renal system	9(15%)
• Absent one kidney (Lt or Rt)	8(88.8%)
• Potter syndrome	1(11.1%)
Digestive system	8(13.3%)
• Tracheo-esophageal fistula	4(50%)
• Ano-rectal malformations	2(25%)
• Hirschsprung disease	2(25%)
Biliary system • Biliary atresia	9(15%)
Genetic	10(16.7%)
• Down syndrome	9(90%)
• Cornelia de Lange syndrome	1(10%)
Facial • Cleft lip and palate (unilateral&bilateral)	14(23.3%)

Table 3: Echocardiographic examination of all patients

Item		**Descriptive statistics (N=60)**
ASD	No	38(63.3%)
	Mild	17(28.3%)
	Moderate	5(8.3%)
	Severe	0(0%)
TR	No	55(91.7%)
	Mild	5(8.3%)
	Moderate	0(0%)
	Severe	0(0%)
PDA	No	43(71.7%)
	Yes	17(28.3%)
PFO	No	54(90%)
	Yes	6(10%)
MR	No	58(96.7%)
	Mild	2(3.3%)
	Moderate	0(0%)
	Severe	0(0%)
VSD	No	42(70%)
	Yes	18(30%)
PASP	Range	(22-85)
	Mean ± SD	40.3±13
	Median/(IQR)	36.5/(32-45)
PASP.cat	Normal	29(48.3%)
	Mild	17(28.3%)
	Moderate	10(16.7%)
	Severe	4(6.7%)
Cardiac anomalies	No	11(18.3%)
	Yes	49(81.7%)

ASD: Atrial Septal defect; TR: Tricuspid regurge; PDA: patent ductus arteriosus; PFO: patent foramen oval; MR: Mitral regurge; VSD: Ventricular septal defect; PASP: Pulmonary arterial pressure

Table 4: Relation between cardiac affection and other congenital malformations

Item	Cardiac affection		P value
	No	Yes	
Genitourinary	5(50%)	5(50%)	0.752
Renal system	1(11.1%)	8(88.9%)	0.046*
Digestive system	2(25%)	6(75%)	0.289
Biliary system	1(11.1%)	8(88.9%)	0.046*
Genetic	1(10%)	9(90%)	0.027*
Facial	1(7.1%)	13(92.9%)	0.003*

Chi square test

*: Significant level at P value < 0.05

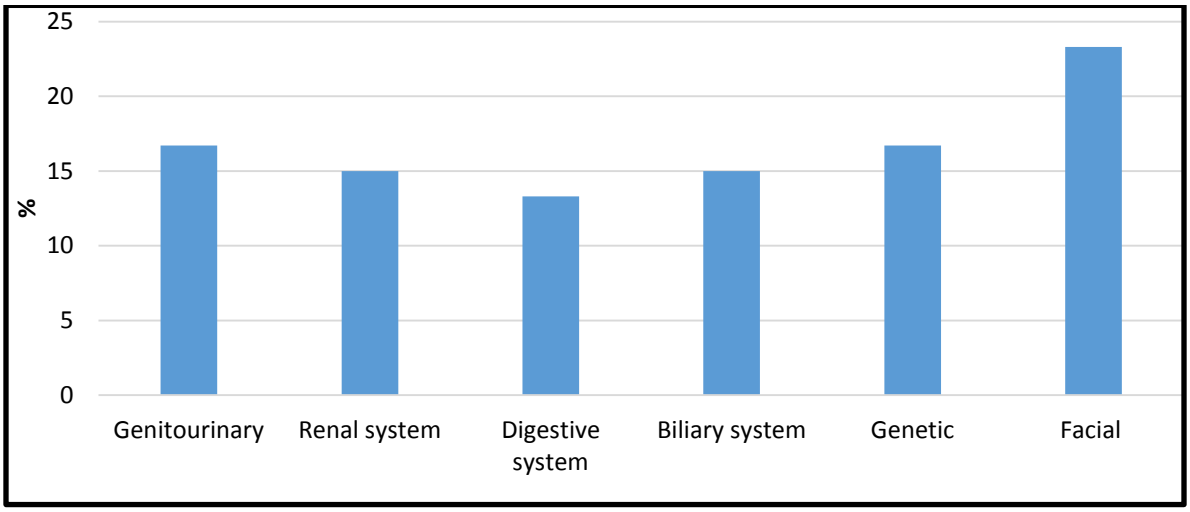

Figure (1): Percentage of cardiac anomalies in different congenital malformations of different systems

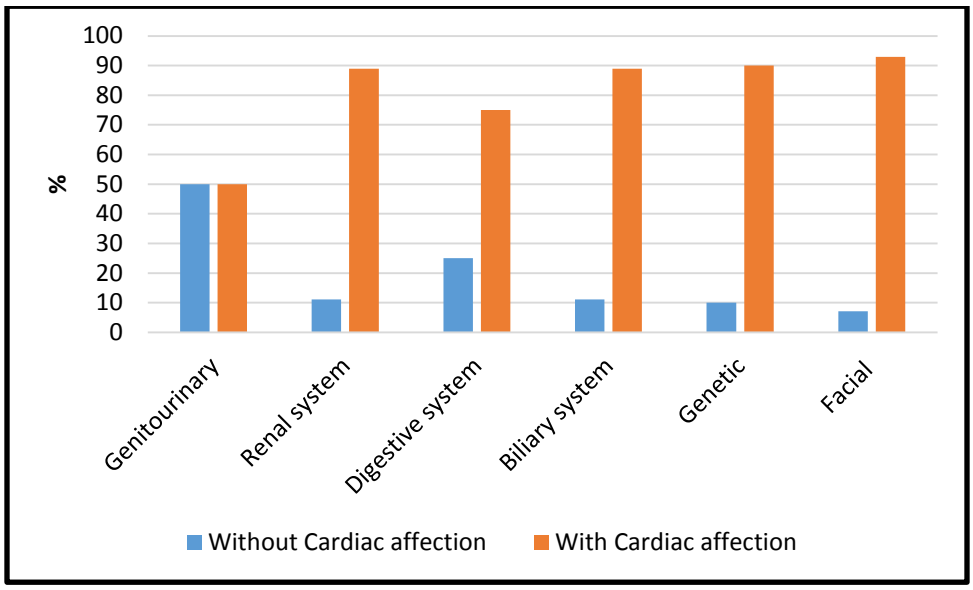

Figure (2): Relation between cardiac affection and other congenital malformations

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