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Measurement of Serum Lipid Level in Children with Congenital Heart Diseases

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ABSTRACT

Background: The lipid profile is an important and independent predictor of coronary heart disease is. This process relates to cholesterol concentration, accumulation and deposition of lipids on the arterial wall.

Objective: The aim of this study was the measurement of serum lipid profile (cholesterol, triglycerides, high-density lipoprotein (HDL) and low-density lipoprotein (LDL) in children with congenital heart diseases and to compare the results with those of healthy children. **Patients and methods:** This case-control study was carried out from July 2020 to December 2020 in Cardiology Unit of Pediatric Department Outpatient Clinic, Zagazig University Hospital on 44 children. Patients were divided into: Group (I): (Case group) included 22 children with congenital heart diseases, and Group (II) (control group) included 22 healthy children. All patients were subjected to dimensional transthoracic echocardiography with color flow Doppler (Vivid 7 dimension apparatus) and Laboratory investigations (total cholesterol, triglycerides, low-density lipoprotein (LDL), high-density lipoprotein (HDL). **Results:** The most frequent cardiac defect was ASD (22.7%) followed by VSD (13.6%), common A-V canal (9.1%), mitral regurgitation (9.1%), pulmonary regurgitation (9.1%), and PDA (9.1%). 18.2% of the studied patients had cyanotic congenital heart disease (CHD) and 81.8% had non-cyanotic CHD. There was statistically significant differences between the studied groups in lipid profile as case group had higher cholesterol, triglyceride, LDL and lower HDL than control group. **Conclusion:** We concluded in this study that patients had significantly higher serum lipid levels than age and sex-matched controls in light of these findings.

Keywords: Congenital Heart disease, Lipids, Dyslipidemia.

INTRODUCTION

Congenital heart diseases (CHD) are structural problems that arise from abnormal formation of the heart or major blood vessels. It is the commonest of all congenital lesions and is the most common type of heart diseases among children [(1)]. The global incidence rate of CHD is 6.8 to 9.0 per 1000 live births. Its most common subtypes are atrial septal defect, ventricular septal defect, patent ductus arteriosus, pulmonary stenosis, and tetralogy of Fallot. Depending on the presence of a right to left shunt, congenital heart disease patients can be divided into two groups; acyanotic and cyanotic [(2)].

Dyslipidemia is an important etiological factor in the development of cardiovascular disease (CVD), which is a leading cause of death worldwide as CVD begins in childhood [(3)]. An important and independent predictor of coronary heart disease is the lipid profile. This process relates to cholesterol concentration, accumulation and deposition of lipids on the arterial wall. The most important consequences of dyslipidemia are atherosclerosis and coronary artery disease due to the occlusion of the coronary arteries, ischemic heart disease (IHD) and myocardial infarction (MI). Many factors such as overweight, hypertension (HTN), diabetes mellitus (DM), smoking and low physical activity lead to increased serum lipid levels and consequently atherosclerosis [(4)].With advances in pediatric cardiology, early physical examination and diagnosis, medical treatment, surgical methods, and postoperative care made the prevalence of CHD in adults has risen in relation to children, and the number of adults living with CHD is expected to continue its upsurge. It is presumed that there are more adults with CHD living than there are children with CHD. Accordingly, control of lipid levels and other risk factors has gained considerable significance [(5)]. So it is suggested to screen and treat dyslipidemia to prevent atherosclerosis since childhood and is important to evaluate prevalence of dyslipidemia in children with congenital heart disease [(4)]. The aim of this study was the measurement of serum lipid profile (cholesterol, triglycerides, high-density lipoprotein (HDL) and low-density lipoprotein (LDL) in children with congenital heart diseases and to compare the results with those of healthy children.

PATIENTS AND METHODS

This case-control study was carried out from July 2020 to December 2020 in Cardiology Unit of Pediatric Department Outpatient Clinic, Zagazig University Hospital on 44 children. Their ages ranged from 2 to 10 years old. The study groups were divided into: Group (I): (Case group): Which include 22 children (11 males and 11 females) with congenital heart diseases, and Group (II): (control group): Which include 22 healthy children (11 males and 11 females).

Ethical approval:

Written informed consent was obtained from all participants' parents and the study was approved by the Research Ethical Committee, Faculty of Medicine, Zagazig University. The work hasd been carried out in accordance with The Code of Ethics of the World Medical Association (Declaration of Helsinki) for studies involving humans.

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Inclusion criteria: Children with congenital heart defects (cyanotic and a cyanotic heart defects) confirmed by echocardiography. Control group of healthy children. Children aged from 2 to 10 years old, both males and females.

Exclusion criteria: Children receiving cholesterol lowering drugs and corticosteroids. Patients with myeloproliferative diseases, chronic liver or kidney diseases and diabetes mellitus which might affect lipid level. Children with heart diseases other than congenital heart diseases.

All patients were subjected to full history taking and full clinical examination. Any patient had tachypnea, tachycardia, grunting and intercostal retraction was considered to have respiratory distress. Echocardiography examination. Laboratory investigations (total cholesterol, triglycerides, low-density lipoprotein (LDL) and high-density lipoprotein (HDL).

Lipid profile blood sample: 3 ml whole blood were collected then centrifuged to determine serum lipid level (total cholesterol, triglycerides, low-density lipoprotein (LDL) and high-density lipoprotein (HDL)). Quantitative determination of cholesterol IVD, Quantitative determination of HDL cholesterol IVD, and Quantitative determination of triglycerides IVD according to **Young [6].**

Statistical Analysis

The collected data were coded, processed and analyzed using the SPSS (Statistical Package for Social Sciences) version 22 for Windows® (IBM SPSS Inc, Chicago, IL, USA). Data were tested for normal distribution using Shapiro Walk test. Qualitative data were represented as frequencies and relative percentages. Chi square test ($\chi 2$) to calculate difference between two or more groups of qualitative variables. Quantitative data were expressed as mean ± SD. Independent samples t-test was used to compare between two independent groups of normally distributed variables (parametric data). P value $\leq$ 0.05 was considered significant.

RESULTS

- There was no statistically significant difference between the studied groups concerning demographic characteristics (Table 1).
- The most frequent cardiac defect was ASD (22.7%) followed by VSD (13.6%), common A-V canal (9.1%), mitral regurgitation (9.1%), pulmonary regurgitation (9.1%), and PDA (9.1%). 18.2% of the studied patients had cyanotic CHD and 81.8% had non-cyanotic CHD (Table 2).
- There were significant differences between the studied groups in lipid profile as case group had higher cholesterol, triglyceride, LDL and lower HDL than control group (Table 3).
- There was no significant difference between cyanotic and non-cyanotic CHD in lipid profile (Table 4).
- There was no significant correlation between age and lipid profile in the studied groups (Table 5).
- There was significant association between sex and lipid profile as females had significantly higher serum triglycerides than males (Table 6).

Table (1): Demographic characteristics of the studied groups

Variables	Case group (n=22)	Control group (n=22)	Test of sig.	P
Age (years):				
Mean ± SD	5.6 ± 2.8	5.6 ± 2.3	MW	0.3
Median	5.0	4.0	1.2	NS
Range	2.0 – 10.0	2.0 – 10.0		
Sex, n (%):				
Male	11 (50.0%)	11 (50.0%)	NA	NA
Female	11 (50.0%)	11 (50.0%)		
Residence, n (%):				
Rural	14 (63.6%)	17 (77.3%)	χ^2	0.3
Urban	8 (36.4%)	5 (22.7%)	1.0	NS
Rank of child, n (%):				
1st	2 (9.1%)	4 (18.2%)		
2nd	8 (36.4%)	10 (45.5%)	χ^2	0.1
3rd	6 (27.3%)	6 (27.3%)	2.5	NS
4th	6 (27.3%)	2 (9.1%)		
Consanguinity, n (%):				
Positive	9 (40.9%)	5 (22.7%)	χ^2	0.2
Negative	13 (59.1%)	17 (77.3%)	1.7	NS
Family history of cardiac diseases, n (%):				
Positive	3 (13.6%)	0 (0.0%)	Fisher	0.2
Negative	19 (86.4%)	22 (100%)		NS

SD: Standard deviation. NA: Not applicable. χ^2: Chi square test, MW: Mann Whitney test. NS: Non-significant (P>0.05)

Table (2): Echo findings of the studied cases

Echo findings	Case group (n=22)
ASD	5 (22.7%)
VSD	3 (13.6%)
Common A-V canal	2 (9.1%)
Mitral regurgitation	2 (9.1%)
Pulmonary regurgitation	2 (9.1%)
PDA	2 (9.1%)
PFO	1 (4.5%)
Coarctation of aorta	1 (4.5%)
Complete endocardial cushion defect	1 (4.5%)
Outlet VSD with pulmonary stenosis	1 (4.5%)
Sever valvular pulmonary stenosis	1 (4.5%)
Truncus arteriosus type 1	1 (4.5%)

CHD: Congenital heart disease. VSD: Ventricular septal defect, ASD: Atrial septal defect. PDA: patent ductus arteriosus, Common A-V Canal: common atrial ventricular canal. PFO: Patent foramen oval. 18.2% of the studied patients had cyanotic CHD and 81.8% had non-cyanotic CHD.

Table (3): Lipid profile of the studied groups

Variables	Case group (n=22)	Control group (n=22)	Test of sig.	P
Total cholesterol (mg/dl): Mean ± SD	130.3 ± 17.6	107.2 ± 8.9	t test 4.0	**<0.001 HS**
Triglyceride (mg/dl): Mean ± SD	115.7 ± 27.1	78.2 ± 14.4	t test 2.6	**0.01 S**
LDL (mg/dl): Mean ± SD	66.4 ± 15.6	38.1 ± 6.7	t test 5.1	**<0.001 HS**
HDL (mg/dl): Mean ± SD	40.7 ± 9.6	53.5 ± 7.5	student t test 3.3	**0.001 S**

SD: Standard deviation. student t test. S: Statistically significant (P<0.05). HS: Highly statistically significant (<0.001)

Table (4): Comparison between cyanotic and non-cyanotic CHD in lipid profile

Variables	Cyanotic CHD (n=4)	Non-cyanotic CHD (n=18)	Test of sig.	P
Total cholesterol (mg/dl): Mean ± SD	132.1 ± 20.2	131.9 ± 17.2	MW 0.9	0.4 NS
Triglyceride (mg/dl): Mean ± SD	96.2 ± 23.6	120.0 ± 29.5	MW 0.4	0.7 NS
LDL (mg/dl): Mean ± SD	63.1 ± 11.4	67.1 ± 14.6	MW 0.4	0.7 NS
HDL (mg/dl): Mean ± SD	40.7 ± 9.5	40.7 ± 9.8	MW 0.4	0.7 NS

SD: Standard deviation. MW: Mann Whitney test. NS: Non-significant (P>0.05)

Table (5): Correlation between age and lipid profile in the studied groups

Lipid profile	Age	
	r	P
Total cholesterol	-0.31	0.2 (NS)
Triglyceride	-0.02	0.9 (NS)
LDL	-0.40	0.09 (NS)
HDL	-0.07	0.8 (NS)

r: Spearman's correlation coefficient. NS: Non-significant (P>0.05)

Table (6): Association between sex and lipid profile of the studied groups

Variables	Males (n=22)	Females (n=22)	Test of sig.	P
Total cholesterol (mg/dl): Mean ± SD	117.1 ± 19.6	120.3 ± 17.2	MW 0.7	0.5 NS
Triglyceride (mg/dl): Mean ± SD	85.2 ± 20.0	108.7 ± 25.6	MW 2.1	**0.03 S**
LDL (mg/dl): Mean ± SD	51.0 ± 11.6	53.5 ± 11.9	MW 1.0	0.3 NS
HDL (mg/dl): Mean ± SD	49.1 ± 11.6	45.1 ± 9.7	MW 1.2	0.2 NS

SD: Standard deviation. MW: Mann Whitney test. NS: Non-significant (P>0.05). S: Statistically significant (P<0.05).

DISCUSSION

The clinical manifestation of congenital heart disease differs depending on the type and severity of the defect [7-8]. There are several risk factors associated with the development of heart diseases, such as smoking, obesity and dyslipidemia. Dyslipidemia is typically spotted as the most significant factor leading to the development of atherosclerotic diseases, mainly the higher concentrations of low-density lipoproteins (LDL) [9]**.** Few data on the impacts of congenital heart diseases are available with regard to the prevalence of dyslipidemia in children. Our study was done to evaluate the lipid profile in children with congenital heart diseases.

In our study, we found that there was no statistically significant difference between the studied groups regarding demographic characteristics, which is in agreement with the study of **Ghaderian *et al.* [4],** who reported that there was no statistically significant difference between the studied groups regarding age and sex. While in **Animasahun *et al.* [10]** study, prevalence was more in males and **Barbiero *et al.* [11]** study found that most participants were males (55.7%), and aged between 6 and 11 years (43.7%).

Our study showed that the most frequent cardiac defect was ASD (22.7%) followed by VSD (13.6%), common A-V canal (9.1%), mitral regurgitation (9.1%), pulmonary regurgitation (9.1%), and PDA (9.1%)**.** In contrast to our study, **Roy *et al.* [8]** found that the commonest lesion was VSD present in 39.1% patients followed by PDA in 17.3%, TOF in 15.5%, ASD in 11.8 %, A-V canal defect in 0.9 %, PS in 1.8 %, COA in 1.8%, TGA in 1.8 % and single ventricle with single A-V canal defect in 0.9%. While, **Ghaderian *et al.* [4]** study showed that VSD, PDA, ASD were the most common heart defects with percentages of 69%, 17% and 10% of total patient respectively. The differences in this study was due to limited number of cases.

We found that 18.2% of the studied patients had cyanotic CHD and 81.8% had non-cyanotic CHD, which is close to the results of **Ghaderian *et al.* [4]** who reported that the case group included 22 patients (22%) with cyanotic CHD and 78 patients (78%) with acyanotic CHD. In addition, **Barbiero *et al.* [11]** found that acyanotic congenital heart disease was presented in 81.1% of patients while cyanotic congenital heart disease was presented in 18.9% of patients. While, **Singh *et al.* [12]** reported that the case group included 4 patients (9.3%) with cyanotic CHD and 39 (90.7%) patients with acyanotic CHD. In contrast **Animasahun *et al.* [10] s**howed that patients with cyanotic congenital heart disease was presented in 56.1% of patients.

Our study showed that there was statistically significant differences between the studied groups in lipid profile as case group had higher cholesterol, triglyceride, LDL and lower HDL than control group**. Ghaderian *et al.* [4]** study agrees with our results where they reported that serum cholesterol, LDL, and TG concentrations were significantly higher in the patients' group than in the control group (p value < 0.05), but disagrees with our study in HDL that was higher in patients' group than in control group. In contrast to our study, **Fuenmayor *et al.* [13]** study showed that dyslipidemia in children with congenital heart diseases revealed rates similar to those found in normal children suggesting that the presence of congenital heart disease does not stand as a risk factor for elevation of LDL.

This study showed that there was no statistically significant difference between cyanotic and non-cyanotic CHD in serum lipid profile**.** This agrees with **Ghaderian *et al.* [4]** study, which showed no statistical difference was detected between patients with cyanotic and acyanotic heart defects in correlation to lipid profile. In contrast, researches of **Fyfe *et al.* [14], Perloff *et al.* [15]** and **Martínez-Quintana *et al.* [16]** demonstrated that patients with cyanotic heart defects have lower total cholesterol and LDL levels than patients with acyanotic heart defects. It has been explained by that patients with cyanotic CHD have hypoxic erythrocytosis that consequently leads to lower cholesterol levels.

As regards age of children in our study, age was from 2 to 10 years, and there was cross matching in

choice of age in both groups (patient and control). There was no statistical significance between age and serum lipid profile, but there was a statistically significant association between sex and lipid profile as females had significantly higher serum triglycerides than males. In contrast to our study, **Ghaderian *et al.*** [(4)] found that in patients group, cholesterol, LDL cholesterol, HDL cholesterol, and TG levels were higher in the males than in the females, but the differences between males and females did not reach statistical significance. While **Rao and Sastry** [(17)] reported that sex and age are two factors associated with difference in serum lipid profile levels. There is a rising trend begins in early life and continues until the fourth decade then remains unchanged (in healthy individuals). In children between 5 to 10 years old, HDL is higher in boys than in girls. HDL levels increase in girls gradually and decrease in boys after this age through life. **Deon *et al.*** [(18)] found that there was no significant serum lipid concentration difference was observed between males and females, but mean serum lipid parameters exceeded the 90th percentiles (age and sex related) except for HDL-C, showing normal concentrations, while in study of **Animasahun *et al.*** [(10)] prevalence was more in males.

The differences observed between results of our study and other studies, could be owing to many factors, for example methodology, type of sample (venous/capillary), time interval between last feeding, preparation of feed (dilution) and genetic composition.

CONCLUSION

We concluded in this study that patients had significantly higher serum lipid levels than age and sex-matched controls. In light of these findings, we recommend screening of lipid profile in children with congenital heart disease to reduce the risk of atherosclerosis. In addition, there was a statistically significant association between sex and lipid profile as females had significantly higher serum triglycerides than males. More studies are needed to determine various affecting factors on lipids in blood and avoid or treat it especially in risky children as who have congenital heart diseases. Moreover, these children must be followed-up.

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