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Total phospholipids and L-Carnitineas predictors of Spontaneous Closure of Atrial Septal Defect and Ventricular Septal Defect in Children at Zagazig University hospitals

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Abstract

Background*: Congenital heart defects (CHD) are common in children. Ventricular septal defect (VSD) is the most common congenital heart defect.Atrialseptal defect (ASD) is a common congenital disorder with a prevalence of approximately 2 per 1,000 live births. phospholipids and the L-carnitine levels may have a valuable and important role in the pathogenesis and prognosis of congenital heart disease The aim was to assess the role of l.carnitine and phospholipids as predictors of spontaneous closure of atrial septal defects and ventricular septal defects.* ***Patients and methods:*** *this was a cohort study whichincludedthirty children dividd into two groups: ASD group and VSD group.Measurement of serum L.carnitine and total phospholipids were done****Results****: there was statistically significant higher total phospholipid among ASD patients with spontaneous closure than regression to ≤ 3 mm than residual >3 mm with no statistically significant difference regarding L. Carnitine. There was statistically significant higher L. Carnitine among the VSD patients with regression to ≤ 3 mm than residual >3 mm. Total phospholipids and L-Carnitine were the statistically significant predictor factors for spontaneous closure of ASD and VSD among the studied group,* ***Conclusion****: Total phospholipids and L-Carnitine were the statistically significant predictor factors for spontaneous closure of ASD and VSD among the studied group.*

Keywords: *predictor- phospholipids- L. Carnitine, ASD ,VSD, , spontaneous closure.*

I. Introduction:

Congenital heart defects (CHD) are common in children, with an incidence of approximately 8 cases per 1000 live births. These defects can cause an array of problems in the primary care of children. **(1)**

Ventricular septal defect (VSD) is the most common congenital heart defect. The incidence of VSD is approximately 2-6 per 1000 live births. **(2)**

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Atrial septal defect (ASD) is a common congenital disorder with a prevalence of approximately 2 per 1,000 live births.There is four types of ASDs: secundum, primum, sinus venosus, and coronary sinus. Secundum ASDs are the most common, making up more than 70% of all ASDs [(3)].

Some of these defects can close spontaneously, or diminish without surgical intervention. However, some patients will suffer from complications such as growth retardation, recurrent infections, congestive heart failure, and even sudden death [(4)].

Predictors of ASDs and VSDs spontaneous closure are dependent on defect size and patient age. Routine clinical follow-up with serial echocardiography is the best way to identify those patients who close spontaneously and those who will require closure. [(5)]

Further investigation is needed to understand the mechanisms and heterogeneity of septal growth and remodeling after birth. Possible mechanisms of a spontaneous ASD and VSD closure include adaptive endothelial migration, limited myocardial proliferation, and fibroblast migration with extracellular matrix deposition. [(3)]

Recent studies have reported that the phospholipids and the L-carnitine levels have a valuable and important role in the pathogenesis and prognosis of congenital heart disease with right or left ventricular volume or pressure overload as in ASD, VSD or PDA. Cell-specific targeting of L-carnitine and phospholipid biosynthetic pathways could serve as a potential strategy for helping in management of congenital heart diseases. [(6)]

The main objective of this study was to assess the role of l.carnitine and phospholipids as predictors of spontaneous closure of atrial septal defects and ventricular septal defects.

II. Patients and Methods

This was cohort study for children up to 2 years of age who were following up ASD or VSD in the Pediatric Cardiology Unit of Zagazig University Hospitals.

Patients: The cases were classified into 2 groups: Group I : comprised 20 patients with ASD. Group II : comprised 10 patients with VSD.

***Inclusion criteria:**All children up to 2 years of age who were following for ASDs and VSDs progress byechocardiography in Zagazig University Hospitals.

Exclusion criteria: Children with ,electrolyte imbalance, cancer, hepatic or kidney disease. Children with aortic stenosis, moderate or severe regurgitation of the mitral or tricuspid valves, pulmonary stenosis, Eisenmenger syndrome.

Methods:

All children enrolled in the study were subjected to the following:

A- Full history taking:

B- Complete clinical examination:

C- Specific Investigations:

➢ Follow up echocardiography at 3 and 6 months showing size of the defects which compared to previous echocardiographic reports.

➢ Examination by Transthoracic echocardiogram, the probe is placed on the chest or abdomen of the subject to get various views of the heart. Modes:

1. 2Dimensional imaging allows structures to be viewed moving in real time in a cross-section of the heart.It is used for detecting abnormal anatomy or abnormal movement of structures

2. M-mode : this modality is obtained at a single angle and then plotted against time to obtain an image. It can be used to watch the movement of structures with time and provides a 1D view, is used for fine measurements.

3. Color Doppler: form of 2D echo in which the doppler shift of the structures is shown as color,show blood flow through the valves to visually indicate the direction of blood flow, show blood flow in abnormal locations such as with septal defects (ASD or VSD).

➢ **Measurement of serum L.carnitine and total phosholipids.**

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.Data were summarized using:The arithmetic mean, The standard deviation (SD). The comparison was done using: Chi- square test (X2), ANOVA (F-test) test, Linear regression Analysis Level of significance: the threshold of significance was fixed at 5% level (P-value).

III. Results:

Table (1): Comparing socio-demographic data among the different defect lesions:-

Variables	***ASD (NO=20)*** mean ± SD	***VSD (NO=10)*** mean ± SD	**t- test**	**p-value**
Age (months)	12.4±4.1	18.5±5.7	3.3	**0.002***
Weight (kg)	9.5±1.3	9.8±1.9	0.4	0.6
Weight percentile	55.3±26.6	43.2±34.6	M.W	0.3

			1.1	
Body surface area	0.43±0.02	0.44±0.06	0.4	0.6
Variables	***ASD*** ***NO (%)***	***VSD*** ***NO (%)***	**χ^2**	**p-value**
Gender				
Male	8 (40.0%)	7 (70.0%)	FET	0.2
Female	12 (60.0%)	3 (30.0%)		
Mode of delivery				
Vaginal	2 (10.0%)	1 (10.0%)	FET	1
C.S	18 (90.0%)	9 (90.0%)		
Order of kid				
1ST	3 (15.0%)	1 (10.0%)		
2nd	10 (50.0%)	5 (50.0%)	2.6	0.6
3rd	6 (30.0%)	2 (20.0%)		
4th	1 (5.0%)	1 (10.0%)		
5th	0.0 (00.0%)	1 (10.0%)		
Feeding				
Breast feeding	11 (55.0%)	4(40.0%)	0.6	0.7
Artificial	9 (45.0%)	6 (60.0%)		
Consanguinity				
Present	2 (10.0%)	1(10.0%)	FET	1
Absent	18 (90.0%)	9 (90.0%)		

*Statistically significant difference ($P \leq 0.05$)M.W=Mann-Witenny U test.

This table shows that there was statistically significant difference between the ASD &VSD patients regarding age at diagnosis with higher age among ASD than VSD group. But regarding body weight, body percentile, body surface area, sex distribution, consanguinity, feeding and mode of delivery, there was no statistically significant difference between the ASD &VSD patients.

Table (2): Comparing clinical data among the different defect lesions:-

Variables	***ASD (NO=20)*** mean ± SD Median	***VSD (NO=10)*** mean ± SD Median	**M.W test**	**p-value**
Disease duration *(days)*	41.3±38.9 29	25.5±22.9 15.0	1.2	0.2
Variables	***ASD NO (%)***	***VSD NO (%)***	**χ^2**	**p-value**
Presence of chest diseases *Recurrent chest infection* *And respiratory distress*	14 (70.0%) 6 (30.0%)	8 (80.0%) 2 (20.0%)	FET	0.7
Heart failure *Yes* *No*	4 (20.0%) 16 (80.0%)	4 (40.0%) 6 (60.0%)	1.3	0.2
Drug history *No* *Lanoxin* *Lasix&capotin* *Lasix* *Capotin*	12 (60.0%) 4 (20.0%) 5 (25.0%) 2 (10.0%) 0.0 (00.0%)	2(20.0%) 4 (40.0%) 6 (60.0%) 1 (10.0%) 1 (10.0%)	8.1	0.1
Defect size at diagnosis *≤ 5 mm* *>5 mm*	15 (75.0%) 5 (25.0%)	5 (50.0%) 5 (50.0%)	1.8	0.2

This table shows that there was no statistically significant difference between ASD &VSD patients regarding disease duration, presence of chest diseases, heart failure, drug history and defect size at diagnosis.

Table (3): Comparing CBC among the different defect lesions:-

Variables	***ASD (NO=20)*** mean ± SD median	***VSD (NO=10)*** mean ± SD median	**t- test**	**p-value**
WBCs*(*1000)*	8.7±3. 7.9	12.4±6.5 10.5	M.W 1.9	0.06
RBCs	4.4±0.6 4.5	4.6±0.6 4.7	0.8	0.4
Platelets*(*1000)*	362.3±95.2 338.1	375.6±70.5 347.0	0.3	0.7
Hb(gm/dl)	10.6±1.5 10.6	11.4±1.4 11.1	1.2	0.2
RDW *(%)*	15.2±1.7 14.9	15.6±3.1 14.4	0.5	0.6
HCT	31.9±4.2 32.5	33.5±3.8 34.3	1.1	0.3
MCV	74.9±9.7 74.7	72.9±9.4 75.0	0.5	0.6
MCH	25.3±3.5 25.5	25.2±2.6 25.6	0.1	0.9

This table shows that there was no statistically significant difference between ASD &VSD patients regarding CBC picture.

Table (4): Comparing Echocardiography among the different defect lesions:-

Variables	***ASD (NO=20)*** mean ± SD median	***VSD (NO=10)*** mean ± SD median	**t- test**	**p-value**
***PA** (mm)*	14.1±5.3 13.5	17.3±3.7 19.0	1.7	0.09
***LPA**(mm)*	6.8±2.2 6.0	9.4±2.1 9.5	3.1	**0.005***
***RPA**(mm)*	6.8±1.6 6.0	8.6±2.7 9.5	2.3	**0.02***
***ESPAP**(mm)*	35.9±5.1 37.0	43.1±14.6 32.0	1.3	0.2
***LA**(mm)*	16.8±4.7 17.0	21.4±4.3 22.0	2.5	**0.01***
***AO**(mm)*	13.1±2.1 13.0	15.9±3.6 16.0	2.8	**0.008***
***LVED**(mm)*	21.3±3.8 20.0	27.5±8.9 26.5	2.6	**0.01***
***LVES**(mm)*	13.7±2.5 13.5	16.9±5.3 15.7	2.2	**0.03***
***IVS**(mm)*	8.1±3.5 6.0	6.9±2.8 6.0	0.8	0.4
***PW**(mm)*	7.4±2.7 6.0	6.4±1.4 6.0	1.1	0.3
EF (%)	71.5±6.6 69.0	72.1±6.5 73.5	0.2	0.8

FS (%)	39.7±4.9 37.5	40±5.1 39.0	0.1	0.9

*Statistically significant difference ($P \leq 0.05$)

This table shows that there was statistically significant increase in LPA, RPA, LA, AO, LVED and LVES among the VSD than ASD patients. But regarding other ECHO findings, there was no statistically significant difference between ASD &VSD patients.

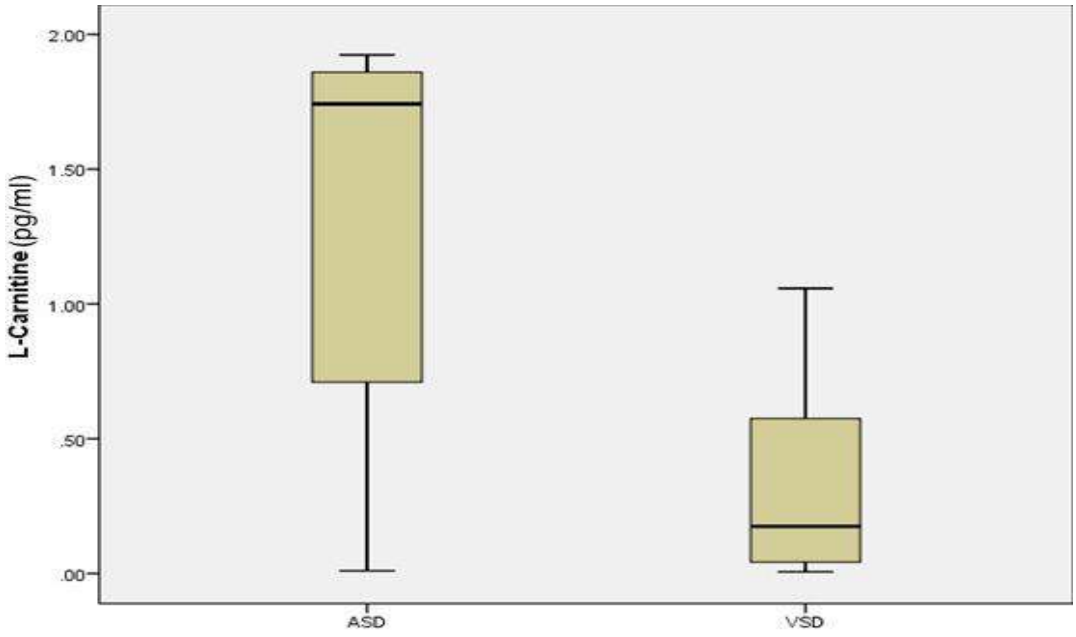

Fig (1): Box plot chart for relation between defect type and the L. Carnitine among the studied group

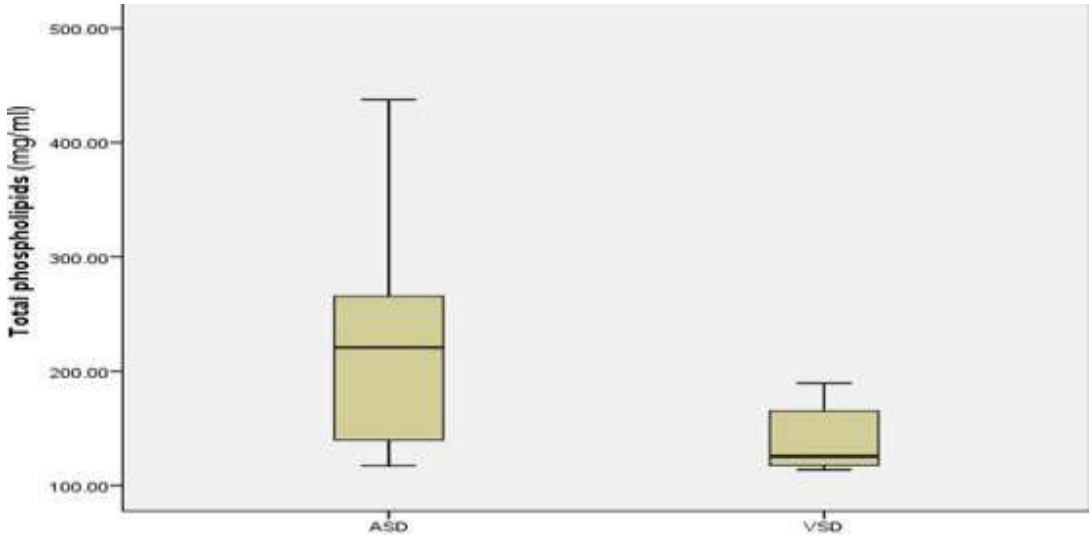

Fig (2): Box plot chart for relation between defect type and the total phospholipids among the studied group

Figure 1 and 2shows that there was statistically significant higher L. Carnitine and total phospholipid

among ASD than VSD patients.

Table (5): Comparing defect size at diagnosis and after the follow up among the different defect lesions:-

Variables	**Defect size** *At diagnosis*	**Defect size** *After follow up*	**W.S.R test**	**p-value**
ASD mean ± SD Median	4.45±2.01 4	2.32±1.4 2	3.6	**0.03***
VSD mean ± SD Median	4.92±3.2 3.6	5.2±3.1 4.25	2.1	0.1

W.S.R=Wilcoxon Signed Rank test.

This table shows that there was statistically significant decrease on the ASD size after the follow up. But regarding VSD, the defect size was increased after the follow up with no statistical significance

Table (6): Relation between the defect type and its outcome among the studied group:-

The defect	*Spontaneous closure NO. (%)*	*Regress to ≤ 3 mm NO. (%)*	*Residual to > 3 mm NO. (%)*	χ^2	**p-value**
ASD (20)	12 (60.0%)	1 (5.0%)	7 (35.0%)	10.8	**0.004***
VSD (10)	0.0 (0.0%)	3 (30.0%)	7 (70.0%)		

*Statistically significant difference (P ≤ 0.05)

This table shows that there was statistically significant difference in the outcome between patients with different defect type, (60.0%) of the ASD had spontaneous closure (5.0%) regressed to ≤ 3 mm and (35.0%) residue to more than 3 mm while (70.0%) of VSD residue to more than 3 mm and 30 % of VSD regressed to ≤ 3 mm.

Table (7): Comparing CBC between ASD patients with different outcome among the studied group:-

Variables	***Spontaneous closure*** **(NO.=12)**	***Regress to ≤ 3 mm*** **(NO.=1)**	***Residual to > 3 mm*** **(NO.=7)**	**F test**	**p-value**
WBCs*(*1000)* mean ± SD	8.9±4.1	7.6	8.5±4.3	K.W 0.06	0.9
RBCs mean ± SD	4.4±0.78	4.1	4.3±0.5	0.1	0.9
Platelets*(*1000)* mean ± SD	365.5±78.3	255	372.1±124.4	0.6	0.5
Hb mean ± SD Range	10.6±1.6	11.4	10.7±1.3	0.1	0.8
RDW *(%)* mean ± SD	15.4±2.1	14.5	14.8±1.3	0.3	0.7
HCT mean ± SD	31.5±4.6	35.3	32.1±3.7	0.3	0.7
MCV mean ± SD	76±12.4	80.2	74.5±2.9	0.4	0.6

MCH mean ± SD	25.3±4.4	25.9	25.2±1.6	0.1	0.9

K.W=Kruskal-Wallis test, F-test=ANOVA, LSD=least significance difference

This table shows that there was no statistically significant difference between the ASD patients with different outcome regarding CBC.

Table (8): Comparing CBC between VSD patients with different outcome among the studied group:-

Variables	***Regress to ≤ 3 mm*** **(NO.=3)**	***Residual to > 3 mm*** **(NO.=7)**	**T test**	**p-value**
WBCs*(*1000)* mean ± SD	9.2±3.6	13.7±7.2	M.W0.9	0.3
RBCs mean ± SD	5.1±0.3	4.3±0.6	2.1	0.06
Platelets*(*1000)* mean ± SD	352.7±20.2	358.4±83.3	0.6	0.5
Hb mean ± SD Range	12.1±1.2	11.1±1.5	0.9	0.3
RDW *(%)* mean ± SD	16.7±5.7	15.2±1.8	0.7	0.5
HCT				

mean ± SD	33.9±4.2	33.3±3.9	0.2	0.8
MCV mean ± SD	66.1±7.5	75.9±9.1	1.6	0.1
MCH mean ± SD	25±1.6	25.4±3.1	0.2	0.8

M.W=Man Witenny test

This table shows that there was no statistically significant difference between the VSD patients with different outcome regarding CBC.

Table (9): Comparing L. Carnitine and total phospholipidsbetween ASD patients with different outcome among the studied group:-

Variables	***Spontaneous closure* (NO.=12)**	***Regress to ≤ 3 mm* (NO.=1)**	***Residual to > 3 mm* (NO.=7)**	**F test**	**p-value**
L. Carnitine *(pg/ml)* mean ± SD	1.54±0.5	0.19±.04	1.11±0.08	2.4	0.1
Total phospholipids *(mg/ml)* ***mean ± SD***	257.4±67.1	266.2±53	141.8±37.8	9.1	**0.002***

F-test=ANOVA test, *Statistically significant difference (P ≤ 0.05)

This table shows that there was statistically significant higher total phospholipid among the ASD patients with spontaneous closure than regression to ≤ 3 ml than residual >3 ml with no statistically significant difference regarding L. Carnitine.

Table (10): Comparing L. Carnitine and total phospholipidsbetween VSD patients with different outcome among the studied group:-

Variables	***Regress to ≤ 3 mm*** **(NO.=3)**	***Residual to > 3 mm*** **(NO.=7)**	**M.W test**	**p-value**
L. Carnitine *(pg/ml)* mean ± SD	0.98±0.7	0.16±0.19	3.1	**0.01***
Total phospholipids *(mg/ml)* ***mean ± SD***	186.2±74.9	138.7±31.2	1.5	0.1

M.W=Man Witenny test, *Statistically significant difference (P ≤ 0.05)

This table shows that there was statistically significant higher L. Carnitine among the VSD patients with regression to ≤ 3 ml than residual >3 ml with no statistically significant difference regarding total phospholipid.

Table (11): Relation between the defect size at diagnosis and its outcome among the ASD studied group:-

The ASD defect size at diagnosis	***Spontaneous closure NO. (%)***	***Regress to ≤ 3 mm NO. (%)***	***Residual to > 3 mm NO. (%)***	χ^2	**p-value**
≤ 5mm (15)	12 (80.0%)	1 (6.7%)	2 (13.3%)	12.4	**0.002***
>5 mm(5)	0.0 (0.0%)	0.0 (0.0%)	5 (100.0%)		

*Statistically significant difference (P ≤ 0.05)

This table shows that there was statistically significant difference in the outcome between ASD patients with different defect size at diagnosis, (80.0%) of the children with defect less than 5 mm had spontaneous closure (6.7%) regressed to ≤ 3 mm and (13.3%) residue to more than 3 mm while (100.0%) of the children with defect more than 5 mm residue to more than 3 mm.

Table (12): Relation between the defect size at diagnosis and its outcome among the VSD studied group:-

The VSD defect size at diagnosis	***Regress to ≤ 3 mm NO. (%)***	***Residual to > 3 mm NO. (%)***	**χ^2**	**p-value**
≤ 5mm (5)	3 (60.0%)	2 (40.0%)	FET	0.1
>5 mm(5)	0.0 (0.0%)	5 (100.0%)		

FET=Fischer Exact Test.

This table shows that there was no statistically significant difference in the outcome between VSD patients with different defect size at diagnosis.

Table (13): Correlation between L. Carnitine and total phospholipids with patients' characteristics and laboratory data among the ASD and VSD patients:

Variables	***L. Carnitine***					
	ASD			***VSD***		
	R	**p**	**Sig**			
Age (months)	0.04	>0.5	NS	0.01	>0.5	NS
Weight(kg)	0.06	>0.5	NS	0.03	>0.5	NS
Body surface area						

	0.07	>0.5	NS	0.09	>0.5	NS
Defect size at diagnosis	**-0.5**	**0.01***	**S**	**-0.6**	**0.001****	**HS**
Defect size after follow up	**-0.4**	**0.02***	**S**	**-0.4**	**0.03***	**S**
WBCs*(*1000)*	0.08	>0.5	NS	0.2	>0.5	NS
RBCs	0.2	>0.5	NS	0.09	>0.5	NS
Platelets*(*1000)*	0.04	>0.5	NS	0.01	>0.5	NS
Hb	0.07	>0.5	NS	0.06	>0.5	NS
RDW *(%)*	0.2	>0.5	NS	-0.2	>0.5	NS
HCT	0.03	>0.5	NS	0.08	>0.5	NS
MCV	0.09	>0.5	NS	0.07	>0.5	NS
MCH	0.01	>0.5	NS	0.08	>0.5	NS
PA *(mm)*	0.06	>0.5	NS	0.01	>0.5	NS
LPA*(mm)*	0.08	>0.5	NS	0.05	>0.5	NS
RPA*(mm)*						

	0.1	>0.5	NS	0.06	>0.5	NS
ESPAP*(mm)*	0.03	>0.5	NS	0.05	>0.5	NS
LA*(mm)*	0.04	>0.5	NS	0.01	>0.5	NS
AO*(mm*	0.2	>0.5	NS	-0.2	>0.5	NS
LVED*(mm)*	0.02	>0.5	NS	0.08	>0.5	NS
LVES*(mm)*	0.09	>0.5	NS	0.06	>0.5	NS
IVS*(mm)*	0.03	>0.5	NS	0.08	>0.5	NS
PW*(mm)*	0.06	>0.5	NS	0.03	>0.5	NS
EF (%)	0.08	>0.5	NS	0.05	>0.5	NS
FS (%)	0.08	>0.5	NS	0.04	>0.5	NS
Total phospholipidsmg/ml	**0.3**	**0.04***	**S**	**0.5**	**0.002***	**S**

*Statistically significant difference ($P \leq 0.05$)

**Statistically highly significant difference ($P \leq 0.001$)

L-Carnitine was statistically significantly positively correlated with total phospholipids (the increase on L-Carnitine was associated with increase on with total phospholipids) and statistically significantly negatively correlated with defect size at diagnosis and after follow up (the higher defect size at diagnosis and after follow up was associated with lower L-Carnitine level) among ASD and VSD patients, with no statistically significant correlation with other variables

Table (16): Correlation between total phospholipids and L.carnitine with patients' characteristics and laboratory data among the ASD and VSD patients:

Variables	***Total phospholipids***					
	ASD			***VSD***		
	R	**p**	**Sig**			
Age (months)	0.01	>0.5	NS	0.2	>0.5	NS
Weight (kg)	0.06	>0.5	NS	0.01	>0.5	NS
Defect size at diagnosis	**-0.4**	**0.02***	**S**	**-0.5**	**0.002***	**S**
Defect size after follow up	**-0.6**	**0.001****	**HS**	**-0.4**	**0.03***	**S**
WBCs	0.08	>0.5	NS	0.2	>0.5	NS
RBCs	0.2	>0.5	NS	0.08	>0.5	NS
Platelets	0.1	>0.5	NS	0.01	>0.5	NS
Hb	-0.1	>0.5	NS	0.01	>0.5	NS
RDW (%)	0.2	>0.5	NS	-0.2	>0.5	NS
HCT	0.02	>0.5	NS	0.08	>0.5	NS
MCV						

	0.09	>0.5	NS	0.07	>0.5	NS
MCH	0.01	>0.5	NS	0.08	>0.5	NS
***PA** (mm)*	0.09	>0.5	NS	0.01	>0.5	NS
***LPA**(mm)*	0.08	>0.5	NS	0.04	>0.5	NS
***RPA**(mm)*	0.1	>0.5	NS	0.2	>0.5	NS
***ESPAP**(mm)*	0.04	>0.5	NS	0.09	>0.5	NS
***LA**(mm)*	0.02	>0.5	NS	0.08	>0.5	NS
***AO**(mm*	0.09	>0.5	NS	0.07	>0.5	NS
***LVED**(mm)*	0.01	>0.5	NS	0.08	>0.5	NS
***LVES**(mm)*	0.09	>0.5	NS	0.01	>0.5	NS
***IVS**(mm)*	0.08	>0.5	NS	0.04	>0.5	NS
***PW**(mm)*	0.01	>0.5	NS	0.08	>0.5	NS
EF (%)	0.09	>0.5	NS	0.01	>0.5	NS
FS (%)						

	0.08	>0.5	NS	0.04	>0.5	NS
L-Carnitine Pg/ml	**0.3**	**0.04***	**S**	**0.4**	**0.01***	**S**

*Statistically significant difference (P ≤ 0.05)

**Statistically highly significant difference (P ≤ 0.001)

Total phospholipids was statistically significantly positively correlated with L-Carnitine (the increase on L-Carnitine was associated with increase on with total phospholipids) and statistically significantly negatively correlated with defect size at diagnosis and after follow up (the higher defect size at diagnosis and after follow up was associated with lower total phospholipids level) among ASD and VSD patients, with no statistically significant correlation with other variables.

Table (17): Multivariate linear regression analysis for predictor factors for spontaneous closure of CHD:-

Variables	**Regression coefficient**	***p***	***95% C.I***
Total phospholipids	**3.5**	**0.03***	**(0.08-0.6)**
L-Carnitine	**0.8**	**0.04***	**(1.4-13.1)**
	ANOVA=2.7 ,p-value=0.01* R2=0.7 Durbin Watson=1.6		

*Statistically significant difference (P ≤ 0.05)

This table shows that total phospholipids and L-Carnitine were statistically significant predictor factors for spontaneous closure of ASD and VSD among the studied group.

IV. Discussion

This study showed that, regarding sex distribution, disease duration, body weight, body percentile, consanguinity, feeding and mode of delivery, there was no statistically significant difference between the patients with different outcome. Our results were supported by study of **Özçekeret al., [7]** as they revealed that spontaneous closure of ASD was observed in 58.9% of patients diagnosed between 1 month and 24 months of age and in 33.3% of patients whose ASD was diagnosed when they were 25–60 months of age. In only 3.3% of patients older than 61 months was spontaneous closure noted. A statistically significant difference was found among the 3 groups regarding spontaneous closure.

Cockerham et al.[8] reported spontaneous closure rates of 22%, 33%, and 3% in patients younger than 12 months old, 1–2 years old, and 2–4 years old, respectively. Present results were in agreement with those of the literature.

A variety of factors have been found to affect the incidence of spontaneous VSD closure. Age at which VSD was diagnosed was one of the most common factors shown to affect the incidence of VSD closure. Results of several studies have suggested that spontaneous VSD closure primarily occurred in the first 2 years of life [9].

Furthermore, in a study by **Ertürk et al.** [10] 90% of defects with diameter of 8mm or more required surgical closure methods.

Their study confirmed previous reports [11] indicating that spontaneous closure can occur beyond infancy. Therefore, the window of opportunity for selective surgery can be determined according to patient age. None of their patients with an ASD size of 9 mm or less needed surgery. In their study, 72.4% of patients needed surgery or trans catheter closure. However, in their study, 8 (4.1%) cases of spontaneous closure of 9 mm ASDs occurred in childhood.

The present study showed that there was no statistically significant difference between the patients with different outcome regarding CBC. The mean LEVD ,LPA and AO were statistically significant higher among the patients with residual >3 ml than regression to ≤ 3 ml than spontaneous closure. But regarding other ECHO findings, there was no statistically significant difference between the patients with different outcome.

Also, **Xu et al.,** [12]demonstrated that the following variables were significantly different and could be identified as potential predictors of spontaneous closure by Student t-test and chi-squared test: DVSD, DVSD/DAR, main pulmonary artery diameter, left atrium sizes, left ventricle sizes, main pulmonary forward blood flow, Qp/Qs, VSD locations, and patients with PDA, membranous septal aneurysm, lung infection scores, Down's syndrome, and anemia.

Cardiovascular disease (CVD) is a key cause of deaths worldwide, comprising 15-17% of healthcare expenditure in developed countries. Current records estimate an annual global average of 30 million cardiac dysfunction cases, with a predicted escalation by two-three folds for the next 20-30years. Although Beta²-blockers and angiotensin-converting-enzymes are commonly prescribed to control CVD risk, hepatotoxicity and hematological changes are frequent adverse events associated with these drugs. Search for alternatives identified endogenous cofactor L-carnitine, which is capable of promoting mitochondrial P-oxidation towards a balanced cardiac energy metabolism. L-Carnitine facilitates transport of long-chain fatty acids into the mitochondrial matrix, triggering cardioprotective effects through reduced oxidative stress, inflammation and necrosis of cardiac myocytes. Additionally, L-carnitine regulates calcium influx, endothelial integrity, intracellular enzyme release and membrane phospholipid content for sustained cellular homeostasis [13].

The current study showed that There was statistically significant higher L. Carnitine among the patients with spontaneous closure than regression to ≤ 3 ml than residual >3 ml, the statistically significant difference was mainly between spontaneous closure and the other groups. Although the regression to ≤ 3 ml had higher L. Carnitine level than residual >3 ml, this difference wasn't statistically significant. There was statistically significant higher total phospholipid among the patients with spontaneous closure than regression to ≤ 3 ml than residual >3 ml.

Our results were supported by study of **Farouk et al., [14]** as they reported that CHD children had a significant low plasma L-carnitine level other than the control group (3.8±1.7pg/ml). Also, there was low plasma L-carnitine level among children with VSD(1.3±0.7pg/ml) other than those with ASD(1.6±0.5pg/ml) and PDA(1.4±0.6pg/ml), p value <0.001for all. It was noticed that there is a marked decrease in the plasma lecithin, cephalin, sphingomyelin and other phospholipids levels in CHD cases in comparison to normal children (p value <0.001). Also, marked changes in the phospholipid profile were observed. There was a significant decrease in lecithin levels in CHD group in comparison to normal children (p value <0.001). The lecithin/cephalin ratio for the control group was 5.62, for ASD was 2.77 and for VSD was 3.19.

In the study in our hands, there was statistically significant difference in the outcome between patients with different defect size at diagnosis, (60.0%) of the children with defect less than 5 ml had spontaneous closure (20.0%) regressed to ≤ 3 ml and (20.0%) residue to more than 3 ml while (100.0%) of the children with defect more than 5 ml residue to more than 3 ml. (60.0%) of the children with defect less than 5 ml had spontaneous closure and (20.0%) residue to more than 3 ml while (100.0%) of the children with defect more than 5 ml residue to more than 3 ml.

In the study of**Behjati-Ardakani et al., [15]**, regression of ASD size occurred in 2 (9.5%) infants and 3 (3.7%) children. No spontaneous closure was observed in cases with a defect size > 10 mm, and no spontaneous occlusion was detected in adolescents or adults. Seventy-two percent (n = 139) of patients needed surgical repair or transcatheter closure of the ASD.

The present study showed that there was statistically significant difference in the outcome between patients with different defect type, (60.0%) of the ASD had spontaneous closure (5.0%) regressed to ≤ 3 ml and (35.0%) residue to more than 3 ml while (70.0%) of VSD residue to more than 3 ml. There was statistically significant decrease on the ASD size after the follow up. But regarding VSD, the defect size was increased after the follow up with no statistical significance.

According to**Özçekeret al., [7]**, in only 6 of the 67 cases of ASD with diameter of ≥9 mm was spontaneous defect closure observed. The remaining 61 cases required surgery (n=19; 28.4%), or use of transcatheter occlusion method (n=34; 50.7%) to close the defect. No patient in the group (n=213) with defect diameter between 3 and 5 mm required closure procedure, and defects of 152 (71.4%) patients in this group closed spontaneously. Spontaneous closure also occurred in 31 patients (41.9%) with defect diameter of 6–8 mm. A statistically significant intergroup difference was discovered regarding defect diameter and spontaneous closure of defect (p<0.001).

The current study showed that L-Carnitine was statistically significantly positively correlated with total phospholipids (the increase on L-Carnitine was associated with increase on with total phospholipids) and statistically significantly negatively correlated with defect size at diagnosis and after follow up among ASD and VSD patients with no statistically significant correlation with other variables.

Furthermore,**Farouk et al., [14]**revealed that in ASD cases, theynoticed a significant positive correlation between total phospholipids and both sphingomyelin and Lcarnitine.

In the study total phospholipids and L-Carnitine were the statistically significant predictor factors for spontaneous closure of ASD and VSD among the studied group.

Farouk et al., [14]concluded that the findings of this study prove that the phospholipids and the L-carnitine levels have a valuable and important role in the pathogenesis and prognosis of congenital heart disease with right or left ventricular volume or pressure overload as in ASD or VSD . Cell-specific targeting of L-carnitine and phospholipid biosynthetic pathways could serve as a potential strategy for helping in management of congenital heart diseases.

In the study of **Lee et al., [16]**, ASOs (Atrial septal openings) occur at a relatively high incidence in VLBW (very low birth weight) infants, but most of these close spontaneously within 3 years.

V. Conclusion:

Total phospholipids and L-Carnitine were the statistically significant predictor factors for spontaneous closure of ASD and VSD among the studied group.

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