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CORRELATION OF AGE AND DEFECT SIZE OF ISOLATED SECUNDUM ATRIAL SEPTAL DEFECT WITH PULMONARY ARTERY PRESSURE

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Contribution

IH conceived the idea and planned study. ZUZ, MSJ and SH helped in collection, assembly & interpretation of the data. IH & ZUZ did critical revision of the article for important intellectual content. All authors contributed significantly to the submitted manuscript.

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ABSTRACT

Objective: To find out correlation of age and defect size of isolated secundum atrial septal defect with pulmonary artery pressure measured by cardiac catheterization.

Methodology: It was a cross-sectional study conducted at Cardiology department, Lady Reading Hospital, Peshawar from January 2012 to December 2016 . Eligible patients were included in the study through cardiology out patient department. Patients with other causes of raised PAP were excluded. Diagnosis was made by transthoracic echocardiography while size of defect was measured with trans-esophageal echocardiography. Pulmonary artery pressures (PAP) were measured with right heart catheterization. The data was analyzed by SPSS 20. Correlation of age and ASD size with PAP groups were examined by Pearson correlation (2-tailed) and R value was calculated.

Results: A total of 104 consecutive patients were included with 65.4 % of females. Mean age and defect size were 23.25 ± 12.2 years and 23.36 ± 5.81 mm, respectively. Average systolic and mean PAP were 37.88 ± 12.3 and 24.48 ± 8.19 mmHg, respectively with 49 (47.1%) patients had raised PAP. Age and size were positively correlated with systolic (R=0.220 & 0.198) and mean PAP (R=0.288 & 0.218) respectively , with most significant results in second and third decade of life and defect size of > 20 mm ($p < 0.002$).

Conclusion: Age and ASD size were positively correlated with pulmonary artery pressure. Moreover PAP can be predicted by the age of patients with ASD secundum.

Key Words: Secundum atrial septal defect, Pulmonary artery pressure, Atrial septal defect

INTRODUCTION

ASD is the second most common congenital heart disease with a prevalence of 1.6 per 1000 live births.[1] It usually goes undetected in childhood and there is 97% probability of survival into adulthood.[2,3] Abnormal development of inter-atrial septum can lead to isolated ASD, which is located mostly (70%) at fossa ovalis i.e. secundum type ASD.[4] It is characterized by the left to right shunting of blood causing volume overload of right side of heart and over circulation of pulmonary arteries.

This might result in pulmonary artery hypertension, right heart failure, and arrhythmias. Sometimes paradoxical embolus may occur due to right to left shunt.[5]

Pulmonary hypertension is characterized by > 40mmHg systolic and > 25mmHg mean PAP determined by right heart catheterization and can occur in many conditions.[6] The prevalence of PAH in ASD secundum varies from 9 to 35%, with age, size of defect, female sex and non-closed status are its predictors. [7,-9] Clinically, PAH in un-operated patients with ASDs has been associated with increased mortality, functional limitations, and atrial tachyar-rhythmias.[10-13]

Age as a risk factor for PAH in patients with ASD has been reported, which may be because of longer duration of shunting, physiologic increase in systolic PAP with aging, and/or interactions with co-morbidities. [7,12,14-17] Larger ASDs are associated with greater shunting from left to right atrium, with consequently increased ability to develop PAH.[12,18] This association has been established, As little is known to date about these associations in our population, therefore this study aimed to determine the correlation of age and size of defect in isolated ASD secundum with PAP measured by right heart catheterization.

METHODOLOGY

The cross sectional study was conducted at Cardiology Department, Lady Reading Hospital, Peshawar having a duration of five years from January 2012 to December 2016. Patients with all ages and either gender having isolated ASD secundum of all sizes were included.

Patients with ASD of all other types, associated valvular heart diseases, coexisting congenital heart defects, identifiable causes for PAH, including mitral valve disease, a left ventricular ejection fraction <50%, pulmonary thromboembolic disease, chronic obstructive pulmonary disease, interstitial lung disease, known sero-positivity to HIV, portal hypertension, and obstructive sleep apnea were excluded.

Eligible patients approaching through cardiology out patient department were included in the study by taking informed consent from the patients, parents or guardians after explaining the purpose and benefits of the study.

All patients were subjected to detailed history followed by routine physical examination. Trans-thoracic Echo-cardiography (Siemen's Acuson CV-70) was done for the diagnosis of ASD followed by TOE for the confirmation of diagnosis, measurement of the size and ruling out coexistent congenital heart defects.

Based on age, patients were divided into 6 groups (0-10, 11-20, 21-30, 31-40, 41-50, and >50 years). Based on ASD size, patients were divided into 2 groups i.e. up to 20mm and more than 20mm. Then these patients were subjected to cardiac catheterization under fluoroscopy.

Pulmonary artery pressures (PAP = systolic, diastolic, and mean) were recorded. PAH was considered present if systolic PAP was $\geqslant$ 40 mmHg or mean PAP $\geqslant$ 25 mmHg. Patients were classified according to systolic PAP and mean PAP by cardiac catheterization as having no (< 40 mmHg and < 25 mmHg), mild (40 to 49 mmHg and 25 to 40 mmHg), moderate (50 to 59 mmHg and 41 to 55 mmHg), or severe ($\geqslant$ 60mmHg and >55mmHg) PAH based on classification used by other studies.

The collected data was stored and analyzed in SPSS version 20 for windows. Continuous data like age, ASD size, and PAP (systolic, diastolic and Mean) were calculated as mean, and standard deviation. Categorical variables like age groups, gender, ASD size groups and PAP groups were represented as frequencies and percentages.

Correlation of age and ASD size with PAP groups were examined by Pearson correlation (2-tailed) and R value calculated. Stratified analysis was performed to control any effect modification due to different age, and size groups.

Stratified analysis were performed to determine the age, and defect size group that correlated best with pulmonary artery hypertension. R and p value were calculated.Binary Logistic Regression model was performed to determine significant predictors of PAH.

RESULTS

A total of 104 patients were included in this study with the mean age of 23.25 ± 12.2 years. About 36 (34.6%) were males . The mean size of defect was 23.36 ± 5.81 mm. Mean of systolic PAP and mean PAP were 37.88 ± 12.3 and 24.48 ± 8.19 mmHg, respectively with 49 (47.1%) patients had raised PAP. (Table 1)

The Pearson correlation R between age and PAP were 0.220, 0.261, and 0.288 for systolic, diastolic and mean PAP with p value of 0.025, 0.007, and 0.003 respectively. Similarly Pearson correlation R between size defect and PAP were 0.198 and 0.218 for systolic and mean PAP with p value of 0.044 and 0.026 respectively. R value between size and diastolic PAP was not significant. (Table 2).

The age, and defect size group that correlated best with pulmonary artery hypertension were 11-20 and 21-30 years and > 20mm as shown in Table 3. Binary logistic regression were significant for age with systolic and mean PAP i.e. p value of 0.002 and 0.018. (Table 4)

Table 1: Demographic Variables of Study Population (n=104)

Variable	MEAN	SD	FREQUENCY	%AGE
Age (years)	23.25	± 12.2	-	-
Age Groups				
0-10 years	-	-	16	15.4%
11-20 years	-	-	35	33.7%
21-30 years	-	-	23	22.1%
31-40 years	-	-	19	18.3%
41-50 years	-	-	9	8.7%
>50 years	-	-	2	1.9%
Gender				
Male	-	-	36	34.6%
Female	-	-	68	65.4%
ASD size (mm)	23.36	± 5.81	-	-
= 20mm	-	-	30	28.8%
>20mm	-	-	74	71.2%
Systolic PAP (mmHg)	37.88	± 12.3	-	-
Normal	-	-	55	52.9%
Raised	-	-	49	47.1%
Mild	-	-	29	27.9%
Moderate	-	-	14	13.5%
Severe	-	-	6	5.81%
Diastolic PAP (mmHg)	15.18	± 5.84	-	-
Normal	-	-	61	58.7%
Raised	-	-	43	41.3%
Mean PAP (mmHg)	24.48	± 8.19	-	-
Raised	-	-	49	47.1%
Mild	-	-	47	45.2%
Moderate	-	-	2	1.9%
Severe	-	-	0	0%

Table 2: Association of Age and ASD Defect Size with Pulmonary Artery Pressure in Study Population (n=104)

		Systolic PAP		Diastolic PAP		Mean PAP	
		Correlation value	Sig	Correlation value	Sig	Correlation value	Sig
Age	Pearson Correlation R	0.220	0.025	0.261	0.007	0.288	0.003
ASD size	Pearson Correlation R	0.198	0.044	0.171	0.082	0.218	0.026

Table 3: Stratified Analysis Displaying Different Age and Size Groups Correlation with PAH in Study Population (n=104)

	Systolic PAP		Diastolic PAP		Mean PAP	
	R	p-Value	R	p-Value	R	p-Value
AGE (years)						
0 – 10	0.005	0.986	0.301	0.257	0.358	0.173
11 - 20	0.373	0.027	0.605	0.000	0.531	0.001
21 - 30	0.507	0.014	0.640	0.001	0.619	0.002
31 - 40	0.025	0.918	0.283	0.241	0.044	0.859
41 - 50	0.464	0.208	0.667	0.050	0.495	0.176
>50	--	--	--	--	--	--
SIZE (mm)						
= 20	0.114	0.549	0.151	0.412	0.026	0.891
>20	0.250	0.032	0.125	0.288	0.087	0.463

Table 4: Binary Logistic Regression Model Showing Age and Defect Size for Determining PAH (n=104)

	Systolic PAP			Mean PAP		
	B	S.E	p-Value	B	S.E	p-Value
Age	0.059	0.019	0.002	0.043	0.018	0.018
Defect Size	0.056	0.039	0.152	0.072	0.039	0.064

DISCUSSION

The prevalence of PAH in our study was 47.1%, as compared to 58.6% of Haque, et al. study, most of whom were likely to be older and have larger defects.[20] About 39.7% of females in our study had pulmonary hypertension, compared to 55.1% of Haque et al. study.[20] This study showed that there is significant relationship of pulmonary artery pressure with age of the patient and size of defect.

Age as a risk factor in ASD patients for PAH has been proven previously .[7,12,14-16] With aging, there will be longer duration of left-to-right shunting, which causes physiological increase in pulmonary artery pressures. Secondly, interactions with other co-morbidities which occurred with aging may also play some role. Yong et al. showed that older age was independently associated with the development of at least moderate or severe PAH, a finding consistent in our study.[9] Most of these studies showed strong association in second and third decade, which has also been proved in our study. The prediction of PAH in unrepaired ASD with increasing age has been proved in this study.

It is certainly true that R-value and p-value in Humenberger, et al. study were quite more significant i.e. 0.65 and <0.0001, than our study i.e. 0.22 and 0.025, respectively. However, the sample they included were mostly elders with mean age of 49 ± 17.4 years, in contrast to our sample in which mean age was less than half of that i.e. 23.25 ± 12.2 years.[22] Moreover, they didn't compare mean PAP with age and lastly, they were unable to show prediction value of age in untreated ASD secundum patients.[22]

The relationship of defect size with systolic PAP has been reported in a study done by Yong.[9] But in this study, its correlation with both mean and systolic PAP has been reported. This is in contrast to the study done in less than 5 years children by Po Z, et al. which showed no relationship between ASD size and PAP.[21] A possible mechanism for raised PAP in our study may be increased flow through larger defect leads to pulmonary endothelial damage with resultant leukocyte activation and mediators release, causing vasoconstriction and vascular hypertrophy eventually.[19] However, prognostic significance of ASD defect size in terms of prediction of PAH is yet to be proved. Further studies are, of course, required to prospectively prove the prediction value of ASD defect size.

ASD of other types, and those with Eisenmenger syndrome and associated defects were not included, and not all patients with isolated ASD (for instance, absent superior or inferior rim who were not supposed to intervene percutaneously) were subjected to cardiac catheterization which are the limitations of this study. So to make a firm comment all ASD types and associated defects must be included.

CONCLUSION

Both age and defect size in isolated secundum ASD patients were significantly associated with systolic, diastolic and mean pulmonary artery pressure. Furthermore, pulmonary artery hypertension can be predicted by the age of patients,

which means elder un-operated ASD patients will have more PAH, but cannot be predicted by the defect size of ASD secundum patients.

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