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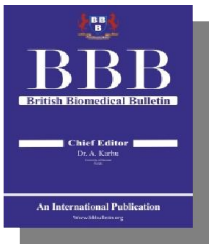

Original

Effect on Natural Course of Pulmonary Vascular Diseases in Isolated Atrial Septal Defect at High Altitude

Farooq Ahmad Ganie*[1], GH. Nabi Lone[1], Khursheed A khan[2], Rumana H. Makhdoomi[3], Hafeezulla Lone[1], Mohd Lateef Wani[1], Imran hafeez[2], Mohd Arif Kelam[4] and Masaratul-gani[5]

[1]*Department of cardiovascular and thoracic surgery, SKIMS, Soura, Kashmir - 190 011*
[2]*Department of cardiology, SKIMS, Soura, Kashmir - 190 011*
[3]*Department of pathology, SKIMS, Soura, Kashmir - 190 011*
[4]*Department of General medicine, SKIMS, Soura, Kashmir - 190 011*
[5]*Department of J and K Health services, SKIMS, Soura, Kashmir - 190 011*

A R T I C L E I N F O

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Corresponding author: Senior Resident Cardiovascular and thoracic surgery SKIMS Soura Srinagar
E-mail address:
farooq.ganie@ymail.com

A B S T R A C T

Background: Development of pulmonary vascular disease (PVD) has been considered a risk factor in the long-term course of ASD (atrial septal defect). Lung biopsy remains the gold standard to confirm the degree of severity in pulmonary vascular disease in patients with isolated ASD**.**

Objective: To determine the effect on natural course on pulmonary vascular diseases in isolated ASD patients at high altitude .To assess the histological degree of pulmonary vascular diseases in isolated ASD patients.

Material and Methods: This study was carried in the Department of Cardiovascular and Thoracic Surgery Sher-i-Kashmir Institute of Medical Sciences between 1st September 2010 to 31st November 2012.Patients with isolated ASD was included in the study. Isolated ASD Patients. Ostium secundum (OS) type. Patients residing at more than 3,500ft above sea-level. All patients were subjected to cardiac cath prior to surgery**.** Pulmonary vascular resistance was calculated in all patients. Lung Biopsy (which was taken during repair of ASD before patient was put on cardio pulmonary bypass) was sent for histopathological examination. Histopathological examination of the specimen was done by a single histopathologist. Severity of the pulmonary vascular disease was assigned a Score between 1 - 4.

Results: histopathological score of one was seen in none whereas 5.6% of the patients (n=2) had a histopathological score of 2; 44.4 % (n=8) had a histological score of 3 and 50% (n=9) had a histological score of 4. Most of our patients (94.4%; n=17) had a higher histopathological score of 3 & 4.

Conclusion: No formal study has been conducted so far to analyze the effect of high altitude on pulmonary vascular disease in Atrial Septal defect. All of our patients had established pulmonary vascular changes at the time of presentation. Severity of the pulmonary vascular disease as proved by histopathological

scoring and Cath data was quite high. This is in contrast with those residing at low altitude as reported in the literature. Therefore, it seems that high altitude has a strong bearing on the natural course of the disease, its complications and outcome after surgery.

Introduction

Congenital cardiac diseases account for 0.8 to 1% of all the live birth disorders [1] . Atrial septal defect (ASD) is a common recognized congenital cardiac anomaly in adults but is very rarely diagnosed and even less commonly results in disability in infants [2] . Ostium Secundum type – most common ASD may go unrecognized for decades because symptoms are mild or absent and physical signs are subtle. An atrial septal defect may first come to light on a routine chest X-ray[3]. Patients usually are asymptomatic early in life, although occasional reports exist of congestive heart failure and recurrent pneumonia in infancy [2]. Dyspnoea and fatigue are earliest symptoms of an Osteum Secondum ASD[4,5]. Recurrent lower respiratory tract infection is common especially in children. Atrial arrythmias, pulmonary obstruction and heart failure are exceedingly rare in paediatric age group in contrast to adults where these are present more often. The timing of operative intervention is critical since the presence of pulmonary vascular disease manifest as severe elevation in pulmonary vascular resistance (PVR), is the primary impediment to a successful outcome[6,7]. Choosing the best final for surgery is difficult because clinical[8] electrocardiographic[9], echo-cardiographic[10] and hemodynamic[11]. Findings do not always distinguish reversible from irreversible disease. It is not possible to predict in which patient pulmonary vascular disease will progress despite successful surgical repair[12,11] nor is it possible to identify those who will survive but with an abnormal pulmonary circulation as judged by inappropriate increase in pulmonary arterial pressure on exercise [13] .Cardiac catheterization: is considered the gold standard for the diagnosis of Pulmonary hypertension (Ph)[14] . Pulmonary biopsy: is reserved for cases where histopathological diagnosis is necessary such as vasculitis granulomatous disease veno-occlusive disease pulmonary vascular disease in congenital heart disease [15] .atrial septal defect (ASD) is one of the most frequent lesions in the spectrum of congenital heart disease in adulthood. Due to the lack of specific and severe symptoms diagnosis can be missed during childhood. Development of pulmonary vascular disease (PVD) has been considered a risk factor in the long-term course of ASD. Lung biopsy remains the gold standard to confirm the degree of severity in pulmonary vascular disease in patients with isolated ASD.[15]

Materials and Methods

This study was carried in the Department of Cardiovascular and Thoracic Surgery Sher-i-Kashmir Institute of Medical Sciences between 1st September 2010 to 31st November 2012.Patients with isolated ASD were included in the study. Isolated ASD Patients. Ostium secundum (OS) type. Patients residing at more than 3,500ft above sea-level. Exclusion criteria were Age more than 36 years and less than 5 years. ASD with associated other cardiac anomalies. All patients were subjected to cardiac cath prior to surgery**.** Pulmonary vascular resistance was calculated in all patients. Lung Biopsy (which was taken during repair of ASD before patient was put on cardio pulmonary

bypass) was sent for histopathological examination. Histopathological examination of the specimen was done by a single histopathologist. Severity of the pulmonary vascular disease was assigned a Score between 1-4.

The scoring was done as follows:

- No intimal thickening ……score of 1.
- Proliferating intimal cells ….....score of 2.
- Fibrously thickened intima…...score of 3.
- Tunica media destroyed by mural necrosis…….... score of 4.

Results and Observations

Our study included a total of 18 patients. The mean age of our patients was 21.7 ± 7.4[12,37] years with youngest patient being 12 years and oldest being 35 years old. tab.1. 55.2 % of the patients were in their 2nd decade of life where as 33.5 % were in their 3rd decade of life. In our study 33.3% of the patients (n=6) were males and 66.7% were females (n=12). tab.2 . In our study the mean weight of patients was 55.3 ± 6.9 kgs with a minimum of 40kgs and maximum of 65kgs

The mean BSA of our studied subjects was 1.54 ± 0.12 with a minimum of 1.33 and a maximum of 1.68 m^2. Most of our patients (50%) were having NYHA class I symptoms at presentation whereas 38% were in NYHA class II and 11% in NYHA class III. None of our patients was having class IV symptoms at presentation. The most common abnormality on ECG IN OUR patients was a right axis deviation and right ventricular hypertrophy (66.6%; n=12). PR interval prolongation was present in 44% of the patients and 22% patients had rhythm abnormality (atrial fibrillation). All our patients were having pulmonary arterial hypertension with 55.4% (n=12) having severe PAH and 44.6% (n=8) having moderate PAH. None of our patients was having mild PAH on presentation. In our study correlating the severity of pulmonary arterial hypertension with the defect size revealed that in 8 patients with defect size of > 30mm, 5 patients (62%) were having severe pulmonary hypertension and 3 (38%) were having moderate pulmonary hypertension on echocardiography.

In our study the mean pulmonary arterial pressure (mPAP) on cardiac catherization was 54.5mmHg with a minimum of 35 mmHg and maximum of 70 mmHg whereas mean left atrial pressure (m LAP) was 7.6 mmHg with a minimum of 5 mmHg and maximum of 10 mmHg. The mean Qp/Qs ratio in our patients was 2.7 with a minimum of 2.06 and maximum of 4.5 and the mean pulmonary vascular resistance (PVR) was 5.1 woods units with a minimum of 2.61 and maximum of 7.1 woods units.

In our study subjects the histopathological score of one was seen in none whereas 5.6% of the patients (n=2) had a histopathological score of 2; 44.4 % (n=8) had a histological score of 3 and 50% (n=9) had a histological score of 4. Most of our patients (94.4%; n=17) had a higher histopathological score of 3 & 4. Correlating the mean pulmonary artery pressure (54.50 ± 10.72) with pulmonary vascular resistance (5.13±1.44) the p value was statistically significant (p=0.03) signifying a direct correlation between mPAP and PVR. The correlation between sPVR (5.13±1.44) and histopathological score (3.44±0.61) was also statistically significant (p= 0.008) signifying a higher histopathological score with increasing pulmonary vascular resistance. Correlation of histopathological score and age was also statically significant (p=0.008) suggesting a higher histopathological score with increasing age

Discussion

Pulmonary arterial hypertension, a common complication in congenital heart disease patients with left to right shunt is one of the principal determinants of the clinical

course and the feasibility of surgical repair [16]. Left to right shunt results in increase in pulmonary blood flow, which causes a progressive elevation of pulmonary vascular tone and/or obstructive obliterative structural changes in the pulmonary vascular bed. If not treated this eventually increases pulmonary vascular resistance and presents as increased pulmonary arterial pressure[17-19]. In these patients; surgical outcome in operable cases depends on the degree of pulmonary arterial pressure and pulmonary vascular resistance. In patients with high pulmonary arterial pressure, there may be a reversal of shunt leading to inoperability [7,20] . It would be ideal to perform corrective surgery before the pulmonary vascular changes become irreversible, but there is no gold standard for assessing the severity of pulmonary vascular disease. Intra-operative lung biopsy is a technically simple investigation that can be used for the same purpose[7,21] . Our study included a total of 18 patients. With youngest patient being 12 years and oldest being 35 years old. In our study 33.3% of the patients (n=6) were males and 66.7% were females (n=12). The mean age of patients in our study was 21.7 years which was much less than reported by Yamaki *et al* in their studies in 1986 [22] and 1987 [23] in whom the mean age was 36 and 34 years. Our patients presented at a relatively younger age which probably can be attributed to high altitude with its consequent hazards leads to early symptoms. However the sex distribution was almost similar between our patients of ASD with PAH (66.7% females and 33.3% males) and that reported by Yamaki *et al* in their studies in 1986 and 1987 (60% females and 40% females).

In our study the mean pulmonary arterial pressure (mPAP) on cardiac catherization was 54.5 mm Hg with a minimum of 35 mmHg and maximum of 70 mmHg whereas mean left atrial pressure (m LAP) was 7.6 mmHg with a minimum of 5 mmHg and maximum of 10 mmHg. The mean Qp/Qs ratio in our patients was 2.7 with a minimum of 2.06 and maximum of 4.5 and the mean pulmonary vascular resistance (PVR) was 5.1 units with a minimum of 2.61 and maximum of 7.1 woods units. Correlating the mean pulmonary artery pressure (54.50 ± 10.72) with pulmonary vascular resistance (5.13±1.44) the p value was statistically significant (p=0.03) signifying a direct correlation between mPAP and PVR. Our findings were comparable to that of Reddy *et al*[24]. M Vogel *et al*[25]. Who reported an increase in the incidence of raised pulmonary artery pressure and resistance between age groups 18 to 40 and over 40 years was observed, but there was no further increase of incidence in patients over 60 years old. In our study subjects the histopathological score of (1) was seen in none whereas 5.6% of the patients (n=2) had a histopathological score of (2) 44.4 % (n=8) had a histological score of (3) and 50% (n=9) had a histological score of (4). Most of our patients (94.4%; n=17) had a higher histopathological score of 3 & 4. The correlation between mPVR (5.13±1.44) and histopathological score (3.44±0.61) was also statistically significant (p= 0.008) meaning herby higher histopathological score with increasing pulmonary vascular resistance. Correlation of histopathological score and age was also statically significant (p=0.000) suggesting a higher histopathological score with increasing age. However our results were not consistent with George Cherian *et al*[26] who reported that Pulmonary hypertension was present in only 13% of patients under 10 years and in only 14% aged 11 to 20 years. This can be easily explained by the fact that his study group did not hail from high altitude. The study was conducted in patients residing at low altitude. Our results were contrary to what has been reported by Shigeo Yamaki *et al*[23] in their study they found a higher percentage of score of (1) and (2) findings on histopathology. But

the study was conducted in population residing at low altitude living near sea level. Our higher grades of (3) and (4) scores on histopathology can be attributed to the fact that our patients were residing at a high altitude from sea level.George H. Khoury, *et al*[27] reported a similar incidence of associated pulmonary hypertension in the children living at moderately high altitude (9.7 per cent) which is higher than has usually been found in studies of children living near sea level. Conclusion: Atrial septal defect is one of the most common congenital heart defects in adults. The debate about the incidence of pulmonary vascular disease, the severity of pulmonary vascular disease in patients living at high altitude from sea level, ideal age for closure and prevention of pulmonary vascular disease is still going on. But the exact incidence of pulmonary artery diseases in patients with atrial septal defect living at high altitude appears variable; however to our knowledge there has not been a formal study which has studied the incidence of pulmonary hypertension in patients residing at high altitude. We have concluded that the incidence of pulmonary vascular disease is very high in patients residing at high altitude as our all patients had pulmonary vascular changes at the time of presentation. The severity of the pulmonary vascular disease in our patients was on higher side as reported in literature. This Signifies that patients residing at high altitude develop early the pulmonary vascular disease and the severity is more.

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Table 1. Cardiac Cath parameters in studied subjects with respect to age and sex

Age(yrs)	Sex	CARDIAC CATH PRESSURES					
		m PAP	m LAP	Qp	Qs	Qp/Qs	PVR
18	F	60	8	9.92	3.89	2.5	5.25
16	F	52	10	8.7	3.2	2.7	4.82
21	F	60	8	10	4.2	2.3	5.2
35	M	45	9	12	5.1	2.4	3
22	F	48	6	10	4.5	2.2	4.2
35	M	35	8	7.9	3.6	2.1	3.41
32	M	38	6	9.5	4	2.37	3.36
17	F	40	6	13	4.9	2.65	2.61
23	M	62	8	12	4	3.1	4.5
19	F	48	6	6.8	3.3	2.06	6.17
20	F	68	8	12	2.79	4.3	5
13	M	64	5	11.8	2.6	4.5	5
14	F	52	10	6	2.8	2.1	7
12	F	70	8	9	3	3	6.89
32	F	60	10	7	3.11	2.5	7.1
22	F	56	6	9	3	3	5.5
19	F	53	8	6.8	3.3	2.06	6.61
20	M	70	8	9	3	3	6.89

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Table 2. Cardiac Cath parameters in studied subjects

	N	min	max	Mean
m PAP	18	35	70	54.5
m LAP	18	5	10	7.6
Qp	18	6	13	9.4
Qs	18	2.6	5.1	3.5
Qp/Qs	18	2.06	4.5	2.7
PVR	18	2.61	7.1	5.1

Table 3. Histopathological Findings in studied subjects

	Score	N	%
Histopathological Score	1	0	0
	2	1	5.6
	3	8	44.4
	4	9	50
Total		**18**	**100**

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