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## Editorial

# Relationship of high altitude and congenital heart disease



### Keywords:

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chronic right ventricular pressure overload.<sup>3</sup> Unacclimatized person at high altitude develops hypoxic pulmonary vasoconstriction and rapid ascent can lead to subacute/chronic mountain sickness (Monge's disease) and high altitude pulmonary edema. This original article focuses on these aspects at physiological level and also in various cardiorespiratory diseases with special focus on congenital heart disease (CHD).

## 1. High altitude

High altitude typically refers to elevations over 2000 m/6360 ft, but no single value is an adequate definition for all patients. During the ascent to high altitude, barometer pressure declines exponentially, and in keeping with Dalton's law, the partial pressure of oxygen falls accordingly.

Pressure chambers and air travel serve as a poor option to study the effect of hypoxemia on human physiology. Most natural is the systemic effects of high altitude on the natives and persons visiting hilly areas from low lands.<sup>1</sup>

The basis of the effects of high altitude comes from studies performed on aviators, mountaineers and natives of high lands.

More than 140 million people worldwide live at more than 2500 m above the sea level and around 80 million live in Asia.

## 2. High altitude and physiological adaptation

Peripheral chemoreceptor afferent activity rises hyperbolically as hypoxia increases and there is a phenomenon of ventilatory acclimatization. Initially due to acute hypoxia, heart rate increases, along with myocardial contractility and cardiac output. Later on, cardiac output falls at rest and on exercise with decrease in left ventricular work but increase in right ventricular work and pulmonary pressures.<sup>2</sup> Coronary circulatory flow increases along with progressive changes in right ventricular function, rising pulmonary pressures and

## 3. High altitude and cardiovascular illness

Although high altitude has a negative effect on preexisting respiratory diseases, we will focus on cardiovascular illnesses. High altitude has an adverse effect on the person from low altitude with rapid ascent and also on the person with underlying coronary artery disease, congestive heart failure, arrhythmias, systemic hypertension, and respiratory illness.<sup>4</sup>

## 4. High altitude and congenital heart diseases

As the original article highlights, high altitude has been linked with high incidence of CHDs like patent ductus arteriosus (PDA) and atrial septal defect (ASD) and their progression.<sup>5</sup> Both PDA and ASD are suspected clinically and later confirmed on investigations, especially Echocardiography. Transthoracic Echocardiography has limitations in detecting all cases of ASD, as there is a possibility of underestimation of this lesion. In the Baltimore-Washington infant study (Ferencz C, Rubin JD, *Am J Epidemiol.* 1985 Jan;121(1):31–6.), ASD was found in 0.0317%, and in the New England Regional Infant Cardiac Program (Donald C. Fyler, *Pediatrics* 1980), it was 0.0073%. The prevalence of ASD at the three high altitudes sites in the study at Qinghai Province 1988 was 2.4%.<sup>6</sup> The prevalence of PDA was 0.0089% and 0.01381% in Baltimore-Washington & New England Study. It was 1.2% at high altitude in Qinghai Province, which is much higher than the two larger studies. Failure of lower oxygen tension to constrict the ductus leads to patency of ductus arteriosus while the presence of high pulmonary vascular

**Table 1 – Percentage-wise specific echocardiographic diagnosis of CHD in Dharan.<sup>11</sup>**

Diagnosis	Number	Percentage
<b>Acyanotic heart disease</b>	<b>58</b>	<b>69</b>
VSD	49	58.3
ASD	4	4.8
ECD	2	2.4
Dextrocardia	3	3.6
<b>Cyanotic heart disease</b>	<b>26</b>	<b>31</b>
TOF	11	13.1
TAPVC	3	3.6
TGA with VSD	1	1.2
Unspecified	11	13.1
<b>Grand total</b>	<b>84</b>	<b>100</b>

VSD: ventricular septal defect, ASD: atrial septal defect, ECD: endocardial cushion defect, TOF: tetralogy of Fallot, TAPVC: total anomalous pulmonary venous connection, TGA: transposition of great arteries.

Adapted from: Incidence of congenital heart disease in tertiary care hospital, Shah GS, Singh MK, Pandey TR; Shah GS, Singh MK, Pandey TR; Kathmandu University Medical Journal (2008), Vol. 6, No. 1, Issue 21, 33-36.

resistance and right atrial pressure at high altitude inhibits early closure of foremen ovale. With physical development of the child and stretching of fossa ovalis along with incompetence of flap, ASD is established. Analogy can be drawn from high prevalence of ASD in TOF as the right ventricular pressure is high and right ventricular compliance is low from birth (JACC, 1988). At high altitude, these two anomalies are due to hypoxemia-induced failure of normal neonatal processes. Even the type of PDA at highland as compared to lowland is different, with larger ductal diameter, Type A lesions and high pulmonary arterial pressure (Bialkowski, 2003)<sup>7</sup> being more challenging for catheter closure.

The prevalence of CHD in India varies from 2.25 to 5.2/1000 live births.<sup>8</sup>

High altitude gives insight into the pathophysiology of both cyanotic and acyanotic heart disease in an interesting way. The patients with cyanotic CHD have more blunted hypoxic ventilatory response, which develops as early as 7-8 years, while the most blunted ventilatory response is seen in patients with maximum desaturation, which is corrected

**Table 2 – Percentage-wise, sex-wise and age-wise specific echocardiographic diagnosis of CHD in Srinagar, data from Skims, Srinagar.<sup>12</sup>**

CHD type	≤1 month		2 months to 1 year		2-5 years		6-12 years		>12 years		Total		Grand total (%)
	Male	Female	Male	Female	Male	Female	Male	Female	Male	Female	Male (%)	Female (%)	
<b>Cyanotic</b>													
TOF	10	2	13	10	4	5	2	1			30	18	48 (48)
TGV	10	1	5	7		2	1		1		17	10	27 (27)
Single ventricle	2		4	1							6	1	7 (7)
TAPVC	1		2	1	2						5	1	6 (6)
Tricuspid atresia	1	1									1	1	2 (2)
DORV	2	2	2	1		1	1				5	4	9 (9)
Truncus arteriosus									1		1		1 (1)
Total cyanotic CHD	26	6	26	20	6	8	4	1	2		65 (7.5)	35 (4.0)	100 (100.0)
<b>Acyanotic</b>													
ASD	31	29	37	40	17	16		2	1	3	86	90	176 (22.9)
VSD	20	25	64	66	29	19	7	7	1	3	121	120	241 (31.4)
VSD + (PDA/ASD/PFO)		2	16	4			1				17	6	23 (2.9)
PDA	47	39	30	34	14	12	1	6		1	92	92	184 (23.9)
AV canal defect	4	5	7	12	1	2	1				13	19	32 (4.1)
PS	7	3	15	13	7	6	3	1	1		33	23	56 (7.3)
Bicuspid aortic valve	1		1			1		1			2	2	4 (0.5)
Dextrocardia	2		2		1						5		5 (0.6)
Cardiomyopathy	1		7	9	4	7	1	2			13	18	31 (4.0)
Aortic stenosis	1		1		1			3			3	3	6 (0.7)
MVP MR	2		3	1	1	1	1				4	4	8 (1.0)
Coarctation of aorta									1		1		1 (0.1)
Total	116	103	180	181	75	64	15	22	4	7	390 (45.0)	377 (43.5)	767 (88.6)
Grand total	142	109	206	201	81	72	19	23	6	7	455 (52.4)	412 (47.5)	867

CHD: congenital heart disease, TOF: tetralogy of Fallot, TAPVC: total anomalous pulmonary venous connection, DORV: double outlet right ventricle, ASD: atrial septal defect, VSD: ventricular septal defect, PDA: patent ductus arteriosus, PFO: patent foramen ovale, AV: atrioventricular, PS: pulmonary stenosis, MVP: mitral valve prolapse.

Adapted from: Khurshid Ahmed Wannani, Naveed Shahzad, Prevalence and spectrum of congenital heart diseases in children; <http://www.heartindia.net/article.asp?issn=2321-449x;year=2014;volume=2;issue=3;page=76;epage=79;aulast=Wannani>.

**Table 3 – Table showing relative prevalence of CHD at high altitudes.<sup>13</sup>**

Altitude (meters above sea level)	Gender	Predominant diagnosis
2260	M	PDA
	F	ASD
3000	M	ASD
	F	RHD (MR + AR)
4500	M	PDA, pulmonary hypertension
	F	ASD

once the patient is surgically treated and normalized. Another important distinction between native highlander and patients with cyanotic heart disease is the fact that though both have arterial hypoxemia, highlanders have lowered alveolar oxygen tension while patients with cyanosis have normal oxygen tension.<sup>9</sup> For patients with VSD, left to right shunting of blood decreases at high altitude. Patients with single ventricle physiology and postoperative Glenn and Fontan tolerate high altitude very poorly due to hypoxia and increased pulmonary vascular resistance.<sup>10</sup>

Studies performed in Northern India, especially the hilly areas of Jammu and Kashmir, India, revealed that 88.5% of all CHD were the acyanotics, and 11.5% were cyanotic heart patients. Among the acyanotic heart diseases, VSD was the most frequent lesion seen in 31.2%, followed by PDA in 24.3% children. Among the cyanotic heart diseases, TOF was the most frequent cyanotic heart disease seen in 48.0% patients. The prevalence of CHD was 1.1/1000 hospital attending patients.<sup>11</sup>

Another database from the Himalayan area showed that acyanotic heart disease was detected in 69% cases while cyanotic heart disease was detected in 31% cases. Among acyanotic heart disease, ventricular septal defect (VSD) was found in 58.3%, ASD in 4.8%, endocardial cushion defect (ECD) in 2.4%, and dextrocardia was found in 3.6%. Among cyanotic heart disease, tetralogy of Fallot (TOF) accounted in 13.1%, total anomalous pulmonary venous connection (TAPVC) in 3.6%, transposition of great arteries (TGA) with VSD in 1.2% and unspecified cases of heart disease were found in 13.1%. The prevalence of CHD was 5.8/1000 hospitalized children.<sup>12</sup>

These values are at par with the results shown in the original article (Tables 1 and 2).

Table 3 denotes the relative prevalence of CHD at high altitudes and the predominant cardiac anomaly at high altitude. The combined prevalence of ASD and PDA increased progressively with altitude. In addition, there may have been deaths caused by CHD again reducing the prevalence. Both of these factors led to underestimation of the prevalence of many other CHDs.

Operability issues of highlanders with CHD depends on the degree and reversibility of pulmonary hypertension which can be decided on the basis of clinical examination, ECG, chest X-ray, and cath lab studies.

Surveillance data from Sichuan Basin also reveal geographical clustering of CHD possibly due to high ecological exposure

to heavy metals like cadmium, arsenic, lead, as well as contribution from ammonia-nitrogen pollution, the costal effect.<sup>14</sup>

## 5. Conclusions

In India, there is a strong possibility of underreporting of cases due to lack of medical care and fatalities with no proper record of deaths due to CHD, as well as lack of trained personnel to carry out reliable echocardiographic studies.

The relevant original article also highlights the practical problems in India, which lead to underestimation of true prevalence of CHD at high altitude.

## Conflicts of interest

The author has none to declare.

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