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RETROSPECTIVE OBSERVATIONAL STUDY OF HIGH ALTITUDE PULMONARY EDEMA CASES TREATED IN A HIGH ALTITUDE TERTIARY CARE SETUP

Anaesthesiology

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ABSTRACT

Background- High altitude pulmonary edema (HAPE) is an altitude sickness that can be life threatening if not detected and managed correctly. HAPE is a noncardiogenic pulmonary edema which typically occurs in lowlanders who ascend rapidly to altitudes greater than 2500-3000 m. Early symptoms of HAPE include a nonproductive cough, dyspnoea on exertion and reduced exercise performance. Later, dyspnoea occurs at rest. HAPE mainly occurs due to exaggerated hypoxic pulmonary vasoconstriction and elevated pulmonary artery pressure. It has been observed that HAPE is a high permeability type of edema occurring also due to leaks in the capillary wall ('stress failure'). Slow descent is the most effective method for prevention. The most common cause of death related to high altitude, HAPE is completely and easily reversed if recognized early and treated properly.

Methods: We performed a serial retrospective study of 220 patients with HAPE admitted to our hospital in 2019. We reviewed the medical records and summarized the clinical, geographical and ascent characteristics of these cases, disease grading and average stay in hospital.

Results: Among 220 patients of HAPE 58% were mild 21% moderate 8% severe and 5% serious. Recurrent cases were 8%. The maximum cases were in the age group 25-30 years 24.54%. Average stay in hospital was 7.4 days.

Conclusion: Age was not found to be associated with increased or decreased risk of HAPE, nor was number of days spent in high altitude, this underlines the significance of proper acclimatization. Going to higher altitudes increased the risk of HAPE.

KEYWORDS

High Altitude Pulmonary Edema, High altitude medicine, critical care.

INTRODUCTION:

The sublime and savage beauty of the mountains call forth many mountaineers to experience its majestic peaks. From historical times when high altitude mountains were called "Headache mountains", we have come a long way in identifying the whole spectrum of altitude sickness.[1] High-altitude illness may result from short-term exposures to altitudes in excess of 2000 m (6560 ft). This illness comprises a spectrum of clinical entities that are probably the manifestations of the same disease process. High-altitude pulmonary edema (HAPE) and cerebral edema are the most ominous of these symptoms, while acute mountain sickness, retinal hemorrhages, and peripheral edema are the milder forms of the disease. The rate of ascent, the altitude attained, the amount of physical activity at high altitude, and individual susceptibility are contributing factors to the incidence and severity of high-altitude illness.

High altitude pulmonary edema (HAPE) is an altitude sickness that can be life threatening if not detected and managed correctly. The symptoms of HAPE typically appear 2 to 3 days after reaching altitudes of 2500 m or greater.[2]

Pathophysiology: HAPE is a non-cardiogenic form of pulmonary edema resulting from a leak in the alveolar capillary membrane. The various mechanisms believed to be responsible are pulmonary arterial vasoconstriction resulting in circulatory shear forces and a consequent permeability leak and antidiuresis possibly mediated by increased antidiuretic hormones, which contribute to fluid retention. The inciting factor appears to be excessive hypoxia.[3]

The mechanism of pulmonary arterial vasocnstriction can be explained by Euler-Liljestrand mechanism. It is a natural reflex that affects only the lungs in hypoxia and was first described by Euler and Liljestrand in 1946.[4] Vaso-constriction in this context exclusively affects the pulmonary circulation. In all other vessels of the body, hypoxia causes vasodilation. As the pulmonary circulation contracts, all other vessels dilate to allow more oxygen-carrying blood to pass through. The non-homogenous pulmonary vasoconstriction results in areas of hyperperfusion leading to a stress failure of the pulmonary endothelium and extravasation of protein-rich fluid into the pulmonary interstitium and alveoli. The hypoxic pressor response is primarily due to the vasoconstriction of small muscular intrapulmonary arteries (IPA) with an internal diameter of 100–500 m.[5] Exposure of the basement membrane to the protein-rich edema fluid results in secondary inflammation, activation of coagulation and generation of microthrombi in the lungs. Pre-existing inflammation e.g. pre-existing Viral infection may make the endothelium more prone to disruption.

Spirometric studies have shown that with increasing altitude, both forced vital capacity (FVC) and forced expiratory volume in one second (FEV1) are reduced by up to 25% (74.8% / 74.6% of baseline. These findings were consistent with increasing pulmonary restriction at high altitudes. Portable spirometry may provide clinically relevant information (impending pulmonary edema) in high-altitude travelers.[6,7,8]

HAPE generally begins with a subtle, nonproductive cough, shortness of breath with exertion, and difficulty walking uphill.

A cardinal clinical feature of HAPE is the early progression from dyspnea with exertion to dyspnea at rest. In about 50 percent of cases, HAPE is accompanied by acute mountain sickness.[9]

Table 1: Clinical criteria for diagnosing High Altitude Pulmonary Edema (HAPE)10

1. History of recent gain in altitude along with any two of the following symptoms
(a) Cough
(b) Dyspnoea at rest
(c) Chest discomfort
(d) Weakness / fatigue

AND

2. Any two of the following signs
(a) Crackles / wheeze at least one lung field
(b) Central cyanosis
(c) Tachycardia
(d) Tachypnoea

Table 2 : Classification of HAPE based on severity [11]:

Grade	Symptoms	Heart rate (beats/min)	Respiratory rate (breaths/min)	Chest X-ray
Mild	Dyspnoea on moderate exertion Able to perform light activity	< 110	< 20	Minor opacities involving < ¼ of one lung field

Moderate	Dyspnoea at rest Weakness, fatigue on slight effort, cannot perform light activity Headache with cough	110 – 120	20 – 30	Opacities involving at least ½ of one lung field
Serious	Severe dyspnoea, Loose recurrent productive cough Wheezy, difficult respiration Obvious cyanosis Weakness Headache Nausea at rest	121 – 140	31 – 40	Opacities involving at least ½ of each lung field or unilateral exudates involving all of one lung field
Severe	Clouded consciousness, stupor/ coma Unable to stand/ walk Severe cyanosis Bubbling rales Copious bloody sputum Severe respiratory distress	> 140	> 40	Bilateral opacities involving > ½ of each lung field

Treatment can be divided into Pharmacological and Non-Pharmacological.

Nonpharmacologic interventions:
oxygen is first-line therapy for HAPE and should be provided first. Second is rest and warmth, strenuous physical exertion and cold stress both elevate PA pressure and can exacerbate HAPE. In remote high-altitude settings where supplemental oxygen is unavailable, descent should begin as soon as HAPE is suspected.[12] If available lightweight portable hyperbaric chambers may be life-saving.[13]

The use of a breathing mask providing pressure on expiration (EPAP) a type of continuous positive airway pressure (CPAP) has shown to improve gas exchange in HAPE and is useful as a temporizing measure.[14]

Pharmacologic interventions:
Acetazolamide - Used mainly for prophylaxis.
Nifedipine - Nonspecific calcium channel blocker that acts by reducing pulmonary vascular resistance and PA pressure, it is used for treatment of moderate to severe HAPE. Clinical trials have shown no benefit from it's use. [15]

Tadalafil and **sildenafil** - Phosphodiesterase-5 (PDE-5) inhibitors that augment the pulmonary vasodilatory effects of nitric oxide by inhibiting the degradation of cyclic guanosine monophosphate (cGMP), the intracellular mediator of NO. They have been shown to be effective as prophylaxis for HAPE, but neither has been studied as treatment.[16]

Salmeterol - Long acting β agonist has been found to prevent HAPE in 50 percent of subjects in one small study, and thus appears less effective than other agents.[17]

Dexamethasone - Although glucocorticoids may have a role in prophylaxis, they have not been studied as treatment for HAPE.

MATERIALS AND METHODS:
We performed a serial retrospective study of 220 patients with HAPE admitted to our hospital after getting clearance from ethics comittee in 2019. We reviewed the medical records and summarized the clinical, geographical and ascent characteristics of these cases, days spent in high altitude and average stay in hospital.

RESULTS:
Incidence: In our hospital total admissions for HAPE in 2019 were 220 out of which 58% were mild 21% moderate 8% severe and 5% serious. Recurrent cases were 8%.

21% required ICU admission and 5% were on CPAP.
Total number of days spent in hospital on average was 7.4 days.

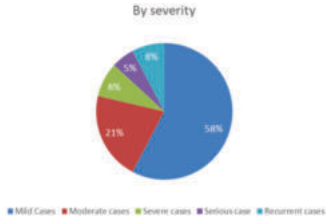

Fig 1: Distribution of total cases with regards to severity

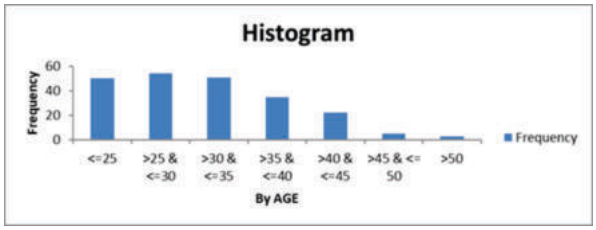

Fig 2: Distribution with regards to age group

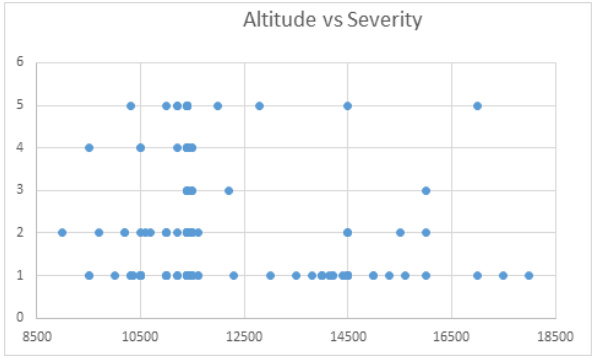

Fig 3: Distribution of cases at various altitudes

X axis – Altitude , Y axis- 1 Mild 2 Moderate 3 Serious 4 Severe 5 Recurrent HAPE

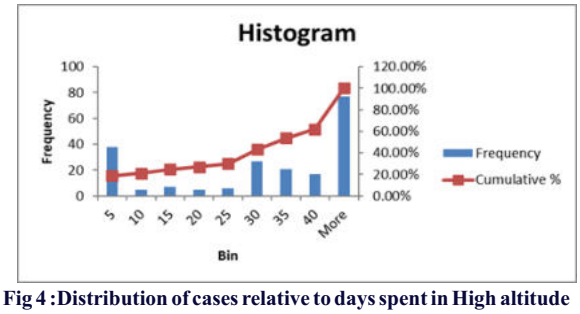

Fig 4 :Distribution of cases relative to days spent in High altitude

DISCUSSION:
Most of the cases 58% fall under mild HAPE and are treatable with bed rest and O2. Age was not found to be associated with increased or decreased risk of HAPE, nor was number of days spent in high altitude this underlines the significance of proper acclimatization. Going to higher altitudes increased the risk of HAPE. Once the patients were admitted to our hospital for HAPE the average number of days spent as inpatient was 7.4.

Apart from encountered stresses like rapid ascent, cold, exercise, viral infection other factors also affect susceptibility. Genetics, ↓ NO synthesis, blunted hypoxic ventilatory response, brisk hypoxic pulmonary vascular response, ↑ sympathetic tone, decreased clearance, uneven HPV.[11] In an unselected population airlifted to an altitude of 5500m incidence of HAPE was up to 15%.[18]

A Cochrane systematic review in 2018 concluded that there was limited evidence to determine the effect of non-pharmacological and pharmacological interventions in treating acute high altitude illness. However, the clinical benefits and harms related to these potential interventions remain unclear.[19] Most of the studies included in this systematic review were conducted in Northern Alps none in India.

A study was conducted in Leh in 2016 on whether patients with HAPE needed any other intervention apart from oxygen. The trial compared three modalities of therapy (Therapy 1: O2 with oral dexamethasone 8□mg q8 hours [n□=□42], Therapy 2: O2 with sustained release oral nifedipine 20□ mg q8 hours [n□ =□ 41], and Therapy 3: only O2 [n□ =□ 50]). Bed rest was given to all patients. The study concluded that oxygen and bed rest alone are adequate for HAPE and adding either dexamethasone or nifedipine does not hasten recovery.[20] Drug prophylaxis for prevention of HAPE should only be considered for individuals with a prior history of HAPE.

In our setup bed rest and O2 continue to be the therapy for all mild and moderate cases with addition of nifedipine and CPAP for severe and refractory cases of HAPE. Education regarding altitude illness is very important in preventing morbidity and mortality.

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Conflict Of Interest: None

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