

Pulmonary Embolism at High Altitude: Analysis of Risk Factors

Naimat Ullah Khan, Muhammad Adil, Muhammad Zaman, Abdul Rahim Palwa*, Muhammad Tahir**, Muhammad Rameez Nawaz

Combined Military Hospital Skardu/National University of Medical Sciences (NUMS) Pakistan, *Armed Forces Institute of Radiology & Imaging/
National University of Medical Sciences (NUMS) Rawalpindi Pakistan, **Rahbar Medical and Dental College, Lahore Pakistan

ABSTRACT

Objective: To analyze the risk factors for pulmonary embolism stationed at high altitudes with high altitude as one of the determinants.

Study Design: Retrospective longitudinal study.

Place and Duration of Study: Combined Military Hospital Skardu Pakistan, from Jan 2016 to Jan 2020.

Methodology: A total of 25 consecutive cases with pulmonary embolism reported to this hospital during the study period were enrolled. Medical records of all patients were retrospectively analyzed to determine the risk factors. In addition, patient demographic data, clinical features, and laboratory and radiological findings were recorded.

Results: Mean age of the patient was 30.68 ± 5.37 years with a range from 23 to 40 years, the mean height of deployment was 17223.00 ± 3577.00 feet, while the mean duration of stay was 53.92 ± 44.76 days. Dyspnoea (84%) was the commonest clinical presentation followed by palpitation, chest pain, headache and haemoptysis. Most patients (88%) were non-smokers, while no patient had known significant risk factors. Thrombophilia and vasculitic screening were negative for all patients. In the absence of any significant hereditary or acquired risk factor, high altitude remains the only thrombogenic risk factor patients deployed at heights.

Conclusion: Stay at a high altitude is a major risk factor for pulmonary embolism in young patients without any other known risk factor.

Keywords: High altitude, Pulmonary embolism, Thrombotic diseases.

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INTRODUCTION

Thrombotic events are comparatively common in the high-altitude area and are known to occur in young patients stationed at heights without obvious risk factors associated with a hypercoagulable state at sea level. However, individuals are exposed to potential thrombogenic risk factors at high altitudes. Extremes of temperature, hypoxia, immobility, dehydration and smoking leading to a hypercoagulable state are impending factors leading to thrombotic states like cerebral venous sinus thrombosis, pulmonary embolism, deep vein thrombosis, splenic and retinal vein thrombosis.¹

Venous Thromboembolism comprising deep venous thrombosis and pulmonary embolism (PE) is the most commonly diagnosed cardiovascular event after myocardial infarction and stroke. PE is a common entity with varied manifestations ranging from benign to fatal. Acute PE leads to about 10,000 deaths annually in the US, only.² PE arises when a thrombus from the leg or pelvic vein dislodges and embolizes to the pulmonary artery or its branch leading to obstruction

of pulmonary capillary bed.³ Despite advancements in diagnostics and therapeutics, PE remained an under-diagnosed and challenging entity. It demands not only timely and accurate diagnosis but also effective treatment. Otherwise, death is not an uncommon result.⁴ Missed diagnosis accounts for increased mortality rather than the failure of treatment.

Massive PE describes acute PE in persistent hypotension requiring inotropic support or systolic BP <90 mmHg for at least 15min, breathlessness and sustained bradycardia, whereas submassive PE is acute PE without hypotension with either right ventricular dysfunction or necrosis.⁵ Early risk stratification is important. The presence of clinical features of shock is linked with poor prognosis and requires immediate intervention.

PE is one of the common presentations in an acute emergency ward. The patient may present typical features, including shortness of breath, pleuritic chest pain and hemoptysis. Clinical presentation may be dyspnea over days to weeks or syncope with least respiratory symptoms. Therefore a high degree of clinical suspicion of PE should be made in all patients with unexplained cardiopulmonary symptoms.⁶

Correspondence: Dr Muhammad Adil, Combined Military Hospital, Skardu, Pakistan

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Risk factors always offer major help towards establishing the diagnosis. However, their absence does not rule out the diagnosis. It often happens due to the interplay of multiple risk factors that contribute to the disease process. Multiple risk factors have been identified in the pathophysiology of PE, including hereditary disorders and acquired factors.

Protein C, S, antithrombin III deficiency, and factor V-laden mutations are hereditary, while prominent acquired factors include age, smoking, immobilization, obesity, surgery, trauma, hypertension, and previous history of thrombotic diseases.⁷ In addition, there are certain less established risk factors, including chronic disease hepatitis B and C, connective tissue disorders, high altitude, and increased plasma homocysteine level.⁸

Recent advancement in the management of suspected cases of PE has improved diagnostic accuracy and has a well-standardized treatment regime. However, diagnostic algorithms remained the same over the last decade and are mainly based on assessing clinical pretest probability, D-dimer level and imaging, mainly pulmonary CT angiography, which can diagnose even small filling defects in the pulmonary circulation. Clinical probability scores and D-dimer are widely used to filter out cases of PE with low probability in cases where ionizing radiations are not advised.⁹

Although much work has been done explaining various aspects of pulmonary embolism, including risk stratification, diagnosis and management, limited data describes the thrombotic illnesses, including pulmonary embolism, in soldiers stationed at high altitudes. Keeping this in mind, we conducted this study to evaluate the profile of patients deployed and analyze the role of causative and underlying risk factors in patients with PE at high altitudes.

METHODOLOGY

This retrospective longitudinal study was undertaken at Combined Military Hospital, Skardu Pakistan, from January 2016 to January 2020. The Institutional Ethical Review Board approved the study protocols of Combined Military Hospital, Skardu Pakistan (IERB approval certificate no. 001 dated 25 Jul 2020).

Inclusion Criteria: Serving personnel deployed at a high altitude area above a height of 8000 feet who presented with clinical features of pulmonary embolism and were subsequently diagnosed with pulmonary embolism were included in the study.

Exclusion Criteria: Those with the previous history of thromboembolic event, procoagulant disorder and presence of pre existing condition that increases the risk of pulmonary embolism were excluded from the study.

All patients in our hospital with high altitude sickness were assessed and managed by doctors at respective altitudes or evaluated at forwarding treatment centres by specialized doctors.

A total of 25 consecutive cases aged 18-45 years reported to this hospital with clinical features and later diagnosed with PE were analysed retrospectively from their clinical records for study enrollment. These included patients with a history of dyspnea, chest pain, hemoptysis, tachypnea, and tachycardia and/or on initial investigations had chest X-ray findings or ECG changes consistent with pulmonary embolism. All patients underwent routine haematological parameters, including Blood CP, LFT, RFT, D Dimers, coagulation profile, and CXR and ECG. Diagnosis of pulmonary embolism was made based on pulmonary CT Angiography findings. In addition, CT scans brain, CTV brain and Doppler legs were performed in selected patients with clinical features suggestive of dural venous sinus thrombosis and deep vein thrombosis. After initial management, these patients were further transferred to tertiary care hospital for further evaluation, including thrombophilic screening, connective tissue profile and plasma homocysteine level. Thrombophilia profile includes Protein C, S, antithrombin III and anticardiolipin antibody levels, while connective tissue disorder assessment includes RA and ANA levels.

All data, including demographic data (age, height of deployment, duration of stay, known risk factors), clinical features, ECG and radiological findings and laboratory findings, were recorded on pre-designed proforma. Statistical Package for Social Sciences (SPSS) version 21.0 was used for the data analysis. Descriptive statistics (mean, standard deviation range and frequencies) were used to analyze data.

RESULTS

A total of 25 patients deployed at high altitudes (>8000 feet) having PE were enrolled in the study. The mean age of the patient was 30.68 ± 5.37 years, ranging from 23 to 40 years. The majority of the patients were in the age range of 25 to 30 years. The mean height of deployment was 17223.00 ± 3577.00 feet (range 8000-21300 feet), while the mean duration of stay was 53.92 ± 44.76 days (range 2-208 days). Dyspnea (n=21, 84%)

was the commonest clinical presentation followed by chest pain (n=17, 68%), palpitation (n=13, 52%), headache (n=8, 32%), haemoptysis (n=7, 28%), leg swelling (n=4, 16%) and syncope (n=1,4%). Most patients (n=22, 88%) were non-smokers, while no patient had known significant risk factors. Haemoglobin was raised in most patients ranging from a minimum of 12.20 to a maximum of 18.70, while D-Dimer was raised in only 12% (n=3) patients. Associated thrombotic complications were listed in Table, along with other clinical features and ECG findings.

Table: Demographic, Clinical and Laboratory Features of Study Population

Characteristics	(n=25)
Age (years)	30.68± 5.37
Altitude where symptoms begin (feet)	17223.00±3577.00
Duration of stay (days)	53.92±44.76
Smoker n (%)	3 (12)
Past history of thrombotic disease	0(0)
High risk cases (History of surgery, trauma, tumor)	0(0)
Hemoglobin level (g/dl)	16.44±1.79
D-Dimer value n (%)	
<250	22 (88)
250-500	3 (12)
Thrombophilic / Autoimmune screening	All Negative
ECG Findings n (%)	
Sinus tachycardia	19 (76)
Non-specific T wave inversion	13 (52)
Right Bundle Branch Block pattern	4 (16)
S1Q3T3	2 (9)
Associated Complications	
Hemorrhagic Infarct	2 (8)
Dural venous sinus thrombosis	2 (8)
Dural venous sinus thrombosis with infarct	1 (4)
Deep vein thrombosis lower limbs	5 (20)

All patients were screened for thrombophilic and vasculitic diseases and found negative. In addition, none of the patients had raised homocysteine levels or had a previous history of thrombotic disease, trauma, tumour or surgery. In the absence of all other risk factors, high altitude remains the only potent thrombogenic risk factor in the studied population.

DISCUSSION

People living at high altitudes are prone to altitude-induced maladies. High altitude illnesses, including acute and chronic mountain sickness, high altitude pulmonary oedema and cerebral oedema, have been extensively investigated and studied in the literature. However, there is a scarcity of data correlating thrombotic disorders with high altitude. Spontaneous arterial or venous thrombosis after a short climb

or prolonged stay at a high altitude has been reported in the literature and is associated with significant morbidity and mortality. Young patients deployed at an altitude ranging from 10,000 feet to 22,000 feet with a mean stay over ten months are at 30 times higher risk of developing thrombosis.¹⁰ It has been shown in various studies that factors like heme concentration, hypoxia, dehydration, enforced immobilization and use of constrictive clothing at high altitude due to severe weather conditions may cause blood to clot.

Our studied population consisted of study participants deployed at moderate to very high altitudes. Gene-rally, they were from plains and have to stay for a considerable period. Most patients were young, under the age of 40 years, with the majority in the age range of 25-30 years. Khalil KF *et al.* described a similar age group in their study on young patients who developed PE at high altitudes.¹¹ Dyspnea was the most common clinical presentation in these patients, which is in accord with the PIOPED study. The most common ECG change is sinus tachycardia, followed by non-specific T wave inversions, which have been described in several studies.¹² In our study, D-dimers were raised only in 12% of the patients, which is contrary to international data. Mohsin *et al.* found that D-dimers are 91-96% sensitive in PE.¹³

In our study, risk factors of PE were compared in the studied population, and high altitude was found to be an independent risk factor. None of the patients had undiagnosed underlying known risk factors, while thrombophilic and vasculitic screening was negative. In a study by Khalil *et al.* most patients (50%) had high altitude as an independent risk factor.¹¹ A similar study by Dutta *et al.* involving patients with the same profile and exposed to the similar climatic condition described comparable results.¹⁴ According to them, hereditary conditions contributes only 17% to the disease burden in patients at high altitude, making idiopathic factors a major contributor. Similar studies, mostly done in the neighbouring country where several people were deployed at extremely high altitudes, demonstrate that staying at this altitude is a significant risk factor.^{15, 16}

Polycythemia at high altitudes can be attributed as one of the factors leading to thrombosis. A hypoxic environment at a high altitude causes an increase in haemoglobin concentration in response to adapt. Kotwal *et al.* have noted a significant rise in haemoglobin levels in patients deployed at high altitudes.¹⁷ Our studied population also demonstrated a substan-

tial increase in haemoglobin levels. This raised haemoglobin may be attributed to hypoxia-driven blood synthesis and dehydration.

Although limited data is available on the studied subject, there is a need to conduct a case-control study with a large sample size to identify the underlying aetiology and risk factors contributing to pulmonary embolism. This will evolve not only the health care delivery system but also patient care as a whole, especially in the case of people deployed at high altitudes. By defining high altitude as one of the potent thrombogenic factors, not only can time management be done, but also preventive measures can be adopted. By combining patient presentation, clinical suspicion and risk factor, the diagnosis can be streamlined, and management can be rationalized.¹⁸ Once the disease is suspected, early descent is the mainstay of treatment and instituting other drug therapy. In addition, early and timely evacuation should be made in suspected cases to save a precious life.

CONCLUSION

Stay at high altitude is a major risk factor for pulmonary embolism in young patients without any other known risk factor. However, further studies are still needed to study the underlying aetiology, pathophysiology and risk factors contributing to this condition.

Conflict of Interest: None.

Author's Contribution:

NUK: Conception, Literature, search, proof reading, MA: Data collection, literature search, article drafting, MZ: Literature search, proof reading, data collection, ARP: Literature search, data entry and analysis, MT: Literature search, proof reading.

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