INTRODUCTION

Pulmonary embolism (PE) remains an under diagnosed and potentially lethal entity despite advances in diagnosis, management and prevention of the disease. With accurate diagnosis and effective treatment, death is uncommon except in patients with massive pulmonary embolism and hemodynamic instability. Majority of deaths can be ascribed to a missed diagnosis rather than failure of treatment.

Pulmonary embolism usually arises from clots originating from deep venous system of the calf, or more rarely from pelvic, renal and axillary veins. Deep venous thrombosis (DVT) and pulmonary embolism are now considered as spectrum of the same disease.

Massive pulmonary embolism (MPE) is defined as PE with systolic blood pressure less than 90 mmHg or drop in systolic pressure of more than 40 mmHg from the baseline over a period of 15 minutes, not explained by hypovolemia, sepsis or new arrhythmia.

Diagnosis of PE should be suspected in patients with otherwise unexplained respiratory complaints. Progressive dyspnea, pleuritic chest pain, hemoptysis are the cardinal symptoms as given in the Prospective Investigation of Pulmonary Investigation Diagnosis (PIOPED) study which also incorporates the modified Well's criteria. Patients with massive PE may be in a state of shock with hypotension, tachypnea and tachycardia.

Pulmonary embolism is associated with numerous risk factors including advanced age, previous history of DVT, trauma, immobilization, surgery, obesity, underlying malignancy, pregnancy, prolonged estrogen therapy, cerebrovascular accident, hereditary thrombophilic disorders like Protein C and S, anti-thrombin-III deficiency, anti-phospholipid anti-body syndrome and factor-V leiden mutation etc. In addition to these well known risk factors, there are certain less well established factors including chronic hepatitis B and C, raised plasma homocystein levels, certain connective tissue disorders and residence at high altitude.

Pulmonary embolism has known to occur in soldiers working at high altitude who are young and do not have the usual risk factors. Preliminary studies done in India where, like Pakistan, thousands of troops are serving in the mountains of the Himalayas, indicate that prolong stay at high altitude has been associated with deep
venous thrombosis (DVT), splenic, retinal vein and dural sinus thrombosis. Unusual environmental conditions like extreme cold, hypoxia, prolonged immobility, polycythemia, smoking and dehydration contribute to this hypercoagulable state.7

There are few non-invasive tests available to diagnose PE which have got a low sensitivity and specificity. D-dimer is the only sensitive test available. The imaging modalities for confirmation of PE are expensive, not widely available and require expertise. These include ventilation-perfusion (V/Q) scintigraphy and spiral CT chest.8

Intravenous unfractionated heparin, sub-cutaneous heparin, low molecular weight heparin, antifactor Xa inhibitors and coumarin anti-coagulants are the effective therapies available for treatment of pulmonary embolism.9

The objective of this study was to diagnose pulmonary embolism, determining the frequency of different risk factors of the disease and consider high altitude as one of the factors.

METHODOLOGY

It was cross-sectional, analytical study, undertaken in the Department of Pulmonology, Military Hospital, Rawalpindi, from December 2006 to December 2007.

Soldiers between 18-45 years of age who were suspected to have pulmonary embolism were included as given by the PIOPED study incorporating the modified Well's criteria.3,4 This included patients who presented with history of dyspnea, chest pain or hemoptysis, had tachypnea, tachycardia, rales, pleural effusion, gallop rhythm or loud P2 and on preliminary investigations had either a raised D-dimer value, an X-ray evidence of pulmonary infarct or an ECG abnormality suggestive of PE.10

Soldiers initially suspected to have PE but subsequently found to have alternate pathologies like pneumonia, tuberculosis, high altitude pulmonary edema (HAPE) were excluded.

High altitude was defined as a height above 8000 ft, with a minimum stay of 4 weeks, so that soldiers are acclimatized to that environment.7

Informed consent was taken. Clinical features of the disease were noted in detail. Preliminary investigations included an X-ray chest, an ECG, arterial blood gases (ABGs) analysis and a D-dimer value. Ventilation-perfusion (V/Q) lung scan and/or spiral CT scan of chest were done to confirm the diagnosis. All the soldiers remained indoor till the final diagnosis was confirmed hence there was no drop out.

Patients were evaluated for presence of risk factors of the disease.3-5 These included underlying malignancy, immobilization, recent surgery, trauma, previous history of DVT etc. Thrombophilic screening for Proteins C and S, anti-thrombin-III and anticardiolipin antibody levels were done. Connective tissue profile including RA and ANA levels, infectious disease screening for hepatitis B and C and syphilis and plasma homocystein levels were also noted. Soldiers fulfilling the criteria to be at high altitude as being evacuated from a height of more than 8000 ft were separated and their approximate height from sea level was noted.

The cost of this study was borne by the Pakistan Army. Data was collected through a carefully designed structured questionnaire and analyzed by SPSS version 11. Age, symptoms, signs, ECG, radiographic features, D-dimer value and mode of diagnosis (whether V/Q scan or spiral CT) were compared by using simple frequencies. Risk factors were also analyzed by frequencies.

RESULTS

Majority (86%) of soldiers were between 20-40 years of age. Dyspnea was the commonest symptom occurring in 40% of soldiers followed by chest pain and hemoptysis. Important physical signs included tachypnea (42%) and tachycardia (14%).

D-dimer was used as the preliminary non-invasive test for suspected pulmonary embolism. Only 10% of patients had D-dimer value less than 250.

Radiological criteria as given in the ICOPER study were used.11 The commonest radiological feature was pleural effusion (40%) followed by peripheral oligemia (12%), pulmonary artery enlargement (6%), pulmonary congestion (4%), basal atelectasis and pulmonary infarct.

ECG changes included non-specific T-wave inversion as the most frequent abnormality (44%), along with right sided changes (28%) including right axis deviation, right bundle branch block(RBBB) and right ventricular hypertrophy (RVH), while the classical S1Q3T3 pattern was less common (12%).

Spiral CT chest was diagnostic in 56% of patients, with 28% demonstrating a thrombus and 28% an infarct, it was in conclusive in another 34% of patients.

Perfusion lung scan was diagnostic in 80% of patients, as it was interpreted as a "high probability perfusion scan" when compared with a ventilation scan or an X-ray chest. Perfusion scan of a patient with PE is shown in the Figure 1.

High altitude was the commonest known risk factor in Table I. Only 2 patients had an underlying malignancy, one diagnosed as colonic carcinoma on colonoscopic biopsy and the other patient had metastatic carcinoma with the primary unknown, confirmed on bone marrow trephine biopsy.

Table I. Only 2 patients had an underlying malignancy, one diagnosed as colonic carcinoma on colonoscopic biopsy and the other patient had metastatic carcinoma with the primary unknown, confirmed on bone marrow trephine biopsy.
DISCUSSION

Military Hospital (MH), Rawalpindi is the only center where soldiers are transferred from military posts located at high altitude for definitive management.

In this study, most of the patients were under 40 years of age, by virtue of being serving soldiers. Dyspnea was the most frequent complaint and it was in accordance with the PIOPED study.

D-dimer was used as the preliminary inexpensive test for suspected pulmonary embolism and it was raised in 90% of patients which is in accordance with the international studies showing a sensitivity of 91-96%.12,13 X-ray chest was interpreted as in the ICOPER study.11 Unlike the ICOPER study where the commonest radiological feature was cardiomegaly; in this study, pleural effusion was the most common (40%) X-ray abnormality. It should be borne in mind that pleural effusion was the second most frequent abnormality in the ICOPER study with an occurrence of 23%.

The most common ECG abnormality in these patients was non-specific T-wave inversion in chest leads in accordance with other international studies.14

The sensitivity of spiral CT chest for diagnosis of PE was (56%) in this study, while ventilation-perfusion lung scan was the modality confirming PE in more than 80% of patients. Those patients showing an intermediate or low probability V/Q scan, because of high clinical suspicion, underwent a spiral CT chest for confirmation of the diagnosis.15

In this study, risk factors of PE were compared using simple frequencies and high altitude was found to be an important factor. Patients with high altitude as a risk factor were separated but their approximate height from sea level was not compared as there was no control group i.e. persons at that particular height who never developed pulmonary embolism. This may be a source of bias in this study.

Except a single study, there is no national data to compare the results of this study.16,17 Few international studies, mostly done in India, where like Pakistan, thousands of militants are serving at high and extreme altitudes, have clearly demonstrated prolonged stay at height expected to a significant risk of venous thrombosis and PE.18-22

It has been postulated that after ascent to high altitude, there is an initial hypercoagulable state due to transient increase in platelet count, heightened factor X and XII activity, shortening of prothrombin time, impaired clot retraction and platelet dysfunction.19 After few weeks, process of acclimatization occurs with an increase in hematocrit and decrease in clotting factor levels towards normal. But as the patient stays there for a prolonged period (postulated as more than 5 months), a hyperfibrinogenic state due to increase in factor VIII levels develops, which along with increase in platelet count and platelet adhesiveness, and heightened thromboxane activity, increase the risk of VTE and the risk continues till the patient remains at height.19,21

In this study, the minimum duration of stay at high altitude was one month, while the mean duration was not recorded. In other studies this has been varying between 5-24 months and this risk is higher with prolonged stay and with higher altitude.17,19 The height from sea level ranged from 8500 to 22000 ft with around 90% of patients evacuated from a height of more than 17000 ft.

There are a number of limitations of this study. For exclusion of other causes of PE, a detailed history and thorough physical examination was performed, connective tissue and vasculitic screen, infectious disease profile along with plasma homocystein levels and thrombophilic screening were done. Factor V leiden mutation is the commonest hereditary abnormality pre-disposing to PE. Serum levels of this mutation are not routinely performed in the Armed Forces Institute of Pathology (AFIP) which is the reference laboratory for MH, Rawalpindi. This may be a source of bias in this study. Few cases of pulmonary embolism in this study might have been attributable to this hereditary abnormality which could not be detected.
It appears that the population under study is a source of bias. As all symptomatic cases from high altitude are transferred to MH, Rawalpindi as a routine, so an increased frequency of cases of PE was attributable to height in this study (around 50%). If another similar study is designed to diagnose PE in another referral center like PNS Shifa, Karachi, which receives soldiers from low land, probably not many cases will be obtained. A similar study in India has clearly demonstrated that soldiers working at high altitude are 24.5 times at increased risk of VTE as compared to soldiers in plains.19 A study for comparing risk of PE in high altitude residents and lowlanders is required. Another study should assess the effects of different altitudes on the incidence of pulmonary embolism.

This study has got certain future strategic implications. Millions of Pakistani soldiers are working at high altitude mountains of Himalayas and Karakarum. By establishing height as a risk factor, many lives can be saved. Soldiers can use measures like elastic stockings and low dose heparin to prevent PE. If the disease is suspected, then early treatment can be instituted. Descent should be the first step in management in addition to pharmacological treatment. Whenever evacuating a patient from high altitude, it should be borne in mind that PE is a completely treatable disease and a number of deaths can occur if a delay in evacuation is done. Over diagnosis is better than under diagnosis.

**CONCLUSION**

Pulmonary embolism occurs at an increased frequency in soldiers working at high altitude. Well designed clinical trials are required in future to evaluate the effect of high altitude on soldiers working at mountains of the Himalayas and Karakarum.

**Disclosure:** This article is a dissertation based study.

**REFERENCES**


