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Pulmonary Embolism

Original Article
Pak Armed Forces Med J 2020; 70 (4): 1061-65

ASSOCIATION OF RISK FACTORS IN MILITARY PERSONNEL WITH PULMONARY EMBOLISM STATIONED AT HIGH ALTITUDE AND SEA LEVEL

Rizwan Azam, Laima Alam, Jamal Ahmed, Mehmood Iqbal Malik, Zahra Asif Sukhera, Bushra Arif

Pak Emirates Military Hospital/National University of Medical Sciences (NUMS) Rawalpindi Pakistan

ABSTRACT

Objective: To compare the risk factors of pulmonary embolism between military personnel living at sea level and high altitude.

Study Design: Prospective cross sectional.

Place and Duration of Study: Pak Emirates Military Hospital (PEMH) and Combined Military Hospital (CMH) Rawalpindi, from Oct 2018 to Mar 2019.

Methodology: A total of 52 young soldiers presenting with pulmonary embolism were segregated into two equal groups according to the altitude. A thorough history and clinical examination was followed by a battery of biochemical, immunological and radiological tests for confirming diagnosis, establishing complications and ruling out possible cause(s) of pulmonary embolism.

Results: Soldiers with pulmonary embolism evacuated from high altitude had a lower body mass index (BMI) (23.5 ± 0.4) and were relatively younger (33.3 ± 1.6 years). The most common presenting symptom was dyspnoea (94.2%) followed by pleuritic chest pain (77%). Majority (92.3%) of the subjects from high altitude had no risk factors for vascular thrombosis in comparison to low landers (77%). Smoking and a relatively high platelet count were the only findings in the soldiers posted at high altitude.

Conclusion: In conclusion, high altitude is an uncommon but known cause of pulmonary embolism in army personnel residing at high altitudes. No risk factor other than smoking and a relatively higher platelet count was found in these patients.

Keywords: High altitude, Hypercoagulability, Hypoxia, Pulmonary embolism, Soldiers, Thrombophilia.

INTRODUCTION

High altitude is a less known cause of pulmonary embolism, demanding a high level of suspicion and can cause death if missed[1]. Pulmonary embolism at high altitude can masquerade as High Altitude Pulmonary Edema (HAPE), pneumonia, bronchitis, asthma and cardiovascular events[2]. The risk factors for pulmonary embolism include hereditary thrombophilic conditions (like Protein C and S, antithrombin III deficiency, Factor V Leiden mutation, homocysteinemia), surgery, prolonged bed rest, vasculitis, trauma, chronic blood stasis, old age, deep venous thrombosis, pregnancy and post-partum period, obesity, malignancy and estrogen use[3].

Spontaneous vascular thrombosis has been documented at rates as high as 30 times in young male military personnel at heights from 3000 meters to 6500 meters[4]. These findings led to the speculation that high altitude which leads to hypoxia activates a pro-coagulant state. High altitude causes erythrocytosis through erythopoeitin activation[5], platelet dysfunction with thrombocytosis and high platelet adhesion that is not mediated by thrombopeitin[6] and a transient hypercoagulability that does not settle in individuals who stay at high altitudes for longer periods[6].

This study was conducted to look in to the risk factors and compare the clinical features, laboratory findings and radiological imaging among soldiers presenting with pulmonary embolism at sea level and high altitude areas.

METHODOLOGY

A total of 52 soldiers with diagnosed pulmonary embolism irrespective of the cause were segregated equally into two groups, depending upon the altitude they were posted at, through

Correspondence: Dr Rizwan Azam, Classified Medical Specialist, PEMH Rawalpindi Pakistan

Received: 07 May 2019; revised received: 20 Jun 2019; accepted: 24 Jun 2019

simple convenience samplingwith a standard error of 0.069 and a relative standard error of 13.97 for a confidence interval of 95% using National Statistical Services Calculator. Exclusion criteria included ages below 18 years and above 50 years, previous history of pulmonary embolism, those on anti-coagulation or pro-coagulation drugs and patients with already diagnosed pro-coagulant states.

A detailed medical history including symptoms, previous medical, surgical, drug and family history especially pertaining to risk factors for pulmonary embolism was taken from each of the patient after getting a written informed consent. Soldiers evacuated from high altitude were further interrogated about the altitude above sea level, total duration of stay and whether they were acclimatized to the high altitude or not. All of the patients were subjected to a thorough examination including vitals, BMI, severity of the disease and its complications.

Pulmonary embolism was diagnosed by clinical history, examination, D-dimers and CT pulmonary angiography[7]. Blood samples were drawn for complete blood count (CBC), haematocrit, platelet count, total leucocyte count (TLC), international normalization ratio (INR), erythrocyte sedimentation rate (ESR), quantitative C reactive protein (CRP), D-dimers and rheumatoid factor (RA factor), anti-neutrophil antibodies (ANA), anti-smooth muscle antibodies (ASMA), anti-ribonucleotide protein (RNP), anti Ro antibodies, anti-La antibodies, anti Jo-1 antibodies, anti Scl 70 antibodies, anti-citrullinated cyclic peptide antibodies (anti-CCP) and ANCA as immunological panel[8]. The thrombophilia panel included anti-thrombin III deficiency, Factor V Leiden mutation, Protein C deficiency, Protein S deficiency, β2 microglobulin, homocysteine levels and HLA B5/51 assay[9]. Tumour markers sent included carcinoembryonic antigen (CEA), CA 19-9, alpha feto protein (AFP) and prostate specific antigen (PSA)[10]. An ECG was also done for all the patients.

Imaging modalities for confirming diagnosis, establishing complications and ruling out possible cause of pulmonary embolism included chest x-ray, 2D Echo, spirometry, Doppler ultrasound of lower limbs venous system, ultrasound abdomen and CT pulmonary angiography[11].

Quantitative data was presented as frequencies and percentages whereas descriptive statistics were used to calculate mean ± SD of the continuous data. Quantitative data was analysed using chi square statistics. Non parametric normal variables (Haemoglobin, haematocrit and BMI) were compared using independent t test whereas, non-parametric non-normal variables were analysed using Mann Whitney U test.

RESULTS

The mean age and body mass index (BMI) of the patients (52 males) presenting with pulmonary embolism was 35.15 ± 9.9 years and 24.68 ± 2.8, respectively with those posted at high altitudes (26 males) representing younger age group and lower BMIs (table-I). The most common clinical feature among both the groups was dyspnoea, followed by pleuritic chest pain. The only statistically significant clinical features between the two groups were temperature and diastolic blood pressure, both lower for the sea level residents (table-I).

A statistically significant relation was found between high altitude residents with pulmonary embolism and smoking (p=0.092). No other risk factor was found significant for either of the groups with majority having no risk factors.

The only significant laboratory finding was the platelet count (p=0.006) with high altitude residents having a raised value. Most of the patients had normal ECG (77%), chest x-ray (69.2%), 2D echocardiography (88.5%), Doppler of lower limb venous system (84.6%) and spirometry (76.9%) (table-II).

The patients evacuated from high altitude areas were stationed at an average of 13,431 feet above sea level for an average of 57 days.

Majority of the high altitude residents (88.5%) were acclimatized during their ascent.

DISCUSSION

Pulmonary embolism accounted to 60,000 to 100,000 deaths per year in the United States, 340 deaths in the year 2015 in Australia and 2300 deaths alone in the United Kingdom in 2012[12]. The challenge lies within early diagnosis and prompt treatment, modality of treatment and the choice of investigation to avoid further harm. The commonest clinical features of pulmonary embolism are pleuritic chest pain and dyspnoea, though these are the commonest symptoms presenting as overall in the emergency departments[13].

Vascular thrombosis including fatal pulmonary embolism is quite common in young personnel posted at high altitude without the usual risk factors and also in the natives of high altitude that are sent to extreme of heights[14]. Dickinson *et al* presented a case series of multiple deaths related to pulmonary embolism in a group of trekkers who were not acclimatized in the absence of any known risk factor other than high altitude[15]. Presti *et al* demonstrated an incidence of 0.9% of chronic pulmonary embolism in a set of high altitude dwellers, again with no previous risk

Table-I: Demographics and clinical features in patients with pulmonary embolism.

Variable	Total (n=52)	Sea level (n=26)	High altitude (n=26)	*p*-value
Age (years ± SD)	35.15 ± 9.9	37.1 ± 2.2	33.3 ± 1.6	0.359
BMI (m/kg^2 ± SD)	24.68 ± 2.8	25.9 ± 0.6	23.5 ± 0.4	0.001
Chest pain				
No	12 (23)	8 (30.8)	4 (15.4)	0.188
Yes	40 (77)	18 (69.2)	22 (84.6)	
Hemoptysis				
No	24 (46.2)	14 (53.8)	10 (38.5)	0.266
Yes	28 (53.8)	12 (46.2)	16 (61.5)	
Dyspnoea				
No	3 (5.8)	-	3 (11.5)	0.074
Yes	49 (94.2)	26 (100)	23 (88.5)	
Risk factors				
None	44 (84.6)	20 (77)	24 (92.3)	0.225
Sepsis	2 (3.8)	2 (7.7)	-	
DVT	2 (3.8)	2 (7.7)	-	
Varicose veins	4 (3.8)	2 (7.7)	2 (7.7)	
Smoking				
No	30 (57.7)	18 (69.2)	12 (46.2)	0.092
Yes	26 (50)	8 (30.8)	14 (53.8)	
Pulse (per min ± SD)	86.1 ± 14.4	88.9 ± 3	83.2 ± 2.5	0.377
RR (per min ± SD)	18.8 ± 1.7	18.7 ± 0.3	18.9 ± 0.3	0.541
Temperature (0F ± SD)	98.2 ± 0.5	98.3 ± 0.1	98.4 ± 0.1	0.039
Oxygen saturation (% ± SD)	94.8 ± 4.3	93.9 ± 1.1	95.7 ± 0.3	0.652
Systolic BP (mmHg ± SD)	120.8 ± 11	121 ± 2.3	120 ± 2.0	0.940
Diastolic BP (mmHg ± SD)	73.8 ± 6.0	76.2 ± 1.3	71.5 ± 0.8	0.009
ECG				
Normal	40 (77)	20 (77)	20 (77)	0.446
S1Q3T3	6 (11.5)	4 (15.4)	2 (7.7)	
T wave inversions	4 (7.7)	2 (7.7)	2 (7.7)	
Tachycardia	2 (3.8)	-	2 (7.7)	

DVT: Deep Venous Thrombosis, RR: Respiratory Rate, BP: Blood Pressure, ECG: Electrocardiography

factors[16]. A study from Pakistan establishing the risk factors for pulmonary embolism at high altitude among military personnel dwelling at high altitude showed that 50% of the cases had no risk factor other than high altitude[17].

Multiple studies have established the role of erythrocytosis, thrombocytosis and increased platelet adhesiveness in response to hypoxia, extreme cold, dehydration (secondary to low humidity, high respiratory rate and insensible water loss), smoking and prolonged inactivity at high altitude[14]. Due to these findings, trekkers and soldiers are advised against dehydration, immobility, alcohol and caffeinated drinks, staying in cramped positions and exposing themselves to unnecessary cold[18]. The use of pressure stockings and prophylactic aspirin has been advocated but not included in the guidelines as yet[19].

Table-II: Biochemical and radiological profiles of patients with pulmonary embolism.

Variable	Total (n=52)	Sea level (n=26)	High altitude (n=26)	*p*-value
Haemoglobin (g/dl ± SD)	14.6 ± 2.1	14.2 ± 0.4	14.9 ± 0.4	0.206
Haematocrit (± SD)	43.2 ± 4.9	42.2 ± 0.9	44.2 ± 1.0	0.149
Platelets (109/uL ± SD)	281 ± 90.2	257 ± 19.3	306 ± 14.7	0.006
CRP (±SD)	51 ± 77.3	60.9 ± 17.3	41.1 ± 12.7	0.141
ESR (mm/hr ± SD)	86.1 ± 16.4	26.2 ± 3.8	22.8 ± 2.6	0.912
INR (± SD)	1.2 ± 0.7	1.3 ± 1.8	1.2 ± 0.05	0.96
Homocysteine (umol/L ± SD)	13.7 ± 20.7	20.3 ± 4.8	7.2 ± 2.6	0.052
Blood Group				
A+	20 (38.5)	10 (38.5)	10 (38.5)	1.00
B+	20 (38.5)	10 (38.5)	10 (38.5)	
O+	8 (15.4)	4 (15.4)	4 (15.4)	
AB+	4 (7.7)	2 (7.7)	2 (7.7)	
Chest X-Ray				
Normal	36 (69.2)	20 (77)	16 (61.5)	0.085
Consolidation	6 (11.5)	2 (7.7)	4 (15.4)	
Pleural effusion(s)	2 (3.8)	2 (7.7)	-	
Consolidation and effusion	2 (3.8)	2 (7.7)	-	
Infarct	2 (3.8)	-	2 (7.7)	
Non specific	2 (3.8)	-	2 (7.7)	
Pulmonary edema	2 (3.8)	-	2 (7.7)	
2D Echo				
Normal	46 (88.5)	22 (84.6)	24 (92.3)	0.048
Pulmonary HTN	2 (3.8)	-	2 (7.7)	
Right heart failure	4 (7.7)	4 (15.4)	-	
Spirometery				
Normal	40 (76.9)	18 (69.2)	22 (84.6)	0.381
Obstruction	6 (11.5)	4 (15.4)	2 (7.7)	
Obstruction with restriction	4 (7.7)	2 (7.7)	2 (7.7)	
Restriction	2 (3.8)	2 (7.7)	-	
Doppler Study				
Normal	44 (84.6)	20 (77)	24 (92.3)	0.225
Left popliteal vein thrombosis	4 (7.7)	2 (7.7)	2 (7.7)	
Right femoral vein thrombosis	2 (3.8)	2 (7.7)	-	
Superficial vein thrombosis	2 (3.8)	2 (7.7)	-	

CRP: C Reactive Protein, ESR: Erythrocyte Sedimentation Rate, INR: International Normalization Ratio

Our study compared the risk factors of pulmonary embolism between two groups of young military personnelliving in completely opposite conditions. As shown in multiple similar studies, no risk factors other than smoking and a relatively increased platelet count (physiological) were found to be significant. The low landers in comparison had a relatively higher serum homocysteine levels and a higher incidence of DVT.

LIMITATION OF THE STUDY

The limitations like sample size, population bias including only male subjects and the lack of information like dehydration and platelet adhesion studies are the few lacunae that need to be filled. However, the extensive workup and comparing two groups of soldiers posted at different altitudes are the strengths of our study.

CONCLUSION

In conclusion, high altitude is an uncommon but known cause of pulmonary embolism in army personnel residing at high altitudes. No risk factor other than smoking and a relatively higher platelet count was found in these patients.

CONFLICT OF INTEREST

This study has no conflict of interest to be declared by any author.

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