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Study of clinical profile and management of patients with pulmonary thromboembolism at a tertiary care center in South Gujarat, India

Manoj Ganvit [1], Chiragkumar D. Patel [1], Snehal R. Patel [1], Priyanka D. Patel [2]*

ABSTRACT

Background

Pulmonary thromboembolism (PTE) is a common health problem that causes high mortality and morbidity. Its epidemiology is difficult to determine as it may be asymptomatic, or its diagnosis may be an incidental finding. Delayed diagnosis is a common cause of death; if caught early the risk may be temporary and reversible. Clinical manifestations of acute pulmonary embolism are highly variable. The aim of this research was to study patients' clinical profiles and the association of risk factors with pulmonary thromboembolism diagnosis.

Methods

The study was carried out between August 2016 to July 2018. Patients were enrolled in the study if they met the inclusion criteria: aged 18 years and above, admitted at the tertiary care centre of a civil hospital in Ahmedabad, South Gujarat, India, with clinical features suggestive of acute pulmonary embolism, and who demonstrated a thrombus in pulmonary arteries by echo or computed tomography pulmonary angiogram (CTPA). Participants underwent detailed evaluation including history, clinical examination and laboratory investigation. Detailed history regarding risk factors of pulmonary embolism was taken in all patients. All patients underwent basic relevant biochemical investigations, specifically D-dimer and cardiac biomarkers, Chest x-ray, 2D echocardiography, computed tomographic pulmonary angiography and ultrasonography of the lower limbs.

Observations

According to the New York Heart Association (NYHA) classification, 56% of the patients fell in Class III and 28% in Class II. 60% patients smoked, 28% were alcoholic and 28% had chronic lung disease; 14% had a history of immobilization for a minimum of 2 weeks; 8% had history of blood transfusion; 6% had previously suffered a stroke; 6% had recently undergone major surgery and 4% had a malignancy.

Conclusion

The clinical presentation and the investigations including electrocardiography, chest radiography and analysis of arterial blood gases, lack adequate specificity to confirm or rule out pulmonary embolism. Echocardiography, cardiac biomarkers and simplified Pulmonary Embolism Severity Index (PESI) score are helpful for treatment and prognosis purposes.

Keywords: Pulmonary thromboembolism, Risk factors, Clinical profile

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1 Department of Medicine, GMERS Medical College and Hospital, Valsad, Gujarat, India
2 Department of Pharmacology, Government Medical College, Surat, Gujarat, India

***Corresponding author** Manoj Ganvit, Senior Resident, Department of Medicine, GMERS Medical College and Hospital, Valsad, Gujarat, manojganvit2016@gmail.com

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INTRODUCTION

Pulmonary thromboembolism (PTE) is an occlusion of pulmonary arterial circulation by a blood clot formed elsewhere, usually in the deep veins of the leg; less than 5% of venous thrombosis occurs in other sites. It is a major health concern with high mortality and morbidity. Nearly 10% of untreated PTE is fatal in the first hour.[1] The incidence of PTE is estimated to be approximately 60-70 per 100,000, and that of venous thrombosis approximately 124 per 100,000 in the general population.[2,3] Mortality rate among diagnosed and treated pulmonary embolism patients ranges from 3-8% and mortality increases to about 30% in untreated cases.[1] Delayed diagnosis is a common cause of death in PTE. In the last decade it has been found that PTE is not a disease, rather it is a complication of venous thromboembolism (VTE).[4] Venous thromboembolism (VTE) includes PTE and deep vein thrombosis (DVT), which encompasses a single disease category. VTE along with stroke and myocardial infarction rank as three major cardiovascular killers. Pulmonary embolism is seen in 60–80% of patients with DVT but more than half these patients remain asymptomatic.[5] VTE may be lethal in the acute phase or lead to chronic disease and disability but it is also often preventable. The epidemiology of PTE is difficult to determine as it is often asymptomatic, and its diagnosis may be an incidental finding.[6] Pulmonary embolism is a major cause of mortality, morbidity and hospitalization.

The clinical manifestations of acute pulmonary embolism are highly variable, ranging from pulse-less electrical activity to mild dyspnoea, new or worsening dyspnoea, chest pain or hypotension. PTE when suspected during a routine diagnostic session includes biomarkers (e.g., D-dimer), and/or imaging modalities such as computed tomography angiography or a ventilation-perfusion scan. Additional evaluations may be performed with troponins, B-type natriuretic peptide (BNP), Pro-BNP, and/or echocardiography.[7] PTE is commonly classified as massive (high-risk), sub-massive (intermediate-risk), and low-risk to help determine the required treatment. Massive pulmonary embolism accounts for 5-10% of cases.[4] PTE often appears in the presence of a temporary or reversible risk factor such as surgery, trauma, immobilization, pregnancy, oral contraceptive use or hormone replacement therapy within the last 6-12 weeks before diagnosis. Risk stratification scores are used to determine management and the risk of complications and associated mortality.[8]

The reporting of pulmonary thromboembolism is not given much importance in Asian countries in general and in India in particular. The present study was carried out to study the clinical profile and associated risk factors in patients diagnosed with pulmonary thromboembolism.

METHODS AND MATERIALS

Researchers at the Medicine Department, Civil Hospital and B.J. Medical College, Ahmedabad carried out an observational study over a period of two years from Aug 2016 to July 2018. Institutional Human Research Ethics Committee permission was taken before starting the study. Patients were screened for enrollment according to inclusion and exclusion criteria. Inclusion criteria were: all patients aged 18 years and above admitted to the tertiary care center, Civil Hospital Ahmedabad, with clinical features suggestive of acute pulmonary embolism, and who demonstrated a thrombus in pulmonary arteries by echo or computed tomography pulmonary angiogram (CTPA). Patients with suspected pulmonary embolism and D-dimer positive patients without demonstration of a thrombus in the pulmonary artery were excluded from the study. Patients were included in the study only after giving written informed consent.

Fifty patients of pulmonary thrombus with CTPA showing thrombus in pulmonary arteries fulfilled inclusion criteria and were included in the study. Patients underwent detailed evaluation including history, clinical examination and laboratory investigation. Detailed history regarding risk factors of pulmonary embolism was taken from all patients. All patients underwent basic and relevant biochemical investigations. Clinical probability was assessed by

using Wells Simplified Score, which can rule out (or not) the likelihood of pulmonary embolism.
Patients with high probability of pulmonary embolism were evaluated with D-dimer and cardiac biomarkers. 2D echocardiography was carried out on all patients to look for Right Atrial (RA)/Right Ventricle (RV) dilatation, RV dysfunction, right ventricular systolic pressure (RVSP), thrombus in MPA and its branches, left ventricular function and ejection fraction. Chest x-rays were taken to look for other causes of dyspnoea. Computed tomographic pulmonary angiography (CTPA) was undertaken in all patients to look for thrombus, location, number and RV function. Ultrasonography of the lower limbs was carried out in all patients. Patients were risk-stratified on basis of ESC guidelines (2014) into low risk, intermediate and high-risk categories.[9] By taking into consideration issues such as cardiac enzymes and simplified PESI score, patients with sub-massive pulmonary embolism were further divided into intermediate high and low risk groups and were managed accordingly.

All the patients assessed to be in the high and intermediate risk group, and two patients with intermediate low risk group, received thrombolysis in addition to standard UFH and oral anticoagulant therapy. All low-risk patients were treated with standard heparin therapy, followed by oral anticoagulation. Twenty-seven patients were given tenecteplase, three were given streptokinase and one was given alteplase as thrombolytic agents. Statistical studies were carried out using IBM SPSS programme version 20. Quantitative variables were expressed as the mean±standard deviation and qualitative variables were expressed as percentage (%). Categorical variables were compared using the chi-square test. A nominal significance was taken as a two tailed p value <0.05.

RESULTS

In total, 50 patients who were newly diagnosed with acute pulmonary thromboembolism were included in the study. Their mean age was 48.3 years. Among these patients, 38 (76%) were male and 12 (24%) were female. Median blood pressure was 114/72 mm of hg. Median heart rate was 106/min. (Table 1). As seen in Table 2, all patients were classified according to NYHA classification: 6% of patients fell in Class I, 28% in Class II, 56% in Class III and 10% in Class IV. The most common clinical presentation was dyspnoea (100%) followed by chest pain (88%). Other common symptoms were cough (42%), anxiety (30%) and haemoptysis (10%) (Fig 1). Out of the 50 patients, 30 (60%) were smokers, 14 (28%) were alcoholic, 14 (28%) had chronic lung disease, nine (18%) had a history of congestive heart failure, seven (14%) had a history of immobilization for a minimum of two weeks, four (8%) had a history of blood transfusion, three (6%) had previously suffered a stroke, three (6%) had undergone major surgery within 6 weeks and two (4%) had malignancy. Half of the patients had two or more risk factors. Seven (14%) patients had no risk factor; 18 (36%) had one risk factor, 18 (36%) patients had two risk factors, six (12%) had three risk factors and one (2%) patient had four risk factors (Figure 2).

All recruited patients underwent blood investigations. Mean haemoglobin was 12.79 gm/dl; mean serum creatinine was 1.15mg/dl; mean SGPT 45IU/L, mean troponin-I was 1.52 ng/ml; mean D-dimer value was 5512, mean PT was 20.64 and mean APTT was 46.93 (Table 3). The most common finding in ECG was sinus tachycardia (88%) followed by ST-T changes (44%), right axis deviation (38%), $S_1Q_3T_3$ pattern (32%) and incomplete RBBB (30%) (Table 4). Amongst 50 patients, 40 (80%) patients had a normal chest radiograph. Of the remaining 10 (20%) patients, three (6%) had pleural effusion, five (10%) had cardiomegaly, and two (4%) had fibrosis suggestive of an old pulmonary Koch's. 2D echo was used as a screening tool in all patients in the study. Out of the 50 patients, 34 (68%) had RV dysfunction, which was assessed by TAPSE (mean TAPSE 13.78±2.26). RA and RV dilatation was present in 44 (88%) of patients. Mean RVSP was 63.8 mmHG. The majority of patients had tricuspid regurgitation at presentation; 42 (84%) had moderate TR and 5 (10%) had severe TR. Definitive evidence of thrombus in MPA and its branches were observed in 13 (26%) patients on 2D echo screening. All 50 patients underwent CTPA, of whom 24 (48%) had a dilated main pulmonary artery; 8 (16%) had saddle thrombus; 23 (46%) had right main

pulmonary artery partial thrombus; 30 (60%) had left pulmonary artery partial thrombus and 24 (48%) had thrombus seen in segmental and sub-segmental vessels. Lower limb venous ultrasonography was also carried out in all patients; 31 (62%) patients had evidence of deep venous thrombosis; 25 (50%) patients had proximal and six (12%) patients had distal vein thrombosis (Table 5). Risk stratification of patients was based on ESC 2014 guidelines with help of four variables: shock, RV dysfunction, simplified PESI score and cardiac enzymes. Out of the 50 patients, two (4%) were assessed as high risk, 27 (54%) had intermediate-high risk; 7 (14%) patients had intermediate-low risk and the rest (14; 28%) of the patients belonged to the low-risk group (Table 6). Thirty-one (62%) patients were managed with thrombolysis plus anticoagulation; 19 (38%) were treated with anticoagulation. All patients from the high-risk (n=2) and intermediate-high risk (n=27) groups were thrombolysed, but only two out of seven from the intermediate high-risk group and one from the low-risk group were thrombolysed (Table 6).

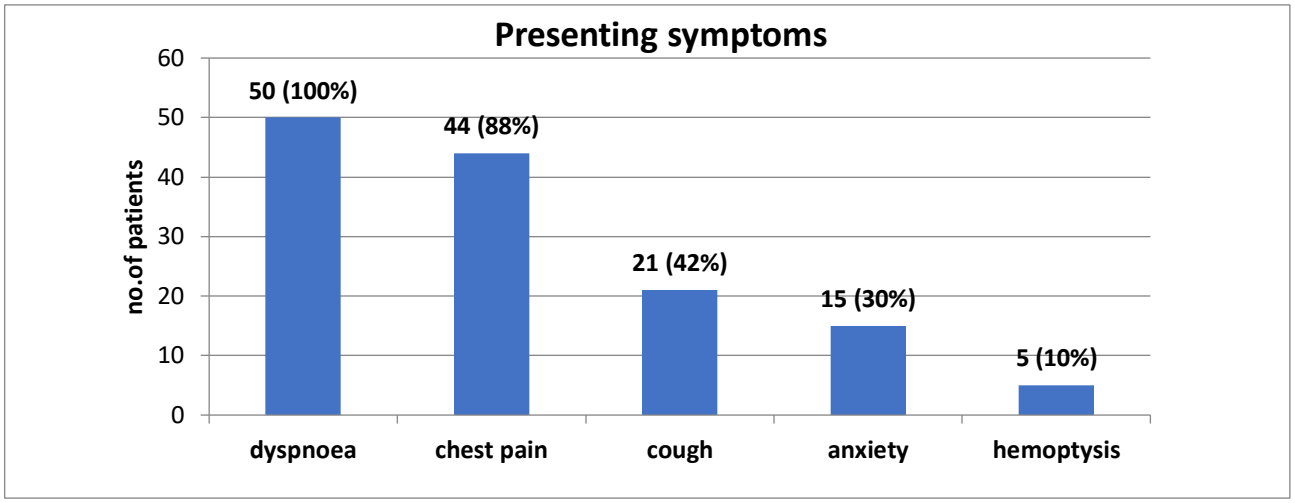

Fig 1 Number and percentage of patients presenting with symptoms

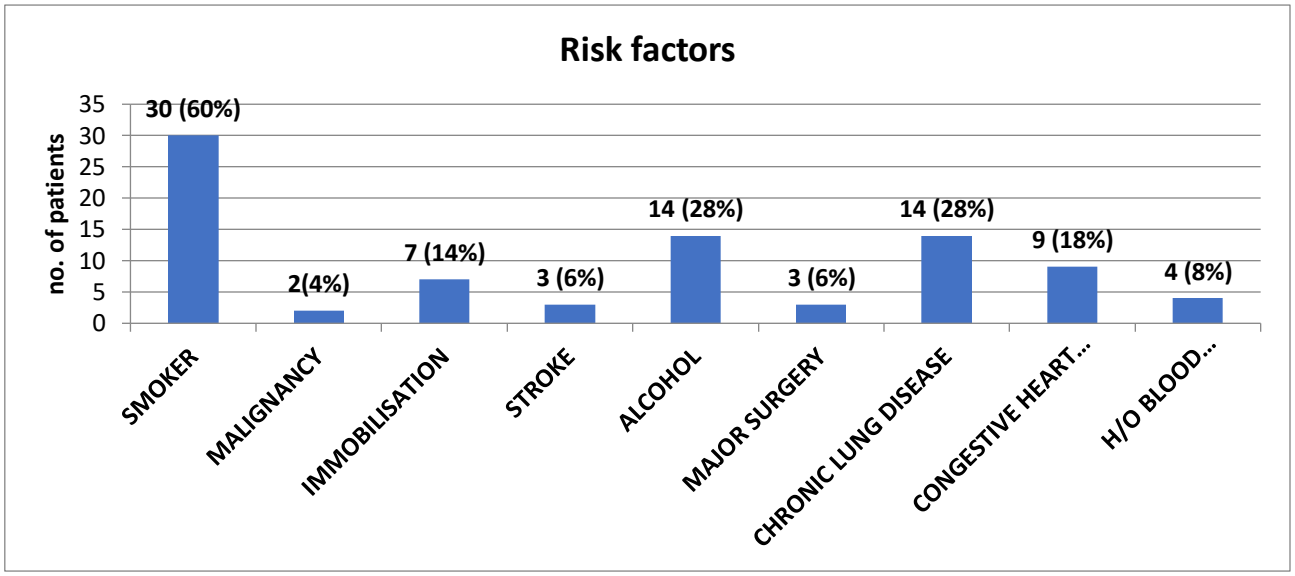

Fig 2 Associated risk factors for pulmony thromboemolism

Table 1 Demographic features of patients

Demographic features	Mean±SD, or n= (%)
Age	48.3±14
BP	114.12±4.96
HR	106±13
Male	38 (76%)
Female	12(24%)

Table 2 Classification of all patients according to NYHA Class

Symptoms	No. of patients
NYHA class I	3 (6%)
NYHA class II	14 (28%)
NYHA class III	28 (56%)
NYHA class IV	5 (10%)

Table 3 Laboratory investigations

Laboratory findings	n=50
Blood glucose	146.58± 49.36
Haemoglobin	12.79±1.35
S.Creatinine	1.15±0.74
SGPT	45±21.1
TROP-I	1.52±1.13
D-dimer	5512.28±2328.53
PT	20.64±8.44
APTT	46.93±19.01

Table 4 ECG Findings among all patients

ECG Changes		
1	Sinus Tachycardia	44 (88%)
2	ST-T changes	22 (44%)
3	Right axis deviation	19 (38%)
4	Incomplete RBBB	15 (30%)
5	S1Q3T3	16 (32%)

Table 5 Findings on various radiological investigations

S. No	Findings on investigations	No. of patients (%)
Chest X-ray findings		
1	Normal	40 (80%)
2	Pleural effusion	3 (6%)
3	Cardiomegaly	5 (10%)
4	Fibrosis	2 (4%)
2D echo findings		
1	Moderate-severe TR	47 (94%)
2	RV dysfunction	34 (68%)
3	Definite Evidence of Thrombus In MPA and its branches	13 (26%)
4.	Pulmonary arterial hypertension	44 (88%)
5.	RA/RV dilatation	44 (88%)
CT pulmonary angiography findings		
1	MPA dilated	24 (48%)
2	Saddle thrombus	8 (16%)
3	RPA partial thrombus	23 (46%)
4	LPA partial thrombus	30 (60%)
5	Segmental and sub-segmental occlusion	24 (48%)
Lower limb Doppler study findings		
1	Proximal venous thrombosis	25 (50%)
2	Distal venous thrombosis	6 (12%)

Table 6 Risk stratification and no. of patients thrombolysed

Category	No. of patients	No. of patients thrombolysed
High risk	2(4%)	2 (6.4%)
Intermediate-high risk	27(54%)	27 (87.09%)
Intermediate-low risk	7(12%)	2 (6.45%)
Low risk	14(30%)	0

DISCUSSION

Acute pulmonary embolism is associated with a significant mortality rate – as high as 30% if untreated, whereas the death rate of diagnosed and treated pulmonary embolism is 8%. Up to 10% of acute PE patients die suddenly.[10]

This prospective observational study gives insight on the clinical profile of 50 hospitalized patients with a confirmed diagnosis of acute pulmonary embolism based on CT pulmonary angiography. The mean age was 48.3 years, and the greater percentage of males (n=38, 76%) than females (n=12, 24%), is consistent with another study carried out in Chennai.[18] In that study, the mean age of patient population was 52.1 years, 62.8% were males and 37.2% were females. A further study carried out in Karnataka showed a mean age of 47.2 ± 13 years, with most cases in men.[11] The majority of the studies done in the Western world show a higher incidence of acute PE among those aged above 60-65 years[12, 13].

Risk factors for venous thromboembolic disease and pulmonary embolism are well characterized in the literature. Risk factors are present in almost 96% of patients with confirmed venous thromboembolic disease.[14] In the present study it was found that most of the patients had at least one risk factor for PTE indicating the importance of looking for known risk factors. Smoking was a major risk factor, present in 60% of the patients. Others studies[15] have also shown smoking to be the major risk factor for acute pulmonary embolism, found in 41.5% of patients. The landmark study PIOPED II[16] also depicted smoking as one of the major risk factors, found in 43% of the patients, which is similar to this study's findings. Chronic lung disease was found to be another important risk factor. In the present study, chronic lung disease was present in 28% of patients, which is comparable to PIOPED II study in which it was observed in 26% of patients.

The most common clinical presentation of patients in this study was dyspnoea (100%) followed by chest pain (88%), cough (42%) and hemoptysis (10%). This is consistent with other studies carried out in India,[15] which show the most common clinical presentation to be dyspnoea (100%), followed by chest pain (52%), syncope (30%) and cough (40%).[17] Another study also showed dyspnoea to be the predominant symptom (71.7%), followed by syncope (17.0%), cough (15.1%), chest pain (7.6%) and haemoptysis (3.8%).[15] This suggests that finding solitary dyspnoea in a patient provides a strong suspicion for pulmonary embolism.

In addition to clinical symptoms, the ECG is also essential in directing the physician towards the diagnosis. There is no isolated ECG abnormality that is definitively associated with pulmonary embolism. However, certain constellations of ECG abnormalities have been shown to be reasonably specific. The most common finding was sinus tachycardia, followed by ST-T changes, RAD, incomplete RBBB and $S_1Q_3T_3$ pattern. Other ECG studies have found sinus tachycardia, RV strain pattern, $S_1Q_3T_3$ pattern and RBBB,[18] ST-T depression in 80% of patients and low voltage in patients with pulmonary embolism.[17] $S_1Q_3T_3$ pattern with presence of S and Q waves in limb leads 1 and 3, respectively, has been observed, with inversion of T-wave in limb lead 3 in 29% of patients and T-wave inversions in leads V1-4 and R/S>1 in V1 in 12% of patients.[19]

In our study 68% of participants had evidence of right ventricular dysfunction; right atrium and right ventricular dilatation was present in 88% of patients. The majority of patients in the study had tricuspid regurgitation (TR) at presentation: 82% moderate and 10% severe. Definitive evidence of thrombus in MPA and its branches were observed in 26% patients on 2D echo screening. A previous study[15] from South India showed pulmonary arterial hypertension as a main finding in 85% of patients. Other findings were RV dysfunction and definite evidence of thrombus in many patients; moderate to severe TR in 73% of patients and RV dilatation and dysfunction in 86% of patients,[17] which is consistent with present study. This suggests important screening tools are needed in cases of a suspected acute pulmonary embolism, especially if there is no prior cardiopulmonary disease history. The abnormality in the other study was mainly in the form of a raised pulmonary artery pressure.

CT pulmonary angiography findings show that 48% of patients had a dilated main pulmonary artery; 16% had saddle thrombus; 46% had right main pulmonary artery partial thrombus; 60% had left pulmonary artery partial thrombus; and 48% patients had thrombus seen in segmental and sub segmental vessels. Previous studies have shown 83% of patients with thrombus located in the main and lobar arteries and 16.7% had thrombus in sub-segmental vessels;[18] MPA thrombus in 40% of patients, thrombus in MPA branches in 40% of patients and segmental and sub segmental occlusion 20% of patients, with 31 (62%) showing evidence of DVT in venous Doppler.[17]

As per this risk stratification, all massive pulmonary embolism patients required thrombolysis. For sub-massive pulmonary embolism patients, the use of thrombolysis is to be balanced against risk of death and bleeding; minor pulmonary embolism should be treated with anticoagulation. Two out of seven patients in the intermediate low-risk group were given a thrombolytic agent and rest, and were treated conservatively. None of the low-risk group patients received thrombolysis in the present study. The number of high-risk patients who were saved with early initiation of treatment, without any major bleeding, demonstrates the importance of clinical suspicion and prompt intervention. High clinical suspicion can help to prevent mortality.

There is no proper consensus about management of the intermediate-risk group patient.[20] Thrombolysis in the intermediate-risk group is associated with increased bleeding complications and reduced mortality.[21] The intermediate high-risk group were haemodynamically stable but they had RV dysfunction and elevated cardiac enzymes, for which they needed strict monitoring and early intervention to prevent haemodynamic collapse and early mortality. All patients in this group in our study survived and benefited from thrombolysis in terms of prevention of early haemodynamic compromise and reduced 30-day mortality as well as reduced chances of developing recurrent PTE. The approach also prevented late complications such as PAH, persistent dyspnoea and moderate TR, leading to improvement in quality of life. All low risk patients were managed with parenteral anticoagulation and discharged on oral anticoagulation.

CONCLUSION

Pulmonary thromboembolism presents with a wide clinical spectrum, from asymptomatic disease to life threatening massive PTE that causes hypotension and cardiogenic shock. The clinical presentation and the investigations, including electrocardiography, chest radiography and analysis of arterial blood gases, lack adequate specificity to confirm or rule out pulmonary embolism. We found echocardiography, cardiac biomarkers and simplified PESI score to be helpful for treatment and prognosis purposes. Risk stratification into high, intermediate and low risk will guide further appropriate treatment of patients and prevent under and over treatment.

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