Pulmonary Embolism, Clinical parameters versus Computed Tomography Pulmonary Angiogram.

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ABSTARCT

Objective: Pulmonary embolism (PE) is a deadly disease with substantial morbidity and possibly fatal consequences. The treatment success of PE depends on prompt and accurate detection, correct risk stratification, and well-observed anticoagulation. Therefore, this study assessed the clinical manifestation and its association with outcomes in patients with pulmonary embolism.

Methodology: This descriptive cross sectional study was conducted at the coronary care unit of Hayatabad Medical Complex, Peshawar. The duration of the study was from 15th August 2014 till 15August 2021. A total of 153 patients having age above 18 years for both genders with suspected pulmonary embolism having presenting complaint such as dyspnea, tachycardia (heart rate > 100 bpm), cyanosis, hypotension (blood pressure < 90/60 mmHg), hemoptysis, syncope with clinical evidence of DVT, postoperative status, obesity (body mass index ≥ 30 kg/m2), malignancy, immobilization (bed rest for >3 days) were included in the study. Chi square test is applied to find out the association between variables and clinical outcomes. Pearson correlation was applied to correlate variables with Wells score.

Results: The mean age of the study participants was 48.03±15.49 years. The correlation analysis showed that among the patient characteristics studied, weight (p=0.004), right ventricle size (p=0.005) and pulse (p<0.001) had a significant correlation with the Wells score where the correlation of all these characteristics with the Wells score was found to be positive. Among the signs and symptoms, cyanosis was significantly associated with the clinical outcome (p=0.022). Moreover, presence of hypertension was marginally insignificantly associated with the clinical outcome (p=0.061).

Conclusion: This study concluded that clinical manifestation such as cyanosis was significantly associated with clinical outcome. Most of the patients showed positive clinical signs of deep-

venous thrombosis. Despite of high and moderate probability of PE patients, mostly patients survived due to timely detection and prompt management.

Keywords: Cyanosis, deep vein thrombosis, hemoptysis, pulmonary embolism.

INTRODUCTION

Pulmonary embolism (PE) is a frequent complication of deep vein thrombosis (DVT) and can be fatal. The prevalence of pulmonary embolism (PE) ranges from 39 to 115 per 100000 individuals per annum while in case of DVT it ranges from 53 to 162 per 100,000 individuals [1-3]. Generally, mortality rate is higher in relation with, and 100,000 people die annually due to PE in the US [4]. It is predicted that PE occurs predominantly in males as compared to females [4].

Clinically, the frequent symptoms that manifest in PE are pleuritic chest pain, dyspnea, cough, blood in sputum, presyncope, or syncope. In case of central PE, dyspnea may be acute and severe, while it may be frequently mild and temporary in small peripheral PE. The most commonly reported symptom is chest pain usually caused by irritation in pleural space owing to distal emboli instigating pulmonary infarction [5]. Additionally, infrequent symptoms are arrhythmias (e.g., atrial fibrillation), syncope, and hemodynamic failure. Hemodynamic collapse is not very common but a critical manifestation, as it shows central or extensive PE with severely worsened hemodynamic backup system of body. Syncope can happen and related with a greater incidence of hemodynamic instability and right ventricular malfunction [6]. Immense PE manifests in the form of hypotension, cardiac arrest or shock. Electrocardiography (ECG) reveals fluctuations of S1Q3 pattern, S1Q3T3 pattern, inverted T waves, notched S wave in lead V1 and right bundle branch block that may be observed in patients with right heart stress [7].

Risk factors that cause PE can be categorized as acquired and genetic. Genetic risk factors involve thrombophilia like factor V Leiden mutation, prothrombin gene mutation, deficiency of protein C, deficiency of protein S, and hyperhomocysteinemia. On the other hand, acquired risk factors are bed rest for longer time period, traveling for > 4 hours (either by air, car, train or bus), and current orthopedic surgery, indwelling venous catheter, fatness, gestation, malignancy, addiction of cigarette and use of oral contraceptive medications [8].

Clinically, the risk of PE is divided on the basis of the Wells score or the Geneva score. A three-tier standard of arrangement (0–1: low risk; 2–6: moderate risk; >6: high risk) supports risk

stratification of pulmonary embolism in dependable method [9]. A two-tier standard of arrangement (≤4 PE unlikely; >4 PE likely) method advises execution of a D-dimer test on "PE unlikely" patients and a CT angiography (CTA) for "PE likely" patients [10]. D-dimer is a plasmin-derived degradation product that exhibits higher sensitivity and negative predictive value in identification of venous thromboembolic disease (VTE) [11]. A value of <500ng/mL indicating negative D-dimer test in a low or intermediary pre-test eliminates the probable chances of acute PE, thus no more tests are needed. Whereas, CTA is necessary for further evaluation in cases of positive D-dimer test [10].

Prompt diagnosis and management is mandatory to prevent the life threatening condition in pulmonary embolism. The chest X-ray is invaluable in identification of PE, as such. It is helpful to eliminate other reasons of acute chest pain like pneumonia, pneumothorax or pulmonary edema, though, quite definitive radiographic irregularities may be observed in acute chest pain [12].Therefore, the diagnosis depends on noninvasive imaging modalities owing to non-specific symptoms that correctly envisage or eliminate the detection of acute PE. Over the past decades, diagnostic approaches for predicting PE have undergone important modifications [13]. In spite of quick technical developments and three-dimensional resolution, the effectiveness of computed tomography (CT) angiography has still been documented in vascular imaging. Mainly, after the development of multi detector row CT [14], CT pulmonary angiography (CTPA) has become the imaging modality of choice in the identification of acute PE [15]. CTPA is more beneficial than conventional invasive X-ray pulmonary angiography and nuclear ventilation-perfusion (V/Q) imaging technique. CT is a commonly accessible, quick and non-invasive method that is capable to directly envisage emboli and might reveal alternate diagnoses [15].

In spite of appropriate detection and anticoagulant treatment, mortality rate following diagnosis of acute PE is still 8% to 15% [16]. The prediction of management of acute PE generally relies on remaining pulmonary circulation and the severity of right ventricular (RV) dysfunction [17]. Recently, one of the studies has revealed that CT allows the detection of acute right-sided heart collapse. Additionally, CT can also envisage the undesired clinical effect by using the RV/left ventricular (LV) diameter ratio or RV ejection fraction in PE patients [18].

In Pakistan, PE remains generally an unidentified, misdiagnosed and mismanaged clinical problem amongst hospitalized patients because of inaccessibility of targeted investigations and

unsatisfactory acquaintance among general practitioners. In fact, there scarce data exists in Pakistan on pulmonary embolism. Therefore, this study was intended to assess the clinical features and parameters, treatment strategies and outcome of pulmonary embolism (PE) in a coronary care center of Peshawar.

METHODOLOGY

This descriptive cross sectional study was performed at the coronary care unit of Hayatabad Medical Complex, Peshawar using non-probability purposive sampling technique. The duration of the study was from 15th August 2014 till 15August 2021. A total of 153 patients having age above 18 years for both genders with suspected pulmonary embolism having presenting complaint such as dyspnea, tachycardia (heart rate > 100 bpm), cyanosis, hypotension (blood pressure < 90/60 mmHg), hemoptysis, syncope with clinical evidence of DVT, postoperative condition, obesity (body mass index ≥ 30 kg/m2), malignancy, immobilization (bed rest for >3 days) were included in the study. On the other hand, patients having previous known pulmonary interstitial pathologies such as Asthma, Chronic obstructive pulmonary disease (COPD), interstitial lung disease (ILD), congenital heart diseases with primary or secondary pulmonary hypertension, Cardiogenic shock, acute myocardial Infarction, Congestive heart failure and pneumonia were excluded from the study.

After taking detailed history of patients with suspected pulmonary embolism, they were admitted in coronary care unit. All Patients were examined to check cyanosis, DVT, pulse rate, blood pressure and oxygen saturation. Investigative parameters including hematological tests (such as serum creatinine, D-dimers), 12 Channel ECG, chest x-ray, Echocardiography and CTPA was performed by using 64 slice helical CT machine. Doppler ultrasound of lower limb was done for DVT.

Data was analyzed by using SPSS version 23.0. For qualitative variables frequency and percentages were documented. Chi square test was used to find out the association between variables and clinical outcomes. Pearson correlation was applied to correlate variables with Wells score. P-value of <0.05 was reflected as statistically significant.

RESULTS

The mean age of the study participants was 48.03±15.49 years. The correlation analysis showed that among the patient characteristics studied, weight (p=0.004), right ventricle size (p=0.005) and pulse (p<0.001) had a significant correlation with the Wells score where the correlation of all these characteristics with the Wells score was found to be positive (Table 1).

The study results further showed that among the signs and symptoms studied, only the presence of cyanosis was significantly associated with the clinical outcome (p=0.022), where those who did not have cyanosis were more likely to be alive at the end of follow up than those who had cyanosis (94.6% vs. 83.3%). Moreover, presence of hypertension was marginally insignificantly associated with the clinical outcome (p=0.061) where those who did not have hypertension were more likely to be alive at the end of follow up than those who had hypertension (92.2% vs. 80.0%) (Table 2).

Table 1: Correlation between Patient Characteristics and Wells Score

Variables (n=153)	Wells Score	
	ρ	p
Age	-0.03	0.711
Height	0.09	0.269
Weight	0.229	0.004
BMI	0.134	0.099
Ddimer[1]	0.009	0.918
Systolic Blood Pressure	-0.131	0.107
Right Ventricle Size	0.225	0.005
Pulmonary Artery Hypertension	0.102	0.21
Pulse	0.284	<0.001
SPO2	-0.119	0.143

[1]n=125

Table 2: Relationship of Signs and Symptoms with Clinical Outcome

Variables (n=153)	Clinical Outcome		p
	Dead	Alive	
	Count (%)	Count (%)	
Chest Pain			
Yes	1 (6.2)	15 (93.8)	0.613
No	14 (10.2)	123 (89.8)	
Cyanosis			
Yes	10 (16.7)	50 (83.3)	0.022
No	5 (5.4)	88 (94.6)	
Palpitation			
Yes	6 (9.1)	60 (90.9)	0.796
No	9 (10.3)	78 (89.7)	
Hemoptysis			
Yes	5 (12.5)	35 (87.5)	0.505
No	10 (8.8)	103 (91.2)	
History of Surgery			
Yes	3 (11.1)	24 (88.9)	0.801
No	12 (9.5)	114 (90.5)	
Obesity			
Obese	4 (8.2)	45 (91.8)	0.789
Overweight	7 (11.9)	52 (88.1)	
Normal Weight	4 (8.9)	41 (91.1)	
Diabetes Mellitus			
Yes	2 (15.4)	11 (84.6)	0.479
No	13 (9.3)	127 (90.7)	
Hypertension			
Yes	5 (20.0)	20 (80.0)	0.061
No	10 (7.8)	118 (92.2)	
Right Ventricle Enlargement[1]			
Yes	1 (4.2)	23 (95.8)	0.732
No	2 (6.2)	30 (93.8)	
IVC Filter			
Yes	Nil	7 (100)	0.372
No	15 (10.3)	131 (89.7)	
History of DVT			
Yes	3 (4.9)	58 (95.1)	0.098
No	12 (13.0)	80 (87.0)	

Doppler Ultrasound of Lower Limb			
DVT Present	4 (7.8)	47 (92.2)	0.187
Normal	3 (5.8)	49 (94.2)	
Not Done	8 (16.0)	42 (84.0)	
Probability of PE			
High	5 (9.4)	48 (90.6)	0.785
Moderate	10 (10.4)	86 (89.6)	
Low	Nil	4 (100)	
[1]n=56			

DISCUSSION

A quick effectual treatment of PE depends on appropriate diagnosis along with correct management [19]. Hence, clinical presentations in combination with risk factors might be responsible for valuable facts in detecting highly vulnerable PE patients. Though, clinical presentations of PE were frequently non-specific. The clinical manifestation differs, reliant on the dissemination and dimension of emboli obstructing the pulmonary vessels along with age and previous medical history of the patients [20, 21]. This study demonstrated accompanied signs and symptoms, risk factors related with the PE that were supportive for the general practitioner to diagnose this serious and probable deadly disease.

D-dimer is a fibrin degradation product produced from degradation of blood clot by the process of fibrinolysis [22]. Thrombosis can be diagnosed by the levels of D-dimer in blood [22]. Earlier researches indicated that D-dimer levels were significantly increased in patients with acute PE [23,24]. However, few researches were controversial regarding level of D-Dimer for detecting PE because D-dimer levels can be elevated due to other diseases [25, 10]. Whereas, few researches recommended that D-dimer might be used alone for PE detection to avoid CTPA scans [26]. Additionally, D-dimer levels associate with the degree of PE on CTPA scans [27]. Similarly, another research studied patients with PE and revealed that D-dimer levels were significantly elevated in patients diagnosed with PE on CTPA as compared to those patients undiagnosed with PE on scan (p=0.001)[28]. These findings were inconsistent with the present research that showed D-dimer levels were insignificantly associated with the degree of PE (p=0.918).

The identification of PE remains confusing owing to nonexistence of generally related clinical presentations in this disease. Some researchers reported the commonly associated signs and symptoms in this disease [29-34]. One of the studies found that hemoptysis along with pleuritic pain were the most common clinical presentation in patients with PE [29]. However, these findings were inconsistent with another research wherein few PE patients presented with pleuritic pain and hemoptysis [35]. Usually, hemoptysis has been considered as classical clinical presentation of PE although reported only in 11.8% patients of PE in their research [35]. Furthermore, another research explained that reduced frequency of hemoptysis can be connected to the extensive accessibility of CT scans, permitting prompt detection and appropriate anticoagulant therapy in patients with PE, consequently stopping the development of pulmonary infarction [36]. The present study was corroborated with the above reported researches and revealed that mostly PE patient clinically manifested with hemoptysis were alive due to early detection and timely management that halted the progression of disease. On the other hand, chest pain, cyanosis and palpitation were also the other classical symptoms in the presentation of PE.

Venous thromboembolism is an important, but comparatively less frequently diagnosed health dilemma [37]. The danger of PE and DVT is a regular alarming distress in the intensive care unit (ICU), hospitalized, and disabled patients. Therefore, prompt detection of DVT is needed to avoid excessive expiries from PE [37]. Similarly, a research by Agunloye *et al.* conducted in Ibadan South-Western Nigeria, on suspicious cases of DVT following Doppler sonography revealed that the clinical signs of DVT were present in only 46.6% cases [38]. These findings were opposing to another research by Ismail *et al.* performed in Kano that documented positive results in 55.8% patients [39]. Additionally, another study in Jos, North Central Nigeria by Salaam *et al.* revealed that 56.3% cases had clinical signs of DVT [40]. In contrast, a Brazilian study by Baroncini *et al.* assessed 528 suspected cases and observed decreased incidence of DVT [41]. The present study did not supported the above researches and revealed, most of the patients showed positive clinical signs of DVT following Doppler ultrasound in 47(92.2%) cases that were alive while 4(7.8%) patients were died due to delayed detection. Early detection of DVT improves the survival of patients.

Likewise, another researchon 1,090 consecutive patients who were admitted to the emergency department for suspicious cases of PE. In order to improve diagnostic capability, they grouped

the suspected cases of PE according to clinical score into high, intermediate, or low probability of PE. Out of 486 patients, 49% cases had a low probability of PE (less than or equal to 4), 50(10.3%) cases had confirmed PE. On the other hand, high probability (score >/=9) was observed in 63 patients whereas moderate probability (score of 5-8) found in 38% patients [42]. The present study was inconsistent with the above mentioned research and showed, probability of PE was high in 48(90.6%) patients and moderate probability was observed in 86(89.6%) for survivors whereas 5 (9.4%) cases were died with high probability and 10(10.4%) were died with moderate probability.

This study had few restrictions. This research did not explore the etiological factor of PE. The clinical outcomes might be well under-represented owing to its reliance on general practitioner assessment. Therefore, more researches are needed to endorse the investigative importance of clinical features.

CONCLUSION

This study concluded that clinical manifestation such as cyanosis was significantly associated with clinical outcome. Most of the patients showed positive clinical signs of deep-venous thrombosis. Despite of high and moderate probability of PE patients, mostly patients survived due to timely detection and prompt management. Early detection of deep-venous thrombosis improves the survival of patients.Furthermore, clinical presentation of PE along with Computed Tomography Pulmonary Angiogram delivers higher sensitivity and specificity.

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