Correlation Of Serum Albumin And Red Cell Distribution Width (RDW) With Deep Vein Thrombosis And Pulmonary Embolism – A Retrospective Study

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Abstract: Background: Venous thromboembolism (VTE), including deep vein thrombosis and pulmonary embolism, is a severe and potentially lethal disease, with serious short and long-term complications and a potentially fatal outcome**.** Objective: To determine the correlation of Serum Albumin and Red cell Distribution Width(RDW), with deep vein thrombosis and pulmonary embolism. Materials & Methods: A retrospective study was carried out from the archive of patients with an event of VTE admitted in the General Medicine ward, Jhalawar Medical College, Jhalawar, Rajasthan. Patients' demographics, presenting symptoms, laboratory tests particularly RDW and Serum Albumin, medications, interventions, and outcomes were collected. Result: A total of 131 cases were evaluated. Majority of the patients (48.8%) were in age group 45-64 years. The mean duration of hospitalization stay of venous thromboembolism (VTE) patients was 6.6 ± 1.4 days. Mean RDW (%) of the total study participants was 15.3 ± 1.4. Mean serum albumin of the total study participants was 3.3 ± 0.8. Conclusion: Majority of the patients were found with higher RDW and Low Serum Albumin. [Ramdev Natl J Integr Res Med, 2021; 12(2):01-05]

Key Words: Deep vein thrombosis, Pulmonary embolism, Red cell Distribution Width (RDW), Serum Albumin.

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Introduction: Venous thrombo-embolism (VTE), including deep vein thrombosis and pulmonary embolism, is a severe and potentially lethal disease, with serious short and long-term complications and a potentially fatal outcome.[1] The annual incidence is approximately 1–3 per 1000 adults in developed countries.[2] Recent studies such as COPER and EMPEROR have shown that some important prognostic risk factors associated with death from pulmonary embolism (17 %) were age (over 70 years), cancer, congestive heart failures, chronic obstructive pulmonary disease, systemic arterial hypotension, tachypnea and the mortality rate directly attributable to pulmonary embolism was only 1%.[3,4] These prognostic risk factors are often used to identify provoked VTE. [5]

Red cell distribution width (RDW) is a parameter of the complete blood count (CBC) that describes the size variation of red blood cells (RBC). It is routinely measured by most of the modern hemocytometers and is calculated by dividing the standard deviation of the mean corpuscular volume (MCV) by the respective actual MCV, and is expressed as percentage. Besides the conventional use of RDW for discriminating between different forms of anemia, a number of studies have suggested that RDW could be a potentially useful marker in a variety of other diseases, such as heart failure, atrial fibrillation, lung cancer or inflammatory disorders, frequently associated with a worse prognosis. An association between high RDW and risk of cardiovascular thrombotic disorders, as well as with increased mortality in patients with cardiovascular diseases has also been described. In a population-based study high RDW was reported predisposing to venous thromboembolism (VTE).[6]

Several studies confirmed the inflammatory response in Acute pulmonary embolism suggesting the potential value of inflammatory markers in the diagnosis and prognosis in these cases. Elevated RDW indicates a greater difference in RBCs size and was found to have a graded association with CRP and ESR independent of confounding factors.[7] Low serum albumin was also associated with increased risk of venous thromboembolism in several renal pathologies associated with protienuria,[8,9] although some studies have not found this association.[10] An explanation for such association is either that hypoalbuminemia may be a marker of inflammation as albumin is a negative acute phase reactant, or it is a reflection of renal loss of albumin and anti-thrombotic proteins creating a hypercoagulable state.

Folsom and colleagues investigated the association between albumin and incident venous thromboembolism in the general population from two large prospective population-based cohorts: the ARIC study (n = 15,300) and the Cardiovascular Health Study (n = 5400), and concluded that low serum albumin is a marker of venous thromboembolism risk.[11]

There are few studies on the correlation of Serum Albumin and RDW with deep vein thrombosis and pulmonary embolism. A retrospective analysis was done to explore the correlation of Serum Albumin and Red cell distribution width (RDW) with deep vein thrombosis and pulmonary embolism among the patients admitted in General Medicine Ward in Jhalawar Medical College, Jhalawar. Study was started with Objective to determine the correlation of Serum Albumin and RDW with deep vein thrombosis and pulmonary embolism.

Materials & Method: The study was done retrospectively. A secondary data analysis was carried out on information collected from the hospital, of patients with an event of VTE admitted to Hospital between 01.01.2018 to 31.12.2020 in the wards of General Medicine Department, Jhalawar Medical College, Jhalawar. The study population consisted of patients admitted with confirmed diagnosis of deep vein thrombosis and/or pulmonary embolism.

Inclusion criteria for the present study were patients aged 18 years or older, definite diagnosis of venous thromboembolism (VTE) and complete data available in medical records. Patients' demographics, presenting symptoms, laboratory tests, medications, interventions, and outcomes were collected using available records of the hospital. We focused on the data of two markers of inflammation: Albumin which is a negative acute phase reactant (so lower level is associated with a higher degree of inflammation) and RDW (higher level is associated with a higher degree of inflammation). Data collected was coded, entered in MS Excel 10. Statistical analyses were performed using SPSS (Windows trial Version 21.0) Continuous variables were summarized with the mean and standard deviation and categorical variables by absolute frequencies and percentages.

Results: A total of 131 subjects were admitted with diagnosis of venous thromboembolism (VTE) (deep vein thrombosis and/or pulmonary embolism) during study period. Majority of the patients (48.8%) were in age group 45-64 years. 27.5% patients were aged 65 years or older and 23.7% were in age group 18-44 years. The mean age of the study population was 56.13 ± 18.21 years. Out of 131 patients, 48.1% were males and 51.9% were females (Table 1).

Table 1: Demographic Characters Of The Patients

Characters	Variables	Number	Percentage
Gender	Males	63	48.1
	Females	68	51.9
Age (Years)	18-44	31	23.7
	45-64	64	48.8
	65 or Older	36	27.5

Majority of the patients (61.8%) admitted with Chief complaint of pain in the affected leg while 27.5% were presented with Swelling or Redness or Warmth of the affected leg. Sudden shortness of breath was the chief complaint of 21.4% patients and 18.3% reported chest pain at the time of admission. Cough was reported by 8.4% subjects. Majority of the patients (80.9%) were admitted first time in hospital for venous thromboembolism and 19.1% patients had history of previous admission for VTE.

Majority of the patients (44.3%) were admitted for 3-6 days duration in hospital followed by 38.9% patients for 7-9 days duration. The mean duration of hospitalization stay of venous thromboembolism (VTE) patients was 6.6 ± 1.4 days. (Table 2) On hospital admission, 31.3% were already on anticoagulant medications.

Table 2: Clinical Profile Of The Patients

Characters	Variables	Number	Percentage
Clinical Presentations*	Pain In The Affected Legs	81	61.8
	Swelling/Redness/Warmth Of The Leg	36	27.5
	Sudden Shortness Of Breath	28	21.4
	Chest Pain	24	18.3

	Cough	11	8.4
	Other Symptoms	20	15.3
Length Of Hospitalization Stay	< 3 Days	7	5.3
	3-6 Days	58	44.3
	7-9 Days	51	38.9
	≥ 10 Days	15	11.4

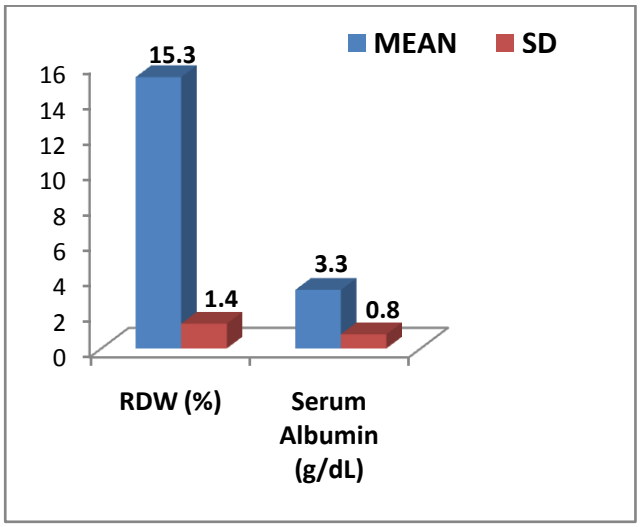
*Multiple responses Laboratory tests closest to the admission time point were chosen for data analysis in present study. Table 3 depicts laboratory parameters of the patients at the time of admission. Majority of the patients (64.1%) were found with RDW ≥ 14.5% while 35.9% the patients were found with RDW <14.5%. Majority of the patients (59.5%) were found with Mean serum albumin < 3.5 g/dL while 40.5% were found with Mean serum albumin ≥ 3.5 g/dL.

Table 3: Laboratory Parameters Of The Patients

Laboratory Parameters	Variables	Number	Percentage
RDW	≥ 14.5%	84	64.1
	< 14.5%	47	35.9
Serum albumin	< 3.5g/dL	78	59.5
	≥ 3.5g/dL	53	40.5

Figure 1 illustrates mean value of RDW and serum albumin with two standard deviations on either side. Mean RDW (%) of the total study participants was 15.3 ± 1.4 (25th–75th percentile: 14.1–16.8). Mean serum albumin of the total study participants was 3.3 ± 0.8.

Figure 1: Mean RDW And Serum Albumin In Venous Thromboembolism



Discussion: Venous thrombosis is a well known health problem in bed ridden patients. Very few studies have been done in Indian patients to assess risk factors of DVT and need for prophylaxis. Most important consequence of DVT is Pulmonary Embolism and chronic venous insufficiency. Frequent location of DVT is in lower limbs, and 10% of the DVT cases are idiopathic in origin.[12] Pulmonary embolism is a an emergency condition. Mortality rate of diagnosed and treated pulmonary embolism ranges from 3 to 8%, but increases to about 30% in untreated pulmonary embolism.[1] Most of the deaths occur when the diagnosis is delayed or never made. Despite diagnostic advances, delays in pulmonary embolism diagnosis are common and represent an important issue.[13]

Present study was carried out retrospectively to determine the correlation of Serum Albumin and RDW with deep vein thrombosis and pulmonary embolism among the patients admitted in wards of General Medicine Department in tertiary care institute of Jhalawar District, Rajasthan. A total of 131 subjects were admitted with diagnosis of venous thromboembolism (VTE) (deep vein thrombosis and/or pulmonary embolism) during study period and included in present study.

In study by Varsha S. Dabadgha et al[12], 30 patients were assessed, out of which 80% were males and 20% females. The age group, most commonly affected was 31-44 yrs (36.67%) followed by 45-60 years (26.67%) and >60 years (26.67%). In study by S. Calwin Davidsingh et al[13], 62.8% were males and 37.2% were females among 35 patients. Mean age was 52.1 years. In our study, majority of the patients (48.8%) were in age group 45-64 years. 27.5% patients were aged 65 years or older and 23.7% were in age group 18-44 years. The mean age of the study population was 56.13 ± 18.21 years.

We assume that the increased incidence of VTE in elderly is because of immobilization, malignant diseases and comorbidities such as DM, COPD, HRT use, CHF which are more prevalent in the elderly than young and middle aged individuals. In our study, out of 131 patients, 48.1% were males and 51.9% were females. Our study does not support previous studies [12, 13] in which the

probability of VTE were higher in men than in women. In study by S. Calwin Davidsingh et al[13], the most common clinical presentation was dyspnea (91.4%) followed by syncope (22.8%). The other symptoms were chest pain (17.1%), fever (11.4%) and cough (11.4%). In our study, majority of the patients (61.8%) admitted with Chief complaint of pain in the affected leg. 21.4% were admitted with history of Sudden shortness of breath and 18.3% reported chest pain at the time of admission. In our study, mean serum albumin of the total study participants was 3.3 ± 0.8. Majority of the patients (59.5%) were found with Mean serum albumin< 3.5 g/dL. Hypoalbuminemia is a common finding and independent predictor for unfavorable prognosis. The prognostic value of albumin measurement for short-term VTE prediction in hospitalized patients remains unclear.

In the APEX trial (Clinical Trials.gov identifier: NCT01583218), a stepwise increase in VTE (P< 0.0001) was observed with lower level of albumin. Patients at the bottom albumin quartile (<35gm/l) had a twofold greater odds for developing VTE compared with top quartile (> 42gm/l) (OR= 2.119 [95% CI, 1.592-2.820]; this finding supports our study. Hesham R Omar et al[15] reported that patients with massive APE had significantly lower albumin level (median (IQR): 2.8 (2.2, 3.0) vs. 3.2 (2.8, 3.6) gm/dL, P < 0.001) compared with non-massive APE. ROC curves showed that albumin had an AUC of 0.750 (P < 0.001) in predicting a massive APE. The optimal cutoff values for albumin that had the highest combined sensitivity and specificity for predicting APE was ≤3 gm/dL for albumin.In our study, Mean RDW (%) of the total study participants was 15.3 ± 1.4 (25th–75th percentile: 14.1–16.8). Majority of the patients (64.1%) were found with RDW ≥ 14.5%. Red cell distribution width (RDW) has been associated with venous thromboembolism (VTE) in recent studies.[16]

Trygve S Ellingsen et al[16] found that individuals with RDW in the highest quartile (RDW≥13.3%) had 50% higher risk of an incident VTE than those in the lowest quartile (RDW≤12.3%). The association was strongest for unprovoked deep-vein thrombosis (HR highest vs lowest quartile of RDW: 1.8, 95% CI 1.1-3.1). VTE patients with baseline RDW≥13.3% had 30% higher risk of all-cause mortality after the initial VTE event than VTE patients with RDW<13.3%. Paolo Bucciarelli et al[17] conducted a Case–control study on 730 patients with a first objectively-confirmed VTE episode and reported that Individuals with RDW above the 90th percentile (> 14.6%) had a 2.5-fold increased risk of VTE compared to those with RDW ≤ 90th percentile, independently of age, sex, body mass index, other hematological variables and renal function (adjusted odds ratio: 2.52 [95%CI:1.42-4.47]).

Limitations: Our study is done retrospectively with a limited sample size. We couldn't get the data of D- dimer, FDP, fibrinogen, factor viii levels and APTT level due to unavailability of investigation facilities in Jhalawar medical college. As a result we couldn't evaluate hypercoagulable tendency of low serum albumin.

In our retrospective study we included inhospital patients and not OPD patients. Serum albumin was measured in hospitalized patients who were already diagnosed with VTE. So, it is not clear whether low serum albumin and increased RDW is a consequence of VTE or it is a cause of VTE. There are other confounding variables that effect albumin level and may have altered the results such as chronic inflammatory conditions and liver disease.[15]

Conclusion: Majority of the patients were found with higher RDW and Low Serum Albumin. Mean value of RDW among study participants was in higher range while Mean value of serum albumin was found in lower range. Further studies having case control design with large sample size should be carried out which can better establish association of these factors with venous thromboembolism.

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