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Original Article

Thrombocytopenia as a Predictor of Severity of Pneumonia in a Tertiary Care Center in Nepal

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ABSTRACT

Introduction: Community-acquired pneumonia is an infectious disease with a global burden. Thrombocytopenia can be an effective and inexpensive tool in predicting the severity of pneumonia which can be useful in the primary care level. The objectives were to identify the clinical and laboratory predictors of hospitalized patients with pneumonia, determine the incidence of thrombocytopenia in those patients, its association with severity, compare it with leucocyte count, assess severity using clinical prediction scores, need of mechanical ventilation, need of transfer to intensive care unit and mortality.

Methods: This was a prospective observational study conducted at Tribhuvan University Teaching Hospital, Kathmandu, Nepal with a sample size of 111. After informed consent, diagnosed and admitted cases of community-acquired pneumonia were examined after which patients' demographic and clinical data, as well as laboratory parameters including white cell count and platelets, were filled in proforma. Clinical prediction scores for pneumonia were calculated and the need for mechanical ventilation, inotropes, transfusions as well as mortality assessed. Patients were followed up until discharge to see the severity of pneumonia.

Results: The incidence of thrombocytopenia among patients with pneumonia was 36.9% (41 out of 111). The overall mortality rate was 9%. More pneumonia patients having thrombocytopenia (14.6%) died than pneumonia patients having leukocytosis (13.8%). There was a significant association between thrombocytopenia and severity of pneumonia, both alone, (p = 0.007, OR = 4.03) and on adjusting for the WBC and GCS (p=0.017, OR=3.81). Significant associations were found between thrombocytopenia and the need for ICU in patients with pneumonia (p=0.001), mechanical ventilation (p = 0.001), presence of edema, confusion, age variation (p=0.024) and septic shock (p=0.021).

Conclusions: Thrombocytopenia is associated with severity in patients hospitalized with community-acquired pneumonia. Thrombocytopenia is an effective predictor of the severity of pneumonia.

Keywords: Nepal; Platelet Count; Pneumonia; Thrombocytopenia

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INTRODUCTION

Community-acquired pneumonia remains a significant cause of morbidity and mortality due to infection all over the world.[1] Thrombocytes are blood components responsible for wound healing and clotting.[2] Thrombocytopenia has been found to have an even greater impact than the total white blood cell count according to various studies.3,4 Thrombocytopenia can help to detect the severe forms of pneumonia earlier and thus help in the proper management of the cases at an early basis.[5-7]

The objectives of this study were to identify the clinical and laboratory predictors of hospitalized patients with pneumonia, to determine the incidence of thrombocytopenia in pneumonia patients, to investigate the association of thrombocytopenia at admission with the severity of pneumonia, to compare the platelet count and leukocyte count as predictors of morbidity and mortality in hospitalized patients with pneumonia and to assess the severity of pneumonia using the SMRT-CO8 (Systolic BP < 90 mmHg, Multilobar Chest X-Ray involvement, Respiratory Rate, Tachycardia, Confusion, Oxygen low) score and CURB-65[9,10] (new mental Confusion, blood Urea raised more than 7 mmol/L, Respiratory Rate ≥ 30/min, systolic Blood Pressure < 90 or diastolic blood pressure ≤60 mmHg, Age ≥ 65 years) score and their correlation with thrombocytopenia.

MATERIALS AND METHODS

This was a prospective observational study conducted at Tribhuvan University Teaching Hospital (TUTH), Kathmandu, Nepal with a study duration of 2 years. The study was approved by the Institutional Review Board (IRB) of Tribhuvan University Institute of Medicine, Maharajgunj, Kathmandu, Nepal, with Reference Number 196(6-11-E) 2071/072 and patients or their relatives signed informed consent.

Inclusion Criteria were cases of community-acquired pneumonia admitted in the Respiratory ward of the Internal Medicine department of TUTH and age >15 years. Exclusion Criteria were: patients with a history of recent hospitalization within the preceding two weeks for a different complaint, patients receiving chemotherapy or immunosuppression, patients with a history of organ transplant, Human immunodeficiency virus (HIV) positive patients, patients with established mycobacterial infection, patients with a diagnosis of hematological malignancy, metastatic cancer, aplastic anemia, immune thrombocytopenic purpura, leukemia, lymphoma.

Criteria for diagnosis:

Community-acquired pneumonia was defined in this study as the presence of new pulmonary infiltrates on chest radiograph at the time of hospitalization associated with at least one of the following: an abnormal temperature ($<35.6^\circ C$ or $>37.8^\circ C$); new or increased cough or an abnormal serum leukocyte count (leukocytosis, shift to left, leukopenia). Thrombocytopenia was defined as a platelet count of ≤150,000/μL. It was further reclassified into mild, moderate, severe categories, defined as 100,000/μL to 150,000/μL, 50,000/μL to 100,000/μL and ≤ 50,000/μL respectively.

Sample Size calculation

$$= \frac{Z^2 P(1-P)}{\frac{(1.96)^2 \times 0.07(1-0.07)}{3.8416 \times 0.0651}} \overline{0.2501}0025$$
$$= \frac{}{0.0025}$$
$$= 100.04$$
$$\approx 101$$

Where,

Z =1.96 for 95% Confidence Interval

P = prevalence (7%)1

d = desired precision (kept here as 0.05)

Accounting for 10% data loss,

101 + 10% of 101 =101+ (0.10 × 101) =110.5≈111

Sampling method used was convenience sampling. Data was filled up in the proforma sheets and relevant physical examination was done. The severity of pneumonia was assessed by the CURB-6510 (new mental Confusion, blood Urea raised more than 7 mmol/L, Respiratory Rate ≥ 30/min, systolic Blood Pressure < 90 or diastolic blood pressure ≤ 60 mmHg, Age ≥ 65 years) and SMRT-CO8 (Systolic BP < 90, Multilobar chest X-Ray involvement, Respiratory Rate, Tachycardia, Confusion, Oxygen saturation) scores as well as the need for inotropes, need of mechanical ventilation, transfer to Intensive Care Unit as well as mortality. The patients were followed up until discharge from the hospital.

Data from pro forma sheets were transferred to Microsoft Excel 2013 spreadsheets. Statistical Package for the Social Sciences (SPSS) (Released 2011. IBM SPSS Statistics for Windows, Version 20.0. Armonk, NY) was used for data analysis and R version 3.5.1 was used for data visualization. The test of significance was applied by cross-tabulating the categorical variables and applying the chi-Square test. Multivariate logistic regression methods were used to assess the association between thrombocytopenia and the severity of pneumonia. p-value of <0.05 was considered statistically significant. 95% confidence interval were calculated where appropriate.

RESULTS

Most patients in this study were in the age group of 71-80 years (18.9%), followed by 51-60 years (15.3%). Males comprised of 43.24% and females of 56.76% (Figure 1). A vast majority of cases were from outside the Kathmandu valley (79.28%). Most of the cases were referred from other hospitals (52.25%)

In this study, 36.9% of the patients had thrombocytopenia. Among these, 16.22% had mild, 11.71% had moderate and 9.01% had severe thrombocytopenia (Figure 2). In this study, the minimum platelet count was 17000/µL, maximum 725000/µL, mean 219216/ µL with SD of 138160.90/ µL. Baseline descriptive statistics of different variables for all cases are elucidated in Table 1.

The patients having thrombocytopenia were 2 times more likely to have severe pneumonia based on CURB-65, but the relation was not significant. The likelihood of developing severe pneumonia in thrombocytopenic patients was around 4 times more based on SMRT-CO scores and the relation was significant. The likelihood increased to 4 times when combining CURB-65 and SMRT-CO scores and the relation was highly significant. When adjusting for WBC and GCS too, similar results were obtained. The study found that there was a statistically significant association between thrombocytopenia and severe pneumonia which was given by combined high SMRT-CO and CURB-65 scores, alone by SMRT-CO score and when adjusted for WBC and GCS (Table 2).

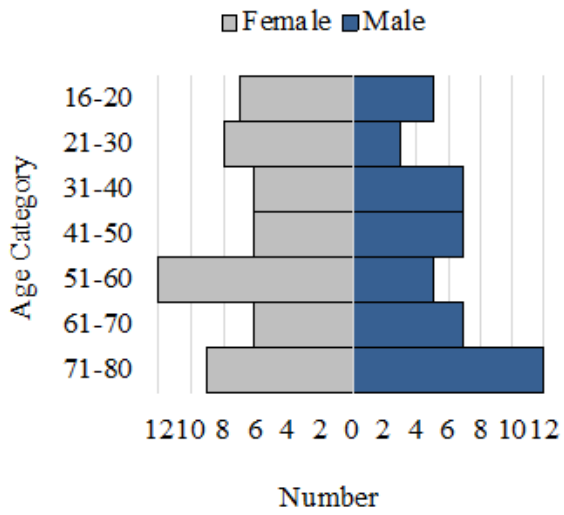

Figure 1: Population pyramid of the total cases of pneumonia (n=111)

The overall mortality rate was 9%; 6.2% in males; 11.1% in females, highest in age group 71-80 years (18.9%). More pneumonia patients having thrombocytopenia (14.6%) died than pneumonia patients having leukocytosis (13.8%).

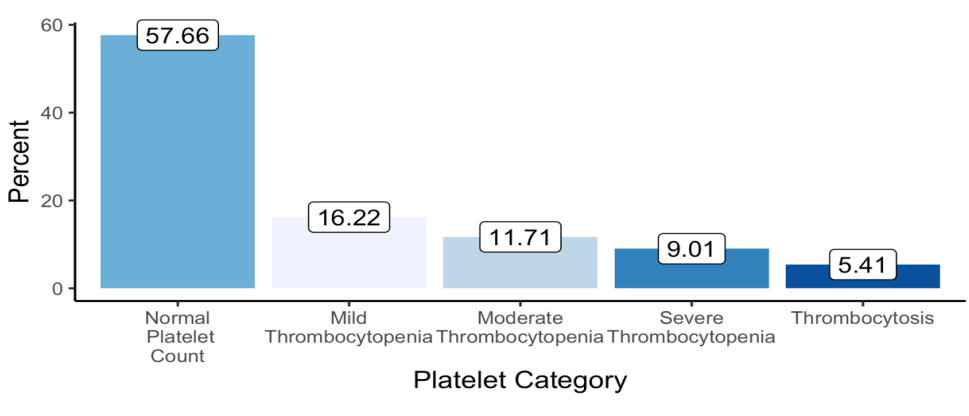

Figure 2: Distribution of patients according to platelet category.

Table 1: Baseline descriptive statistics of different variables for all cases

Variables	Minimum	Maximum	Mean	Std. Deviation
Respiratory Rate (/min)	18	64	26.87	7.46
Pulse (/min)	60	140	98.29	15.66
Systolic BP (mmHg)	70	160	107.65	19.40
Diastolic BP (mmHg)	40	100	68.47	12.81
Temperature (°F)	95	105	98.76	1.55
Saturation (% in Room Air)	52	99	86.41	9.09
GCS	6	15	14.79	1.15
Hemoglobin (g/dL)	4.3	19.4	11.59	2.47
WBC count (/µL)	2890	38300	13284	6727.15
Platelets (/µL)	17000	725000	219216	138160.90
Sodium	108	153	134.61	7.91
Potassium	1.8	6.4	3.89	0.82
Urea	1.5	38	8.31	6.40
Creatinine (µmol/L)	26	565	107.28	88.24
Random Blood Sugar (mmol/L)	1	25	7.51	3.60

Mortality increased as the platelet counts declined, with 22.2% of the patients with severe thrombocytopenia dying (Figure 3). There was a highly significant association between thrombocytopenia and the need of ICU in patients with pneumonia (p=0.001) as well as need of mechanical ventilation (p = 0.001). Significant associations were found with presence of edema, confusion, age variation (p=0.024) and also between thrombocytopenia and septic shock (p=0.021).

DISCUSSION

The incidence of thrombocytopenia among patients with pneumonia in the current study was 36.9% (41 out of 111). This was in stark contrast to the study by Mirsaeidi et al.4 in which only 5.4% (27 out of 500) had thrombocytopenia. This finding from the current study was slightly similar to the study by Brogly et al.[5] in which it was found that 25% (202 out of 822) patients having pneumonia had thrombocytopenia. The study by Prina et al.11 found that 2% of the sample population (53 out of 2,423) had thrombocytopenia, but this might have been due to the case definition of thrombocytopenia as < 105/µL. In the study by Samaha et al.12 the incidence of thrombocytopenia was found to be

Table 2: Logistic regression analysis comparing thrombocytopenia along with CURB-65, SMRT-CO and both combined scores

	Crude OR	95.0% C.I. for OR		p-value	Adjusted* OR	95.0% C.I. for OR		p-value
		Lower	Upper			Lower	Upper	
CURB-65	1.65	0.75	3.6	0.21	1.31	0.58	2.97	0.52
SMRT-CO	3.48	1.55	7.82	0.003	3.51	1.48	8.31	0.004
Both combined	4.03	1.48	11	0.007	3.81	1.27	11.41	0.017

*Adjusted for WBC and GCS

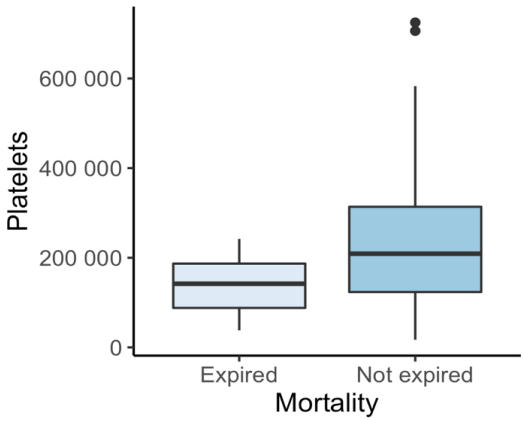

Figure 3: Boxplot showing platelet count among survivors and non-survivors.

19% (33 patients out of 173).

In the current study, the percentage of pneumonia patients dying was higher in those having thrombocytopenia than those having leukocytosis, similar to the study by Mirsaeidi et al.4 There was a significant association between thrombocytopenia and severity of pneumonia, both alone, (p = 0.007, OR = 4.03) and on adjusting for the WBC and GCS (p=0.017, OR = 3.81) similar to Mirsaeidi et al.4 (p<0.0009). Similar results were obtained on comparing septic shock and thrombocytopenia (p=0.021) in the present study and that of Brogly et al.5 (p=0.0002). Thrombocytopenia was more prevalent among females than among males in the present study, which was different from that of Msaouel et al.[13]

The rate of pneumonia was consistently higher among men than among women, across all age groups and for both hospitalized patients and outpatients with pneumonia, although the difference was not always statistically significant according to the 3-year long observational study by Jackson et al.[14] However, in the present study, the rate of pneumonia was higher among men than among women in the age groups 16-20, 21-30, 51-60 and 81-90 years only.

In the current study, there was no significant association between thrombocytopenia and leucopenia (p=0.084) and leukocytosis (p = 0.520). This was in contrast to the study by Prina et al.,[11] where it was found that there was a weak but significant positive correlation between platelet count and leukocyte count (r = 0.21, p <0.001).

The patients having thrombocytopenia were 2 times more likely to have severe pneumonia based on CURB-65, but the relation was not significant. The CURB-65 score lacked specificity for predicting the need for critical care interventions in a retrospective analysis done in Boston which was similar to our study in which CURB-65 alone to classify severe pneumonia had no significant relation with thrombocytopenia.[15]

In this study, 58.5% of the patients having thrombocytopenia had CURB-65 scores of 2, 3 or 4 and 44.3% of the patients having no thrombocytopenia had CURB-65 scores of 2, 3 or 4. This finding was similar to that from the Mirsaeidi et al.[4] Study, in which 18% of the non-survivors had CRB-65 scores 2, 3 or 4 and 82% of the survivors had CRB-65 scores of 2, 3 or 4. In both the studies, p value for CURB-65 and thrombocytopenia was not statistically significant.

CONCLUSION

Severe pneumonia is still a killer disease in the world. Thrombocytopenia is an effective and inexpensive tool in predicting the severity of pneumonia which was demonstrated by our study. Platelet count can be used in peripheral areas of Nepal where radiological services may be easily inaccessible. Usage of platelet count for predicting pneumonia severity will help to identify more severe forms earlier, necessitate timely referrals and management for greater survival. It can foretell the course of pneumonia, which can make clinicians able to administer stronger treatment modalities at an earlier stage.

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