

Reliability of Haematological Parameters and Ratios Obtained from Automated Haematology Analysers in Predicting the Clinical Condition of the Patient - A Study from a Tertiary Care Hospital in New Delhi

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ABSTRACT

BACKGROUND

Modern automated analysers provide various haematological parameters which have gained a lot of clinical significance. Of these, platelet indices are the most recent one which need to be explored in various diseases. The present study was conducted to evaluate the significance of platelet indices, neutrophil-to-lymphocyte ratio (NLR), monocyte-to-lymphocyte ratio (MLR), and mean platelet volume-to-platelet count in critically ill patients.

METHODS

This is a prospective study carried out in emergency laboratory of pathology department. 100 patients of intensive care units (ICU) and non-intensive care units (Non-ICU) visiting to the emergency department were included in the study. Forty-five age and sex matched control patients were taken. The ethylenediamine tetra acetic acid (EDTA) blood sample was analysed on automated analyser. Platelet indices, NLR, MLR and mean platelet volume to platelet counts were calculated in ICU, Non-ICU and control groups. All these values were compared among these groups.

RESULTS

The study included 400 patients (200 critically ill and 200 non-critically ill) and 45 healthy controls from normal population. The male to female ratio in critically ill and non-critically ill patients was 1.3 : 1 (113 : 87) and 1.08 : 1 (104 : 96) respectively. The critically ill patients had significant leucocytosis (P = 0.019) with neutrophilia (P = 0.005) and lymphopenia (P = 0.048) when compared to non-critically ill patients. There was a significant difference of NLR (P = 0.010), MLR (P = 0.027) and MPV : Platelet count (P = 0.045) in these two groups. However, platelet count and platelet indices were not showing any significant difference in these groups.

CONCLUSIONS

In the era of modern auto analysers, we should try to utilize the maximum information that could be provided by these machines in forms of various indices and ratios. The present study highlights that neutrophilic leucocytosis with lymphopenia is seen in critically ill patients when compared to non-critically ill patients and normal control population. NLR, MLR and MPV to platelet ratios are also of great importance whereas platelet count and platelet indices are always not helpful in categorization of severity of the patient's condition.

KEYWORDS

Intensive Care Unit Patients, Neutrophil Lymphocyte Ratio, Monocyte Lymphocyte Ratio, Mean Platelet Volume

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BACKGROUND

Complete blood count (CBC) is a routinely done basic investigation which provides significant information about patient's condition. This includes white blood cells (WBC), red blood cells (RBC) and platelets. Neutrophils are the most abundant WBCs which play a critical role in critically ill patients and can be used as an therapeutic target in these patients.¹ Numerous studies in literature have documented correlation between neutrophil to lymphocyte ratio (NLR), monocyte to lymphocyte ratio (MLR) and mean platelet value (MPV) to platelet ratio (MPV : Platelet) in critically ill patients with respiratory, cardiac, metabolic or inflammatory diseases. But none of these studies had compared these values from those of non-critically ill patients.²⁻⁵ These ratios are race specific; thus requires a reference value of the normal population of that particular demographic area to assess the accurate correlation in various diseases and patient groups.^{6,7}

Platelets play an important role in both physiological and pathological conditions like coagulation, inflammation, thrombosis and maintenance of vascular integrity.^{8,9} Modern automated analyser provide platelet indices which provide information about platelet count, morphology and proliferation kinetics.¹⁰ Initially these parameters were used to study various haematological disorders but recently their role is being discovered in critically ill intensive care patients. Thrombocytopenia and elevated mean platelet volume are directly related with prognosis of ICU patients.¹¹

However, the comparison of platelet count in critically ill and non-critically ill patients is not done in any of the previous studies. The present study aims to compare and demonstrate whether there is any significant difference of NLR, MLR, platelet count, platelet indices and ratios in critically ill patients, non-critically ill patients and normal population.

METHODS

This is a prospective study done in emergency laboratory, Department of Pathology over a period of one month (February 2020 to March 2020). 200 patients of each critically ill as well as non-critically ill patients and 45 normal individuals were included in the study. The critically ill patients were those who were admitted in intensive care units of various departments. Non-critically ill patients were those who were admitted to routine wards of various department.

Patients with less than 18 years of age/known leukaemia were excluded from the study. 45 medically fit age and sex matched individuals were taken as control. Two ml EDTA sample was collected by venepuncture and was processed within 2 hours. The platelet indices and white blood cell differential (DLC) were analysed in whole blood using a blood cell counter (Horiba Medical Pentra XLR). Platelet indices and ratios were calculated. WBCs, DLC, platelet indices and various ratios (NLR, MLR and MPV : Platelet count) were compared within critically ill, non-critically ill

patients and controls. Leucocytosis was defined as more than 10×10^9 WBC/L, neutrophilia as more than 7.7×10^9 neutrophils/L.^{12,13} Thrombocytopenia was defined as platelet count below the lower limit of 1.5 lakhs/cumm.¹⁴ It was divided into four grades from Grade 1 to 4.¹⁵

- Grade 1: 75,000 – 1, 50,000/cu.mm
- Grade 2: 50,000 – 75,000/cu.mm
- Grade 3: 25,000 – 50,000/cu.mm
- Grade 4: < 25,000/cu.mm

Statistical Analysis

Statistical analysis was done by statistical package for social sciences (SPSS) version - 23. Unpaired t test was used and P value of < 0.05 was considered as significant.

RESULTS

The study included 400 patients (200 critically ill and 200 non-critically ill) and 45 healthy controls from normal population. The male to female ratio in critically ill and non-critically ill patients was 1.3 : 1 (113 : 87) and 1.08 : 1 (104 : 96) respectively. The mean WBC was $12.60 \pm 5.95 \times 10^9/L$ in critically ill patient and $11.29 \pm 5.16 \times 10^9/L$. The rise in WBC was significant in critically ill patients with a P value of 0.019. The neutrophil count was significantly higher (P = 0.005) while lymphocyte count was significantly lower (P = 0.048) in critically ill patients than those of non-critically ill patients. On comparing these values with those of control population this difference was statistically significant in both the critically ill versus control group and non-critically ill versus control group (Table 1 & 2).

Variables	Critically Ill			Non - Critically Ill			P - Value
	Mean	SD	Median	Mean	SD	Median	
RBC	3.690	1.039	3.620	3.795	0.900	3.880	0.280
HB	10.787	2.929	10.500	11.167	2.870	11.150	0.191
HCT	32.220	8.345	31.650	33.115	8.083	33.450	0.277
MCV	88.440	9.393	87.000	88.040	12.095	87.500	0.712
MCH	29.576	3.573	29.400	29.524	4.712	29.550	0.887
MCHC	33.427	1.518	33.400	33.294	2.621	33.550	0.535
RDWCV	14.699	2.113	14.500	15.030	2.690	14.400	0.171
RDWSD	46.500	6.283	46.000	47.485	8.379	45.000	0.184
PLT	201.580	127.528	174.000	194.980	124.103	168.000	0.600
MPV	10.312	1.401	10.400	10.426	1.509	10.200	0.432
PCT	0.201	0.119	0.183	0.194	0.105	0.181	0.525
PDW	19.777	3.739	19.500	20.336	4.287	20.150	0.165
WBC	12.601	5.952	11.450	11.294	5.155	10.100	0.019
NEU	75.105	10.799	76.600	71.771	12.487	74.750	0.005
LYM	18.355	10.759	16.150	20.342	9.248	18.350	0.048
MON	4.116	2.140	3.850	4.244	2.726	3.700	0.602
EOS	2.069	2.062	1.400	2.352	2.278	1.700	0.194
BAS	0.802	0.710	0.600	0.774	0.867	0.600	0.719
LIC	1.554	2.333	0.800	1.487	5.068	0.600	0.864
NLR	5.759	4.357	4.639	4.739	3.414	3.992	0.010
MLR	0.301	0.253	0.224	0.251	0.191	0.199	0.027
MPV : Platelet	0.083	0.076	0.060	0.110	0.175	0.061	0.045

Table 1. Descriptive Comparison between Critically Ill and Non-Critically Ill Patients

The mean NLR, MLR, MPV, MPV : Platelet count and platelet count were 5.76 ± 4.36 , 0.30 ± 0.25 , 10.31 ± 1.4 femtoliter (fl), 0.08 ± 0.08 and 201.58 ± 127.53 cells/cumm in critically ill patients and 4.74 ± 3.14 , 0.25 ± 0.19 , 10.42 ± 1.50 fl, 0.11 ± 0.18 and 194.98 ± 124.10 cells/cumm in non-critically ill patients.

This shows that NLR (P = 0.010), MLR (P = 0.027) and MPV (P = 0.432) were higher in critically ill patients but MPV to platelet ratio (P = 0.045) and platelet count (P = 0.600) were higher in non-critically ill patients. However, among these only the difference of NLR, MLR and MPV to platelet ratio was significant between critically ill and non-critically ill whereas platelet count and indices were not statistically significant (Table 1).

Thrombocytopenia was seen in 79 critically ill patients and 80 non-critically ill patients (Table 3). Ten non-critically ill patients (12.5 %) had severe grade 4 thrombocytopenia whereas only 1 critically ill patient had grade 4 thrombocytopenia.

Variables	Critically Ill	Non - Critically Ill	Controls	Critically Ill Versus Control	Non - critically Ill Versus Control
	Mean	Mean	Mean	P - Value	P - Value
RBC	3.690	3.795	5.006	0.000	0.000
HB	10.787	11.167	15.116	0.000	0.000
HCT	32.220	33.115	42.509	0.000	0.000
MCV	88.440	88.040	85.295	0.034	0.144
MCH	29.576	29.524	30.270	0.220	0.305
MCHC	33.427	33.294	35.539	0.000	0.000
RDWCV	14.699	15.030	13.127	0.000	0.000
RDWSD	46.500	47.485	40.295	0.000	0.000
PLT	201.580	194.980	223.795	0.263	0.137
MPV	10.312	10.426	9.911	0.094	0.043
PCT	0.201	0.194	0.218	0.349	0.135
PDW	19.777	20.336	17.866	0.003	0.001
WBC	12.601	11.294	7.677	0.000	0.000
NEU	75.105	71.771	65.389	0.000	0.001
LYM	18.355	20.342	29.184	0.000	0.000
MON	4.116	4.244	2.977	0.001	0.003
EOS	2.069	2.352	2.459	0.227	0.761
BAS	0.802	0.774	0.673	0.232	0.444
ALY	1.775	2.052	2.068	0.051	0.930
LIC	1.554	1.487	0.280	0.000	0.116
NLR	5.759	4.739	2.321	0.000	0.000
MLR	0.301	0.251	0.104	0.000	0.000
MPV : Platelet	0.083	0.110	0.052	0.008	0.030

Table 2. Descriptive Comparison between Critically Ill, Non-Critically Ill Patients and Normal Control Population

Group	GRADE 1	GRADE 2	GRADE 3	GRADE 4	Total
Critically ill	55 (69.6 %)	12 (15.19 %)	11 (13.92 %)	01 (1.27 %)	79 (100)
Non-critically ill	56 (70 %)	10 (12.5 %)	04 (5 %)	10 (12.5 %)	80 (100)

Table 3. Categorization of Critically Ill and Non-Critically Ill Patients Based on the Severity of Thrombocytopenia

DISCUSSION

Complete blood count is a routinely done basic investigation in all patients which includes hemogram and differential leucocyte count. In the present study WBCs were significantly raised in critically ill ($12.6 \times 10^9/L \pm 5.95$) and non-critically ill ($11.25 \times 10^9/L \pm 5.16$) patients when compared to normal control population ($7.68 \times 10^9/L \pm 1.76$). A study Bertolino et al. reported that there is transient leucocytosis in patients attending the emergency rooms which can be due to physical stress or medications and this settles down in one or two days once they are admitted to respective units.¹⁶ Another study done by Asadollahi et al. showed that more than 40 % hospitalized patients have WBCs > $10 \times 10^9/L$.¹⁷ In the present study WBCs were significantly higher in critically ill patients in comparison to non-critically ill patients (P = 0.019). This finding was in

concordance to Asadollahi et al. who stated that mortality is directly related to leucocytosis in the hospitalized patients.¹⁷

Among the WBCs, neutrophils are the most abundant cells. The result of immune response to various insults is increase in neutrophils and decrease in lymphocytes. When the insult persists there are large number of neutrophils and their apoptosis is slow resulting in neutrophilic leucocytosis.¹⁸ According to a study by Djordjevic et al. neutrophils were raised ($10.40 \times 10^9/L$) and lymphocytes were decreased ($0.95 \times 10^9/L$) in critically ill patients with pancreatitis, peritonitis, trauma or sepsis.¹⁹ Our study also had similar results with a significant increase of neutrophils in critically ill patients ($9.46 \times 10^9/L$) in comparison to both non-critically ill patients ($8.11 \times 10^9/L$) and control group ($5.02 \times 10^9/L$) with a P value of 0.005 and < 0.0001 respectively. This neutrophilic difference was also statistically significant between non-critically ill and control group (P value = 0.001). Similar to Djordjevic et al. study the lymphocyte count were also reduced in both the critically ill ($2.31 \times 10^9/L$) and non-critically ill patients ($2.29 \times 10^9/L$) in present study with a P value of 0.048.¹⁹ This finding highlights the fact that although neutrophils are raised whereas lymphocytes were reduced both in critically and non-critically ill hospitalized patients they are more significant in critically ill patients.

Platelet count is one of the most routinely used parameter by the clinicians but on the contrary platelet indices like MPV, platelet distribution width (PDW) and procalcitonin (PCT) which are available with the help of automated blood counters since a long time are not in much clinical application due to difficulties in standardization and calculation of reference values. Also, their diagnostic utility is not completely clarified. Reference values of platelet indices should be calculated for a particular population rather than comparing it with others and arriving to a conclusion. In the present study the platelet count was lower in non-critically ill patients ($194.98 \times 10^9/L \pm 124.10$) than the critically ill patients ($201.58 \times 10^9/L \pm 127.53$). Although both the groups had lower platelet count than the control group ($223.80 \times 10^9/L \pm 66.84$), but these differences were not statistically significant. A study by Khurana et al. showed that around 37 % of critically ill patients have thrombocytopenia.²⁰ The results of the present study were different from previous studies which concluded that critically ill patients have lower platelet counts than those of non-critically ill patients. This difference can be attributed to vigorous treatment of thrombocytopenia by frequent transfusions along with adequate and timely medication as well as care of the critically ill patients in our institute. The present study had thrombocytopenia in 39.5 % of critically ill patients (grade 1 - 69.6 %, grade 2 - 1.26 %, grade 3 - 1.39 %, grade 4 - 1.27 %) and 40 % of non-critically ill patients (grade 1 - 70 %, grade 2 - 12.5 %, grade 3 - 5 %, grade 4 - 12.5 %). (Table. 3)The results were similar to a study by Elgohary et al. that showed thrombocytopenia occurs in 15 % to 60 % of critically ill patients.²¹

Mean platelet volume and PDW were raised whereas PCT was reduced in both critically ill patients and non-critically ill patients but this difference was not significant when compared to normal control population. MPV in critically ill

patients studied by Djordjevic et al. (9.05 fl.) and Oral et al. (8.19 fl) were lower than that of present study.^{19,22} None of these values showed significant difference in the present study when compared to other studies hence was not of any importance.^{19,22,23}

Initially CBC was done for diagnosis of anaemia, leukaemia, certain neoplasms, immunodeficiencies and infections. Nowadays, the derived parameters like neutrophil to lymphocyte ratio (NLR), monocyte to lymphocyte ratio (MLR) and MPV : Platelets are found to be associated with activity, morbidity and mortality of various diseases. In critically ill patients, infections, inflammation, systemic lupus erythematosus, active rheumatoid arthritis and Takayasu's arteritis NLR and MLR are significantly increased in comparison to control patients.²⁴⁻²⁸ In the present study also when critically ill and non-critically ill patients were compared to control population both the NLR and MLR were significantly raised with a P value of less than 0.0001 (Table 2). On further comparison of NLR and MLR between critically ill and non-critically ill patients, both the values were slightly higher in critically ill patients and statistically significant (P = 0.010 and 0.027 respectively). This shows that the raised NLR and MLR values are not specifically raised for critically ill patients in fact these are raised in all sick patients irrespective of the underlying pathology.

MPV : Platelet ratio was 0.083 in critically ill patients, 0.110 in non-critically ill patients and 0.052 in control patients. This ratio was raised in both critically ill and non-critically ill patients and the difference between both the groups was statistically significant with a P value of 0.008. Here also the non-critically ill patients had higher MPV : platelet ratio than the critically ill patients with was in contrast to previous studies which had high MPV : Platelet in intensive care unit patients.²⁰ This is due to high platelet count in critically ill patients compared to non-critically ill patients in the present study.

Previous studies have compared the particular diseased persons with control population only and not with other diseased persons visiting the hospitals. These studies have compared only survivors and non survivors but they have not compared the critically ill and non-critically ill patients. To our knowledge this is the first study to compare the above entities in critically ill, non-critically ill and healthy persons. As no studies are without limitations, the present study does have limitations: We have not studied the role of different haematological indices & ratios in predicting the prognosis or outcome of the patients, patients were not categorized based on the underlying pathology and the sample size was small.

CONCLUSIONS

Modern day autoanalyzer provide ample information about the condition of the patient when interpreted correctly. The WBCs are markers of immediate insult of immune system in the form of neutrophilic leukocytosis in hospitalized patients with more significance in critically ill patients. The platelet count and indices may not be always helpful. NLR, MLR and

MPV to platelet ratios provide more precise information about the critical condition of the patients.

Data sharing statement provided by the authors is available with the full text of this article at jebmh.com.

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