Original Article

Pathology Section

The Study of Correlation between Different Complete Blood Count Parameters in Acute Coronary Syndromes

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ABSTRACT

Introduction: Red Blood Cell (RBC) count, White Blood Cell (WBC) count, Platelets and their indices correlates with increased risk and severity of Acute Coronary Syndrome (ACS).

Aim: To assess various haematological parameters like WBC, Absolute Neutrophil Count (ANC), Absolute Lymphocyte Count (ALC), Neutrophil Lymphocyte ratio (NLR), Mean Platelet Volume (MPV), Platelet Distribution Width (PDW) and all RBC parameters in patients diagnosed with ACS as risk predictors.

Materials and Methods: A prospective hospital based study was carried out on 116 cases with ACS and 116 controls (age and sex matched) from 1st November, 2015 to 30th June, 2017 considering the inclusion and exclusion criteria.

Results: The incidence of ACS in males (72.4%) was more as compared to females (27.6%). The most commonly affected age group was 5th decade. Total WBC count, ANC, ALC, NLR, MCHC, MPV and PDW showed significant association in ACS compared with healthy control group and in concordance with biochemical or electrocardiography results.

Conclusion: The study concludes that Total WBC count, ANC, ALC, NLR, MCHC and PDW parameters can give clinician a helping hand in diagnosis, assessing severity and timely interventions in cases of ACS admitted in intensive care units.

INTRODUCTION

Ischemic Heart Disease (IHD) is a group of syndromes with similar pathophysiology resulting from imbalance between myocardial supply and demand [1]. According to World Health Organisation, coronary vascular disease represents one-third of all global deaths. In India, 1/4th of mortalities are due to cardiovascular diseases [2,3].

Patients with IHD are classified into two groups:

• Patients with chronic Coronary Artery Disease (CAD)

• Patients with ACS

ACS represents patients with ST-elevation myocardial infarction on their presenting electrocardiogram and non-ST elevation ACS. The latter includes non-ST elevation myocardial infarction and those with unstable angina [4].

High blood cell counts, mainly neutrophil counts, platelet counts, their ratios and various other haematological parameters are strong and independent predictor of cardiovascular disease. As this is indirectly related to inflammation leading to increase in total count, neutrophil count, platelet hypersensitivity and platelet activation, so changes in these parameters will invariably be helpful in diagnosis and risk stratification in IHD [2,4].

The most sensitive and specific biomarkers of myocardial damage are Troponin T and I, level of both begin to rise within 2-4 hours and reaches peak value at 48 hours. Creatinine kinase enzyme begins to rise within 2 to 4 hours of onset of event and peaks at about 24 hours and comes back to normal within approximately 72 hours [1,4].

Patients admitted in coronary care units undergo excessive testing usually done in focused attempts to diagnose various coronary events. Despite the important influence of blood elements on the process of formation of arterial thrombus and in various stages of atherosclerosis, these routine haematological parameters which are easily recorded by automated cell counters which are available in most of the laboratories are traditionally not considered as bio-markers for identifying high risk patients.

The purpose of study was to contribute further to improve the efficacy of these haematological parameters as prognostic markers in ACS, which will lead to saving of enormous number of life, even in limited resource setting [5-7].

After a thorough search of literature, studies have been done in relation to platelets in region of north Karnataka but this study is exclusive in regards for inclusion of parameters of RBCs, WBCs and platelets.

MATERIALS AND METHODS

A prospective hospital based study was carried on 232 subjects from 1st November 2015 to 30th June 2017. There were 116 patients with ACS which were included in the study and compared with 116 normal healthy controls (age and sex matched) having a normal electrocardiogram and no past history of IHD.

The study was undertaken after obtaining approval from ethical committee. After taking the informed consent, all patients were interviewed as per Performa prepared and then complete clinical examination was done. The blood samples were collected from antecubital vein using aseptic precautions and analysed by standard procedure using 6 part differentiated automated Haematology analyser (Sysmex XN1000) [8]. Peripheral smear of all cases were studied. Relevant investigations like electrocardiogram and cardiac enzymes were performed.

Inclusion criteria: Patients diagnosed with myocardial infarction and unstable angina was included in study.

Exclusion criteria: Patients of coronary artery disease with haematological malignancies, systemic inflammatory disease and infectious causes, were excluded from study.

STATISTICAL ANALYSIS

For continuous variables, the summary statistics of mean, Standard Deviation (SD) were used. For categorical data, the number and percentage were used in the data summaries. Chi-square (χ^2)/ Freeman-Halton Fisher-exact test was employed to determine the

significance of differences between groups for categorical data. The difference of the means of analysis variables between two independent groups was tested by unpaired t-test. If the p-value was <0.05, then the results were considered to be statistically significant otherwise it was considered as statistically non-significant. Data were analysed using SPSS software v.23.0. and Microsoft office 2013.

RESULTS

A total of 232 subjects participated in the study, which were divided into 116 case group and 116 in control group, with 84 males and 32 females in case group. Age distributions between male and females were calculated, which indicates that as age increases male to female ratio decreases. In younger age group (3rd decade), it is 4:1 but as age increases, ratio reduces from 2.90:1 to 2.11:1 in 5th decade and 6th decade, respectively [Table/Fig-1,2].

Age (yrs)	Male		Female		M:F ratio	p-value
	N	%	N	%		
31-40	8	9.5	2	6.3	4.0	
41-50	17	20.2	4	12.5	4.25	
51-60	29	34.5	10	31.3	2.90	0.632
61-70	19	22.6	9	28.1	2.11	
>70	11	13.1	7	21.9	1.57	
Total	84	100.0	32	100.0	2.6	

[Table/Fig-1]: Age distribution by sex among cases.

Age (years)	Case		Control	
	N	Percent	N	Percent
31-40	10	8.6	13	11.2
41-50	21	18.1	18	15.5
51-60	39	33.6	37	31.9
61-70	28	24.1	30	25.9
>70	18	15.5	18	15.5
Total	116	100	116	100

[Table/Fig-2]: Age distribution by study groups.

The mean value for total WBC count (x10^3 per μl) in case and control group were statistically significant with p-value <0.001 at 5% level of significance. Mean values in study and control group came out to be giving statistically significant p-value <0.001 in both ANC and ALC. One of the important parameter which was derived in our study was Neutrophil to Lymphocyte ratio (NLR), had significant p-value of <0.001 [Table/Fig-3].

Parameters	Case		Control		p-value
	Mean	SD	Mean	SD	
WBC (x10^3 per μL)	12.5	3.9	7.5	1.4	<0.001*
ANC (x10^3 per μL)	10.2	4	4.7	1.2	<0.001*
ALC (x10^3 per μL)	1.9	0.9	2.4	0.6	<0.001*
N/L	7.3	5.8	2.1	0.7	<0.001*

[Table/Fig-3]: Comparison of mean WBC parameters among study group.
*significantly distributed at 5% level of significance

In present study, various other RBC parameters which were also evaluated, like Haematocrit (%) (HCT), Mean Corpuscular Volume (MCV), Mean Corpuscular Hemoglobin (MCH) (g/dL), p-value of all these parameters was statistically non-significant. But out of all RBC parameters, a MCHC (g/dL) was significant with p-value <0.001 [Table/Fig-4].

PDW (fl) and MPV (fl) were two of platelet parameters considered in this study. The p-value of these both platelet parameters (MPV, PDW) was statistically significant [Table/Fig-5].

Parameters	Case		Control		p-value
	Mean	SD	Mean	SD	
Hb (g/dL)	13.1	2.7	13.1	1.7	0.967
HCT (%)	39.2	7.2	40.6	4.9	0.103
RBC (10^6/μL)	4.6	0.8	4.9	2.6	0.238
MCV (fl)	86.1	9.7	87.1	9.1	0.448
MCH (pg)	28.6	4.0	28.2	2.5	0.344
MCHC (g/dL)	33.1	2.0	32.2	1.4	<0.001*

[Table/Fig-4]: Comparison of mean RBC parameters among study groups.
*significantly distributed at 5% level of significance

Parameters	Case		Control		p-value
	Mean	SD	Mean	SD	
PDW (fl)	11.7	2.2	11.1	2.1	0.032*
MPV (fl)	10.2	0.9	9.9	0.9	0.014*

[Table/Fig-5]: Comparison of mean platelets parameters among study groups.
*significantly distributed at 5% level of significance

DISCUSSION

Extensive research in the past decade has led to establishing atherosclerosis as an inflammatory disease, which has opened potential for new parameters in predicting Coronary Heart Disease (CHD). Although myocardial infarction is traditionally considered an older patients disease which are above 45 years but now-a-day's lot of younger men and women are also getting affected. There is an increase in the prevalence of heart disease among specific ethnic groups like Asian Indian origin, these people are at risk of myocardial infarction at a much younger age as compared to rest of the world population due to association with complex coronary artery abnormalities. In this context, potentially 80% of cardiovascular disease cases are preventable due to modifiable risk factors but still mortality continues to rise, mainly because of ineffective and insufficient preventive measures [4,9-11].

Almost all of the cellular elements of blood like WBCs, RBCs and Platelets are involved in pathogenesis of atherosclerosis and its complications. These cellular elements not only plays a role in development of CHD, but can also help in predicting any recurring event and even death in previously diagnosed CHD patients [4].

In the present study, overall male to female ratio was 2.6:1, but among the various age groups between males and females, as age increases it was noted male to female ratio has decreased. In younger age group (3rd decade) it was 4:1 but as age increases ratio reduced to 1.57:1 (>70 years). The most affected group were in 5th and 6th decade with least were in 3rd decade (8.2%) [Table/Fig-1,2]. It is widely accepted that post-menopausal women lose the protective action of endogenous oestrogen on vascular endothelium, which lead to increased risk of CAD which was comparable with the findings of present study. An average age of onset of CVD is younger among Indians than the rest of the world. Affected age for the developed world is >45 years but in Indian set-up affected age is between 35 to 64 years, which correlates with this study where 75.8% of subjects were between 4th to 6th decades of life [12]. Study subjects above 70 years accounted for 15.5% of present case subjects. In present study mean age for case group was 57.91±11.36 years and 57.99±11.64 years in control group.

The prevalence of CVD is higher in males than females though the mortality due to CVD is higher among females. The Framingham study showed that women have a lower incidence of CAD than men do, until the age of 75 years [12,13].

The leukocyte count has been correlated with CHD since 1920s. Large number of studies has been conducted in CHD free populations over several decades to show positive correlation between leukocyte count and risk of CHD [14].

Not just high neutrophil count but also lymphopenia also contributes to worse clinical outcome with ST-elevation myocardial infarction. Thus, NLR has emerged as an effective indicator of inflammatory state in various clinical studies [15]. NLR has also emerged as an indicator of early and late clinical outcomes in patients of ST-elevation myocardial infarction undergoing primary percutaneous coronary intervention [16].

In various studies done by Demir K et al., [17], Zhang GY et al., [18], Selcuk H et al., [19], Erkol A et al., [20], Bajari R et al., [21] have shown that NLR is not only an independent predictor of presence of CAD but also can be helpful in long term mortality prediction [17-21]. Present study results as shown in [Table/Fig-6], were also indistinguishable from these studies between coronary pathology and NLR.

Other studies	Control group	Case group	p-value
Nunez J et al., [15]	-	-	<0.01
Naz S et al., [16]	1.61	3.67	<0.01
Demir K et al., [17]	1.7±0.57	2.95±1.29	<0.01
Zhang GY et al., [18]	-	3.64±1.94	<0.01
Seluck H et al., [19]	2.04±1.01	2.86±1.57	<0.01
Erkol A et al., [20]	4.1±3.2	6.9±5.5	<0.01
Bajari R et al., [21]	4.1±3.39	7.92±3.46	<0.01
Present study	2.1±0.7	7.3±5.8	<0.01

[Table/Fig-6]: Showing comparison of NLR ratio with other studies [15-21].

Total WBC counts, ANC, ALC, NLR were showing significant association with ACS. The result represents a strong correlation with presence of neutrophils. These neutrophils release proteolytic neutral proteases which lead to detachment of endothelial cells from vessel walls along with adherence of platelets to sub-endothelial collagen. In activated stage, neutrophils also release large amount of chemotactic agent Leukotriene B4 and also many inflammatory mediators [22,23].

In RBC parameters like Hb, HCT, RBC, MCV, MCH, MCHC were studied and only MCHC was the only affected parameter which was significantly correlating in the case group but the possible mechanism is not well understood, it was proposed in literature that MCHC has to be considered as an inflammatory marker [24].

In platelet parameters, MPV and PDW both were statistically significant in ACS patients. These results were comparable to other studies done in literature [25-28]. Main mechanism is the result of inflammatory cytokines and acute cellular response due to inflammation. Though few studies also showed no significant correlation between platelet parameters. Larger studies are required to further validate the results.

LIMITATION
Larger sample size studies are required to substantiate the results. The present study has not segregated smokers/non-smokers and parameters of lipid profile were not considered. Follow-up of patients and outcome has to be considered. Platelets with qualitative disorders and causes of reactive platelets were not assessed.

CONCLUSION
The study concluded that various complete blood count parameters were analysed in patients with ACS and found to be statistically significant except MCHC. These parameters should be utilised for prognostication and timely management of patients admitted in ICU diagnosed with ACS as they are readily available and inexpensive.

FUTURE RECOMMENDATIONS
- For routine CBC haematology report in addition, we recommend to include ANC, ALC, NLR, MPV and PDW for the patients admitted in intensive care unit for reason of CVD.

- Awareness and utility of these new parameters to the residents and critical care specialists for timely intervention in ACS patient management for better outcome.

- NLR can also be used for risk stratification in cases of previously diagnosed IHD patients.

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