Original Research Article

A STUDY OF HAEMATOLOGICAL INDICES AND THEIR CORRELATION WITH IN-HOSPITAL MORTALITY & MORBIDITY IN ACUTE CORONARY SYNDROME

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Abstract

Background: Coronary Artery Disease (CAD), an emerging pandemic is causing significant morbidities and mortalities across the globe. ACS is a life threatening manifestation of CAD. It warrants an early risk stratification and timely intervention. Prompt Clinical Evaluation, ECG and Biomarkers remain corner stone in approaching ACS. Recently, Haematological indices, have gained attention because of their significant associations in predicting outcomes of CAD. We carried out a prospective cross-sectional study among ACS patients to find the association of Red Cell Distribution Width (RDW), Haemoglobin Corrected RDW (HbCRDW), Red Cell Width Volume Index (RWVI), Neutrophil/Lymphocyte Ratio (NLR) and Platelet Distribution Width (PDW) with in-hospital Major Adverse Cardiac Events (MACEs) such as Recurrent Angina, Clinical LVF, LV Dysfunction by ECHO, Arrhythmias and Death.**Methods:** A total of 100 patients diagnosed to have ACS (Unstable Angina, STEMI, NSTEMI) and admitted in our hospital were enrolled for the study. The significance of association between the haematological parameters of interest with the MACEs were found using Fisher Exact Test. **Results:** The mean age of study participants was 55.72±11.07 years with 74% of them being males. 36% were Diabetic, 41% were hypertensive and 19% had both as major CAD risk factors. The distribution of ACS was a majority 68% with STEMI, 21% with Unstable Angina and 11% with NSTEMI. 81 of them underwent Coronary Angiogram and subsequently 49 patients had revascularisation procedure within their in-hospital stay. Frequency of occurrence of In-hospital MACEs were 17% Recurrent Angina, 42% Clinical LVF, 57% LV Dysfunction (mild-25%; moderate-21%; severe-11%), 18% Arrhythmias and 10% Mortality. Using Fisher-Exact test, RDW (>15%) had a significant association with Recurrent Angina (P=0.012) and LV Dysfunction (P=0.09). Higher tertiles of HbCRDW & RWVI had significance in predicting Recurrent Angina with P values of 0.013&0.043 respectively. Higher tertiles of NLR (>3.75) was statistically significant in prediction of Clinical LVF (P=0.086) and Arrhythmias (P=0.080). None of the studied parameters were found to have significance in predicting in-hospital mortality.**Conclusion:** RDW and its derived indices HbCRDW, RWVI are strong predictors of in-hospital Recurrent Angina among ACS patients. In addition, Higher values of RDW are also useful in predicting LV dysfunction. Though, there was no significant relationship between PDW and MACEs, NLR is found significant in predicting clinical LV failure and arrhythmias.

Keywords: Coronary Artery Disease, morbidities and mortalities, ECG, arrhythmias.

Introduction

Coronary Artery Disease (CAD) is one of the leading cause of mortality and morbidity in Industrialised nations and developing countries like India.

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CAD contributed to 23% of total deaths and 32% of adult deaths in India between 2010-13. India's burden of CAD is worse compared to global average, since our nation has a higher age-standardised death rate due to CAD. In its CAD epidemiology, the country is peculiar in its dubious distinction of a steep rise in Pre Mature Death due to CAD evidenced by 59% increase over the past two decades[(1).]

Acute Coronary Syndrome (ACS) is the life threatening

manifestation of CAD. Among the patients presenting to the emergency services, chest pain due to myocardial ischemia is attributed to 8-10% of total admissions.[2] Hence, predicting the clinical outcomes and risk stratifying the patients admitted with ACS becomes essential. There are many cardiac biomarkers available to predict the outcomes of patients with ACS.

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They are supportive in taking clinical decisions with respect to in-hospital acute phase management. In addition, they are also utilised to serve the purpose of assessing the long term prognosis[3]. The major limitations of conventional cardiac biomarkers are: they are expensive, they are still not available in all Indian centres.

In the recent years, Haematological Indices such as Red Cell Distribution Width (RDW), Neutrophil/Lymphocyte Ratio (NLR), Platelet Distribution Width (PDW), Mean Platelet Volume (MPV) are studied in predicting the risks and outcomes of patients with ACS. The said parameters have been found to be having an independent association with ACS outcomes and severity of CAD. Since they are widely available at cheaper prices, their association with outcomes of ACS is regarded with potential significance.[4]

The exact mechanism behind the association of Haematological indices and their correlation with severity of CAD is under clinical research. There are very few studies which compared the different haematological indices from all three cell lineages, namely Red Cell, White Cell and Platelets with the clinical outcomes of patients having ACS.

This study is an effort to analyse haematological indices representing all three cell lineages and their correlation with clinical outcomes of ACS. As with earlier studies, the need for the study was to analyse their significance in predicting the mortality and morbidity in patients with ACS.

Aims and Objectives

1. To study the correlation of Red Cell Distribution Width Indices, Neutrophil- Lymphocyte Ratio, Platelet Distribution Width with In-hospital Mortality and Morbidity in patients presenting with Acute Coronary Syndrome.
2. To observe the trends in values of RDW Indices, Neutrophil/Lymphocyte Ratio, Platelet Distribution Width in Patients of Acute Coronary Syndrome.
3. To assess if there is any association of each individual indices with adverse outcomes of Acute Coronary Syndrome in terms of In Hospital Mortality & Morbidity - MACE (Major Adverse Cardiac Events).

Material and methods

This study was carried out in the Department of General Medicine and in collaboration with Department of Cardiology in Mahatma Gandhi Medical College and Research Institute during the period of January 2016 to January 2017. This study was ethically approved by the Institutional Ethical Committee.

This study was an observational clinical study with 100 cases of Acute Coronary Syndrome. Cases were selected from those who were admitted for ACS under Department of General Medicine and Cardiology. Study was carried out after obtaining written and informed consent from the study participants.

BRIEF EXPLANATION OF THE PROCEDURE

STUDY SUBJECTS:

Hundred patients of ACS (ST Elevation MI, Non ST Elevation MI and Unstable Angina) diagnosed as per Clinical presentation, ECG changes and Cardiac Biomarkers were included in the study. Following criteria was laid for exclusion from the study. They are as follows:

- Active Malignancy
- Hemato-proliferative Diseases
- Inflammatory Rheumatic Disease
- Acute or Chronic Inflammatory or Auto-Immune Disease
- Sepsis
- Recent Blood Transfusion
- Anaemia Hb<7g/dl

- On Haematinics

METHODOLOGY:

As a part of routine Standard Operating Procedures, Patients presenting to the Emergency Department of Mahatma Gandhi Medical College with Chest Pain, Breathlessness with high index of suspicion of ischemia/infarction will be subjected to rapid Clinical Evaluation.12 leaded ECG will be taken. Blood samples will be taken for Cardiac Biomarkers CK-Total,CK-MB Fraction and Troponin I. Along with them as a part of routine investigations Complete Blood Count will be performed. An aliquot of 5 ml blood of each subject will be taken in a typical biochemistry tube, which will be centrifuged at 2000 rpm for 10 minutes to obtain serum. For analyses of Hematlogical Indices under study, aliquots of 2 ml blood will be taken in the EDTA (ethylendiamine tetra acetic acid) tubes, which will be examined within 30 minutes by automated analysers.

Diagnosis of ACS will be confirmed with typical symptoms, ECG findings and laboratory findings. The diagnosis of AMI will be established by the three criteria accepted by World Health Organization (WHO): (1) ischemic type chest pain; (2) Changes in serial ECG tracings typical for AMI; and (3) presence of at least two criteria of typical course of rise and fall of serum cardiac biomarkers. The diagnosis of unstable angina pectoris will be established by the presence of unstable chest pain stratified using Braunwald Criteria and typical electrocardiographic findings in the absence of elevated CK-MB and Troponin levels.

With the above procedure, whenever a patient was diagnosed to have acute coronary syndrome, those patients were contacted immediately. Details of the study were explained to them if they are hemodynamically stable and conscious enough to understand. Else the details were explained to the closest kin available who was responsible for taking decisions for the patient. Permission was sought in the form of written consent and the study was conducted.

Their haematological report was accessed and the values were noted down. The Red Cell Derived Indices such as Hemoglobin Corrected RDW (HbCRDW) and Red Cell Width Volume Index (RWVI) are derived using following formulae.

HbCRDW= (RBC*RDW)/Hemoglobin

RWVI = PCV*RDW

All the patients in study continued to get the standard treatment for ACS and they were followed up on daily basis from the day of admission till discharge to observe for the following Major Adverse Cardiac Outcomes (MACE)

- Death
- Clinical Left Ventricular Failure
- Cardiac Arrhythmias
- Left Ventricular Dysfunction
- Recurrent Angina

1. In addition other clinical data relevant to the study such as Age, Sex, Diagnosis, Diabetes, Hypertension, Thrombolysis agent, Angiogram findings were recorded.

DATA COLLECTION:

The data was noted down for individual patient in a standard case proforma. Then it was transferred to a master chart in excel format and subjected to statistical analysis.

STATISTICAL METHODS:

Descriptive and inferential statistical analysis has been carried out in the present study. Results on continuous measurements are presented on Mean ± SD (Min-Max) and results on categorical measurements are presented in Number (%). Significance is assessed at 5 % level of significance. The following assumptions on data is made,

ASSUMPTIONS:

1. Dependent variables should be normally distributed,

2. Samples drawn from the population should be random, Cases of the samples should be independent.

3. Analysis of variance (ANOVA) has been used to find the significance of study parameters between three or more groups of patients, Chi-square/ Fisher

Exact test has been used to find the significance of study parameters on categorical scale between two or more groups.

SIGNIFICANT FIGURES

+ Suggestive significance (P value:0.05<P<0.10)

* Moderately significant (P value:0.01<P ≤ 0.05)

** Strongly significant (P value : P≤0.01)

Statistical software: The Statistical software namely SAS 9.2, SPSS 15.0, Stata 10.1, MedCalc 9.0.1,Systat 12.0 and R environment ver.2.11.1 were used for the analysis of the data and Microsoft word and Excel have been used to generate graphs, tables etc**.**

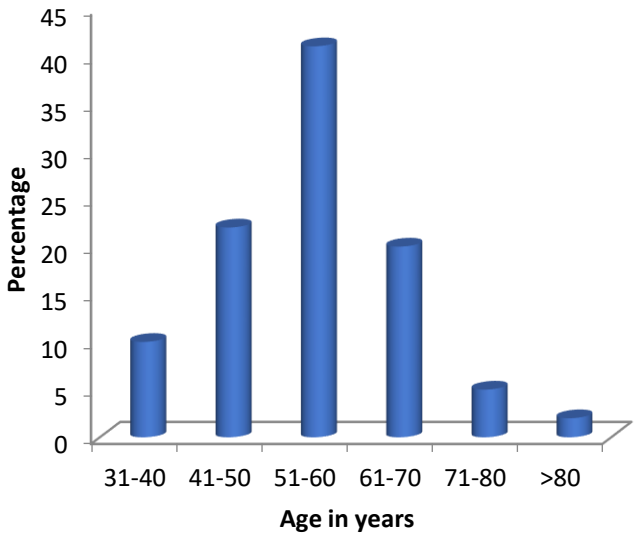

Figure 1: Age distribution of patients studied

Observations

Baseline Characteristics of Study Population:

Mean Age is 55.72±11.07 years and gender distribution of the patients are tabulated in Table 1 and 2.

Table 1: Age distribution of patients studied

Age in years	No. of patients	%
31-40	10	10.0
41-50	22	22.0
51-60	**41**	**41.0**
61-70	20	20.0
71-80	5	5.0
>80	2	2.0
Total	100	100.0

Table 2: Gender distribution of patients studied

Gender	No. of patients	%
Female	26	26.0
Male	74	74.0
Total	100	100.0

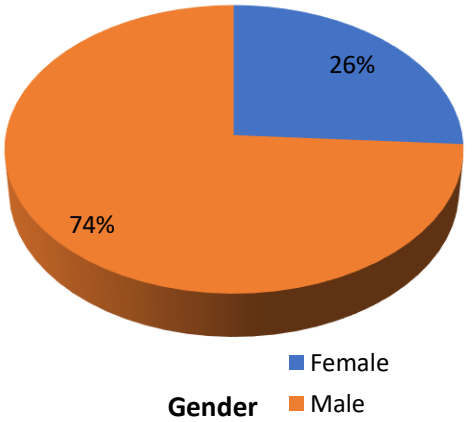

Figure 2: Gender distribution of patients studied

Distribution of the type of Acute Coronary Syndrome diagnosis is listed in following table.

Table 3: Diagnosis distribution of patients studied

Diagnosis	No. of patients	%
IWMI	**42**	**42.0**
USA	21	21.0
AWMI	26	26.0
NSTEMI	11	11.0
Total	100	100.0

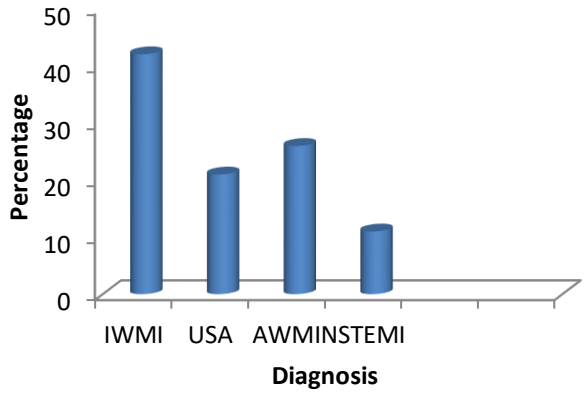

Figure 3: Diagnosis distribution of patients studied

Out of the above, 26% of them met the criteria for thrombolysis and were thrombolysed. The various agents used for thrombolysis were Streptokinase (15 patients), Reteplase (6 patients) and Tenecteplase (5 patients).

Table 4: Thrombolysed Type

Thrombolyis Agent	No. of patients	%
Nil	74	74.0
STK	15	15.0
TNK	6	6.0
RET	5	5.0
Total	100	100.0

Among the patients studied, 36% of them were diabetics, 41% of them were hypertensives and 19% of them were both diabetic and hypertensives. Out of the 100 patients, 81 of them underwent Coronary Angiography (CAG). The various findings in CAG are tabulated below.

Table 5: Findings in CAG

Findings	No. of patients

Single Vessel Disease	38
Double Vessel Disease	14
Triple Vessel Disease	10
Recanalsied RCA	7
Recanalised LAD	6
Recanalised LCX	2
Branch Vessel Disease	1
Normal Coronaries	2
Rescue PCI arrest	1
Total	81

Out of the study patients, revascularisation procedures were done for 49 patients. Procedures done are tabulated.

Table 6: Revascularisation procedures

Procedure	No. of patients	%
PTCA to RCA	19	32.20
PTCA to LAD	12	20.34
PTCA to LCX	7	11.86
PTCA to RCA&LAD	3	5.08
CABG	8	13.56
Total	49	100

CLINICAL VARIABLES STUDIED:

The frequency of occurrence of major adverse cardiac events namely Recurrent Angina, Clinical LV faiure, LV Dysfunction, Arrhythmia and Death are tabulated below.

Table 7: R.Angina distribution of patients studied

R.Angina	No. of patients	%
No	83	83.0
Yes	17	17.0
Total	100	100.0

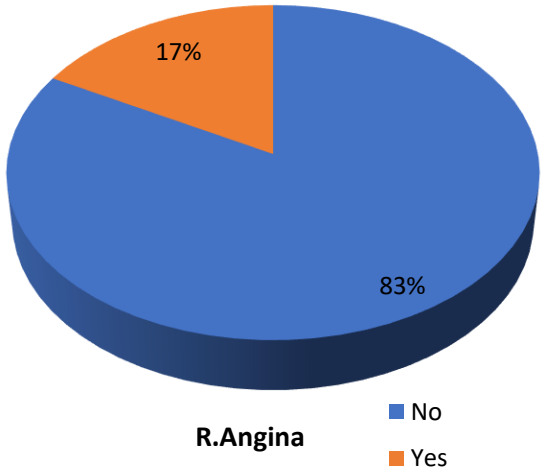

Figure 4: R.Angina distribution of patients studied

Table 8: Clinical LVF distribution of patients studied

Clinical LVF	No. of patients	%
0	58	58.0

1	42	42.0
Total	100	100.0

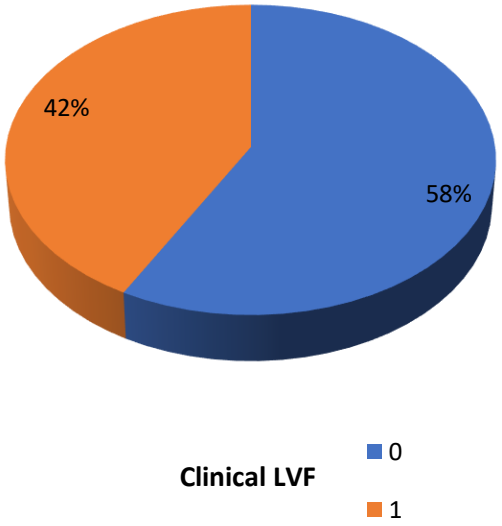

Figure 5: Clinical LVF distribution of patients studied

Table 9: LV Dysfunction distribution of patients studied

LV Dysfunction	No. of patients	%
Normal	43	43.0
Mild	25	25.0
Moderate	21	21.0
Severe	11	11.0
Total	100	100.0

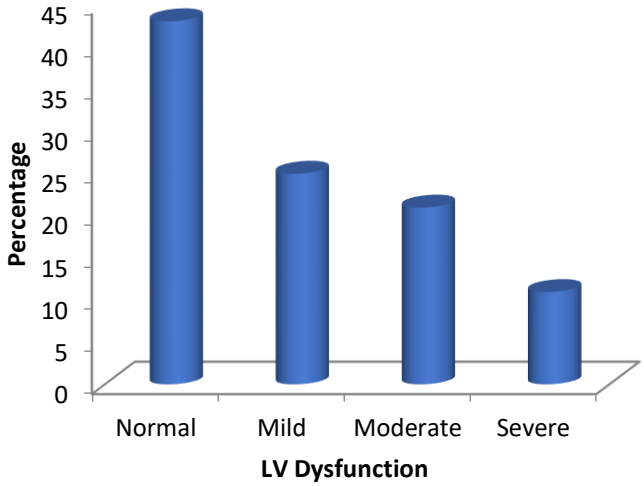

Figure 6: LV Dysfunction distribution of patients studied

Table 10: EF distribution of patients studied

EF%	No. of patients	%
≤30	10	10.0
31-44	21	21.0
45-54	25	25.0
≥55	43	43.0
Ventricular Sepetal Rupture	1	1.0
Total	100	100.0

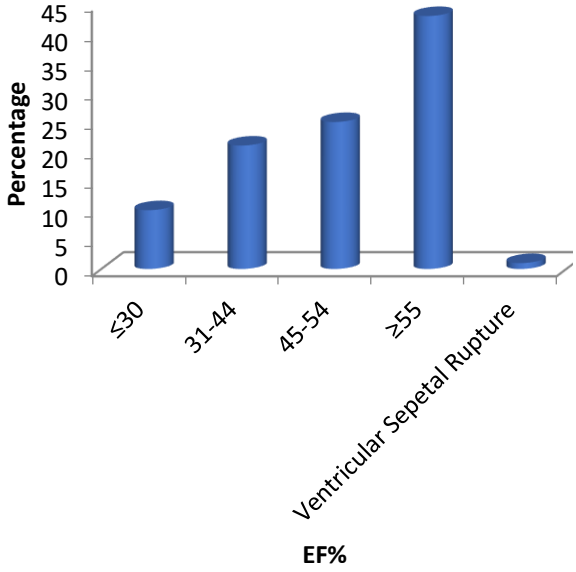

Figure 7: EF distribution of patients studied

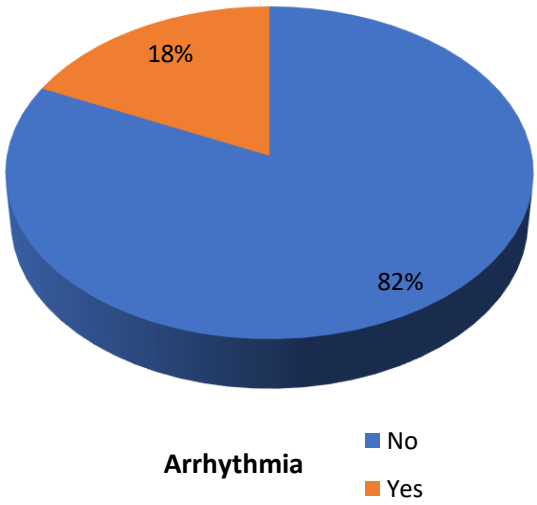

Figure 8: Distribution of Arrhythmias

Table 11: Arrhythmia distribution of patients studied

Arrhythmia	No. of patients	%
No	82	82.0
Yes	18	18.0
Total	100	100.0

Table 12: Distribution of Arrhythmias

Arrhythmia Type	No. of patients	Mortality
Atrial Fibrillation	5	-
Atrial Flutter with Variable AV Block	1	-
Junctional Rhythm with Bradycardia	1	-
Ventricular Tachycardia	6	5*
Sinus Bradycardia Arrest	3	3
Complete Heart Block	2	2

*1 patient who had Polymorphic VT on presentation, who went into cardiac arrest was

successfully revived, except whom the remaining 5 patients had in-hospital mortality.

Table 13: Death

Death	No. of patients	%
No	90	90.0
Yes	10	10.0
Total	100	100.0

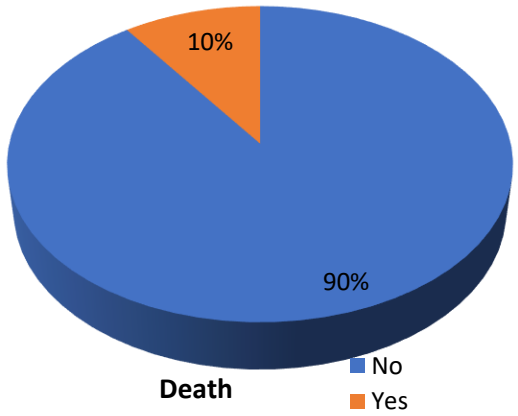

Figure 9: Death

ASSOCIATION OF THE STUDIED PARAMETERS WITH MACE

MACE 1 – Recurrent Angina

Out of the hematological parameters studied, Red cell Distribution Width (RDW) and its derieved indices namely Hemoglobin Corrected RDW (HbCRDW); Red Cell Width Volume Index (RWVI) had a significant association with occurence of in-hospital Recurrent Angina among patients admitted with ACS.

RDW values >15% , Higher tertiles of HbCRDW (>56223), RWVI (>5.8) show a statistically moderate significance with P values of 0.012, 0.013 and 0.043 respectively for their association with recurrent angina.

Neutrophil-Lymphocyte Ratio (N/L Ratio) Platelet Distribution Width (PDW) did not have any statistical significance with occurence of Recurrent Angina.

Table 14: RDW distribution in relation to R angina of patients studied

RDW	R Angina		Total
	No	Yes	
≤12%	2(2.4%)	0(0%)	2(2%)
12-15%	54(65.1%)	5(29.4%)	59(59%)
>15%	27(32.5%)	12(70.6%)	39(39%)
Total	83(100%)	17(100%)	100(100%)

P=0.012*, significant, fisher Exact test

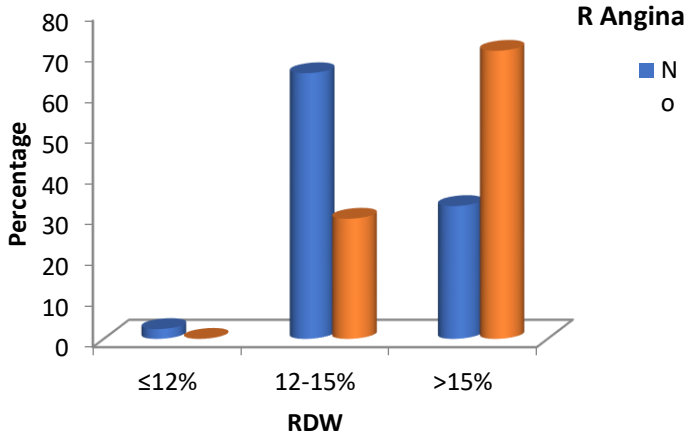

Figure 10: RDW distribution in relation to R angina of patients studied

Table 15: Distribution of R.Angina in relation to tertile distribution of HbCRDW

	Tertile HbCRDW			Total (n=100)	P value
	48147 (n=33)	**48147-56222 (n=34)**	**>56223 (n=33)**		
R Angina					

• No	32(97%)	28(82.4%)	23(69.7%)	83(83%)	0.013*
• Yes	1(3%)	6(17.6%)	10(30.3%)	17(17%)	

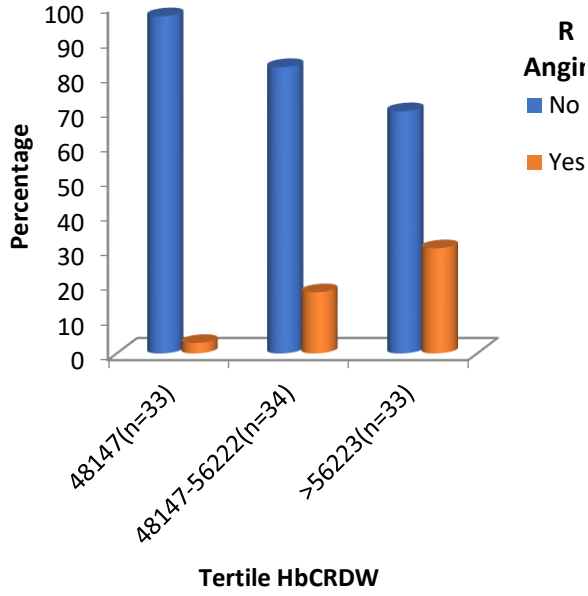

Figure 11: Distribution of R.Angina in relation to tertile distribution of HbCRDW

Table 16: Distribution of R.Angina in relation to tertile distribution of RWVI

variables	Tertile RWVI			Total (n=100)	P value
	4.99 (n=33)	4.99-5.79 (n=34)	>5.80 (n=33)		
R Angina					
No	29(87.9%)	31(91.2%)	23(69.7%)	83(83%)	0.043*
Yes	4(12.1%)	3(8.8%)	10(30.3%)	17(17%)	

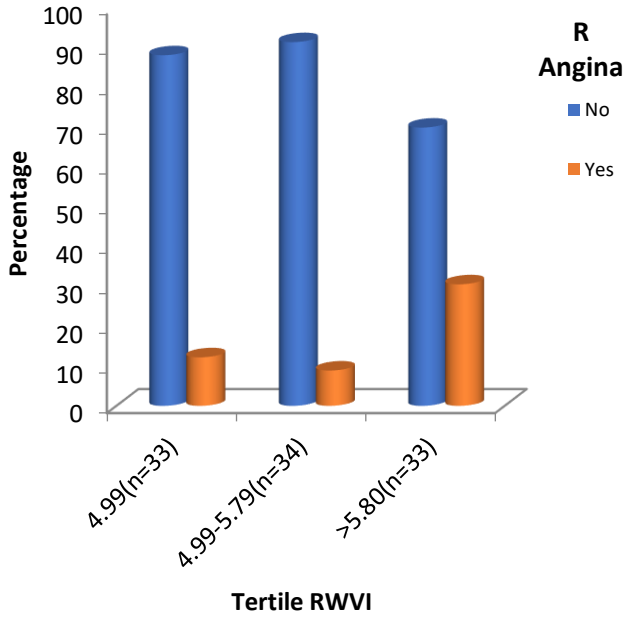

Figure 12: Distribution of R.Angina in relation to tertile distribution of RWVI

MACE 2 – Clinical LV Failure:

Higher tertile of N/L ratio (>3.75) has a statistically suggestive significance (P=0.086) in predicting the occurrence of In-Hospital Clinical Left Ventricular Failure.

Table 17: Distribution of Clinical LVF in relation to tertile distribution of N/L ratio

variables	Tertile NL Ratio			Total (n=100)	P value
	<2.13 (n=32)	2.13-3.75 (n=35)	>3.75 (n=33)		
Clinical IVF					
0	21(65.6%)	23(65.7%)	14(42.4%)	58(58%)	0.086+
1	11(34.4%)	12(34.3%)	19(57.6%)	42(42%)	

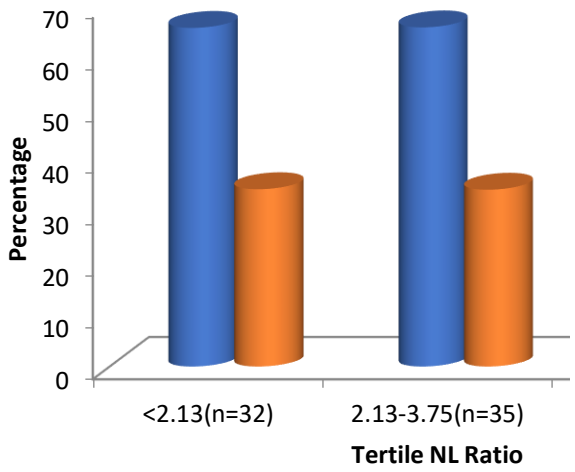

Figure 13: Distribution of Clinical LVF in relation to tertile distribution of N/L ratio

Other parameters such as RDW, HbCRDW, RWVI and PDW did not have any significant association with clinical LV failure.

MACE 3 – LV DYSFUCNTION

There was statistically suggestive significance (P=0.09) between higher RDW values and degree of LV Dysfucntion by Echocardiogram.

Table 18: RDW distribution in relation to LV dysfunction of patients studied

RDW	LV dysfunction				Total
	Normal	Mild	Moderate	Severe	
≤12 %	1(2.3%)	1(4%)	0(0%)	0(0%)	2(2%)
12-15 %	26(60.5 %)	10(40 %)	13(61.9 %)	10(90.9 %)	59(59%)
>15 %	16(37.2 %)	14(56 %)	8(38.1 %)	1(9.1%)	39(39%)
Total	43(100 %)	25(100 %)	21(100 %)	11(100 %)	100(100%)

P=0.090+, significant, fisher Exact test

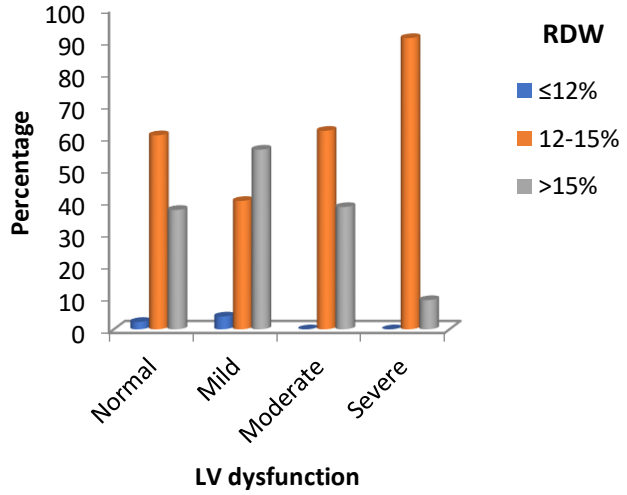

Figure 14: RDW distribution in relation to LV dysfunction of patients studied

Other parameters such as N/L Ratio, HbCRDW, RWVI and PDW did not have any significant association with LV Dysfunction.

MACE 4 – ARRYTHMIAS:

Of all the parameters, ***Higher tertile of Neutrophil/Lymphocyte Ratio (NLR) had a statistically suggestive significance (P=0.080) in predicting occurrence of arrhythmias.***

Table 19: Distribution of Arrhythmia in relation to tertile distribution of N/L ratio

Variables	Tertile NL Ratio			Total (n=100)	P value
	<2.13 (n=32)	2.13-3.75 (n=35)	>3.75 (n=33)		
Arrhythmia					
No	28(87.5%)	31(88.6%)	23(69.7%)	82(82 %)	0.080+
Yes	4(12.5 %)	4(11.4 %)	10(30.3%)	18(18 %)	

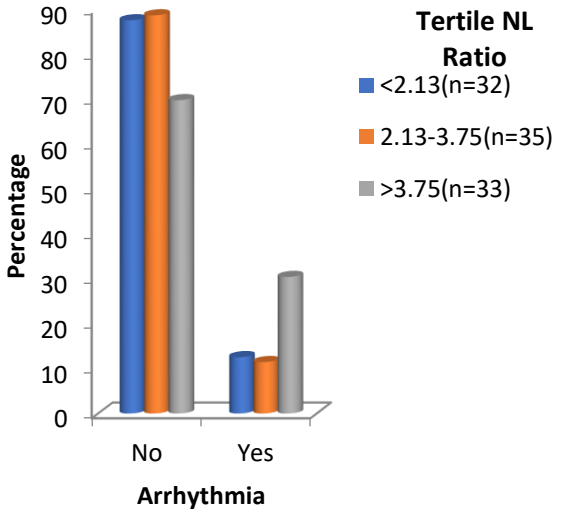

Figure 15: Distribution of Arrhythmia in relation to tertile distribution of N/L ratio

MACE 5 DEATH:

All the haematological parameters studied did not show any statistically significant association with in hospital mortality.

Discussion

Recently a number of studies have been carried out to correlate Hematological indices and outcomes in various chronic systemic diseases including CAD. This phenomenon in clinical research has gained ground because of altered haematopoiesis secondary to underlying common pathophysiology – ''Chronic Inflammation''. Chronic Inflammation is the root cause of Atherosclerosis, which is the basic pathophysiologic mechanism in the development of ACS.[4]

Only few studies have demonstrated relationships of all three cell lineages (Erythrocytes, Leucocytes and Thrombocytes) with outcomes of ACS in a single study[5].

Hence we evaluated the relationship of Red Cell Distribution Width (RDW), Red cell indices such as Hemoglobin Corrected RDW (HbCRDW), Redcell Width Volume Index (RWVI), Neutrophil/Leucocyte Ratio (NLR), and Platelet Distribution Width (PDW) with the occurrence of Major Adverse Cardiac Events (MACE) during in-hospital stay among patients admitted with Acute Coronary Syndrome (ACS).

RED CELL INDICES:

In our study, Red cell indices, RDW, HbCRDW and RWVI showed a significant association with the occurrence of Recurrent Angina. In addition, Higher RDW values had a significant positive correlation with worsening Left Ventricular dysfunction. In a similar South Indian study carried out by JV Narayana et al. among 100 ACS patients, RDW was a useful prognostic marker of MACE at 30 days but not in in-hospital MACE, whereas HbCRDW, RWVI were useful in predicting in-hospital MACE. It held true in our study as they showed significant association with Recurrent angina.[6]

Gianni et al. proved with 979 ACS patients that RDW was a useful predictor for medium term MACE (at 3months). A value of >14.8% showed a significant association [7].

An Israel based study involving large cohort of ACS patients (1,709) showed independent association of higher RDW with risk of increased heart failure and mortality following ACS irrespective of presence or absence of anemia.

In a larger community cohort study by Arbel et al., involved the database of 2,25,006 patients with a hemogram done. They were followed up for a median 6 years for the risk of CV morbidity and all cause mortality. It was found out that higher RDW (>17%) was associated with increased CV morbidity and mortality irrespective of presence or absence of anemia.

Though in our study we excluded patients with haemoglobin less than 7g/dl, RDW was not associated with in-hospital mortality risk. It may be implied that a larger cohort of patients with a longer follow up is further needed to assess any significance.

NEUTROPHIL/LYMPHOCYTE RATIO (NLR)

In the setting of acute inflammation, Neutrophil activation leads to pro-thrombotic state. It is explained by the phenomenon of increased Neutrophil Extra Cellular Traps (NETs) at the site of coronary thrombi. Serum Markers of NETs are shown to be increased in STEMI patients.

On the other hand, lymphocytes (T Helper Cells and B2) are anti-atherosclerotic. Vaduganathan et al. showed that a reduction of 10% of lymphocytes are associated with adverse CV outcomes.

Hence, many studies have been found out NLR to be associated with adverse outcomes in CAD. In our study, we found higher tertile of NLR (>3.75) was associated with Clinical Left Ventricular Failure and occurrence of arrhythmias during in-hospital stay among ACS patients.

In a similar study done by Akpek et al. among 418 STEMI patients undergoing PCI, NLR was found to be an independent correlate for in-hospital MACEs as well as development of no reflow[8].

Chatterjee et al. found significance of pre-procedural NLR in predicting occurrence of Ventricular arrhythmias during PCI in their retrospective case control study.

Also, Ozdemir et al. found higher NLR to be associated with lower Left Ventricular Ejection Fraction, in his study involving 262 CAD patients undergoing Myocardial Scintigraphy.

A meta analysis of 13 studies conducted by Wang et al. on patients who underwent Coronary Angiography or Revascularisation. It found out that the relative risk (RR) of CV events and all cause mortality was higher with higher NLR. Tamhane et al. studied a large cohort of 2,833 ACS patients, for whom a highest tertile of NLR was associated with increased in-hospital mortality (8.5% vs 1.8%) as well as mortality at the end of 6 months (11.5% vs 2.5%) compared to lowest tertile. However in our study there was no statistical significance between NLR and in-hospital mortality.

PLATELET DISTRIBUTION WIDTH (PDW)

Platelets play a central role in the process of atherosclerosis, hence the development of CAD. Platelet aggregation and activation along with endothelial inflammation are key consequences of post plaque rupture culminating in ACS. Hence platelet indices are studied to assess the outcomes in ACS. In Our study, PDW, grouped in tertiles, was included as the platelet parameter to correlate with in-hospital MACE. There was no statistical significance of PDW found in our study to predict MACE.

There has been conflicting reports from different studies with respect to PDW being an useful marker in ACS. Like our study, Ozdemir et al. in his study did not find PDW to be statistically significant in elucidating myocardial perfusion abnormalities in ACS patients. In contrast, Belker et al. in his study of 502 ACS patients, found a higher PDW >17% was significantly associated with higher Gensini Score and hence the severity of CAD.

Cetin at al. had found among 260 patients, grouped into STEMI and stable CAD, a significant association between PDW and occurrence of STEMI as well as higher PDW is associated with thrombolysis failure[9].

It is also found that most studies use tertile values of PDW for analysis, including our study[10]. In 2012, a South Indian study done among 500 healthy subjects had attempted to define normal range of PDW for adult male and female as 9 fL -16.56 fL and 8 fL -13.28 fL respectively[11]. A Sudanese based study included 300 subjects derived normal ranges for males as 8.7-15.7 fl and females as 7.8-16.2 fl[12]. Farias et al. finds among 231 patients that a PDW range of 10-17.9% as normal[13]. It is observed that variability in defining normal ranges is primarily due to different standards of automated analysers as reviewed by Zoller et al.[14, 15]. Hence there is a need for standardisation in measurements of platelet indices for a more consistent results.

Limitations

The limitations of our study were as follows:

(1) This was a non-randomized trial, single centred study with a relatively small number of patients. Hence it was subject to selection bias.
(2) The follow up was done only till the patient's discharge or in-hospital mortality. Hence midterm and long term outcomes are not assessed.
(3) While higher tertiles of parameters such as RDW, NLR had been found useful in predicting MACE, still normal ranges for these parameters remains to be standardised. Hence furthermore randomised multicenter trials are needed to arrive at ranges of normal values for a uniform standardisation.
(4) In our study, we did not compare the prognostic value of haematological indices with other cardiac biomarkers (Cardiac Troponins) and inflammatory markers (Hs-CRP, NT Pro BNP).

FURTHER SCOPE FOR THE STUDY

Though there was significant association of haematological parameters (RDW/NLR) with in-hospital MACEs, there is a potential to conduct the study for a longer term with higher number of subjects to substantiate their clinical utility. Due to their potential significance as evidenced in our study as well as in plenty of recent clinical studies, there is a need to standardise the methodologies for measuring haematological indices. In addition, it provides an opportunity for haematopathologists and clinicians to work together to fill up the bigger vacuum existing in our understanding of the novel mechanisms occurring in ACS contributing to rise in these particular haematological parameters.

Conclusion

Red Cell Distribution Width (RDW) and its derived indices Haemoglobin Corrected RDW (HbCRDW),

Redcell Width Volume Index (RWVI) are strong predictors of Recurrent Angina in hospitalised ACS patients. In addition, Higher values of RDW are also useful in predicting LV dysfunction. Though, there was no significant relationship between Platelet Distribution Width (PDW) and MACEs, Neutrophil-Lymphocyte Ratio (NLR) is found significant in predicting clinical LV failure and arrhythmias. The studied parameters showed good correlation with morbidities but no significant association with in-hospital mortality. Hence, in view of their potential significance, cheap and wide spread availability, further studies in large scale are warranted to transform them from research domain to clinical utility.

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