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RESEARCH ARTICLE

A COMPARATIVE STUDY OF ABSOLUTE LYMPHOCYTE COUNT (ALC), NEUTROPHIL LYMPHOCYTE RATIO (NLR) AND RED CELL DISTRIBUTION WIDTH (RDW) AMONG COVID 19 DEATH AND SURVIVAL GROUP

Mahesh Dave[1], Sahil Kharbanda[2,*], Abhishek Nyati[3], Ravi Manglani[4], Manasvin Sareen[5], Devender Sukhwal[6] and Ramgopal Saini[7]

[1]Senior Professor & Ex Head of Department, Department of Medicine, RNT Medical College, Udaipur, Rajasthan, India
[2,3,4,5,6]Resident Doctor, Department of Medicine, RNT Medical College, Udaipur, Rajasthan, India
[7]Assistant Professor, Department of Medicine, RNT Medical College, Udaipur, Rajasthan, India

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Corresponding author:
Sahil Kharbanda

ABSTRACT

Background-At the end of 2019, a novel coronavirus was identified as the cause of a cluster of pneumonia cases in Wuhan, a city in the Hubei Province of China. It rapidly spread throughout the world. Identifying patients at highest risk for severe disease is important to facilitate early, aggressive intervention and to mitigate the crises occurring throughout the world. Biomarkers were needed for patient stratification into those likely to develop severe disease and with high risk of mortality. Present study aims to find out those indicators. **Methods:** Total patients admitted over a period of 1 year from 1st April 2020 to 31th March 2021 in Dedicated COVID Hospital of RNT Medical College and MB hospital Udaipur was 4304 out of which 620 died and 3498 got discharged, 186 couldn't be followed up as they took leave against medical advise. From death group (620 patients) and Survival group (3498 patients), 400 patients were selected randomly from each group and were analysed and comparison was made between both the groups including parameters like ALC(Absolute lymphocyte count), NLR (Neutrophil Lymphocyte)ratio and RDW(Red cell distribution width). **Results:** Median age in death and survival group was 62.03 and 47.18 respectively. Mean Absolute lymphocyte count was 0.88 and 0.93 in death and survival group respectively. Mean Neutrophil -Lymphocyte ratio in death and survival group was 8.37 and 4.34 respectively. Mean RDW- CV was 1.86 and 1.67 in death and survival group respectively. **Conclusion:** From the present study we conclude that Decreased ALC and Elevated NLR are a reliable indicator of death as an outcome in COVID 19 disease whereas RDW was high in COVID19 patients but had no significant relationship with outcome of the disease.

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INTRODUCTION

Coronaviruses are important human and animal pathogens. At the end of 2019, a novel coronavirus was identified as the cause of a cluster of pneumonia cases in Wuhan, a city in the Hubei Province of China. It rapidly spread, resulting in an epidemic throughout China, followed by an increasing number of cases in other countries throughout the world. In February 2020, the World Health Organization designated the disease as COVID-19, which stands for coronavirus disease 2019[1].Coronavirus disease 2019 (COVID-19) is an acute respiratory illness caused by infection with severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2).

COVID-19 has a high rate of hospitalization, critical care requirement, and mortality.[2-3] Lymphocytopenia[4]is observed as an independent risk factor for outcomein COVID-19 patients. Mechanisms leading to lymphocytopenia are the inflammatory cytokine storm which is the key factor behind the observed lymphopenia and COVID-19 infection which can result in exhaustion of T cells.[5] Another marker of inflammation is Neutrophil-lymphocyte ratio (NLR)[6] The neutrophils are increased in bacterial infection and lymphocytes are reduced during viremia. Examining these two parameters can greatly help assess the COVID-19 infection. A recent study concluded that neutrophil/lymphocyte ratio (NLR) is associated with the progression of the COVID 19 infection and can be utilised by the physicians to identify high risk or deteriorating patients at

an early stage.[7] Red cell distribution width (RDW) is a red blood cell parameter that measures variability of red cell volume/size (anisocytosis). Depending on the types of hematology analyzer instruments, RDW can be reported statistically as coefficient of variation (RDW-CV) or standard deviation (RDW-SD). RDW-SD (expressed in fL) is an actual measurement of the width of the red blood cell (RBC) size distribution histogram and is measured by calculating the width (in fL) at the 20% height level of the RBC size distribution histogram.This parameter is therefore not influenced by the average RBC size (mean corpuscular volume, MCV). RDW-CV (expressed in %) is calculated asratio of 1 standard deviation of RBC volume and MCV and expressed as percentage.Since RDW-CV is mathematically derived from MCV, it is therefore affected by the average RBC size (MCV).[8,9]RDW obtained from a standard complete blood count (CBC) is a convenient and inexpensive biochemical parameter representing the variability in size of circulating erythrocytes.[10]

Elevated RDW is associated with an increased risk for all-cause mortality; mortality from heart disease, pulmonary disease, sepsis, influenza, and cancer; complications associated with heart failure, severity of coronary artery disease and viral hepatitis, advanced stage and grade for many cancers; and the development of diabetes, chronic obstructive pulmonary disease, stroke, anemia, and many other conditions.[11] RDW appears to be a nonspecific marker of illness that has the potential to provide general quantitative risk stratification that may be particularly useful for a new and unknown disease. Previous studies have found evidence in some specific conditions that RDW elevation is caused by delayed clearance of older RBCs[12].Because RBCs characteristically decrease in cellular volume across their lifespan, persistence of these older, smaller cells thus increases volume variance and this clearance delay coincides with and offsets a net decrease in RBCproduction.[12]These reports suggest the possibility that an elevated RDW in some circumstances may reflect a clinical state in which RBC production and turnover have slowed in the setting of increased production and turnover of leukocytes or platelets such as would occur in inflammation.[13]

Identifying patients at highest risk for severe disease is important to facilitate early, aggressive intervention and to mitigate the crises occurring throughout the world. Biomarkers are urgently needed for patient stratification into those likely to develop severe disease and with high risk of mortality and those at low risk to prioritize our efforts and resources. Several demographic and blood parameters have been identified to be related to disease but very few have been identified to be directly related to mortality. So in this need of hour we need to find out parameters easily accessible, cheap at cost which correlates with disease severity and mortality. ALC, NLR and RDW are component of Complete blood count (CBC) which is routinely done in all patients and is cost effective. In this study, our aim was to investigate whether an association exist between mortality risk and lymphocytopenia, elevated NLR and raised RDW.

Aims and Objective

- To find out ALC, NLR and RDW in death group.
- To find out ALC, NLR and RDW in survival group.
- To compare these parameters between both groups and its correlation with mortality risk.

METHODS

Total patients admitted over a period of 1 year from 1st April 2020 to 31th March 2021 in Dedicated COVID Hospital of RNT Medical College and MB hospital Udaipur was 4304 out of which 620 died and 3498 got discharged, 186 couldn't be followed up as they took leave against medical advise. From death group (620 patients) and Survival group(3498 patients), 400 patients were selected randomly from each group and were restrospectively analysed from their admission tickets. Clinical data and biochemical investigations including ALC, NLR and RDW were compared between both the groups. Inclusion Criteria- RT PCR confirmed case of SARS-CoV-2 infection above the age of 18 years admitted in Dedicated COVID hospital. Exclusion Criteria-Patient younger than 18 years of age. Confidentiality and ethical issues were considered during the study and necessary permission was taken.

RESULTS

Table No. 1 and 2 shows the distribution of patients according to age. Among age groups, maximum patients were from ≤50 years (55.8%) from survival group and 61-70 years(32.1%) years from death group followed by 51-60 years (19.5%) from survival group and ≥70 years (22.9%) from death group. Regarding gender, no. of males were294 from survivor group (73.5%) and 288(72%) from death group as compared to females which were 106(26.5%) and 112(28%) in survivor and death group respectively. Table No. 3 depicts distribution of comorbidities among death group and survival group.

Out of 400 patients from Death group 283 (70.7%) had comorbidities and only 170 (42.5%) had comorbidities among survival group. Diabetes was most common comorbidity present in death group(47.9%) followed by Hypertension (39.3%)whereas Hypertension was most common comorbiditiy among survival group(20.4%) followed by Diabetes(16.8%). Other comorbidities like CAD (10.7%) and CKD(5.7%) were also more prevalent in death group as compared to survival group. Table No. 4 depicts patients with elevated RDW- CV (>14.5). Total 694 out of 800 patients had elevated RDW- CV value out of which 326(81.4%) were present in death group and 368 (92.0%) in survival group. Table No. 5 depicts comparison of variables between death and survival group. Mean age in death group and survival group was 62.03 and 47.18 respectively. Mean Total leukocyte count (TLC) was 10.5 and 7.97 in death and survival group respectively. Mean Absolute lymphocyte count was 0.88 and 0.93 in death and survival group respectively. Mean Neutrophil -Lymphocyte ratio in death and survival group was 8.37 and 4.34 respectively. Mean RDW- CV was 1.86 and 1.67 in death and survival group respectively.

Table 1. Distribution of Age

Age	Group		Total
	Death	Survival	
≤50 years	72(17.9%)	223(55.8%)	295(34.8%)
51-60 years	109(27.1%)	78(19.5%)	187(23.7%)
61 – 70 years	128(32.1%)	88(22.1%)	216(27.7%
≥70 years	91(22.9%)	11(2.7%)	102(13.8%)
Total	400	400	800

Table 2. Distribution of Sex

Sex	Group		
	Death	Survival	Total
Male	288(72%)	294(73.5%)	582 (72.7%)
Female	112(28%)	106(26.5%)	218 (27.3%)
Total	400	400	800

Table 3. Distribution of Comorbidities

Comorbidities	Group	
	Death	Survival
Diabetes Mellitus	136(47.9%)	67(16.8%)
Hypertension	157(39.3%)	82(20.4%)
CAD	27(10.7%)	7(1.8%)
CKD	23(5.7%)	4(0.9%)
Hypothyroidism	17(4.3%)	17(4.4%)
Any	283(70.7%)	170(42.5%)

Table 4. Distribution of patients with elevated RDW-CV (>14.5)

RDW- CV	Group		Total
	Death	Survival	
≤14.5	74(18.6%)	32(8.0%)	106(13.8%)
>14.5	326(81.4%)	368(92.0%)	694(86.2%)
Total	400	400	800

Table 5. Comparison of variables between groups

	Group	N	Mean	SD	P
AGE	Death	400	62.03	12.48	0.000
	Survival	400	47.18	15.11	
TLC	Death	400	10.51	5.60	0.001
	Survival	400	7.97	5.89	
NC	Death	400	77.85	11.42	0.000
	Survival	400	65.15	15.82	
LC	Death	400	13.09	7.49	0.000
	Survival	400	24.73	14.17	
ALC	Death	400	1.24	0.88	0.000
	Survival	400	1.65	0.93	
PC	Death	400	173.76	108.50	0.013
	Survival	400	208.88	113.73	
HB	Death	400	11.88	2.13	0.000
	Survival	400	13.10	2.06	
HCT	Death	400	35.74	6.09	0.000
	Survival	400	40.12	5.63	
NLR	Death	400	8.37	5.82	0.000
	Survival	400	4.34	3.82	
RDWCV	Death	400	16.08	1.86	0.647
	Survival	400	16.19	1.67	
RDWSD	Death	400	40.66	5.97	0.084
	Survival	400	39.50	4.26	

DISCUSSION

This study was retrospective comparative observational study done over a period of 1 year (1st April 2020 to 31stMarch 2021)in patients who were admitted in Tertiary Dedicated COVID Hospital of RNT Medical College, Udaipur. Total patients admitted were 4304 out of which 620 died and 3498 got discharged, 186 couldn't be followed up as they took leave against medical advise. From death group (620 patients) and Survival group (3498 patients) 400 patients were selected randomly from each group and were restrospectively analysed from their admission tickets. Clinical data and biochemical investigations including ALC, NLR and RDW were compared between both the groups and their role as prognostic value was found out. In the present study we found out that, maximum patients were from ≤50 years (55.8%) from survival group and 61-70 years(32.1%) years from death group followed by 51-60 years (19.5%) from survival group and ≥70 years (22.9%) from death group. Median age of death and survival group was 62.03 and 47.18 in death and survival group. Sharma D et. al[18] found nearly similar results in their study i.e symptomatic patients were older than the asymptomatic patients with median age of symptomatic patients being 60 years old while median age of asymptomatic patients was 30 years old.As the age increases risk of death from COVID 19 diseases increases. Regarding gender, no. of males were294 from survival group (73.5%) and 288(72%) from death group as compared to females which were106 (26.5%) and 112(28%) in survivor and death group respectively. Males are affected more, Possible explanation of this would be males are more involved in outdoor activities, smoking, drinking and tendency to remove face mask more frequently. Percentage of males and females in either group is comparable which explains sex is not associated with increased mortality. In present study Out of 400 patients from Death group 283 (70.7%) had comorbidities and only 170 (42.5%) had comorbidities among survival group. Diabetes was most common comorbidity present in death group (47.9%) followed by Hypertension (39.3%)whereas Hypertension was most common comorbiditiy among survival group followed by Diabetes(16.8%). Similar results was found in study by Dosi R et al[14]in which comorbidity was present in 47.1% of adult group and 71% of dead patients. The most common morbidity in the adult group was found to be hypertension followed by diabetes seen in 25%, and 21.5% people respectively. The most common comorbidity in deceased patients was found to be diabetes followed by hypertension seen in 35.5% and 32.2% respectively. Mean Absolute lymphocyte count was 0.88 and 0.93 in death and survival group respectively. Results were found to be significant(P value 0.00) This tells us about role of ALC as prognostic marker of severity and death due to COVID 19. Wang D et. al[4] also found out similar results that is lymphocytopenia is associated with mortality due to COVID 19 disease. Mean Neutrophil-Lymphocyte ratio in death and survival group is 8.37 and 4.34 respectively. Results were found to be significant (P value 0.00) This tells us about role of NLR as mortality marker. This was in accordance with study done Yang AP et. al[15] and Chan A et. al [16]according to which NLR can be considered independent biomarker for indicating poor clinical outcome. Total 800 out of 694 patients had elevated RDW- CV value out of which 326(81.4%) were present in death group and 368 (92.0%) in survival group. This tells us about role of RDW as a marker of having COVID19 disease and not as a prognostic outcome. Mean RDW- CV is 1.86 and 1.67 in death and survival group respectively. This study explains Elevated RDW may be associated with COVID 19 disease but its has no role as prognostic marker of severity and death due to COVID 19 (p value 0.647 i.e insignificant) .This was not in accordance with Foy et. al[17] which said RDW measured at admission and during hospitalization was associated with a statistically significant increase in mortality. But was in accordance with study done by Sharma D et. al[18]which found out that RDW was found to be higher in COVID 19 patients, however it had no significant relationship with appearance of symptoms or severity of the disease.

Conclusion

From the present study we concluded that Decreased ALC and Elevated NLR are a reliable indicator of severity in COVID19 disease whereas RDW is high in COVID 19 disease but has no significant relationship with severity and mortality due to this disease.

Early recognition of the severe cases allows for early triaging and timely initiation of management. These markers are routine laboratory test and are cost-effective and easily accessible. They may be useful in risk stratification of hospitalized patients with COVID-19.

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