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Original Research Paper

ASSOCIATION OF ABSOLUTE LYMPHOCYTE COUNT & RDW WITH COVID19 PNEUMONIA SEVERITY

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ABSTRACT:

Background and Aim: In February 2020, the WHO designated the disease COVID-19, which stands for Coronavirus disease 2019 & was declared pandemic on 11th March 2020.The symptoms may vary from fever, malaise, headache, and myalgia in mild cases to adult respiratory distress syndrome accompanied by multiorgan dysfunction in severe cases. Lymphopenia and elevated RDW were common lab findings among hospitalized patients with COVID 19 RT PCR positive. The aim of this study was to evaluate Absolute Lymphocyte count & RDW in COVID 19 pneumonia patients & correlate with disease severity. **Materials and Methods**: Hospital based descriptive epidemiological study(record based). Patients admitted in MBGH & COVID Dedicated Hospital ESIC, Udaipur wards and ICU diagnosed with COVID 19 pneumonia (based on nasal and throat swab COVID 19 RT PCR positive) were taken into the study. Blood samples for Absolute Lymphocyte count and Red cell distribution width (RDW) at the time of admission were taken and then correlated with clinical severity. **Results:** In our study, we evaluated 110 patients of SARS COVID19 RT PCR positive . Mean RDW% was 14.76, 15.18, 15.78 among mild, moderate and severe category cases respectively. Severe clinical category cases had maximum RDW% of 15.78. Mean ALC with severe cases was 1037.8/mm^3 as compared to 1128/mm^3 and 1371.5/mm^3 among moderate and mild cases respectively. **Conclusion**: Among severe cases 37(71.15%) had RDW ≥14.5% whereas 15(28.85%) had RDW <14.5% which was statistically significant. Severe cases had more severe lymphopenia as compared to mild & moderate cases. Therefore elevated RDW and lower Absolute Lymphocyte Count correlated with clinical severity of the disease.

Keywords: COVID19, Red Cell Distribution Width(RDW) , Absolute Lymphocyte Count(ALC).

INTRODUCTION:

At the end of 2019, a novel coronavirus was identified as the cause of cluster pneumonia cases in Wuhan, China. It rapidly spread, resulting in an epidemic throughout China, followed by pandemic disease. In February 2020, the WHO designated the disease COVID-19, which stands for Coronavirus disease 2019.The virus that causes COVID-19 is designated severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2);previously it was referred to as 2019-nCoV[1,2].After an incubation period that ranges from 1-14 days of exposure, SARS usually begins as a systemic illness marked by the onset of fever, malaise , headache ,and myalgia and is followed by in 1-2 days by a non productive cough, rhinorrhea , sore throat ,dyspnea , loss of taste and smell, nausea, vomiting , abdominal pain . Approximately 25% patients have diarrhea. Chest x rays can show a variety of infiltrates, including patchy areas of consolidation- more frequently in peripheral and lower lung fields-or interstitial infiltrates, which can progress to diffuse involvement .In severe cases, respiratory function may worsen during second week of illness and progress to frank adult respiratory distress syndrome accompanied by multiorgan dysfunction. High risk factors for severe disease include age>60years, cardiovascular disease including hypertension and CAD, diabetes mellitus and other immunocompromised states, chronic liver/lung/kidney disease, cerebrovascular disease and obesity[3]. Leucopenia or normal white blood cell count and lymphopenia (ALC<1.0 *10^9/L) is seen in COVID 19 infected patients. Lymphopenia is a result of defective immune response to the virus. SARS CoV-2 is believed to inhibit bone marrow hematopoeisis via certain receptors causing lymphopenia.[4]Medication used in COVID 19 treatment like steroid also results in lymphopenia[5].Lymphopenia is prominent laboratory finding in patients with SARS and more commonly in patients with severe disease in comparison to non severe disease[6].Lymphopenia is observed in around

60% of cases with SARS CoV-2 infection at initial symptomatic phase[7]. Red cell distribution width (RDW) measures the anisocytosis, a condition of heterogeneity in volume of circulating RBCs[8]. Elevated RDW signifies inflammation due to various mechanisms. Pro inflammatory cytokines such as interferon gamma and tumor necrosis factor alpha which interferes with iron metabolism and capacity of bone marrow to produce RBC, which leads to anemia and increased RDW. RDW also increase due to decreased life span of RBCs from bone marrow because of increased oxidative stress associated with inflammation. Increased RDW during admission is associated with increased risk of mortality. RDW more than 14.5% at the time of hospitalization was associated with increased mortality risk (from 11% to 31%). RDW elevates when RBC production kinetics have slowed as compared to increased WBC and platelet kinetics[9].Clinically COVID 19 Pneumonia can be categorized into mild, moderate and severe. Mild severity include patients with uncomplicated upper respiratory tract infection having mild symptoms such as fever, cough, sore throat, malaise, nasal congestion, headache without any evidence of breathlessness or hypoxia(normal saturation:>93%)Moderate severity include patients with pneumonia with no signs of severe disease having clinical features of fever, cough, dyspnea and or hypoxia including SpO2 90-93% on room air and respiratory rate more or equal to 24/min. Severe disease presents with severe pneumonia with signs with pneumonia plus one of the following: Respiratory rate >30 breaths/min, severe respiratory distress, SpO2 <90% on room air. Severe disease can be further subcategorized into ARDS, Sepsis and Septic shock.

AIMS AND OBJECTIVES:

- To evaluate Absolute Lymphocyte count & RDW in COVID 19 pneumonia patients & correlate with disease severity.

MATERIAL AND METHODS:

Patients presented with sign and symptoms of COVID 19 pneumonia were investigated with RT-PCR(Reverse Transcription-Polymerase Chain Reaction) using throat and nasal swab specimen from upper respiratory tract. These patients tested positive on RT-PCR were classified into mild, moderate and severe category based of clinical severity and treated accordingly. Study variables undertaken for study were Absolute Lymphocyte count and Red cell distribution width(RDW) at the time of admission. After an informed consent all subjects will thoroughly assessed at presentation, investigated and treated according to the protocol. Patient's detailed clinical history, comorbidities and risk factors, demographic profile and socio-economic status was recorded. The onset of symptoms and signs were recorded. A diagnosis of COVID 19 Pneumonia will be made based on the basis of Clinical Symptoms, COVID 19 RT PCR & radiological imaging (Chest X ray or HRCT Thorax) and Clinical examination.Routine CBC, Absolute Lymphocyte count, RDW, Chest X Ray were done in all patients.

RESULTS:

Total 110 cases were taken for our study.Maximum number of cases was in age ≥65 year (34%)and group 45 to 54 year(20%).The mean age among cases was 49.8± 17.84 years. Age ranges from 19 year to 90 year with SD of 17.84.In our study, majority of cases were Male (55%) as compared to females(45%).In our study, among 110 cases (patients admitted with COVID19), Fever and cough were the most common presenting symptoms and was seen among 105 cases followed by followed by shortness of breath (98), loose motion and bodyache (20) ,headache (12) , vomiting (6) , pain abdomen (4) , altered sensorium (4).4 cases were asymptomatic.In our study population 47 individuals had past history of comorbid illnesses. Among the 47 individuals with comorbid illnesses, the most common comorbidity was hypertension (26) followed by diabetes mellitus(23),thyroid disorder (17), asthma (6), stroke(5), and CAD(4).Mean Hb of the cases -12.15(g/dL) ranging from 4.4 to 16.4 (g/dL) with Standard deviation of 2.08.Mean Hb of male cases -12.3(g/dL) as opposed to female cases of 11.58(g/dL). Out of 110 cases ,35 were of mild severity whereas 23 and 52 of moderate and severe category respectively. Out of 52 severe cases, 26(50%) were males and 26 females(50%).Number of cases with absolute lymphocyte count ≥1000/mm^3 were 65 whereas 31 patients had ALC 500-999 mm^3 and 14 cases had ALC <500/mm^3 . Mean RDW% is 14.76, 15.18, 15.78 among mild, moderate and severe cases respectively. Severe clinical category cases has maximum RDW% of 15.78. Out of 110 cases 70 cases has RDW ≥14.5%(63.6%) compared 40 cases with RDW <14.5%(36.4%).Among severe cases 37(71.15%) has RDW ≥14.5 whereas 15(28.85%) had RDW <14.5%. . Out of 110 cases 39 died while 71 recovered.35.5% mortality was reported in our study population. Among mild category cases only 1(2.86%) patient died while rest 34 recovered as compared to moderate category cases where 2(8.7%) patients died out 23. Mortality in severe category cases is 69.24%. In females out of 26 severe cases 19(73%) died as compared to 18(69.23%) cases in males.The mortality was maximum of 78.6% for patients with severe lymphopenia(ALC<500/mm^3). Patients with no lymphopenia(ALC ≥1000/mm^3) had mortality of 23% whereas in mild to moderate lymphopenia(ALC 500-999/mm^3) cases mortality was 34.1%.In our study, dead patients had statistically significant (p value <0.05) lower Absolute Lymphocyte count than discharged. Among 14 patients with ALC<500/mm^3

only 3(21.4%) patients recovered while 11(78.6%) succumbed to death.In our study mortality among patients with RDW ≥14.5% 27 cases(69%) was higher than that with RDW <14.5% of 12 cases(31%).This distribution was statistically significant (p value <0.001).Total 47 out of 110 cases had comorbid disease .Out of 47, 20(43%) cases succumbed to death whereas 27(57%) recovered.Whereas in patient with no comordity , 17(27%) out of 63 patients died rest 46(73%) recovered.

Table 1:Age wise distribution of study population

Age group	N	%
<25 year	7	6.4 %
25-34 year	11	10 %
35-44 year	15	13.6 %
45-54 year	22	20 %
55-64 year	17	15.5%
≥65 year	38	34.5 %
Total	110	100.0%

Table 2: Gender wise distribution of cases

Sex	No.	%
Male	60.00	54.6%
Female	50.00	45.4%
Total	110.00	100.00%

Table 3: Distribution of study population with comorbid illnesses

Comorbidity	Frequency	Percentage (%)
Present	47	42.72
Absent	63	57.28
Total	110	100

Table 4: Mean MCV of cases

CLINICAL SEVERITY	MEAN MCV(fL)
MILD	84
MODERATE	89

SEVERE	98

Table 5: Absolute Lymphocyte count with Clinical severity

SEVERITY	ALC ≥1000/mm^3	ALC 500-999/mm^3	ALC <500/mm^3
MILD	29	5	1
MODERATE	14	7	2
SEVERE	12	29	11
TOTAL	55	41	14

Table6: RDW% with clinical severity among cases

CASES	RDW ≥14.5%	RDW <14.5%
MILD	19	16
MODERATE	14	9
SEVERE	37	15
TOTAL	70	40
DEATHS	27	12

Table 7: Mortality and recovery among cases

	Recover		Death	
Clinical Severity	No.	%	No.	%
Mild	34.00	97.14%	1	2.86%
Moderate	21.00	91.3%	2.00	8.7%
Severe	16.00	30.76%	36.00	69.24%
Total	71.00	100.00%	39.00	100.00%

DISCUSSION:

In our study, we evaluated 110 patients of SARS COVID19 RT PCR positive who satisfied our inclusion and exclusion criteria. In the study population the majority (34%) were in the age ≥65 years. The median age of patients in moderate(50years) and severe category(63years)was

higher than that of mild disease(48years).The male : female ratio was 1.20. A similar study at General hospital, Brigham, Boston, Massachusetts by Foy H. Et al[11] reported study mean age as 62±18 years and the sex ratio similar to our study was 1.17. In a similar study at SMS Hospital, Jaipur Rajasthan by Sharma D Et al[10] median age of patients in symptomatic and asymptomatic group was 60 years and 30 years, respectively & the sex ratio was 2:1 unlike our study. As in our study sex show a statistically significant correlation with mortality whereas mean age in survivors was 59.6± (17.6)years as compared to non survivors 74.6 ± (13.4) P<0.001 which was statistically significant. In our study population 47 individuals had past history of comorbid illnesses . Out of 47, 20(43%) cases succumbed to death whereas 27(57%) recovered. Whereas in patient with no comordity , 17(27%) out of 63 patients died rest 46(73%) recovered signifying that cases with comorbid illness had more risk for mortality as compared to cases with no comorbidity. Although mortality among cases with comorbidity was statistically insignificant(p value 0.08) similar to studies done by Henry et al[12] & Lee J et al[15].Normal Total Leucocyte Count(cells/mm^3) is 4000-11000. Mean Total Leucocyte Count(cells/mm^3) among mild , moderate and severe category cases were 7370 , 8288 and 9277 respectively denoting high TLC associated with more severity of cases.Normal MCV is 80-96fL.In our study, mean MVC(fL) among mild , moderate and severe category cases were 84,89 and 98 respectively denoting higher MCV among more clinically severe cases.Normal RDW% is 11-14.5.Mean RDW% was 14.76, 15.18, 15.78 among mild, moderate and severe category cases respectively. Severe clinical category cases had maximum RDW% of 15.78.Out of 110 cases 70 cases has RDW ≥14.5% (63.6%) compared 40 cases with RDW <14.5% (36.4%).Similar to study done by Foy H. Et al[103] & Wang C et al[107] mean RDW% was maximum among severe cases which implies there is significant correlation between RDW with clinical severity (p value=0.004;high statistical significance).In our study mortality among patients with RDW ≥14.5% 27 cases(69%) was higher than that with RDW <14.5% of 12 cases(31%).This distribution was statistically significant (p value <0.001). RDWs was found to be significant predictors of severe illness. The RDW value was found to be significantly higher in patients with severe COVID-19 than in those with milder form of disease.Normal ALC is 1000-4500cells/mm^3.Mean ALC with severe cases was 1037.8/mm^3 as compared to 1128/mm^3 and 1371.5/mm^3 among moderate and mild cases respectively. Number of cases with absolute lymphocyte count ≥1000/mm^3 were 65 whereas 31 patients had ALC 500-999 mm^3 and 14 cases had ALC <500/mm^3 . Number of severe cases with absolute lymphocyte count ≥1000/mm^3 were 12(23%) out of 52, compared to 29 (55.8%)with ALC 500-999 mm^3 and 11 (21.2%) cases with ALC <500/mm^3 . Number of mild severity cases with absolute lymphocyte count ≥1000/mm^3 were 29(82.85%), 5(14.3%)with ALC 500-999 mm^3 and 1 (2.85%) cases with ALC <500/mm^3Number of moderate severity cases with absolute lymphocyte count ≥1000/mm^3 were 14(61%), 7(30%)with ALC 500-999 mm^3 and 2 (14%) cases with ALC <500/mm^3.Our study showed significant association between Absolute Lymphocyte and clinical severity of disease (p value <0.001) similar to previous studies done by Sharma D Et al[10] , Foy H. Et al[11] ,Wagner J Et al[13] . The median lymphocyte count of mild and moderate severe cases was significantly higher than that of severe cases similar to study of Liu J Et al[14] & Lee J Et al[15].There was a significant difference in mortality among cases with lymphopenia(61.5%) compared to their counterparts without lymphopenia (38.5%). p value(<0.001). Mortality in our study was 34.5% i.e 39 cases among 110 patients. Mortality was least among mild category cases of 2.86% as opposed to 8.7% and 69.2% in moderate and severe cases. Our study shows fatality of disease among severe category implying life threatening clinical disease.Female patients had a slightly higher mortality compared to males. In females out of 26 severe cases 19(73%) died as compared to 18(69.23%) cases in males which was statistically insignificant(p value>0.05).In summary, analyses of the clinical data of 110 patients with COVID-19 showed that lymphopenia and increased RDW were common and correlated with the severity of COVID-19. To the best of our knowledge, this study demonstrates the significance of the higher RDW & low absolute lymphocyte count as a marker of disease severity which emphasizes the need to dynamically monitor blood cell counts in the management of COVID-19.

SUMMARY & CONCLUSION:

This study was done to understand the clinical profile of patients with COVID19, categorize them according to the clinical severity (mild, moderate and severe), calculate Absolute Lymphocyte count & RDW% and correlate Absolute Lymphocyte count & RDW with disease severity at the time of admission. Out of 110 cases, 35(38.5%) were of mild severity whereas 23(25.3%) and 52(57.2%) of moderate and severe category respectively. Mean RDW% was 14.76, 15.18, 15.78 among mild, moderate and severe category cases respectively. Severe clinical category cases had maximum RDW% of 15.78.Out of 110 cases 70 cases has RDW ≥14.5% (63.6%) compared 40 cases with RDW <14.5% (36.4%). Among severe cases 37(71.15%) had RDW ≥14.5 whereas 15(28.85%) had RDW <14.5% which was statistically significant. In our study, mean MVC(fL) among mild , moderate and severe category cases were 84,89 and 98 respectively denoting higher MCV among more clinically severe

cases. Mean ALC with severe cases was 1037.8/mm^3 as compared to 1128/mm^3 and 1371.5/mm^3 among moderate and mild cases respectively.. In our study, dead patients had statistically significantly lower Absolute Lymphocyte count than discharged. In our study mortality among patients with RDW ≥14.5% 27 cases (69%) was higher than that with RDW <14.5% of 12 cases(31%) which was statistically significant. Absolute Lymphocyte count & RDW was correlated to predict clinical severity in pneumonia. A statistically significant correlation was made between lymphopenia and elevated RDW ≥14.5% with clinical severity and mortality.

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