Association Between Neutrophil: Lymphocyte Ratio(NLR) And Ct Severity Scoring (CTSS) In Corona Virus Disease-19 (Covid-19) Patients With And Without Comorbidities.

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I.   Introduction:

COVID-19 is the worst pandemic, that has created health, social and economic crisis worldwide.it shook humanity and took like 3 months in India to have a proper treatment guideline for the same. According to the GLOBAL BURDEN OF DISEASES(GBD) by WHO elevated systolic blood pressure stands at top in mortality rank and elevated fasting blood glucose at 4th of the same list of 2019 suggesting burden of hypertension and diabetes world wide, this study mainly encompasses on assessment of NLR and CTSS there by disease progression in diabetics and hypertensive patients compared with non-comorbid patient.

According to NIH (National institute of health) feb-03-2021 guidelines, the disease has been classified clinically into asymptomatic, mild, moderate, severe and critical taking into the account of peripheral oxygen saturation[1] at presentation and radiologically taking number of segments in a lobe involved and aggregating to a score so called CT severity scoring (CTSS) which is highly variable as to consider date from which HRCT-chest is obtained from disease onset[2]. During the illness maximum detioration in health occurred on 5th-12th day from onset of symptoms as per symptomology in covid-19 by CDC. The studies conducted in this regard have explained the cause as to be cytokine storm, acute coronary syndrome, cerebrovascular accidents and multiple organ dysfunctions[3] as major causes due to increased prothrombotic states and IL-6, SrCRP, SrFerritin, D-dimer are widely used investigations to monitor cytokine storm[4] and thereby for intervention and prevention of its deleterious effects.

India is developing country and not all patients can afford all the above-mentioned investigations. This retrospective study encompasses on easily available facility-based investigation complete hemogram available in all phc/chc/tertiary care facility to help and find effect on respiratory system and its probable progression in patients with /without comorbidities by comparing the same with radiological severity during admission and hence help in deciding early measures for treating patients. So far, the studies conducted in this regard have indicated that there is positive correlation between the NLR ratio and disease severity and progression[5] but note has not been made out to see its association in comorbid and non-comorbid patients.

II.   Methods And Material:

This study includes all the patients who had similar symptom of fever, cough and acute shortness of breath which was present since 1-4days of admission and tested positive for COVID-19 via RT-PCR and classified under moderate clinical disease as per CDC guidelines and was admitted in ICU setting in dedicated covid-19 care hospital Government medical college, Kota-Rajasthan. After approval being taken from college ethical committee relevant data (demographic data, history, lab investigations, radiological data) was collected from patients after taking valid informed consent. Study was single blinded as the resident collecting data had no knowledge regarding the purpose of data being collected to eliminate data bias. Retrospective study was then made to achieve relationship between CTSS and NLR ratio between the groups. This study includes 2 groups in which all tested positive for covid-19 via RT-PCR

A)   GROUP-A: patients with no comorbidity

B)   GROUP-B: 1) patients with either hypertension (HTN) or diabetes mellitus type 2 (DM2) both old and newly diagnosed and had HbA1C=more than 6.5% on admission,

2) patients with both HTN and DM2.

All other patients with comorbidities other than HTN, DM2 and also the patients who had additional comorbidity along with HTN, DM2 and age less than 18years were excluded, other causes of acute shortness of

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breath such as CAD, pulmonary thrombo-embolism, acute exacerbation of asthma, pulmonary edema have been ruled out at time of presentation using appropriate clinical and lab methods. a gap duration between admission and obtaining patients HRCT chest for CTSS and blood investigation for NLR was kept constant to 1-2 day from onset of symptom to prevent confounding in study.

III.   Results:

| COMORBIDITY	MIDDLE age	OLD age	YOUNG Age	Grand Total
DM2	7	7	2	16
F	2	2	1	5
M	5	5	1	11
HTN	6	16	0	22
F	1	5	0	6
M	5	11	0	16
HTN, DM2	9	11	0	20
F	3	3	0	6
M	6	8	0	14
NIL	29	20	9	58
F	8	7	1	16
M	21	13	8	42
Grand Total	51	54	11	116

A total of 116 patients were included in the study of which 32 were females and 84 were males. study included two equal groups, group-A(N=58) included non-comorbid patients, group-B(N=58) which included hypertensive(N=22), diabetes type2(N=16), both hypertension and diabetes (N=20) patients out of which 16 were females and 42 were males. median age group was 59years among 116patients with lowest being 37years and highest being 90years. For study purpose age from 18-40 years was considered young,41-60 years as middle age and >60years as old age. Table.1 represents total number of patients included according to their age category and comorbidity.

Below table (2) shows average NLR and average CTSS of the non-comorbid/group-A, comorbid patients/group-B, and also for individual comorbidity and individual age group, Pearson's correlational study was applied to assess linear relationships between NLR and CTSS for the following groups and the respective Pearson's co-efficient value(r) indicated in respective rows, test of significance (p-value) was later applied to know credibility of the strength of association with alpha level of 0.05.

TABLE-2

	GROUP-A	GROUP-B	HTN	DM2	HTN, DM2	YOUNG-AGE	MIDDLE-AGE	OLD-AGE
AVERAGE NLR	10.09	16.25	18.91	11.5	17.08	7.8	14.4	14.46
AVERAGE CTSS	10.24	14.37	13.90	14.06	14.45	8.1	11.7	13.4
PEARSONS COEFFICIENT(R)	0.2518	0.1079	0.110	0.094	0.2108	0.79572	0.281914	0.134
TOTAL PTS (N)	58	58	22	16	20	11	51	54
P-VALUE	0.0282	0.2098	0.31186	0.363271	0.186103	0.001699	0.022524	0.165628

Following are the scatter plot diagrams for association between average NLR and CTSS in comorbid (group-A) and non-comorbid (group-B) patients.
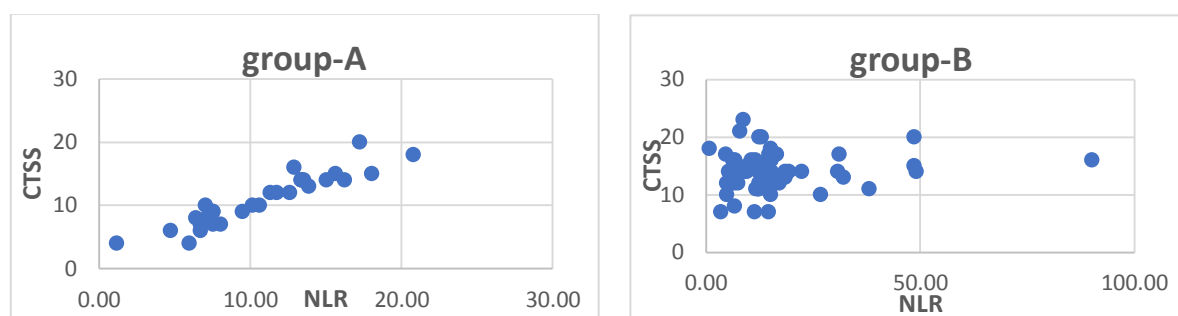
It can be easily noted that there is a linear association in group-A and no such association in group-B patients between NLR and CTSS.

IV. Discussion:

In this study we assessed 116 patients who had typical history of shortness of breath, tested positive for COVID-19 via RT-PCR and moderate illness at presentation their laboratory and radiological data dividing into two groups of comorbid (group-A) and non-comorbid (group-B) patients as described above. The average NLR of group-B was (16.25) found to be significantly higher than that of group-A (10.09) which indicated possibility of higher degree of suppression of lymphocytic cell production or its action in comorbid group and relative neutrophilia, similarly the average CTSS of group-B(14.37) which was significantly higher than that of group-A(10.24) the above findings suggest that patients with comorbidities have more pulmonary involvement than non-comorbid patients at the time of presentation even if the onset of symptoms occurred on same day among both, which signifies the rapid progression of pulmonary damage since onset in comorbid group. There was no significant difference in average CT severity scores of individual co-morbidities but people with hypertension had significantly higher average NLR again suggesting dysregulated immune response in consistent with old age group[7] as shown in above table-2.

Correlational study was made for both the groups and individual comorbidities using Pearson's correlation coefficient (R). R-value of group-A=0.25 and group-B =0.107 which showed positive correlation between NLR and CTSS shows linear relationship in btw the same i.e., as nlr increases CTSS increases but R-value of group B was statistically insignificant as P-value for same (0.209) was found to be >0.05/Alpha-value. This is further evidenced by applying scatter plots for individual NLR and CTSS between patients of two groups as shown in above figures it can be noted that there is linear association in group-A patients (showing straight line arrangement) and no such relation in group-B patients. Analysis of individual co-morbidities yielded similar conclusion as that of collective co-morbid group/group-B also note to be made on no significant correlation in diabetic group R=0.094 gives insight regarding possibility of increased chance of early secondary infection in disease in diabetic patients[8].

Similar study was then applied on age categories without segregating comorbidities it was seen that young age and middle aged people had positive linear relationship btw NLR and CTSS (R=0.79 & R=0.281) and this correlation was statistically significant as P-value was <0.05/alpha-level, but the old age group had no statistically significant correlation as P-value (0.165) was higher than 0.05/alpha-level as this group had higher co-morbidities and also possibility of age related dis-regulation of autoimmune system[9] as this group had higher values of avg NLR and CTSS (14.46 & 11.7 respectively) compared to young (7.8 & 8.1 respectively) and middle (14.40 & 13.4 respectively)aged patients.

V. Conclusion:

COVID-19 is an emerging infection and has varying spectrum of symptoms but the pulmonary involvement has become the most important cause adding to mortality due to infection. ACE2 receptors being the portal of entry for virus lead to downregulation of ACE2 and hence increases pulmonary vascular permeability leading to diffuse alveolar damage (DAD)[10], old age, hypertension being the leading cause due to upregulated receptors[10]. Such a diffuse damage leads to compromise in pulmonary capacitance leading to mortality of patients. This study suggests that patients with hypertension, diabetes mellitus-2 or with both have more rapid progression of disease in terms of pulmonary complications which is not predictable by NLR at time of admission due to dysregulated immune response and have to be considered high risk if presented with symptoms from day-1 and aggressive in-patient supportive management alongside management of particular co-morbidity, to prevent such detioration in health/mortality.

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