A Study on Neutrophil Lymphocyte Ratio in Covid 19 Patients in Tertiary Care Centre

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Abstract

Introduction: COVID-19 pandemic is spread by droplet infectionwith symptoms of fever, cough, diarrhea,dyspnea, fatigue, myalgia, headache, anosmia and ageusia. Morbidity and mortality is higher among elderly and in patients with comorbidities especially Diabetes Mellitus(DM). Biomarkers of inflammation are potential predictors for prognosis in covid patients.

Aim: To analyze the association of NLR in covid 19 patients with symptoms and diabetic status Objective: 1. To studyNLR in covid 19 patients with and without symptoms

2. To study the association of NLR between diabetic and non-diabetic covid 19 patients.

3. To study the association between symptomatology and NLR in diabeticcovid 19 patients.

Methodology: 3000 RT-PCR confirmed Covid 19 patients who attended triage op were included afterEthics committee approval.Patients were grouped as patients with and without symptoms and patients with and without DM.The diabetic Covid patients were also analyzed based on the symptoms. Blood samples onreporting were used for analysis of NLR andparameters analyzed using SPSS23.0 version.

Result: There is no statistically significant difference in NLR among Covid symptomatic and asymptomatic patients. But NLR is markedly raised in covid symptomatic patients with diabetes mellitus.

Key Words: *COVID 19, Diabetes Mellitus, Neutrophil Lymphocyte Ratio*

Introduction

The new coronavirus disease 2019 (COVID-19), caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), is a highly communicable infectious disease.WHOdeclared it as a pandemic in March 2020 and current evidences suggestthat SARS-CoV-2 spreads among people via direct contactroutes and by droplet, airborne and, fomite transmission.[1,2]. The common clinical features of COVID-19 include fever, dry cough, dyspnea, fatigue, myalgia, headache, anosmia, ageusia and diarrhea[3,4]. Patients with severe disease, may develop life threatening complications like, acute respiratory distress syndrome (ARDS), metabolic acidosis, coagulopathy, and septic shock[5]. The pathophysiology of complications in Covid 19 patients is under study and new theories are still evolving.One of the proposed mechanisms of complications in Covid infection is Cytokine storm. Cytokine storm syndrome can be triggered by direct target cell lysis with release of cytokines like interferon

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gamma (IFN-γ) or tumour necrosis factor alpha (TNF-α) or by activation of T cells with subsequent cytokine release[6]. These cytokines cause activation of innate immune cells like macrophages and endothelial cells with further cytokine release[7]. Inflammation, plays a key role in progression of COVID-19 pneumonitis and vasculitis. InCOVID-19 patients leukocyte count in the peripheral blood is normal ordecreased with reduced lymphocyte count in the earlystage.Neutrophils are the major constituent of leukocytes and are responsible for first line of defense against pathogens, whereas lymphocytes are regulatory and protective component of immune system[8,9]. However,Systemicinflammation destroys CD4+ T lymphocytes and increases suppressor CD8+ T lymphocytes, thereby resulting in an increased neutrophil-to-lymphocyte ratio (NLR), NLR has been universally accepted as an inflammatory marker[10,11]. In a study conducted byYang et al., NLR was found to be an independent prognostic factor in patients with COVID-19. This reinforces the belief in the relationship between hyper-inflammation and SARS-CoV-2.

Studies conducted by Zhuo F et al, have suggested that, Covid infection and its severity is higher amongst individuals with comorbidities, especially those with diabetes mellitus[12].Diabetics reportedfor12%–22% of patients with COVID-19, higher thanthe incidence in non-diabetic people 9.3%[13]. Diabetes, itself being a chronic inflammatory disease, presents with significantly higher incidence of mortality and multiple organ damages.[14][15].

Identifying early warning signs of covid 19 infection and providing treatment at the right time, helps in reducing the mortality and shorten the hospital stay with better cure rate. Various blood parameters showing immune status of human, have been identified as potential markers in assessing the severity of the disease. But these tests are mostly expensive and time consuming, which challenges the process of early identification and initiation of treatment. In such a case, Complete Blood Count and arriving at NLR is a specific and sensitive indicator of immune status, which is inexpensive with less turnaround time[16]. Hence this study was undertaken to find the association of NLR among symptomatic and diabetic patients in patients attending triage op where patients are segregated for different treatment modalities.

AIM: To analyze the association of NLR in covid 19 patients with symptoms and diabetic status

Objective:

1. To study neutrophil lymphocyte ratio in covid 19 patients with and without symptoms

2. To study association of NLR between diabetic and non-diabetic patients of covid 19.

3. To study the association between symptomatology and neutrophil lymphocyte ratio in diabetic patients of covid 19.

Methodology: The demographic, clinical and laboratory characteristics of RT-PCR confirmed, 3000Covid -19 patients who attended Triage OPD at Chengalpattu Medical college & Hospitalfor a period of one monthwas collectedafter approval from Institutional ethics committee.

Inclusion Criteria: COVID 19 patients of age group 18 to 70 years of both genders

Exclusion criteria: COVID 19 positive pediatric cases, antenatal and postnatal mothers,post-operative cases and sick cases admitted in COVID ICU

Symptoms of COVID 19 such as fever, cough, sore throat, myalgia, diarrhea, anosmia were noted. Comorbidities such as Type 2 Diabetes Mellitus, Hypertension, Coronary Artery Disease, Bronchial asthma, Tuberculosis, Epilepsy, Chronic Kidney Disease on Dialysis and other medical conditions documented were noted. NLR on reporting to triage was noted from Complete Blood Count measured by Automated Sysmex Analyzer.

The patients were clinically categorized from the received data as

1. Patients with symptoms

2. Patients without symptoms

3. Patients with Diabetes Mellitus

\-   Further subdivided as, symptomatic and asymptomatic

.The parameters were analyzed using SPSS 21.0 version.

Results

Results were analyzed by Descriptive statistics, 't' test, p value <0.05 was considered significant.

Table No: 1- Comparison of NLR in Covid patients with and without symptoms

S.no	Covid patients Total(n=3000)	NLR Mean ± SD	p value
1.	Covid patients with symptoms (n=620)	2.309 ± 1.68	0.09
2.	Covid patients without symptoms (n=2380)	2.06 ± 1.56	

Table No: 2- Comparison of NLR in Covid patients with and without Diabetes mellitus

S.no	Covid patients Total(n=3000)	NLR Mean ± SD	p value
1.	Covid with Diabetes mellitus (n=350)	4.45 ± 2.3	0.00004
2.	Covid without Diabetes mellitus (n=2650)	2.02 ± 1.2	

Table No: 3- Comparison of NLR among Diabetic Covid patients with and without symptoms

S.no	Covid patients with Diabetes mellitus Total(n=350)	NLR Mean ± SD	p value
1.	Diabetic patients with symptoms (n=132)	4.93 ± 2.56	0.00012
2.	Diabetic patients without symptoms (n=218)	3.19 ± 1.049	

Discussion

In our study, out of 3000 Covid patients, 620 were symptomatic. On analysing the NLR values among symptomatic and asymptomatic patients, table-1 shows, there was a mild increase in NLR among symptomatic patients (2.309 ± 1.68), compared to asymptomatic patients (2.06 ± 1.56), which was not statistically significant. However, the NLR in symptomatic patient was in higher limit of normal range.This is consistent with study conducted by Jumana Mansur Aljishi et al in Saudi arabia on symptomatic and asymptomatic covid patients.[17]According to Al-Tawfiq et al, and Graselli G et alit was foundthat elevated NLR was significantly associated with illnessseverity, taking into consideration the presence of comorbidities.[18][19]

Among 3000 Covid patients, 350 had Diabetes mellitus. On analyzing their NLR, from table-2, we found that it is significantly higher with a mean value of 4.45 ± 2.3, than that of the covid patients without diabetes mellitus, 2.02 ± 1.2. This is consistent with study done by Anurag et al, in Jharkand.[1]. Richardson et al, stated that the most common comorbidity associated with Covid -19 is Diabetes mellitus.[20]. Studies conducted by Samaras K et al, Marioni et al, showed that Diabetes mellitus is associated with low grade chronic systemic inflammation, presenting with increased inflammatory mediators.[21–23]Various studies conducted by Shiny A et al, Sefil F et al and Luo M et al, have reported that increased NLR in diabetics is linked with poor glycemic control, insulin resistance and cardiovascular events. [24,25][26,27]

Table-3 shows, out of 350 diabetic Covid patients, 132 patients were symptomatic and 218 were asymptomatic. On analyzing NLR among them, it was elevated in symptomatic diabetes mellitus patients (4.93 ± 2.56), compared to asymptomatic diabetic patients (3.19 ± 1.049), which was statistically significant. Guozhen li et al, conducted a retrospective study on clinical characteristics of diabetic patients with covid 19, showing that the patients with DM who landed up in severe category of Covid infection with moderate to severe symptoms, suffered from more complications, showing prominent lymphopenia with increased NLR, when compared with those diabetic covid patients without symptoms.[26,28].

This increased NLR in diabetic Covid patients, has been documented in various studies. But our study shows that, the NLR is markedly increased in diabetic patients with symptoms, compared to asymptomatic diabetic patients, which is also statistically significant. This proves the fact that NLR, can be used as a screening tool, for early identification of high risk cases amongst Covid patients with diabetes.

Significance of NLR in Covid:In covid, viral antigens cause activation of cell mediated immunity and humoral immunity. There occurs a marked interaction withmolecules like vascular endothelial growth factor (VEGF), interleukin-6, interleukin-8, tumor necrosis factor-alpha, interferon-gamma, and granulocyte colony-stimulating factor, resulting in profound inflammatory reactions and altered NLR.According to Ji P et al and Yang X et al, VEGF-A and VEGF-Care notorious contributors to inflammation in SARSCoV2[29][30].In another study conducted by Ciccullo et al, an NLR of greater than four was seen as a predictor of theadmission of COVID-19 patients to the intensive care unit.[31]

The potential mechanisms for increased NLR in diabetic Covid patients, is over-activated inflammation and imbalanced immune response in DM.

Diabetes is a condition related with proinflammatory stage, patients suffer from dysregulated immune response and were found to have altered cytokine profile, signifying the severity of Covid in them as reported in a study conducted by Yang J et al[32,33]A recent clinical study conducted byGuo et al,reported thatcompared to COVID-19 patients without diabetes, peoplewith diabetes had activated inflammatory response[34]. Hyperglycemia wasan independent predictor of a high neutrophil count. In a study conducted by Lim S et al, it showed there were moderatepositive correlations between Fasting Blood Glucose levels and NLRin the critical group of Covid patients with DM.[35,36]

Mehta N et al showed that, use of thiazolidinediones in diabetics, increased the expression of ACE2 receptors, to which corona virus binds.[37] This is reported in a study conducted by Gaoli Liu et al , on role of NLR in prognosis of type 2 diabetics with covid 19,[2]

Conclusion

In our study there is no statistically significant difference in NLR among symptomatic and asymptomatic Covid patients. NLR is increased in diabetic covid patients when compared with Non-diabetic and is statistically significant. The increase in NLR is more in symptomatic Covid patients with DM than in asymptomatic diabetic patients showing the marked increase in inflammation and chances for complication. NLR is a simple tool, which can be estimated at ease, in a triage centre, to assess the immune status and inflammatory response. It also helps in early identification of sick cases, which is ideally done at a triage centre, to categorize the patients, especially in patients with Diabetes mellitus and to refer them promptly, without delay, for initiation of treatment.

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