D-Dimer and Neutrophil - Lymphocyte Ratio as a Prognostic Marker In COVID-19

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Abstract

Background: Novel coronavirus 2 cause a disease which is wide spectrum ranging from mild asymptomatic disease to life threatening disease. The inflammation which is wide spread is the reason for the adverse outcome. There are multiple markers which has been used to identify the severity and the prognosis of the disease.

Aim: To find D-dimer and Neutrophil lymphocyte ratio as a prognostic factor in covid 19-patients

Methodology: This study was done in VMKV Medical College and Hospital, Salem, Tamil Nadu in Emergency Medicine Department., from the period of September 2020 to November 2020.All the Covid positive patients of all age groups of both sexes with or without comorbidity were included. Patients having Non Covid Pneumonitis disorder and chronic haematological were excluded. After getting ethical committee clearance data was collected using Patients information sheet and analysis was done using SPSS 23.p value <0.05 is considered significant.

Results: The mean age increases with the severity of the disease. The patients who have comorbidity have increases risk of developing COVID infection. For predicting the severity of the disease, the cut-off point is 6.2 sensitivity is 100%, specificity is 74% for NLR. For D-dimer the cut-off point is 1.5 the sensitivity is 100% and the specificity is 56%.

Conclusion: Our study shows that the D-dimer and the Neutrophil Lymphocyte Ratio is a good indicator of severity of the disease and has prognostic significance in COVID-19. This also helps in early intervention and preventing mortality

Keywords: Prognostic, D-dimer, Neutrophil Lymphocyte ratio and Salem

Introduction

A Novel Coronavirus (Severe Acute Respiratory Syndrome Coronavirus-2 (SARS COV-2)) was identified on 7th January 2020, in Wuhan China causing a Cluster of respiratory infections.[1,2] I was spreading quickly in China and in the other countries. The mortality rate was 4.76% and the confirmed cases were 285,179 and 13577 deaths occurred by March 23 2020.World Health Organisation declared COVID-19 infection as pandemic on March 2020 as it poses a great threat to human health. It was consuming most of our resources in our health care systems. As the severity of the disease was worst it was found to be useful to find out the risk factors of the patients so that timely action and interventions

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can be done so that the cure rate may increase and the prognosis will be better.[3] As most of the hospitals lacks beds for critically ill patients, we stratify the patients based on their clinical, radiological and laboratory parameters. This categorisation makes ease for the health care workers to classify the patients as mild, moderate and severe. Many laboratory parameters are used for predicting the COVID -19 infection but we have to still evaluate their accuracy of finding the infections severity and prognosis.[4] It is understood that the inflammation caused by the infectious diseases will gives us a evidence that there is a significant role in progression of viral pneumonias like COVID.[5] There is an immune response balance as a result of severe inflammatory responses. So, circulating biomarkers always represent inflammation and are considered as potential predictors for COVID19 patient's prognosis.[6] High neutrophil count, leukocytes and lymphopenia which are initial parameters which helps in discriminating severe and non-severe COVID19 patients.[7,8] Increased D-dimer and the prothrombin time are the indicators which indicates that the patients have worst prognosis .This increase in parameters may be due to dysregulated coagulopathy which occurs in patients with Severe COVID Infections.[9,10] White blood cells in Peripheral blood, Neutrophil lymphocyte ratio, platelet lymphocyte ratio and lymphocyte monocyte ratio are the indicators of the systematic inflammatory response.[11] Neutrophil-Lymphocyte Ratio (NLR) is a quick and convenient index which is often used to detect inflammation in laboratory investigations. It is useful in diagnosing, treating and prognosis of pneumonia.[12] Multiple studies also stated that D-dimer is a prognostic factor which is often indicates the adverse outcome of diseases of respiratory system.[13,14] Thus the aim of our study is to find the role of D-dimer and Neutrophil and lymphocyte ratio as a prognostic marker in COVID 19.

Methodology:

Study area: The study was done in VMKV Medical College and Hospital, Salem, Tamil Nadu in Emergency Medicine Department for a period of 3 months from September 2020 to November 2020.

Sample Size: All those patients who have given consent for the study and fulfilling the inclusion

criteria will be considered. The minimum sample size will be 100.

Inclusion criteria: All those patients who were tested positive for Real time Polymerase chain reaction through nasopharyngeal swab and those with CT thorax positive will be included. Patients age more than 18 and those having lymphocyte count results within 24 hours after admission.

Exclusion Criteria: Non Covid Pneumonitis, Chronic haematological disorder and Patients who don't have lymphocyte record.

Laboratory and imaging methods: With patient's permission blood was drawn and the following blood parameters are seen like Complete Blood Count, Liver Function test, Renal Parameters ratio, D-dimer test, Serum Ferritin test and Serum LDH levels were tested. CT chest and Echocardiogram (ECG) was taken regularly for all patients.

CT scan: The CT scan was taken in supine position. Two radiologist of more than 5 years of experience gives the CT values. The scoring was given out of 25. In case of any mismatch in the CT results, the senior most will be taken as the result.

Data Collection: After obtaining Institutional Ethical Committee Clearance, data was collected like their baseline characteristics like Name, Age, Sex, Comorbid status, Saturation and CT scoring was taken from their patient information sheet.

Statistical Analysis: Once the data was collected, it was entered in MS excel Windows 10. Statistical analysis was done by SPSS 23. Continuous variable was expressed in terms of Mean and Standard deviation. Categorical variables were expressed in terms of numbers(percentages). The association between the categorical variables are found by Chi square test. The association between the groups of continuous variables are found using Mann Whitney test. The continuous variables optimal cut off is found by Receiving operating curve (ROC) analysis. The p value <0.05 will be considered as Statistically significant.

Results:

The analysis was done after classifying the patients into three groups based on their clinical condition, laboratory parameters and CT scoring. The mean age of the study participants in mild covid disease is

51.87±14.55, in moderate covid disease is 53.28±14.25 followed by 56.55±13.81 among the severe covid disease. In our study male preponderance is observed. In mild Covid disease 166(73.5%) were male, in moderate covid disease 125(69.4%) were male whereas in severe covid disease 89(71.2%) were male. Majority of our study participants have Diabetes i.e., 57(25.2%) in mild disease,67(37.2%) in moderate disease and 45(36%) in severe disease. The second comorbidity which is present in our study participants is Hypertension of which 40(17.7%) participants have hypertension in mild disease, 44(24.4%) in moderate disease. The third comorbidity to follow is coronary artery disease followed by Thyroid disease. The moderate covid participants and the severe covid participants group have more participants having comorbidities. The difference between the diabetes and hypertension and thyroid in the covid category patients is statistically significant. In the above table NLR ratio, D dimer, CRP and serum ferritin are described with their median and interquartile range. The difference between the groups were found to be statistically significant. In our study for the predicting severity of disease the NLR Area under curve is .765 and for D-dimer is 0.733. For predicting the severity of the disease, the cut-off point is 6.2 sensitivity is 100%, specificity is 74% for NLR. For D-dimer the cut-off point is 1.5 the sensitivity is 100% and the specificity is 56%

Discussion:

The mean age of the patients having severe COVID 19 diseases is 56.55±13.81which is greater than the mild and moderate COVID patients which tells that as age is more the severity is also more. Males are affected more than female in all the three categories of COVID 19 patients. Similar results also seen in study conducted by Ashwin Kulkarni et al.[15] It is also observed in our study that the patients having comorbidities have more risk of developing COVID 19 infection .So Comorbidity patient have more risk of developing COVID 19 infection. The most common Comorbidity in our study groups is Diabetes followed by Hypertension in turn by coronary artery disease and thyroid. We found that the median values of the parameters like NLR, CRP, D-dimer and Serum ferritin are increasing as the severity of disease increases and it was also found to be statistically significant. Similar results were also seen

in the Wenjing et al [15] but the only thing is they have done multiple tests to find the prognostic effect whereas we did only single test. The area under curve of initial D-dimer, NLR were more than 0.7 which indicates good predictive value similar results also seen in Ashwin Kulkarni et al.,[15] and Weijing et al study.[16] Thus the patients who have a high D-dimer have a increased tendency of getting worse and risk of death is more among them so immediate treatment should be done to prevent the complications. High D-dimer is always linked with micro thrombotic formation, acute myocardial infection, pulmonary infection which may also leads to disseminated intravascular coagulation. Furong Zeng et al.,[17] in the meta-analysis states that inflammatory markers measurement will helps clinicians in monitoring and evaluating the severity and prognosis of COVID-19. Gustavo D et al[18] stated that Neutrophil and Lymphocyte ratio is the simple affordable and alternative test instead of cytokines which are costly. We should also need to do more studies in cytokines and other inflammatory markers.

Limitation:

Our study has some limitations. It is done based on the medical records available in the period of admission and the obtained data. All the laboratory parameters were obtained in the period of admission so the evaluation was not done during the follow up of the patients and their clinical condition. So, we didn't know their correlation. In our study we used cost effective method so some biomarkers like IL-6, LDH, CKMB, troponin and procalcitonin were not evaluated.

Conclusion:

In our study we have done single test but it was found that multiple has to be done for D-dimer and NLR which will give more valuable for COVID-19. It is known from our study that D-dimer and NLR ratio helps clinician in their diagnosis and treatment for preventing the complications related to the biomarkers level.

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Table 1: Demographic characteristics and comorbidities of the study participants:

Characteristics	Mild disease (N=226)		Moderate (N=180)		Severe (N=125)		P value
Age	51.87±14.55		53.28±14.25		56.55±13.81		.716
Sex	M 166(73.5%)	F 60(26.5%)	M 125(69.4%)	F 55(30.6%)	M 89(71.2%)	F 36(28.8)	.800
Diabetes	57(25.2%)		67(37.2%)		45(36%)		.019
Hypertension	40(17.7%)		44(24.4%)		16(12.8%)		.032
CAD	7(3.1%)		5(2.4%)		3(2.4%)		.930
Thyroid	1(0.4%)		8(4.4%)		2(1.6%)		.018

Table 2: NLR, D.dimer, CRP and Serum Ferritin compared with the Severity of the disease

Characteristics	Mild disease (N=226)	Moderate (N=180)	Severe (N=125)	P value
NLR	2.66(4.45-1.86)	2.69(5.28-1.82)	2.72(5-1.89)	0.037
D-dimer	526.50(684.50-398)	763(1092-524)	1350(3320-761)	.000
CRP	18(36.12-5)	23.66(48-10)	25.50(63.50-10.62)	.003
Serum ferritin	135(197-98)	254(464-137)	378(690-231)	.000

Table 3: ROC curve comparison of NLR and D-dimer

Characteristics	AUC	95%CI
NLR	.765	.652-.821
D-dimer	.733.	.682-.784

Table 4:

Characteristics	Cut off	Sensitivity	Specificity	PPV	NPV
NLR	>6.2	100	74	65.80	100
D-dimer	>1.5	100	56	53.20	100