ORIGINAL RESEARCH PAPER

Obstetrics & Gynaecology

THE PREDICTIVE VALUE OF NLR AND CRP IN THE PROGNOSIS OF COVID 19 POSITIVE OBSTETRIC CASES IN THIRD TRIMESTER OF PREGNANCY

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ABSTRACT

Covid 19 infection was like a nightmare for the entire world as nobody could see it coming in such a destructive way. But since we have to deal with it, better be well equipped. Identifying those patients at increased risk of disease severity definitely helps in decreasing mortality. This study is aimed at using NLR and CRP- two lost cost, easily available laboratory tests, in predicting disease severity of Covid19 pregnant women in third trimester. A total of 73 symptomatic pregnant women in third trimester were included in the study. We found out that these two tests were sensitive enough to detect patients who required oxygen support, had high grade fever, persistent cough, headache and needed prolonged hospital stay.

INTRODUCTION:

The ending of 2019 started the onset of a global pandemic related to severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), now known as COVID-19 (coronavirus disease 2019), which have spread rapidly from Hubei Province in China and engulfed the whole world. The World Health Organization initially classified the outbreak of the coronavirus disease 2019 (COVID-19) as a Public Health Emergency of International Concern (PHEIC), and on 11th March, 2020, they upgraded it to a pandemic[1].

Although majority of the cases are usually self-limiting with mild symptoms such as low-grade fever and cough, the disease can be fatal [2]. Numerous studies have illuminated the clinical characteristics and outcomes of general population with COVID-19, but little has been reported about the effects of SARS-CoV-2 infection on pregnant women. To our knowledge, a study by Huang and colleagues reported that the clinical characteristics of nine pregnant women with COVID-19 resembled those in the general population[3]. Another study including ten pregnant patients demonstrated that perinatal SARS-CoV-2 infection had adverse effects on newborns such as fetal distress and even death [4]. Moreover, a case described that a pregnant woman with COVID-19 delivered a healthy neonate with no evidence of SARS-CoV-2 infection during her 30 weeks pregnancy [5]. However, these series of cases had limitations for their small size and lack of control group. Therefore, there are still debates on whether pregnant women have a different disease course and outcomes, considering the physiological changes in cell-mediated immunity and pulmonary function during pregnancy [6].

Pregnant women experience immunologic and physiologic changes, which make them potentially more susceptible to viral respiratory infections, including respiratory syncytial virus, influenza virus, and SARS-CoV [7].This presents an increasing concern towards the need of a reliable and efficient prognostic marker to help in the management of pregnant cases. Neutrophils to lymphocytes ratio (NLR) is an inflammatory ratio that can be easily calculated from routine blood examination. Due to the fundamental meaning of this ratio reflecting an inflammatory load, it is frequently tested and reported as a prognostic factor in obstetric cases [8].

In a study conducted in Spain by Augusto Pereira and associates, they found out that in pregnancy CRP and D-dimer levels positively correlated with severe pneumonia and the neutrophil/lymphocyte ratio decreased as the patients improved clinically [9]. In another study on pregnant patients Arturo Ciccullo and associates found that patients with NLR <3, showed good prognosis, whereas transfer to ICU could be predicted with NLR >4.So, they concluded that increase in NLR in obstetric cases are associated with a poor prognosis [10]. The Federation of obstetrics and gynaecological societies of India (FOGSI) also mentions the presence of lymphocytopenia, thrombocytopenia and elevation of acute phase reactants (e.g.CRP) in covid 19 infected pregnancies[11]. Furthermore, in a notification (dated 13th of June 2020, page no.13) The Ministry of Health and Family Welfare, Government of India recommended that the moderate cases of Covid 19 to be followed up with 48-72 hourly measurement of acute phase reactants including CRP and daily CBC with DLC and absolute lymphocyte count.

GMCH being a Covid Hospital and a tertiary health unit has seen a lot of Covid 19 positive pregnant patients being referred from various peripheral hospitals and covid care centres, hence we decided to do an observational study to better understand the management of obstetric patients and their prognosis in relation with NLR and CRP. This study therefore is also aimed at finding out whether such relationships exist and if so, the utility of such a finding in better management of the patients.

Scientific hypothesis :

Neutrophil to lymphocyte ratio (NLR) and CRP both reflect systemic inflammation. They have been widely known as inflammatory markers. Patients suffering from covid 19 have shown an increase in both these parameters. However their rise during the covid 19 effected obstetric cases have shown to have a poor prognosis and vice versa.

AIMS AND OBJECTIVES :

The objective of this study was to find out the relationship between NLR and CRP with pregnancy outcome in covid 19 patients and the aim is to utilise these findings in the better management of such patients.

Materials and Methods:

Place of study: Covid Ward, Department of Obstetrics and

gynaecology, Gauhati Medical College and Hospital, Guwahati

Duration of study: 6 months (December 2020- May 2021)

Study design: Hospital based observational study

Study participants: Those patients fulfilling the inclusion and exclusion criteria were included in the study.

Inclusion criteria:
a. All pregnant patients with >28 weeks of gestation with covid 19 positive status with symptoms admitted at covid ward GMCH.

Exclusion criteria:
a. Patients with IUFD
b. Patients with any pre-existing haematological or systemic disease that may affect NLR and CRP Values.

Diagnosis and admission criteria:
Diagnosis: Both the Rapid antigen test and RTPCR tests were considered as valid tests for diagnosis.

Admission:
a. Symptomatic patients with SpO2 less than 95% at room air.
b. Those patients who didn't have adequate arrangement at home for quarantine.
c. Patients who wanted to get admitted.
d. Obstetric indication for admission.

Statistical Analysis:
The data was collected as numbers and percentages, and plotted in appropriate tables/charts, Chi-square test was used for analysing the categorical data and positive predictive value was calculated using a 2 x 2 contingency table. A p-value of 0.05 or less was considered as statistically significant.

Method of Sample Collection:
Over the study period all pregnant patients admitted with covid 19 infection fulfilling the inclusion and exclusion criteria were included in the study after obtaining proper written consent. On admission, patients were examined and all the vital parameters were noted. Their blood samples were collected and sent for the required tests for the study. The patients were kept under monitoring and vital parameters noted down from time to time. The required haematological reports were collected and compared with patient's health status (improving or deteriorating). They were followed up till

they tested negative for covid 19 and moved out of the covid ward.

The patients were evaluated for NLR and C-reactive protein (CRP) values. While considering the NLR they were included in two groups – those with NLR < 4 and other with NLR ≥ 4. Similarly with CRP values they were divided between those with CRP of <15 mg/L/dl and ≥ 15 mg/L/dl. These values were taken after considering the pregnancy related changes and guidance from studies performed earlier [12].

RESULTS :
This study was conducted on 73 symptomatic patients who fulfilled the inclusion and exclusion criteria. High grade fever (temperature more than 102°F), Persistent cough (more than 7 days), severe headache(requiring medication) and diarrhoea were the symptoms that were considered for analysis. Patients requiring Oxygen support by mask/nasal prongs for SpO2 below 94% at room air (outside of ICU), admission in ICU and duration of hospital stay more than 10 days were the other parameters that were considered.

Out of the 73 patients 6 patients required ICU care and 67 patients were managed in ward. Out of the 6 ICU patients 3 of them expired. Among those managed at ward 39 patients needed oxygen support (with mask/nasal prongs) and remaining 28 didn't require oxygen support. 47 patients had persistent cough beyond 7 days, 26 patients had high fever (>102°F), 18 patients had severe headache requiring medication and 11 patients had diarrhoea. There were overlapping of symptoms in some as well. Regarding the duration of hospital stay, 46 patients had to stay for more than 10 days.

The study was conducted at a time of when the first wave was ending and the second wave of covid19 infection had just started in India. Though most antenatal patients in the first wave were asymptomatic, but during the second wave majority patients presented with symptoms. From table 1, we found that at NLR ≥4 and CRP ≥15, significant number of patients had oxygen saturation below 94% and required oxygen support, needed more than 10 days of hospital stay, persistent cough more than 7 days , high grade fever and headache. Similarly with CRP ≥15, we had more oxygen requirement, patients with persistent cough, high grade fever and severe headache. ICU admission was not statistically significant in both the group but 50% of ICU admitted patients expired, and they had higher NLR and CRP compared those who survived. Diarrhoea was also not found to be a significant factor in our study.

Table No.1: The values of different parameters and data of statistical analysis

Nos. of patients in each category	NLR		p value	CRP (mg/l)		P Value
	≥4	<4	p	≥15	<15	
O2 requirement (39)	30 (76.92%)	9 (23.08%)	value is 0.004 (<0.05, significant)	33 (84.62 %)	6 (15.38%)	p value is 0.027 (<0.05, significant)
O2 not required (28)	11 (39.29%)	17 (60.71%)		17 (78.57%)	11 (21.43%)	
ICU Admission (6)	5 (83.33%)	1 (16.67%)	p value is 0.366 (>0.05, not significant)	5 (83.33%)	1 (16.67%)	p value is 0.414 (>0.05, not significant)
Patients outside ICU (67)	37 (55.22%)	30 (44.78%)		45 (67.16%)	22 (32.84%)	
Hospital stay > 10days (46)	35 (76.09%)	11 (23.91%)	p value is 0.002 (<0.05, significant)	31 (46.27%)	15 (32.61%)	p value is 0.897 (>0.05, not significant)
Hospital stay <10days (27)	10 (37.04%)	17 (62.96%)		11 (40.74%)	16 (59.26%)	
Persistent cough (47)	28 (59.57%)	19 (40.43%)	p value is 0.041 (<0.05, significant)	43 (91.49%)	4 (85.11%)	p value is 0.005 (<0.05, significant)
Cough <7days (26)	9 (34.62%)	17 (65.38%)		16 (61.54%)	10 (38.46%)	
High fever >102°F (26)	18 (69.23%)	8 (30.77%)	p value is 0.018 (<0.05, significant1)	20 (76.92%)	6 (23.08%)	p value is 0.037 (<0.05, significant)
Fever < 102°F (47)	19 (40.43%)	28 (59.57%)		23 (48.94%)	24 (51.06%)	
Severe Headache (18)	11 (61.11%)	7 (38.89%)	p value is 0.008 (<0.05, significant)	15 (83.33%)	3 (16.67%)	p value is 0.023 (<0.05, significant)
Mild or no headache (55)	13 (23.64%)	42 (76.36%)		27 (49.09%)	28 (50.91%)	
Diarrhoea (11)	6 (54.55%)	5 (45.45%)	p value is 0.190 (>0.05, not significant)	8 (72.73%)	3 (27.27%)	p value is 0.245 (>0.05, not significant)
No Diarrhoea (62)	18 (29.03%)	44 (70.97%)		30 (48.39%)	32 (51.61%)	

In a study conducted by Andrea Lombardi and associates, they found that among other inflammatory markers Neutrophil-lymphocyte ratio and CRP correspond with the disease activity of the covid 19 positive hospitalized pregnant women. Fever, cough, dyspnoea, requirement for oxygen support and ICU admission are more in those patients with higher NLR and CRP. These findings are similar with those of our study [13].

Another study conducted by Zhe zhu and associates concluded that CRP and IL-6 were independent risk factors for the severity of Covid-19[14]. The study conducted by Yuwei Liu and co-workers also found NLR to be an independent risk factor of the in-hospital mortality for Covid-19 patients[15].

CONCLUSION :

This study provides us with the information that both NLR and CRP are sensitive data for prediction of disease severity in covid19 effected pregnant women in the third trimester. Those patients with high NLR and CRP should be treated at hospitals with better facilities because they are at increased risk of disease severity. Another advantage of using these two tests is that these tests are relatively cheaper and done at most of the pathological laboratories across the country.

Consent And Ethical Issues:

Written and informed consent was taken from all patients before enrolling into the study. Ethical clearance was obtained from the Institutional Ethical Committee.

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