

Original Article

# Evaluation of Clinical Characteristics and Laboratory Results of COVID-19 Iraqi Pregnant Women

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## ARTICLE INFO

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## ABSTRACT

**Aims:** To verify the value of simple blood indices as a predictor to COVID-19 infection among pregnant women.

**Methods:** A prospective case-control study was carried in Al-Yarmouk Hospital from April 2020-till until April 2021 .

A total of 80 pregnant women were recruited. Aged range 20-42 years, at 28-36+6 weeks of a singleton pregnancy.

40/80 tested +ve for COVID-19 based on real-time polymerase chain reaction test (PCR). Another 40/80 were taken

as matched controls. **Results:** No statistically significant differences were reported upon comparing the two groups

in terms of age and gestational age, (P-value= 0.341, 0.445, respectively). However, statistically difference were found

for Hb, WBC, neutrophil count, lymphocyte count, platelet count, MPV, RCW, neutrophil/lymphocyte ratio, and

platelets/lymphocyte ratio; all were significantly higher in the study group versus the healthy control with a P-value

<0.0001. **Conclusion:** The neutrophil/lymphocyte ratio may serve as a critical factor determining the severity

of COVID-19-infection in the early stages of the disease. Early detection and treatment of COVID-19 severe cases

reduce the risk of an adverse pregnancy result.

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## INTRODUCTION

A Coronavirus 2 disease (COVID-19) is an acute infectious respiratory disease caused by a new strain of Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2), first demonstrated in china as the patients suffered from flu-like symptoms then followed by severe pneumonia [1]. This contagious disease is rapidly transmitted through respiratory droplets of infected patients via coughing and sneezing, close contact, contact with fomites, and aerosols generated. Then the virus enters through the nasal passage to reach and affect pulmonary cells by stimulating the receptor angiotensin-converting enzyme 2 (ACE2) and priming S protein by using the transmembrane serine protease 2 (TMPRSS2) [2,3]. This explained the necessity of proper diagnosis of positive cases population to restrict the spread of infection [4]. It started in 2019 in china, then spreads globally and become a challenging pandemic disease. Enormous attention has been made to the adverse effects and the underlying mechanisms of COVID-19 with management, particularly during pregnancy [5]. COVID-19 is known to be a capsulated single-stranded RNA virus, the response to the COVID-19 based on the body's immune system resulting in mild infection with complete clearing of the virus from the body or severe disease with its complications and higher mortality. The cytokine storm results from the inflammation associated with COVID-19 is responsible for higher morbidity and mortality; the disease spectrum differs from asymptomatic to severe

symptoms and even death [6]. During pregnancy, there is an adaptation of the immune system for the growth of the fetus, leading to alteration of the immune response towards the viral infection in pregnancy [7].

There is a similarity in the clinical features of the disease among pregnant and non-pregnant patients [9]. The virus can result in severe maternal and neonatal complications, thus requiring strict screening during pregnancy as the results and research in this field are limited [8]. The pregnancy is considered an immunocompromised status; therefore, pregnant women can have COVID-19 infection more than the general population. The management of this rapidly spreading disease during pregnancy is regarded as a significant concern as always there is concern about fetal safety and the scare of vertical transmission with its potential risks[9]. However, there is a similarity in pregnancy risk factors compared to the general population, as the underlying mechanism of vertical transmission is still uncertain. Asymptomatic pregnant women are common, with an uncertainty of clinical significance for COVID 19[10]. There are several immunity parameters in the body to counteract the infection; most of these are delay time and expensive. Therefore, an inexpensive clinical indicator with high sensitivity and specificity like; complete blood count (CBC) out of which are lymphocyte and neutrophil as the first one decreases and the second increases in viral infection and uses them as in other gynaecological and obstetrical approaches [11,12].

In Iraq, early August, the epidemic course was as follows: 140,604 cases, 5,160 deaths, and 101,024 cases recovered from the COVID-19 viral infection. Symptoms reported were variable from asymptomatic - mild symptom as fever, cough, headache, generalized muscle pain, and diarrhoea. More severe course illness showed extreme dyspnea and hypoxia, where intubation and ventilation were needed with death in unfortunate cases[ 8]. Due to the unique challenges among pregnant women, there is a need to assess the viral load, inflammatory response, level of immunity, and antibody production in pregnant patients across different gestational ages. This facilitates proper evaluation of the immunological reactions COVID-19 [3].

While there is a lack of knowledge of the disease's trajectory in pregnant women and data to establish information on the disease this time, we have developed a reasonable database on the previous SARS pandemic in 2013 [13]. The study evaluates the differences in the clinical features and laboratory investigation in pregnant women infected with Covid-19 to nourish the knowledge base to understand the disease course better.

## METHODS

### ***Study design and setting***

A prospective study was carried in Al-Yarmouk Hospital from April 2020-till until April 2021. The Medical Ethical Committees gave the approved form with informed consent, including written and verbal ones were obtained from all recruited patients.

### ***Data collection procedure***

A total of 80 pregnant patients suspected to have COVID-19 admitted to the hospital and screened for the disease. They were aged 20-42 years, and their gestational age at 28-36<sup>+6</sup> week, with a singleton pregnancy. The recruited patients were divided into two groups based on the positive result for the SARC-COVID-19, group one (study group) including 40 pregnant with Covid-19, while group two (healthy control) contained 40 pregnant without COVID-19. Both groups were age and body mass index-matched women. Accurate dating of gestational age calculated based on the last menstrual date and early 1<sup>st</sup>-trimester ultrasound. Complete epidemiological and medical history was taken, including symptoms onset, time of admission, length of hospitalization, cough symptoms, fever, abdominal pain, headache, nausea, and vomiting, besides the obstetrical, gynaecological, and surgical history. Comprehensive general (blood pressure, pulse rate, and temperature) and obstetrical

examination for all patients followed by laboratory tests; consisted of white blood cell (WBC) count, lymphocyte count, neutrophil count, platelet count, Haemoglobin level (HB), mean platelet value (MPV), Red cell distribution (RCW), neutrophil/lymphocyte ratio, platelets/lymphocyte ratio, chest x-ray (CXR), and contrast sonography (CTS) based on the severity of symptoms.

Patients with positive results based on real-time polymerase chain reaction test (PCR), a swab from the nasopharyngeal area, with repeated tests twice/ 2 days and should be done in two different laboratories. Patients included in this study followed the inclusion criteria in which they had positive results for swab and PCR. At the same time, severe cases or those referred for other hospitals, associated medical co-morbidities, twins pregnancies, patients on aspirin or immunosuppressive drugs were all excluded. Cases that passed away were excluded too.

### Statistical analysis

It was performed using SPSS version 22.0 software. The research data were analyzed using the descriptive statistics tool represented by the mean (mean) and standard error of the mean for all diagnostic variables and the results of laboratory tests. The levels of clinical characteristics and the results of laboratory tests were measured for these two groups to clarify whether there is a difference in the clinical characteristics and the results of laboratory tests between both groups. The boxplot was generated to highlight numerical data distribution and skewness by displaying the data quartiles (or percentiles) and averages.

## RESULTS

The study recorded two groups in which group one (study group) consisted of 40 pregnant women infected with Covid-19, and group two (healthy control) consisted of 40 pregnant women without Covid-19.

Table 1. shows the clinical variables and the results of laboratory tests for both groups. There were no statistically significant differences for both groups regarding age and gestational age, (P-value=0.341,0.445, respectively). However, a statistically significant difference was found concerning Hb, WBC, neutrophil count, lymphocyte count, platelet count, MPV, RCW, neutrophil/lymphocyte ratio, and platelets/lymphocyte ratio as they were significantly higher in study group than in the control with a P-value <0.0001.

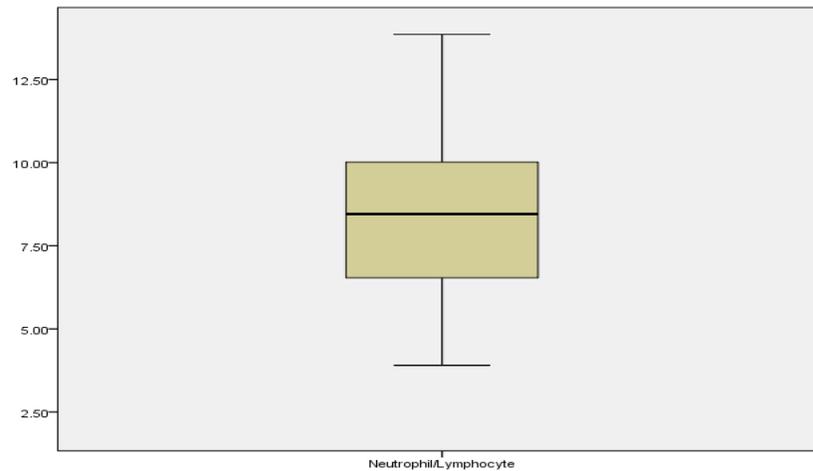
Figure 1. Illustrated the boxplot for the variable Neutrophil/lymphocyte ratio, the average variable (Neutrophil/lymphocyte) for this group is 8.27, and the value of (IQR, Range) is (3.66, 9.95) respectively, which is of great spread. As for the distribution shapes, it is found that the distribution is tilted to the right, and there are no large or small outliers for it, which indicates a difference between the two groups regarding the variable Neutrophil / lymphocyte ratio.

**Table 1. Description of the clinical variables and laboratory tests results for the two groups (group 1; pregnant women with COVID-19, group 2; pregnant women without COVID-19).**

Parameter	Normal range	Gr. 1 pregnant with COVID-19	Gr. 2 pregnant without COVID-19	P-value
Age	-	29.90 ± 1.40	31.60 ± 1.05	0.341
Gestational Age	28-36 <sup>+6</sup> Weeks	32.40 ± 0.60	31.65 ± 0.69	0.445
HB g/dL	9.5-15	11.70 ± 0.42	13.85 ± 0.29	0.000
WBC 10 <sup>9</sup> /L	5.6-16.9	11.61 ± 0.99	4.14 ± 0.27	0.000
NEU X 10 <sup>9</sup> /L	3.9-13.1	17.83 ± 0.68	3.54 ± 0.17	0.000
LYM X 10 <sup>9</sup> /L	1-3.6	2.12 ± 0.13	1.64 ± 0.12	0.008

<b>PLATLET x 10<sup>9</sup>/ L</b>	150-450	195.65 ± 10.03	323.85 ± 15.35	0.000
<b>MPV Femtolitter</b>	8.2-10.4	10.17 ± 0.28	9.67 ± 0.29	0.192
<b>RDW %</b>	11.4-16.6	14.47 ± 0.72	11.79 ± 0.18	0.001
<b>PLT/LYM</b>	-	102.61 ± 7.69	208.39 ± 18.96	0.000
<b>NEU/LYM</b>	-	8.27 ± 0.61	2.39 ± 0.19	0.000

White blood cell (WBC) count, LYM: lymphocyte count, NEU: neutrophil count, HB: Haemoglobin level, (MPV): mean platelet value, (RCW): Red cell distribution, NEU/LYM: neutrophil/lymphocyte ratio, PLT/LYM: platelets/lymphocyte ratio.



**Figure 1. The boxplot for the variable (Neutrophil/lymphocyte) from the group (pregnant women with COVID-19)**

## DISCUSSION

The COVID-19 virus originated in China from a big seafood market in Wuhan then becomes a pandemic spread worldwide [14]. The limited evidence of the probable effect of COVID-19 infection during pregnancy encourages the establishment of several studies on this subject; like other viral impacts on pregnancy, COVID-19 infection leads to an increased rate of miscarriage in early pregnancy besides the higher adverse pregnancy outcome like intrauterine growth restriction, preterm delivery, and increasing the perinatal mortality. Therefore it is crucial to have predictive parameters in order to evaluate the clinical features of COVID-19 disease with its complications [15]. The patient's symptoms may progress from mild to severe within a short duration with increased mortality risk. This could be related to the development of inflammatory storm [3].

According to a study conducted by Na Li et al. white blood cells and lymphocytes display no statistical disparity between cases and healthy controls [16]. However, previous research has found lower lymphocytes and leucocytes in COVID-19-infected hospitalized women. A small sampling bias may be the cause.

Neutrophils were higher in our analysis among COVID 19 cases contradicting wang D et al. study [17]. Platelets counts were reduced in line with Yang X et al., who confirms it is an ominous prognostic sign for infected cases [18]. Platelets serve as a vital bridge between the immune response and the hemostatic system. In addition, viral infections have been shown to affect platelet function [19].

In obstetrics, platelet number was suggested as a possible predictor for cases of preterm labour, including chorioamnionitis. Qiu et al. discussed that the area under the curve for platelet was 0.8 implying a good predictor marker, 95 % CI, 0.76760.8, P<0.05 in cases affected [20,21].

NLR included two subtypes of leukocyte cells, displays the balance of neutrophil and lymphocyte levels in the body with stages of systemic inflammation [22]. More precisely, it reflects a balance between the body's immunity status and the severity of the inflammation. Therefore it can be regarded as an essential marker of systemic inflammation as it can predict the severity of infection [23]. This study displayed the clinical risk parameters, which are easily collected from the laboratory tests.

We found a significant difference between the study group and healthy control regarding NLR as the P-value was  $<0.0001$  and it was higher in infected pregnant women, which suggested the role of NLR as a warning sign for patients deterioration and detected the severity of COVID-19 infection.

Imran et al., in a prospective, cross-sectional study in Pakistan, included 63 patients with the measurement of their NLR, serum albumin, C - reactive protein, serum fibrinogen. The investigators found significant differences between subdivided groups based on diabetic prevalence. There was a positive correlation between C - reactive protein and NLR ( $P < .001$ ,  $P = 0.04$ , respectively) with the Covid-19 severity but a negative correlation regarding serum albumin. They declared the important role of NLR as an independent risk parameter for detecting COVID-19 severity with a sensitivity of 0.83 and specificity of 0.75 [24].

Xia et al. enrolled 63 infected patients with COVID-19 in China, 32 cases with moderate infection and 31 cases diagnosed with a severe infection in a retrospective study. The authors confirm a significantly higher rate of NLR, diabetes, C-reactive protein, serum amyloid, serum albumin levels among severe cases with a P-value  $<0.05$ . Furthermore a positive correlation between NLR, CRP, and diabetes morbidity with the COVID-19 severity. The high NLR was considered as an earlier sign for the severity of COVID-19 infection [25].

Zhong et al. included 539 Chinese patients infected with COVID-19, including 36 infected pregnant women with 36 non-infected pregnant as control matched aged and body mass index in a retrospective study design. They found a significantly higher WBC, neutrophil count, and NLR ratio, Interleukin-6 (IL-6), interleukin-10 (IL-10), and IL-6/IL-10 ratio among patients presented with severe infection with COVID-19 than those non-infected with P-value  $<0.001$ . This indicates immune dysregulation in COVID-19 patients, and pregnant women have the same immune response with the rare occurrence of critical cases [26].

The crucial feature of COVID-19 patients is immune dysregulation, as they could develop a severe clinical illness similar in pregnant and non-pregnant patients. NLR serves as an earlier warning sign for the severe deterioration of COVID-19 patients; therefore permits the physicians and doctors to prepare for the covering of adequate treatment mechanisms.

## CONCLUSION

The NLR ratio could serve as a profound factor in predicting infected patients with COVID-19 in the early stages of the diseases, which give us the objective bases for the earlier diagnoses and treatment of severe COVID-19 infection in pregnant women in order to control and decrease the adverse pregnancy outcome.

### *Disclaimer*

The article has not been previously presented or published and is not part of a thesis project.

### *Conflict of Interest*

There are no financial, personal, or professional conflicts of interest to declare.

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