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Research Article

Early Hematological Changes in Patients with Asymptomatic COVID-19 During Labor

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Abstract

Objectives: This study aimed to find out easy, rapid, and less expensive tests to follow up with COVID-19 patients during labor. Early changes in CBC and inflammatory ratios among asymptomatic women in labor with positive COVID-19 PCR were analyzed.

Methods: Data from 109 women in labor with negative COVID-19 test and 109 patients with asymptomatic COVID-19 positive test. WBCs, neutrophils, lymphocytes, monocytes, and platelets numbers were retrieved from patients on admission. Neutrophil-Lymphocyte-Ratio (NLR), Platelet- Lymphocyte-Ratio (PLR), Monocyte-lymphocyte-ratio (MLR), and systemic-immune-inflammatory-index (SIII) calculated. ROC curve calculated cut-off levels of blood indices in both groups.

Results: WBCs significantly decreased in COVID-19 group (P= 0.045). Lymphocytes and platelets significantly decreased in the COVID-19 group (P =0.03 and P < 0.0001 respectively). Whereas no significant changes in Neutrophil and Monocytes in the COVID-19 group (P=0.123 and 0.66 respectively). No significant difference between NLR, MLR, and SIII in COVID-19 and non-COVID groups (P= 0.78, P=0.2184, and P=0.1188 respectively). PLR decreased significantly in COVID-19 group (P = 0.05). ROC curve determined the cut-off levels of total WBC, lymphocytes, platelets, and PLR. The predictive cut-off level of WBC was 8.85 (sensitivity 35.19 and specificity 82.46, AUC 0.594). The cut-off levels of Lymphocytes and Platelets were ≤1.876 (sensitivity 44.95, and specificity 69.72, AUC 0.575) and ≤249 (sensitivity 77.06 and specificity 55.05, AUC 0.726) respectively.

Conclusion: Early changes in total WBCs, Lymphocytes, Platelets, and PLR can be used as simple tests for early prediction, prognosis, and follow-up of COVID-19 pregnant patients in labor.

Keywords: COVID-19; Neutrophils; Lymphocytes; Monocytes; Platelets; PLR

Introduction

Recently, the world is overwhelmed by the pandemic disease COVID-19 which is caused by a novel coronavirus named severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). It became a global threat to human health. Many studies are conducted on the overall population. Similar to nonpregnant individuals, age, obesity, diabetes, and hypertension are risk factors associated with COVID-19 during pregnancy. Pregnant women may be more vulnerable to COVID-19 because of physiological adaptive changes and immunosuppressive state during pregnancy [1].

The clinical manifestations of coronavirus infections during pregnancy range from asymptomatic or mild disease to severe or fatal disease, similar to cases of infection among nonpregnant patients. The majority of pregnant women who are infected with SARS-CoV-2 were asymptomatic. Approximately, 95% of infected pregnant women had an asymptomatic or mild illness, and 5% developed a severe or critical illness. It was reported that 86% of women who were admitted in labor and who tested positive for SARS-CoV-2 were asymptomatic [2].

Most of the previous reports on the SARS-CoV-2 laboratory results were collected from the general population and limited information is available based on pregnancy and labor status. Moreover, asymptomatic patients in labor with confirmed SARS-CoV-2 infection need to assess their prospective risk for developing severe disease. Detection and combining appropriate cutoffs for certain hematological parameters could help in identifying the prognosis and severity of cases during pregnancy and labor.

Studies have proposed that the hyperinflammatory response created by SARS-CoV-2 is the main cause of disease severity and death in infected patients [3]. It was also shown that hematologic parameters were altered in COVID-19 patients but Pregnancy itself may influence these parameters. Physiological changes during pregnancy regarding leukocytes (neutrophils, monocytes, and lymphocytes) and platelets, may complicate the use of predictive values of these hematological parameters.

COVID-19 laboratory findings in pregnant women are conflicting. A complete blood count (CBC) is the most ordinarily performed hematological laboratory test worldwide. It was found that there is a strong association between COVID-19 positive pregnant patients and a low WBC count [4]. In asymptomatic patients WBC was found to be normal or decreased in COVID-19 pregnant patients; however, in severe cases, the WBC was increased when compared to the non-severe cases. On the other hand, leukocytosis was found in 50% of pregnant women infected with COVID-19 [5].

The functions of neutrophils in viral infections have not been fully explained yet. An increasing number of studies have revealed that neutrophils exhibit both protective and pathologic functions. Neutrophils are now considered as one of the most important immune cells in defending the airway epithelium against the SARS-CoV-2 infection. Neutrophils perform an essential function in the clearance of bacteria and specific mechanisms to combat viruses. Neutrophil numbers were mostly normal or even decreased in non-severe COVID-19 patients compared to healthy controls but were increased in severe infections. However, excessively increased neutrophils producing proinflammatory mediators can cause cytokine storm and Tissue damage, leading to severe pneumonia and death [6].

Lymphocytes are the primary immune barrier against viral infections. SARS-CoV-2 may directly infect lymphocytes and causes profound damage to lymphocytes. In addition, the release of cytokines and chemokines will draw immune cells, such as monocytes and T lymphocytes, from the blood to the infected area, causing lymphopenia in COVID-19 patients. The course of the disease in COVID-19 infection seemed to depend upon differences in lymphocyte regeneration in response to lymphocyte destruction by the virus [7].

Studies showed that lymphopenia was present in almost all symptomatic patients and was considered a sensitive and reliable marker of disease severity and outcomes in COVID-19 infection. Moreover, lymphocyte count was considered to be an important parameter in predicting disease severity and outcome [8]. It was reported that there is a dynamic change in peripheral blood lymphocytes with COVID-19. Lymphocyte percentage in pregnant women with COVID-19 was significantly lower compared with nonpregnant women. A possible reason for this finding is that lymphocytes are depleted because the virus is engulfed [9].

Monocytes had a pivotal function in host defense. They are liable for early pathogen recognition, initiation, and determination of inflammation. It was also responsible for the repair of tissue damage, especially lung injury in respiratory diseases [10]. Blood monocytes provide a window on the systemic immune reaction from production to tissue recruitment, reflecting the impact of infection on the host. Circulating monocytes and tissue macrophages participate in altogether stages of SARS COVID- 19. During the infection, monocytes and macrophages could also be involved within the hypersensitive and exacerbated reactions that contribute to the tissue damage. It was found that activated monocytes infiltrate lungs in patients with COVID-19 and animal models of SARS-CoV-2 infection. Studies reported that monocyte numbers were generally within the normal range but could be in the lower range in the severe patient [11].

Thrombocytopenia was detected in COVID-19 patients. The incidence varies according to disease severity. In general, COVID-19 patients have normal or low platelet counts. Severe cases of Covid-19 had lower thrombocytopenia than mild cases. Lower platelet count was found in a meta- analysis of severe COVID-19 patients compared to the non-severe cases. In Wuhan Hospital, COVID-19 patients admitted with thrombocytopenia had a poor prognosis with an increased risk of inpatient mortality. Lippi et al, decided that platelet counts may determine disease severity [12].

The neutrophil-to-lymphocyte ratio (NLR), is a famous marker of infection and systemic inflammation. It is recognized as a systemic marker of the inflammatory response that is superior to individual levels of neutrophils and lymphocytes in assessing disease progression in viral infections. Raised NLR values advocate a poor prognosis in COVID-19 disease. Elevated NLR was considered as a screening tool at admission to a hospital and identification of high-risk patients. Increasing neutrophil count and a decrease in lymphocyte count in severe cases of COVID-19 may be related to increased NLR levels [13].

Platelet-lymphocyte-ratio (PLR) has also been reported as a parameter that indicates the severity of the infection. PLR was significantly higher in COVID-19 patients. The PLR of patients reflects the degree of cytokine storm, which might provide a new indicator in the monitoring of patients with COVID-19. PLR is a unique biomarker to predict the severity of COVID-19 [14].

Monocyte-lymphocyte ratio (MLR) in blood routine tests

have specific clinical application values in predicting the progress of infectious diseases. Several studies about COVID-19 showed abnormal parameters of lymphocytes and monocytes in the peripheral blood of patients with COVID-19. MLR had a significant positive correlation with the Covid-19 disease severity. MLR also had a predicting value in hospitalized patients with COVID-19 [15].

Systemic immune-inflammation index (SIII), based on lymphocyte, neutrophil, and platelet counts, is an inflammation-related indicator and can reflect the immune and inflammation status of the organism. SIII has been recently proposed as a prognostic indicator in the follow-up of sepsis and patients with cancer as an index defining the instability in the inflammatory response. Few reports about the role of SIII in reflecting the inflammatory situation and predicting the prognosis of patients with COVID-19. SIII was significantly higher in patients with severe Covid-19 disease [16].

Thus, there is a need for alternative, easy, rapid, less expensive, and more accessible tests to follow up covid-19 patients, especially during pregnancy and labor.

This study aimed to analyze early changes in CBC and inflammatory ratios among asymptomatic women in labor and had Covid-19 positive RT-PCR. It was also aimed to find a sensitive cut-off level of inflammatory markers for the prediction and prognosis of early asymptomatic COVID-19 pregnant patients. Incidence of cesarean sections and feto-maternal transmission in asymptomatic patients were also investigated.

Material and Methods

CBC is a routine test done for all patients admitted to Al Yamamah Maternity Hospital for delivery. Mothers and infants were tested by nasopharyngeal SARS-CoV-2 RNA reverse transcriptase-polymerase chain reaction (RT-PCR).

Asymptomatic patients admitted to Al Yamamah Maternity hospital in labor (≥37 weeks) and their results of the COVID-19 test were positively included in this study in the period between January 2020 to December 2021. Patients known to have COVID-19 or had signs and symptoms such as fever, cough, dyspnea, low O2 saturation, or acute respiratory distress were excluded from this study. Any patients with medical complications such as DM, GDM, chronic hypertension, preeclampsia, and cholestasis were also excluded.

Data of 109 asymptomatic patients with COVID-19 positive tests and in labor were collected in this study (COVID-19 or study group). Also, data of 109 patients (≥37 weeks) with negative COVID-19 and in labor (non-COVID-19 group or Control group) were gathered. All cases were matched by age, parity, single fetus, and absence of chronic diseases. Demographic data were collected for all patients from the Hospital's electronic medical record.

Total WBCs, neutrophils, lymphocytes, monocytes, and platelets numbers were retrieved from all patients on admission. Neutrophil-Lymphocyte-Ratio (NLR), Platelet Lymphocyte Ratio (PLR), Monocyte lymphocyte ratio (MLR), and systemic immune-inflammatory index (SIII) were calculated. MLR was calculated by dividing the absolute monocytes counts by the absolute lymphocyte counts. (SII) is calculated by (N×P)/L (N, P, and L represent neutrophil counts, platelet counts, and lymphocyte counts, respectively).

All participants shared in this study have signed a consent form. Also, approval consent was taken by the Medical Ethics Committee of Al Yamamah Hospital.

Statistical Analyses

Statistical analyses were performed using the software SPSS Version 20 (SPSS Inc.). The analysis between the COVID-19-positive and non-COVID groups was performed using an independent sample t- test. Differences between COVID-19-positive and negative groups were considered statistically significant if the p-value was <0.05. Continuous variables were expressed as mean ± SD. ROC curve was used to calculate cut-off levels of blood indices in both groups.

Results

Demographic data are shown in Table 1. No significant difference was found between the COVID- 19 group and the control group regarding age, parity, GA, and mode of delivery. Cesarean section (19.3%) was significantly higher in COVID group (P = 0.05). Also, 2 cases of IUFD (1.8 %) were found in the COVID-19 group. All neonatal specimens tested, were negative by RT-PCR for SARS-CoV-2.

Table1: Summary of Demographic data of Covid-19 and Non-Covid-19 groups.

	Age	Parity	GA	NVD	C/S
COVID-19 (n=109)	29.4±6.76	2.18±1.92	38.71±2.17	86(78.9%)	21(19.3%)
Non Covid group (n=109)	30.85±6.6	2.51±1.90	38.98±1.54	98 (89.9%)	11(10.1%)
P	0.11	0.2	0.29	P=0.076	P = 0.05

Total WBCs were significantly decreased in COVID-19 group compared to non-COVID-19 women in labor (10.58±3.74, 95% CI 9.87 - 11.29 vs 11.54±3.35, 95% CI 10.54 - 11.74, P= 0.05). There were no significant changes in Neutrophil No. between COVID-19 and the normal delivery control group (7.84±3.52 95% CI 7.18 to 8.50 vs 8.53±3.09 95 % CI 7.94 to 9.12, P=0.12). Absolute

lymphocyte No. was found to be significantly decreased (2.03±0.64 95% CI 1.91- 2.15 vs 2.24±0.75 95% CI 2.10- 2.38 P =0.03) in the COVID-19 group compared to the normal labor group.

Although Monocytes were increased in COVID-19 group, the increment was not significant in women with COVID-19 positive vs control group (0.70±0.39 95% CI 0.619- 0.774 vs 0.72±0.28 95% CI 0.67-0.76, P= 0.66).

Platelets were found to be significantly decreased in the COVID-19 group compared to the control group (213.61±53.87 95% CI 203.38-223.83 vs 265.05±60.19 95% CI 253.62-276.47 and P < 233 0.0001).

Inflammatory ratios in Covid-19 and non-Covid-19 groups were calculated. No significant difference in NLR was found between COVID-19 and the control group (4.36±2.46 95% CI 3.89 to 4.82 vs 4.24±2.43 95% CI 3.82 to 4.67, P= 0.78). PLR was decreased significantly in COVID-19 group 237 (1 1 7 . 4 3 ± 5 3 . 8 2 95% CI 107.21-127.64 vs 132.69±62.04 95% CI 120.92- 144.47 and P = 0.05). No significant changes were found in MLR between the Covid-19 and non-Covid-19 groups (0.38±0.22 95% CI 0.33 to 0.42 vs 0.36±0.22 95% CI 0.32 to 0.41, P=0.22). SIII was not significantly decreased in the Covid-19 group compared to no-Covid-19 (958.70±580.29 95% CI 808.53 to 1028.87 vs 1091.37±667.39 95% CI 964.06 to 1218.67 and P=0.12). Previous data and Inflammatory ratios are shown in Table 2.

Table 2: Comparing CBC and inflammatory Ratios in Covid-19 and Non-Covid -19 patients in labor.

	Covid Pregnancy	Non-COVID Pregnancy	P value
	Mean ± SD (95% CI)	Mean ± SD (95% CI)	
Total WBC	10.58±3.74 (9.87 - 11.29)	11.54±3.35 (10.54 - 11.74)	P = 0.05
Neutrophil No	7.84±3.52 (7.18 to 8.50)	8.53±3.086 (7.94 - 9.12)	P = 0.12
Lymphocyte No	2.03±0.64 (1.91- 2.15)	2.24±0.75 (2.10- 2.38)	P = 0.03
Monocytes No	0.70 0.39 (0.619- 0.774)	0.72±0.28 (0.67-0.76)	P = 0.66
Platelets No	213.61±53.87 (203.38-223.83)	265.05±60.19 (253.62-276.47)	P < 0.0001
1-NLR (Neutrophil Lymphocyte Ratio)	4.36±2.46 (3.89-4.82)	4.243±2.43 (3.82-4.67)	P = 0.78
2-PLR (Platelet Lymphocyte Ratio)	117.43±53.82 (107.21-127.64)	132.69±62.04(120.92- 144.47)	P = 0.05
3-MLR (Monocyte Lymphocyte Ratio)	0.38±0.22(0.33 to 0.42)	0.363±0.22 (0.32 to 0.41)	P = 0.22
4-SIII (Systemic Immune Inflammatory Index)	958.70±58.29(808.53 to 1028.87)	1091.37±667.39(964.06 to 1218.67)	P = 0.12

Table 3: Summary of ROC curves.

	AUC	CI	P	Youden Index J	Associated criterion Cut-off level	Sensitivity	Specificity
Total WBC	0.59	0.53 to 0.66	0.01	0.18	≤8.85	35.19	82.46
Lymphocytes No	0.58	0.51 to 0.64	0.052	0.15	≤1.88	44.95	69.72
Platelets	0.73	0.66 to 0.78	<0.0001	0.32	≤249	77.06	55.05
PLR (Platelet/Lymphocyte Ratio)	0.59	0.52 to 0.66	0.018	0.193	≤89.7	36.7	82.57

ROC curve was used to study for positive results (WBC, lymphocyte no., Platelet no, PLR, and SIII) to determine the cut-off level of WBC. The predictive cut-off level of WBC was 8.85 with a sensitivity of 35.19 and specificity of 82.46 (95% CI 0.53 to 0.66). AUC was 0.59 and P =0.01. 35% Of cases < 8.85 in Covid-19 group whereas in control group 17.5% of cases <8.85.

The cut-off level of Lymphocyte was ≤1.88, AUC was 0.58 with a sensitivity of 44.95, and specificity 69.72 (95% CI 0.51 to 0.64). Platelet cut-off level was ≤249, and AUC was 0.73 (sensitivity 77.06 and specificity 55.05, 95% CI 0.66 to 0.78). PLR cut-off level was ≤89.7 and AUC was 0.59 (sensitivity 36.70 and specificity 82.57, 95% CI 0.52 to 0.66). Tab.3 summarizes sensitivity, specificity, and AUC of WBCs, lymphocytes, platelets, and PLR. Figure 1 shows the ROC curve of WBCs, lymphocytes, platelets, and PLR.

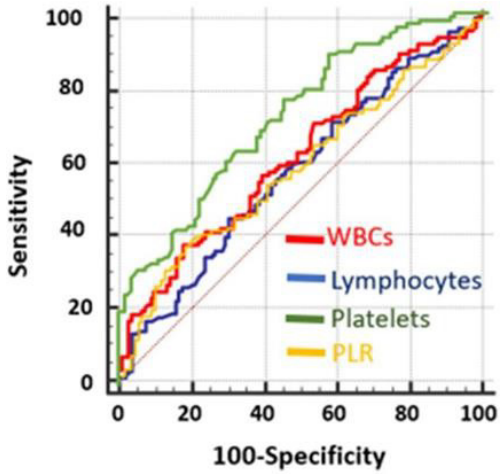

Figure 1: ROC curve of WBCs, lymphocytes, platelets, and PLR.

Discussion

The outbreak of coronavirus disease 2019 (Covid-19) is an ongoing global pandemic disease caused by SARS-CoV-2 and affecting the lives of millions of people worldwide. Preliminary studies showed that systemic inflammatory response played an important role in the progression of the disease. Evidence has indicated that hyperinflammatory responses triggered by SARS-CoV-2 are the main cause of pathogenicity, damage, and functional impairment of major organs in the severe cases of patients who have died during the current viral disease [3]. The influence of COVID-19 on pregnant women is not completely clear. There is growing evidence that pregnant women may be at increased risk of infection with COVID-19 compared with non-pregnant women, particularly in the third trimester [1]. Moreover, there is a possibility of a newly born baby infection.

Laboratory findings of infected pregnant women are different from non-pregnant women. According to various research, the majority of pregnant women had mild to moderate COVID-19 symptoms, with a small percentage developing severe symptoms such as high temperature and pneumonia. In a previous study, 86 percent of women who were admitted in labor and tested positive for SARS-CoV-2 were asymptomatic [2].

Cesarean section in pregnant women with COVID-19 is high and this rate reaches 93% in China [17]. In our study, the incidence of CS in the COVID-19 group (19.3%) was also significantly higher than in the non-COVID group (10.1%, p=0.05). No fetal infection was detected in the COVID-19 group after delivery. It was also reported that there is no evidence for intrauterine transmission of COVID-19 from infected pregnant women to their fetuses [1].

WBC

A complete blood count (CBC) is a common blood test ordered by physicians and interpreted in clinical laboratories. A literature review suggested that hematologic abnormalities in COVID-19 patients may serve as a diagnostic and prognostic tool for predicting illness severity and mortality. WBC is normally elevated during pregnancy due to the physiologic stress induced by the pregnant state.

WBC count in pregnant women infected with COVID-19 was controversial. It was reported that WBC counts were similar among healthy pregnant women and pregnant women with COVID-19 [9]. Other studies reported slightly lower WBC counts in pregnant women with COVID-19 [5,18]. Other researchers found that the WBC count in pregnant women with COVID-19 infection was significantly higher [5]. Zhao, et al. in Reported that patients with increased leukocyte count were more likely to develop a critical illness [19]. This significantly higher level may be due to systemic inflammation response. In our study, during labor, WBC was significantly lower in the Asymptomatic pregnant COVID- 288 19 group compared to the non-COVID group (10.58±3.74, 95% CI 9.87 - 11.29 vs 11.54±3.35, 95% CI 10.54 - 11.74, P= 0.05). Yang H, et al. also found that leucocytes were lower or normal in COVID-19 infected pregnant women [20]. WBC count may differ according to COVID-19 severity.

Neutrophil

Since the beginning of the COVID-19 pandemic, strong evidence has accumulated indicating that neutrophils play a major role in the pathogenesis of the disease, particularly in patients with severe illness. Neutrophil numbers were usually normal in non-severe cases but were increased in severe infections. It was reported that normal and even decreased neutrophils were detected in COVID-19 patients compared to healthy controls [21].

Increased neutrophils in the blood of severely affected patients were noted as a prominent clinical feature of COVID-19. Wang Z, et al. suggested that neutrophilia might be related to the cytokine

storm induced by the invasion of COVID- 19 [5]. It was found that pregnant patients showed enhanced innate immune response evident by higher neutrophils [7]. Leukocytosis and elevated neutrophil ratio were found to be more common in pregnant women infected with COVID-19. On the other hand, in the Li N study, the infected COVID-19 pneumonia groups had lower counts of white blood cells and neutrophils [18]. In our study, neutrophil count in the COVID-19 group, not significantly changed compared to non-infected pregnant women. Similar results were found in other research [22].

Lymphocyte

Dynamic changes of lymphocytes are most consistent in COVID-19 [21]. Fan, et al. reported that the percentage of lymphocytes changed dynamically throughout COVID-19 infection, that this change was more consistent than any other hematological parameter, and that more severe lymphopenia was associated with ICU admissions and non-survivors [23].

It was reported that pregnant COVID-19 patients had lymphopenia upon admission, and lymphocyte counts were particularly low in severe cases hospitalized in ICUs. Lymphocyte count could help to identify the likelihood of disease progression and severity in COVID-19 and therefore aid patient risk stratification and medical management [24].

In this study lymphocyte no. was significantly lowered in asymptomatic COVID-19 pregnant women compared to the control group (2.03±0.64 95% CI 1.91- 2.15 vs 2.24±0.75 95% CI 2.10- 2.38, P= 0.03). None of our infected patients developed severe COVID-19 or died. This result is comparable with Sun, et al results who also found significantly lower lymphocytes in infected pregnant women [4].

Also, Norooznezhad in the analysis of pre-cesarean section CBC found a significant decrease in lymphocytes ratio and absolute lymphocytes count compared to healthy pregnant women [22]. Many other studies also showed decreased or normal lymphocytes count in infected pregnant women with COVID-19 [4] Lymphocyte count was determined to be the most sensitive and reliable parameter in predicting disease severity and outcome [24].

Monocytes

Monocytes play an important role in the immune system and a substantial part in the body's defense against viral infections. Monocytes are thought to be important participants in the pathophysiology of lung damage produced by cytokines storm in COVID-19 [10].

In COVID-19, monocyte numbers were usually within the normal range but could be decreased in severe patients [23]. The mechanism leading to monocytes alteration is still unclear, but a direct viral role can be suspected. In this study monocyte numbers were not significantly differed between asymptomatic COVID-19 and non-COVID-19 groups.

Platelet

Pregnant women have somewhat fewer platelets count than non-pregnant women of the same age, and the number of platelets declines as the pregnancy progresses. Numerous physiological changes that occur during pregnancy could be responsible for lower platelet counts.

Previous research reported that thrombocytopenia was common in COVID-19 patients. In patients with severe COVID-19, the platelet count was markedly reduced, suggesting that changes in platelet levels may be predictive of the patient's prognosis [12]. Thrombocytopenia may occur due to direct infection of bone marrow precursors, leading to abnormal hematopoiesis of platelets, or a cytokine storm destroying progenitor cells. Thrombocytopenia may also be associated with platelet destruction by the immune system as a result of an auto-immune response or by increased platelet consumption due to lung damage [25].

It was reported that no significant difference in platelet count between COVID-19 pregnant women and non-COVID 19 cases [22]. However, in other studies, platelet counts were lower in pregnant with COVID-19 [12]. In this study, platelets were significantly decreased in COVID-19 group compared to 349 non-COVID-19 group (213.61±53.87 (203.38-223.83) vs 265.05±60.19 (253.62-276.47) $P < 0.0001$).

Neutrophil Lymphocyte ratio (NLR)

The NLR is recognized as a systemic marker of the inflammatory response that is superior to individual levels of neutrophils and lymphocytes in assessing disease progression in viral infections. Accumulating evidence suggests that the NLR increases significantly in patients with severe COVID-19 infection and is associated with poor outcomes in acute respiratory distress syndrome [26].

High NLR seems to be consistently increased in patients with severe COVID-19 cases. Feng Z, et al. reported that higher NLR had a prognostic value and can be considered as an independent predictor for severe pneumonia in COVID-19 patients. It was also reported that elevated NLR could be used as a screening tool at admission to a hospital to identify high-risk patients [27].

Limited data are comparing the NLR in healthy pregnant women with that in COVID-19 pregnant women, and the results were inconsistent. It was reported that in pregnant women, the NLR cutoff level was 5.1 (sensitivity 70% and specificity 63%) between normal and those with severe disease [28]. In this study, there was also no significant difference between asymptomatic COVID-19 pregnant patients and non-COVID cases.

Platelet to Lymphocyte Ratio (PLR)

PLR was considered as a marker of a pre-existing inflammation or chronic inflammatory state. Previous research reported that PLR was an indicator of the severity of COVID-19 infection. On hospital admission, a higher level of PLR on admission in COVID-19 patients

was found to be associated with increased morbidity and mortality [29]. PLR can be used as an independent prognostic marker for the severity of COVID-19 [27]. Lira et al reported increased PLR in pregnant COVID-19 cases with a cutoff point of 221(sensitivity was 90% and the specificity 83%, OR 45, 95% CI 4.40–461.7) [28].

In this study, PLR was significantly lower in the asymptomatic COVID-19 group with a cutoff level of 89.7 (95% CI 0.52 to 0.66, sensitivity 36.70, and specificity 82.57). This marked difference in cutoff level maybe because other studies involve mild, moderate, and severe cases of COVID-19 whereas in our study only asymptomatic cases are collected. Lower PLR may reflect early consumption, destruction, and decreased production in platelet and lymphocytes.

The PLR in COVID-19 patients may be associated with the degree of cytokine storm and might provide a novel indicator to monitor patients with COVID-19. Higher levels of PLR were associated with severe COVID-19 cases. Accordingly, the PLR level is considered a novel, cost-effective, and readily available biomarker with a hopeful prognostic role for determining the severity of COVID-19 patients [14]. Low PRL as an inflammatory biomarker may be a good prognostic test to differentiate and predict severe cases of COVID-19.

Other researchers presented conflicting data on the diagnostic and prognostic value of the PLR in patients with COVID-19 where no significant difference was found between infected and non-infected COVID-19 early on hospital admission [30].

Monocyte-Lymphocyte Ratio (MLR)

Previous studies reported a significant positive correlation between MLR with disease severity of patients with COVID-19. MLR was increased with the severity of patients with COVID-19 [31]. The higher MLR in severe cases indicated that the immune system in these cases was severely damaged. Our results showed that asymptomatic COVID-19 are not significantly changed compared to the COVID-19 group.

Systemic Immune Inflammatory Index (SIII)

SIII is an inflammation-related indicator that reflects the immune and inflammation status of the organism, based on lymphocyte, neutrophil, and platelet counts. Recently, SIII was proposed as an innovative predictable marker for COVID-19 patients. Also, SIII might be considered as a remarkable prognostic indicator to assess the clinical outcomes of patients with COVID-19. Patients in the high-SIII group had a higher chance of severe complications, such as multiple organ dysfunction syndromes, ARDS, major cardiovascular adverse events, disseminated intravascular coagulation, secondary infection, sepsis shock, and acidosis [32]. A study by Huang Li et.al found that the cut-off level of SIII ≥ 1293.11 was predictive of severe complications in COVID-19 patients [33]. In our study SIII in the asymptomatic COVID-19 group was no significant changes compared to the non-COVID-19 group.

Conclusion

With the spread of COVID-19, pregnant women are at greater risk because they have a worse prognosis than non-pregnant ladies once they got infected. During pregnancy, physiological changes include decreased functional residual capacity by approximately 20% to 30% and increased oxygen consumption by 20%, making lower respiratory infections less well tolerated.

Pregnant women with asymptomatic COVID-19 infection are rarely investigated. The study of early changes in COVID-19 infection is crucially important. Low WBC count, low lymphocyte, low platelet counts, and low PLR are diagnostic and prognostic values for asymptomatic cases of COVID-19.

In mild COVID patients, a moderate inflammatory response is sufficient to clear the body of the viral pathogen. However, an excessive inflammatory response will cause immune loss, fatal cytokine production, systemic inflammatory response, multi-organ failure, and a series of additional clinical manifestations

Inflammatory index data are cost-effective and easily accessible resources that can assist with the early recognition of severe COVID-19 cases and ensure the timely initiation of the most appropriate treatment. Our data might suggest that, in the early phases of COVID-19, the virus induce an inflammatory response leading to a reduction in the hematological indices. Decrease total WBC, lymphocytes, and platelets were the early changes detected in asymptomatic pregnant women in labor. These parameters may be changed with the increased severity of COVID-19. These results may also serve as prognostic markers in COVID- 19. These early changes of parameters may be very useful for the detection of a pregnant patient who may progress to a severe stage of COVID-19.

More comprehensive studies with larger patient groups are needed to further assessment of our results. It is also needed to follow up on these cases to monitor and predict the severity and prognosis of COVID-19.

Acknowledgement

The Study was approved, and Ethics approval was obtained from the Al Yamamah Ethical committee.

Conflict of Interest

The authors declare that they have no conflict of interest. All authors contributed to the study's conception and design. All authors read and approved the final manuscript.

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