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Comparison of third-trimester blood profile indices in pregnant women with and without COVID-19 infection: A cross-sectional study

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ABSTRACT

Background: The third trimester represents a critical window in pregnancy when these hematologic changes could have the greatest impact. Therefore, understanding how coronavirus disease 2019 (COVID-19) infection influences blood profiles during this period is vital for clinical management and risk stratification. In Kenya, while national guidelines recommend laboratory evaluation, including complete blood count, c-reactive protein (CRP), lactate dehydrogenase (LDH), and coagulation profiles for pregnant women with suspected or confirmed COVID-19, there is a paucity of local data documenting these hematologic trends.

Objective: To investigate hematologic profile differences between pregnant women in the third trimester with and without COVID-19 infection.

Methods: A cross-sectional comparative study was employed to compare hematological parameters in pregnant women with and without COVID-19 between May 1st and August 31st, 2021. We recruited 60 eligible patients from the Nairobi hospital using purposive sampling. We assessed the complete blood count, coagulation profile, lactate dehydrogenase, and C-reactive protein.

Results: Pregnant women with COVID-19 had significantly higher levels of neutrophils, prothrombin time, CRP, and LDH compared to those without, with respective AORs of 9.50 ($p<0.01$), 11.52 ($p=0.001$), and 3.06 ($p=0.078$). No significant differences were observed in white blood cells, basophils, and international normalized ratio after adjusting for age, parity, COVID-19 vaccination, and fetus number.

Conclusion: This study reported significant associations between neutrophil count, prothrombin time, CRP, LDH levels, and COVID-19 infection status in pregnant women. These indices may aid in distinguishing healthy pregnant women from those with COVID-19 infection.

Keywords: COVID-19 infection, pregnant women, third trimester, blood profile

Introduction

Coronavirus disease 2019 (COVID-19), caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) (1), poses significant risks to pregnant women, particularly during the third trimester (2). Pregnancy itself is known to induce

physiological changes that alter the hematological profile of women, ensuring an optimal environment for fetal development (3). However, when combined with the potential effects of COVID-19 infection, these changes may become more complex and raise concerns for both maternal and fetal well-being (4). The third trimester, characterized by advanced gestation, represents a critical period in pregnancy, during which any alterations in hematological parameters could have profound implications. Changes in the blood profiles of pregnant women, including neutropenia, leukocytosis, thrombocytopenia, lymphopenia, eosinophilia, elevated D-dimer, increased ferritin, elevated lactate dehydrogenase (LDH), and elevated C-reactive protein (CRP) are thought to be contributing factors to this increased risk (5-16). In Kenya, the Ministry of Health has published guidelines for the management of COVID-19 in pregnancy, which recommends routine laboratory investigations, including complete blood count, CRP, LDH, and coagulation profile (17). However, there are currently no published data in Kenya on the blood profiles of pregnant women with COVID-19 infection. This study therefore aims to investigate the differences in blood profiles between pregnant women in the third trimester with and without COVID-19 infection.

Methods

Study design and setting

The study was a comparative cross-sectional design conducted at Nairobi Hospital, Nairobi, Kenya, between May 1st, 2021, and August 31st, 2021.

Study population

The study included 60 pregnant women in their third trimester who were admitted to the maternity wing. Participants were selected using a purposive sampling technique, excluding those with comorbid conditions. All pregnant women admitted at the Nairobi hospital between May 1st, 2021, and August 31st, 2021 were included in this study, whereas those with comorbid conditions such as diabetes, tuberculosis, hypertension, and malignancies were excluded. To minimize confounding from other conditions that affect hematological profiles, we screened medical records to exclude participants with known acute infections, malignancies, autoimmune diseases, or hematologic disorders. The structured data tool also captured symptoms and clinical signs to help identify underlying illnesses. Patients with any such conditions were excluded.

Sample size estimation

The sample size of 60 was determined to provide adequate statistical power (80%) to detect meaningful differences or associations between hematological parameters in pregnant women with and without COVID-19 in their third trimester. This sample size was chosen considering the feasibility of recruitment and data collection within the available resources, including time and budget constraints. Conducting a study with a larger sample size would have been challenging due to logistical factors, such as the availability of participants and accessibility to healthcare facilities during the period of curfew and limited services. Thus, the chosen sample size ensured a balance between statistical power and practical considerations for effectively conducting the study.

Data collection and management

A structured data collection tool detailing all the variables of interest was used to collect data from patients' records. Data were collected on patients' demographics, Reproductive/clinical characteristics, and COVID-19 status, as determined by polymerase chain reaction (PCR) testing, and hematological results. The specific blood profiles, including complete blood count, coagulation profile, LDH, and CRP, were obtained from the main laboratory (The Nairobi Hospital) using Architect C8000®. The collected data was counterchecked by the principal investigator for accuracy and consistency and then converted to a password-protected Microsoft Excel sheet.

Data analysis

The data obtained were analyzed using SPSS version 26. The socio-demographic characteristics, including age, COVID-19 vaccination status, parity, and fetus number, were tabulated, and their means were compared between the two groups using chi-square. The medians and interquartile ranges of the specific blood profile results were tabulated and compared across the two groups using the Mann-Whitney U test. A p-value of less than 0.05 was considered statistically significant.

Ethical considerations

Ethical approval was obtained from the Kenyatta National Hospital - University of Nairobi (KNH-UoN) Ethics Committee (registration number P860/11/2021), Nairobi Hospital, (registration number TNH-ERC/DMSR/RP/021/22) and the National Commission for Science, Technology,
and Innovation (NACOSTI) (registration number 496450). Informed consent was obtained from
all participants prior to their inclusion in the study.

Results

Sixty pregnant women were recruited into the study. The mean age of those with COVID-19 infection was 33 ± 5.25 years, while the mean age for those without was 31 ± 5.59 years. Age difference was not found to be statistically significant (p=0.145). There was a trend towards older age in women with COVID-19 infection, with 57% of them being 35 years or older compared to 37% of women without the infection (p=.121). The majority of women in both groups were vaccinated against COVID-19, but the difference between the two groups was not statistically significant (p=.195). The parity status of the women differed significantly between the two groups, with 60% of women with COVID-19 infection being multiparous compared to 84% of women without the infection (p=.120). There was no significant difference between the two groups in terms of fetal number (p=1). (**Table 1**)

Table 1: sociodemographic characteristics and blood profiles among women with and without COVID-19 infection in the third trimester

		Women with COVID-19 infection N=30	**Women without COVID-19 infection N=30**	**P-value**
Age (Mean ± SD)		33 ± 5.25	31 ± 5.59	.145
Age group	<35	13(43%)	19(63%)	.121
	≥35	17(57%)	11(37%)	
Vaccinated	Yes	25(83%)	29(97%)	.195
	No	5(17%)	1(3%)	
Parity	Nulliparous	12(40%)	7(16%)	.120
	Multipara	18(60%)	23(84%)	
Fetus Number	Singleton	28(93%)	29(97%)	1
	Twins	2(7%)	1(3%)	

The p-value in Table 1 represents the result of a chi-square test for the comparison of categorical variables, such as age group, vaccination status, parity, and fetal number, between the two groups (women with COVID-19 infection and women without COVID-19 infection).

Pregnant women with COVID-19 infection had a significantly lower median white blood cell (WBC) count of 5.4 × 10^9/L (normal range: 4.0–11.0 × 10^9/L) compared to 7.1 × 10^9/L in women without COVID-19 (p = 0.005). They also exhibited a lower median neutrophil count of 3.5 × 10^9/L (normal range: 2.0–7.0 × 10^9/L) compared to 4.5 × 10^9/L in the COVID-19 negative group (p = 0.022). Conversely, the basophil count was higher in women with COVID-19, with a median of 0.04 × 10^9/L (normal range: 0.0–0.1 × 10^9/L), compared to 0.02 × 10^9/L in the negative group (p = 0.039). In addition, pregnant women with COVID-19 showed significantly elevated international normalized ratio (INR) and prothrombin time (PT) in seconds, with median INR and PT values both exceeding those of the COVID-19 negative group (p = .004 and p = .001, respectively). The normal range for INR is 0.8–1.2, and for PT is typically 11–13.5 seconds. Pregnant women with COVID-19 infection had significantly higher levels of CRP and LDH compared to the control group (p=0.011 and p<.001, respectively). There were no significant differences between the two groups in terms of lymphocyte percentage, monocyte count, eosinophil percentage, platelet count, red blood cell count, neutrophil-to-lymphocyte ratio (NLR), or platelet-to-lymphocyte ratio (PLR) (**Table 2**).

The table shows that pregnant women with COVID-19 infection had significantly lower levels of neutrophils and elevated PT Seconds, CRP, and LDH compared to those without COVID-19 infection, with AORs of 9.50 (p<.01), 11.52 (p=.001), and 3.06 (p=.078), respectively. Meanwhile, there were no significant differences observed in the levels

of basophils, and INR between the two groups after adjusting for age, parity, and COVID-19 vaccination status, and fetus number (Table 3).

Table 2: Third-trimester blood profiles among women with and without COVID-19 infection

	Women with COVID-19 infection N=30 **Median (Q1-Q3)**	**Women without COVID-19 infection N=30** **Median (Q1-Q3)**	**P-value**
White blood cell count,10^9/L	5.4(4.81-7.00)	7.1(6.21-9.36)	**.005**
Lymphocyte %	1.7(1.25-2.31)	1.8(1.40-2.72)	.695
Neutrophils	3.5(2.49-4.95)	4.5(3.97-6.00)	**.022**
Monocyte	0.4(0.26-0.64)	0.6(0.32-0.81)	.082
Basophil	0.02(0.01-0.04)	0.04(0.02-0.06)	**.039**
Hemoglobin	12.4(10.83-13.40)	12.6(12.18-14.30)	.086
Eosinophil %	1.5(0.3-3.0)	0.9(0.18-1.80)	.407
Platelets *10^9/L	220(200.25-307.75)	272(232.0-324.5)	.399
Red blood cell count*10^9/L	4.4(3.78-4.84)	4.6(4.23-4.93)	.091
Neutrophil lymphocyte ratio (NRL)	1.8(1.20-3.47)	2.3(1.64-3.60)	.104
Platelet lymphocyte ratio	139.2(96.44-208.40)	132.5(106.60-175.13)	.848
International normalised ratio	1.8(1.5-1.9)	1.5(1.2-1.7)	**.004**
Prothrombin time (PT)sec	13(12-15)	11(9.9-13.0)	**.001**
Activated partial thrombin time	33(26.75-37)	27.5(25-33)	.353
C-reactive protein mg/l	32.5(14.40-40)	15.4(12.48-23.50)	**.011**
Lactate dehydrogenase/L	213(198 -245)	97(83.75-114.75)	**<.001**

Table 3: Association of COVID-19 status with selected laboratory parameters after adjusting for age, parity, vaccination status and fetal number

		Pregnant women with COVID-19 infection N=30	**Pregnant women without COVID-19 infection N=30**	**Crude OR (95% CI)**	**P-value**	**Adjusted OR (95%CI) (age, parity, COVID-19 vaccination status and fetus number)**	**P-value**
White blood cell count,10^9/L	<9.5	27(90%)	24(80%)	2.25(0.51,9.99)	0.47	3.52(0.53,23.50)	
	≥9.5	3(10%)	6(20%)	Ref		Ref	.194
Neutrophils	<3.9	18(60%)	4(13%)	9.75(2.71,35.11)	**<0.01**	9.50(2.23,40.52)	
	≥3.9	12(40%)	26(87%)	Ref		Ref	**.002**
Basophil	<0.1	28(93%)	24(80%)	3.50(0.65,18.98)	0.25	4.90(0.30,80.38)	
	≥0.1	2(7%)	6(20%)	Ref		Ref	.266
International normalised ratio	<1.1	3(10%)	4(13%)	0.72(0.15,3.55)	1	0.90(0.14,5.87)	
	≥1.1	27(90%)	26(87%)	Ref		Ref	.913
Prothrombin time Seconds	<12	6(20%)	19(63%)	6.91(2.16,22.10)	**<0.01**	11.52(2.69,49.33)	**.001**
	≥12	24(80%)	11(37%)	Ref		Ref	
C-Reactive protein mg/l	<20	18(60%)	10(33%)	Ref	**0.03**	Ref	

	≥20	12(40%)	20(67%)	3.00(1.05,8.60)		3.06(0.88,10.65)
Lactate dehydrogenase U/L	≥140	30(100%)	5(17%)	-		-
	<140	0(0%)	25(83%)			

Discussion

Our study comparing specific blood profile indices of 30 pregnant women in their third trimester with COVID-19 infection and 30 pregnant women in their third trimester without the infection aligns with previous reports regarding the impact of COVID-19 on hematological parameters. Several studies have reported similar findings, including a decrease in basophil count and neutrophil count, as well as an increase in C-reactive protein (CRP) and lactate dehydrogenase (LDH) levels (18-21). COVID-19 infection was associated with a decrease in neutrophil count, which could be attributed to the virus's ability to suppress the immune response and affect hematopoiesis (18). Increased levels of CRP in COVID-19 patients have been reported, indicating an inflammatory response, which is consistent with our findings (22). Elevated LDH levels in COVID-19 patients were observed, suggesting cellular injury, consistent with our findings (20). However, it is worth noting that there have been studies that reported contrary findings in the context of pregnant women with COVID-19. For instance, there were no significant differences in neutrophil count, basophil count, CRP, and LDH levels between pregnant women with and without COVID-19 (23-24). In another study, neutrophil levels among gravid women with COVID-19 were noted to be reduced. The plausible reasons for the conflicting results could be attributed to various factors. These include differences in the study populations, sample sizes, methodologies, and timing of blood profile assessments. Variations in the severity of COVID-19 cases among pregnant women, differences in underlying comorbidities, treatment regimens, and genetic factors could also contribute to the disparities in findings.

The study's findings also suggest that COVID-19 may affect coagulation function as indicated by the significantly higher INR and prothrombin time in pregnant women with COVID-19 infection compared to those without. These findings are consistent with previous reports that COVID-19 can cause coagulation abnormalities and increase the risk of thrombosis (18,25). Contrary to our findings, a retrospective cohort study on pregnant women with COVID-19 found no significant differences in coagulation parameters, including INR and prothrombin time, between pregnant women with and without COVID-19 (26). Similarly, a multicenter cohort study on pregnant women with COVID-19, reported no significant differences in INR and prothrombin time between the COVID-19 women and those without COVID-19, suggesting that COVID-19 did not significantly affect coagulation function in pregnant women (27). These conflicting findings may be attributed to variations in study designs, sample sizes, inclusion criteria, and the severity of COVID-19 cases among the pregnant women included in the studies. This study found that after adjusting for confounding factors (age, COVID-19 vaccination status, fetus number and parity), COVID-19 infection was associated with a significant decrease in neutrophil count (p=.022), basophil count (p=.039), prothrombin time (p=.001), and an increase in INR (p=.004), c-reactive protein (p=.011), and lactate dehydrogenase (p<.001) compared with the group of women without COVID19.

Conclusion

This study reported significant associations between neutrophil count, prothrombin time, c-reactive protein, lactate dehydrogenase levels, and COVID-19 infection status in pregnant women. These indices may aid in distinguishing healthy pregnant women from those with COVID-19 infection.

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Author contribution

Daniel Oketch conceived the research idea and drafted the manuscript, Diana Ondieki, Omondi Ogutu, and James Amenge framed the research question and provided comments. Pamela Mandela and Kennedy Oduor edited the manuscript.

Conflicts of interest

The authors have no conflict of interest

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