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Hematologic abnormalities and pregnancy outcomes in pregnant women with COVID-19

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Abstract

Background: Since declaring coronavirus disease 19 as a pandemic by the World Health Organization, a great concern was directed toward pregnant women and their fetuses. Despite the substantial impact of COVID-19 disease on pregnancy, there is a scarcity of national researches discussing this important issue.
Objectives: To study the relationship between peripheral blood abnormalities and COVID-19 in pregnant women.
Patients and methods: A case control study was conducted in the labour wards of Baghdad Teaching Hospital in the Medical complex / Baghdad /Iraq during the period from 1st of February till 31st of July, 2021. Fifty pregnant women diagnosed with COVID-19 disease were compared to 50 healthy pregnant women as controls. The pregnant women enrolled in the study were tested by COVID-19-Reverse transcription RT-PCR test upon admission to hospital. The confirmation of COVID-19 diagnosis was done according to the Iraqi guidelines approved by the Iraqi Ministry of Health.
Results: Dyspnea was a significant clinical presentation of pregnant women with COVID-19 disease. Those women had abnormal white blood cell count, lymphocytopenia, high neutrophil to lymphocyte ratio, high platelets to lymphocyte ratio and mild to moderate anemia which were significant when compared to controls. The maternal and neonatal morbidity and mortality rates were higher among pregnant women with COVID-19 disease. Abnormalities in peripheral blood system parameters like lymphocyte count, neutrophils count, platelets count and hemoglobin level were predictors of maternal morbidity and mortality.
Conclusions: The clinical presentations and hematological abnormalities are useful in the diagnosis of COVID-19 disease in pregnant women and may be used as predictors of maternal and neonatal morbidity and mortality.

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Introduction:

Nearly three years have passed since COVID-19 was first encountered in China Causing severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). SARS-CoV-2 had spread rapidly and continues to cause important morbidity, mortality, and social disruption globally. 1, 2 To lessen the transmission risks for pregnant women and health care workers, the International Federation of Gynecology and Obstetrics (FIGO) endorsed the suspension of recurring ANC visits and conducting them through virtual and smartphone connections3, 4, 5. Pregnant women have a higher risk of death due to thrombo-embolism6. Infection with COVID-19 might be an additional potential risk for thrombosis during pregnancy, as reported by some case reports7 suggesting a high death rate among pregnant women infected by COVID-19. Another study suggested the use of thromboprophylaxis during pregnancy until an d until the first ten days postpartum in confirmed COVID-19 infections. 8 In United States, January 22-October 2020, among the more than 450,000 females of reproductive age with COVID-19, the incidence of ICU admissions, invasive ventilation, extracorporeal membrane oxygenation, and death were higher in pregnant than in non-pregnant women of childbearing age9.

Patients and Methods

A case control study was conducted in the labour wards of Baghdad Teaching Hospital in the Medical complex in Baghdad/ Iraq during the period from 1st of February until 31st of July, 2021. All pregnant women aged ≥18 years in the 3rd trimester of pregnancy who had a single viable fetus with no detected abnormalities and were admitted to the maternity unit of Baghdad Teaching Hospital were the background population from which the cases were selected for the current study. The cases were 50 pregnant women infected with COVID-19 disease

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diagnosed by positive reverse transcription polymerase chain reaction (RT-PCR). The controls were 50 healthy pregnant women with negative RT-PCR. The data was collected from the records using a prepared data collection form included demographic, obstetric, clinical, and blood parameters information in addition to pregnancy and neonatal outcomes. The study was approved by the Iraqi Board of Health Specialties. Patient consent was taken verbally. The Chi-square test was used to study associations between variables, while the Fisher Exact test was used for small frequencies. The student t-test was used for differences between means. Statistical significance was determined at P value of ≤ 0.05.

Results

Pregnant women with COVID-19 in the current study had a mean age of 28.9±6.00 years with a range of (19-40 years). Three of the COVID-19 pregnant women (6%) were under the age of 20 years and another three were 40 years old, 46% were in the 20-29 years age group, and 42% in the 30-39 years group. The age group distribution among the controls was not significantly different. The gestational age distribution of the cases was significantly different from that of controls, with 26% of the cases being 28-32 weeks, 32% being 33-36 weeks and 42% being ≥37 weeks. The common clinical presentation of pregnant women with COVID-19 disease was dyspnea (54%), followed by; labour symptoms (32%), fever (4%), fatigue (2%) and headache. The mean BMI and mean parity were not significantly different between the two groups. The mean duration of the COVID-19 disease was 20.6 days, with 62% of the cases having a duration of two weeks or less. The main presentation for COVID-19 cases was dyspnea, while controls presented with labour signs and symptoms, Table 1.

Table 1: Comparison of demographic and clinical characteristics of cases and controls

Variable	Categories / Mean± SD	Study groups				P-Value
		COVID-19		Control		
		No	%	No	%	
Age (Years)	<20 years	3	6.0	0	-	0.1*^{NS}
	20-29 years	23	46.0	32	64.0	
	30-39 years	21	42.0	17	34.0	
	40 years	3	6.0	1	2.0	
Gestational age (Weeks)	28-32 weeks	13	26.0	3	6.0	0.01*^{S}
	33-36 weeks	16	32.0	16	32.0	
	≥37 weeks	21	42.0	31	62.0	
Body mass index (Kg/m^2)	Mean±SD	26.8±4.30		27.2±4.50		0.6***^{NS}
Parity	Mean±SD	2.0±2.00		2.0±1.00		1.0***^{NS}
Clinical presentation	Dyspnea	27	54.0	1	2.0	<0.001*^{S}
	Fatigue	1	2.0	0	-	
	Fever	4	6.0	3	6.0	
	Headache	2	4.0	0	-	

**Chi square test, ***Independent sample t-test, NS=Not significant, S=Significant.*

The mean WBC count of COVID-19 cases was (11.7 x10^3), with 12% having a low WBC count and 14% having a high WBC count. The mean lymphocyte count of COVID-19 cases was (3.5 x10^3), with 50% having a low count and 18% having a high count. Both of the above two counts were significantly different from the controls. The mean neutrophils count of cases was (11.2 x10^3), with 6% having a low count and 30% having a high count, which was not significantly different from the controls. This was also true for the counts of the monocytes, eosinophils and basophils, as can be seen in table 2. The mean of neutrophils to lymphocytes count ratio (NLR) of cases was (30.6) and was significantly higher than the controls, while the mean of monocytes to lymphocytes count ratio (MLR) of cases was (1.2), and not significantly higher than the controls. The mean platelet level of cases was (201.8 x10^9) with 34% having thrombocytopenia and only case having thrombocytosis. The mean platelet to lymphocyte ratio (PLR) was (506). The mean hemoglobin level of cases was (10.3 g/dl) with 34% having mild anemia, 8% having moderate anemia and one case with severe anemia. Non-significant differences were observed between cases and controls regarding the platelet count. The mean PLR was significantly higher among pregnant women with COVID-19 disease (P = 0.009) and a significant association between mild to moderate anemia with the cases (p=0.008), *Table 2*.

Table 2: Comparison of hematological variables of cases and controls

Variables	Categories / Mean±SD	Groups				P-Value
		COVID-19		Control		
		No.	%	No.	%	
WBC count	Low	6	12.0	2	4.0	0.01**^{S}
	Normal	37	74.0	47	94.0	
	High	7	14.0	1	2.0	
Lymphocyte count	Low	25	50.0	3	6.0	<0.001**^{S}

	Normal	16	32.0	40	80.0	
	High	9	18.0	7	14.0	
Neutrophils count	Low	3	6.0	7	14.0	0.1**^{NS}
	Normal	32	64.0	35	70.0	
	High	15	30.0	8	16.0	
Monocytes count	Low	1	2.0	2	4.0	0.5**^{NS}
	Normal	44	88.0	40	80.0	
	High	5	10.0	8	16.0	
Eosinophil count	Normal	40	80.0	39	78.0	0.8*^{NS}
	High	10	20.0	11	22.0	
Basophils count	Normal	44	88.0	44	88.0	1.0*^{NS}
	High	6	12.0	6	12.0	
NLR	Mean±SD	30.6±16.6		5.9±9.8		<0.001***^{S}
MLR	Mean±SD	1.2±0.9		0.9±1		0.3***^{NS}
Platelets count	Thrombocytopenia	17	34.0	10	20.0	0.2**^{NS}
	Normal	32	64.0	37	74.0	
	Thrombocytosis	1	2.0	3	6.0	
PLR	Mean±SD	506±972.7		134.5±91.7		0.009***^{S}
Hb level	Normal	28	56.0	43	86.0	0.008**^{S}
	Mild anemia	17	34.0	4	8.0	
	Moderate anemia	4	8.0	2	4.0	
	Severe anemia	1	2.0	1	2.0	

**Fishers exact test, **Chi-square test, ***Independent sample t-test, NS=Not significant, S=Significant, NLR=Neutrophils count to lymphocytes count ratio, MLR=Monocytes count to lymphocytes count ratio, PLR=Platelets to lymphocyte ratio.*

Six (12%) of the pregnant women with COVID-19 disease died, while none of the control group did, which was statistically significant. Cesarean section was the mode of delivery in 72% of the cases and of the controls. Maternal co-morbidity was reported for 34% of the cases and 22% of the controls. These included gestational hypertension (47.1% and 45.5%), gestational diabetes mellitus (23.5% and 9.1%), acute renal failure (11.8% and none), among others. No statistically significant associations were found, (*Table 3 and Figures 1*).

Table 3: Comparison of maternal outcomes for cases and controls

Variable	Category	Groups				P-Value
		COVID-19		Control		
		No.	%	No.	%	
Maternal outcome	Dead	6	12.0	0	-	0.01*^{S}
	Alive	44	88.0	50	100.0	
Delivery mode	Normal vaginal delivery	14	28.0	14	28.0	1.0**^{NS}
	Cesarean section	36	72.0	36	72.0	
Maternal co-morbidity	Yes	17	34.0	11	22.0	0.1**^{NS}
	No	33	66.0	39	78.0	
Type of maternal co-morbidity	Gestational hypertension	8	47.1	5	45.5	0.2*^{NS}
	Gestational DM	4	23.5	1	9.1	
	Acute renal failure	2	11.8	0	-	
	Asthma	1	5.9	0	-	
	Preeclampsia	1	5.9	0	-	
	Cardiac problems	1	5.9	1	9.1	
	Anemia	0	-	3	27.3	
	Hepatitis B viral infection	0	-	1	9.1	

The mean birth weight for neonates among cases was (2.4 Kg) with 38% born with low birth weight, 4% of born with very low birth weight and 2% born with extremely low birth weight. NICU admission was reported for 60% of neonates among cases compared to 38% among controls. Low APGAR score at 1 minute was found in 94% of neonates among cases and 56% among controls, while low Apgar score at 5 minutes was found in 40% of neonates compared to 14% among controls. Five (10%) of the neonates died among the cases compared to none among the controls. Statistically significant associations were found for the all variables studied, *Table 4 and Figure 2*.

Table 4: Comparison of neonatal outcomes for cases and controls

Neonatal outcomes	Categories	Groups				P-Value
		COVID-19		Controls		
		No.	%	No.	%	
Birth weight	Normal	28	56.0	44	88.0	0.005**s
	Low	19	38.0	5	10.0	
	Very low	2	4.0	1	2.0	
	Extremely low	1	2.0	0	-	
NICU admission	Yes	30	60.0	19	38.0	0.02*S
	No	20	40.0	31	62.0	
Apgar score at 1 minute	Normal	3	6.0	22	44.0	<0.001 *S
	Low	47	94.0	28	56.0	
Apgar score at 5 minutes	Normal	30	60.0	43	86.0	0.003*S
	Low	20	40.0	7	14.0	
Neonatal outcome	Dead	5	10.0	0	-	0.02*S
	Alive	45	90.0	50	100.0	

Discussion:

zDue to physiological changes, pregnant women may be at a higher risk of developing respiratory infections including COVID-19. Therefore, the early detection of COVID-19 infection during pregnancy is essential to prevent future maternal and neonatal complications 10. The findings of the current study, of the common clinical presentations of pregnant women with COVID-19 disease with dyspnea and symptoms and signs of labour with a mean symptoms duration of (20.6 days) are inconsistent with the results of Afshar et al 11 nationwide prospective cohort study in USA which reported that cough, sore throat, fatigue and fever were the common symptoms of COVID-19 disease among pregnant women with mean duration of (37 days). This inconsistency might be due to the poor response of Iraqi pregnant women to symptoms and their late attendance to the health services after the disease has progressed to dyspnea. Similarly, Aslam et al 12 in Pakistan reported different symptoms of COVID-19 disease in pregnant women as compared to normal pregnant. These hematological findings of the current study were consistent with those of Sun et al 13 and Hapshy et al 14, who reported that abnormal hematological findings are important in the diagnosis of cases. The significant abnormality of WBC count among the cases in the current study is consistent with of the findings of Sun et al 15 study in China, who documented a lower WBC count among pregnant women with COVID-19 disease. This finding might be attributed to the late presentation of cases for consultation which leads to conflicting results of WBC counts during COVID-19 infection 16. In our study, a significantly low lymphocyte count was found among the cases, in agreement with the results of Lombardi et al 17, 18 in Italy which stated that lymphocytopenia is a diagnostic marker of the early phase of COVID-19 disease in pregnant women. The high mean NLR among the cases in the current study is in agreement with the findings of Zhang et al 19. The high mean PLR among the cases in the current study is consistent with the results of Lira and Espinosa in Mexico who reported that an elevated PLR is useful in diagnosis of COVID-19 disease during pregnancy 20. The mild to moderate anemia among the cases in the current study is in agreement with the findings of Gajbhiye et al 21 who found a high prevalence of anemia among pregnant women with COVID-19 disease especially in low-income countries. The higher incidence of preterm deliveries among the cases is in agreement with the results of Al-Kuraishy et al 22 and Karasek et al 23 studies. Unfavorable neonatal outcomes were significantly higher among the cases in the current study, similar to the results of Mullins et al 24 PAN-COVID and AAP-SONPM registries in the UK and USA which reported higher neonatal morbidities in pregnant women with COVID-19 disease.

Conclusion:

The clinical presentations and hematological abnormalities are useful in the diagnosis of COVID-19 disease in pregnant women and may be used as predictors of maternal and neonatal morbidity and mortality.

Author's Contributions:

Dr. Huda Mozer AbdAlraheem: writing the project, collecting data, writing draft, and research.

Dr. Rawaa D.M. AlJanabi: supervisor, concept of the study, reviewing

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إختلالات الدم ونتائج الحمل عند الحوامل المصابات بـ فايروس كورونا المستجد

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الخلاصة
الخلفية: منذ إعلان منظمة الصحة العالمية عن مرض فيروس كورونا 19 باعتباره جائحة، أثير قلق كبير حول النساء الحوامل وأجنتهن. على الرغم من التأثير الكبير لمرض فايروس كورونا 19 على الحمل، كان هناك ندرة في الأبحاث الوطنية التي تناقش هذه القضية المهمة.
هدف الدراسة: دراسة الخصائص السريرية والمخبرية للحوامل المصابات بفايروس كورونا 19 وخاصة تشوهات الدم المحيطي.
منهجية البحث: هذه الدراسة هي دراسة حالة ضابطة أجريت في ردهة المخاض والولادة في مستشفى بغداد التعليمي في المجمع الطبي في مدينة بغداد / العراق خلال فترة ستة أشهر طوال الفترة من 1 شباط حتى 31 تموز 2021 على 50 من النساء الحوامل المصابات بمرض فايروس كورونا 19 وعينة من 50 من النساء الحوامل الأصحاء كعناصر تحكم. تم اختبار النساء الحوامل المسجلات في الدراسة عن طريق اختبار البلمرة الاستنساخي عند إدخالهن إلى المستشفى. تم تأكيد تشخيص مرض فايروس كورونا وفقًا للإرشادات العراقية التي تم إقرارها من قبل وزارة الصحة العراقية.
النتائج: كان ضيق التنفس عرضًا سريريًا مهمًا للنساء الحوامل المصابات بمرض فايروس كورونا. كانت النساء الحوامل المصابات بمرض فايروس كورونا يعانين بشكل كبير من عدد خلايا الدم البيضاء غير الطبيعي، وقلة الخلايا اللمفاوية، وارتفاع نسبة خلايا العدلات إلى الخلايا الليمفاوية، وارتفاع نسبة الصفائح الدموية إلى الخلايا الليمفاوية وفقر الدم الخفيف إلى المتوسط مقارنة بالضوابط. كانت معدلات مراضة ووفيات الأمهات والمواليد أكثر بين النساء الحوامل المصابات بمرض فايروس كورونا المستجد. تعتبر الاضطرابات في معلمات نظام الدم المحيطي مثل عدد الخلايا الليمفاوية، وعدد خلايا العدلات، وعدد الصفائح الدموية ومستوى الهيموغلوبين من العوامل المسببة لاعتلال ووفيات الامهات.
الاستنتاجات: إن الأعراض السريرية وإختلالات الدم المحيطي مفيدة في تشخيص مرض فايروس كورونا المستجد أثناء الحمل ويمكن إستخدامها للتنبؤ باحتمالات المراضة والوفيات بين الأمهات المصابات وأطفالهن حديثي الولادة.
الكلمات المفتاحية: نظام الدم المحيطي، نتائج الأم، النساء الحوامل، كورونا فايروس المستجد.