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BLOOD ELEMENTS PROFILE IN A SAMPLE OF IRAQI PREGNANT WOMEN TAKING ANTICOAGULANT TREATMENT BEFORE INFECTION WITH COVID-19 VIRUS

Abd Al- jabbar Falih Al-Rubai[1], Nibras Hatim Khamees[1], Lina A. Salih[2], Samia A. Eleiwe[1,3], Aeshah Makttoof Karnti Al-Khafaji[3], Nuha Abdulmunem Ajel Al –Sabbagh[3], Suad Makttoof Karnti Al-Khafaji[3]

[1]Department of Anatomy, Histology and Embryology, College of Medicine, Al- Mustansiriyah University, Baghdad, Iraq.
[2]Department of Biology, College of Science, University of Baghdad, Baghdad, Iraq.
[3]Department of Gynecology and Obstetrician, Al- Khadhraa Private Hospital Baghdad, Iraq.
Corresponding author Dr. Samia A Eleiwe, E-mail: samiyaa.abbas@uomustansiriyah.edu.iq

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Abstract

Background: Coronavirus disease 2019 (COVID-19) is caused by severe acute respiratory syndrome coronavirus 2, and outbreaks have occurred worldwide, and Iraq was one of the affected total countries. Laboratory test results are an important basis for clinicians to determine patient condition and formulate treatment plans worldwide.

Patients and Methods: This study comprised 150 Iraqi pregnant women at 3rd trimester, who were improved clinically to have COVID-19 infection and were already taking anticoagulant medications for treating another conditions during their pregnancies, concomitantly before and during COVID-19 course of infection. The ongoing study included 450 laboratory test results, as three test values for each pregnant patients who were diagnosed with COVID-19 and non- hospitalized but rather were treated at home since there were no indications for admission to inpatient department at specialized governmental hospitals, because in Iraq, at that time, all the severely affected patients were admitted exclusively to COVID-19 specialized governmental hospitals, and not to any other hospitals whether it was governmental or private hospitals, never the less, the affected patients who were having mild or moderate infections with COVID-19, they were possibly treated at home, private clinic, or even as outer patients at governmental or private hospitals. These cases were regarded as mild or moderate cases or even sub clinical cases that's to say; they were diagnosed by laboratory tests only.

This study was done between 1st of January 2020 to 1st of January 2021, at Department of Gynecology and Obstetrics, Al- Khadraa' Private hospital, Baghdad, Iraq.

The 1st, 2nd and last test results were compared among the three studied groups included in this ongoing study. Group I involved fifty women; those who were pregnant and not affected by COVID-19 infection by clinical features nor by laboratory findings during whole of their pregnancy. Group II was signified fifty women; these were the affected pregnant women who were already taking anticoagulant medications for treating another conditions during their pregnancies, concomitantly before and during COVID-19 course of infection, whereas group III referred to fifty women; comprising the affected pregnant women who were not taking any anticoagulant medications during their pregnancies, before their COVID-19 course of infection. Then statistic comparisons were estimated and the laboratory test's data showed significant differences among these three considered groups. The obtained data were evaluated using a chi-square test and at the level of $P < 0.05$ was regarded the significance using version 23 of SPSS software, to estimate the differences among the three pregnant groups including the control group.

Results: Among all of so many laboratory test data, for any patient with COVID-19 infection, specific records were chosen in this work. These were: White blood cell count, neutrophil count/percentage, platelet count, lymphocyte count, eosinophil count and basophil count as well as hemoglobin level.

Neutrophil-lymphocyte ratio as well as platelet-lymphocyte ratio have been estimated also.

Conclusions: By the results of the laboratory data, it was clear that pathological effect of COVID-19 infection on blood tissue was ameliorated by taking anticoagulant treatment prior to getting infected with COVID-19 viral infection.

This study provided important insight into the association between the risk of disease severity and the uses of anticoagulant medications during pregnancy, concomitantly before and during COVID-19 course of infection, hence, these consequences could be used to simplify patient management.

Keywords: *Pregnancy; COVID-19; platelet; lymphocyte; neutrophils; Hemoglobin; eosinophil and basophil.*

INTRODUCTION

Iraq was one of the moderately "COVID-19" viral infected countries on 2019, 2020 and 2021 years having many disaster stories were existing on the repetitive attacks of COVID-19 viral infection worldwide [1,2]. As any other person so m any pregnant women had infected with COVID-19 viral infection which had been proven to affect variable body tissues and organs among which was the blood tissue cells and other elements [3]. It is well known that blood picture was one of the most important diagnostic sign of infection with COVID-19 virus, plus, it was very important test having prognostic rate [3-5[.

COVID-19 was originally reported in Wuhan, China in December 2019. The agent was diagnosed to be a unique b-coronavirus which is formerly termed severe acute respiratory syndrome coronavirus 2 "SARS-CoV-2"[6]. Patient could have a wide range of this disease from a so mild illness, to severe pneumonia and acute respiratory distress syndrome then sepsis plus multiple body organs failure ended with death [7,8]. A diverse approaches were tried to diagnose the infected patients. At that time, the best diagnosis was the detection of SARS-CoV-2 nucleic acid by real-time polymerase chain reaction "RT-PCR" [9].

Haematological tests could play an imperative role that give prognostic markers in the management of infected persons. Complete blood picture "CBP" abnormalities include a decrease in white blood cell count as well as lymphocyte count, neutrophilia, thrombocytopenia, increased abnormal procalcitonin "PCT", C-reactive protein "CRP"and erythrocyte sedimentation rate "ESR" in the majority of patients. These tests had the most important roles in diagnosis in addition to the stages and severity of the infectious status [10, 11].

Other inflammatory markers were affected in COVID-19 viral infection like C-reactive protein, Erythrocyte Sedimentation Rate (ESR), D-Dimer, Ferritin, Procalcitonin and Lactate dehydrogenase, however, these markers are not useful in predicting the severity of the infection [12].

Anti-coagulant during pregnancy: Two types of anti-coagulant therapy are used during pregnancy: low molecular weight Heparin and Aspirin. The use of anti-coagulant during pregnancy is necessary in many pathological conditions which may threatened the pregnancy well fare such as systemic lupus erythematosus, antiphospholipid syndrome, anticardiolipin syndrome and any pregnant at high risk of getting deep vein thrombosis such as if she had a history of venous thromboembolism, with atrial fibrillation, prosthetic heart valves, left ventricular dysfunction, or even with a history of unexplained fetal loss, in addition to so many other indicating conditions need treatment with anticoagulants, and such treatment of pregnant ladies with anti-coagulants usually needs special care by cardiologist and obstetrician [13].

The aim of the current study was to provide important insight into the association between the risk of COVID 19 severity and the uses of anticoagulant medications during pregnancy, in order to ease patient management.

PATIENTS AND METHODS:

This study comprised 150 Iraqi pregnant women at 3rd trimester, who were improved clinically to have COVID-19 infection and were already taking anticoagulant medications for treating another conditions during their pregnancies, concomitantly before and during COVID-19 course of infection. The ongoing study included 450 laboratory test results, as three test values for each pregnant patients who were diagnosed with COVID-19 and non- hospitalized but rather were treated at home since there were no indications for admission to inpatient department at specialized governmental hospitals, because in Iraq, at that time, all the severely affected patients were admitted exclusively to COVID-19 specialized governmental hospitals, and not to any other hospitals whether it was governmental or private hospitals, never the less, the affected patients who were having mild or moderate infections with COVID-19, they were possibly treated at home, private clinic, or even as outer patients at governmental or private hospitals. These cases were regarded as mild or moderate cases or even sub clinical cases that's to say; they were diagnosed by laboratory tests only.

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Results:

The average count of WBC was noticed to have a slight decreased at group II, whilst it had a significant increase at group III, as shown in table (1).

The average count of Neutrophil had a significant increase in group II (neutrophilia), with more increase at group III, as shown in table (1).

The average count of Lymphocytes count had significant decrease in group II (lymphopenia), with more decrease at group III, as shown in table (1).

The average count of Eosinophil count had decreased in group II, with more decrease at group III, as shown in table (1).

The average count of Basophil count had decreased in group II, with more decrease at group III, as shown in table (1).

The average count of Platelets count had a decrease in group II (thrombocytopenia), with more decrease at group III, as shown in table1.

Hemoglobin in g/dl was noticed to have a little decrease at group II, whilst it had a more decrease at group III, as shown in table(1).

Neutrophil-lymphocyte ratio had increased in group II, and more increased at group III, as shown in table (2).

Platelet-lymphocyte ratio had increased in group II, and more increased at group III, as shown in table (2).

Table 1: Selected blood parameters for the three studied pregnant women groups

Parameter	**Control pregnant not infected by COVID-19 infection ±SD**	**pregnant women taking anticoagulant before COVID-19 infection ±SD**	**pregnant women not taking anticoagulant before COVID-19 infection ±SD**	**L.S.D. (P-value)**
WBC (10^9/L)	6.85±2.01 b	6.71±2.2 b	10.84±3.1 a	2.372 ** (0.0052)
Neutrophil (%)	55.26 ±9.6 b	77.3 ±21.1 a	79.49 ±9.7 a	16.419 ** (0.0001)
Lymphocyte (%)	33.41 ±8.9 a	13.6 ±1.8 b	10.09 ±2.3 b	7.026 ** (0.0001)

Eosinophil (%)	2.10 ±0.7 a	1.91 ±0.6 a	1.02 ±0.3 b	0.877 * (0.0392)
Basophil (%)	0.50 ±0.2	0.48 ±0.10	0.41 ±0.09	0.174 NS (0.895)
Platelets (10^9/L)	274.91 ±97.78	256.21± 96.6	224.82 ±91.81	76.189 NS (0.237)
Hemoglobin (g/dl0	11.10 ±1.31 a	10.62± 2.11 ab	9.76 ±1.41 b	1.126 * (0.049)

a, b, c: Means having with the different letters in same row differed significantly.
* (P≤0.05), ** (P≤0.01).

Table2: Neutrophil-lymphocyte and platelet-lymphocyte ratio in the three studied pregnant women groups.

Parameters/ Ratio	**Control pregnant not infected by COVID-19 infection**	**Pregnant women taking anticoagulant before COVID-19 infection**	**Pregnant women not taking anticoagulant before COVID-19 infection**	**L.S.D. (P-value)**
Neutrophils /Lymphocytes	1.66 ±0.33 c	5.68 ±0.61 b	7.87 ±0.64 a	2.185 ** (0.0001)
Platelets /Lymphocytes	8.23 ±0.75 b	18.84 ±1.58 a	22.28 ±2.07 a	4.076 ** (0.0001)

a, b, c: Means having with the different letters in same row differed significantly.
** (P≤0.01).

DISCUSSION:

In this study all pregnant women were chosen at the 3rd trimester, in order to avoid the normal alterations in WBC level throughout the different stages of pregnancy [14, 15].

The average counting of WBC was noticed to be decreased at group II, whilst it was increased at group III, which could be due to the medical fact that WBC count is different according to severity of the illness as well as presence of complications, and many previous cases showed leucocytosis that associated with severe cases [16, 17]. Neutrophilia had been considered as an indicator for severe illness and could be associated with poor outcome [16-18].

Reduction in lymphocyte number (lymphopenia), which has been found in group II and more in group III is an indication of severely infected patients, and it seems that the significant reduction in lymphocytes is correlated with poor outcome, plus, it is well known to be associated with impaired immunological reaction against viral infection [19, 20, 21].

Eosinophil count had decreased in group II, with more decrease at group III.

Physiologically, tissue-resident eosinophils are mainly represented in the gastrointestinal tract and in the lung, where they have regulatory functions in protective immunity, organ growth and metabolism [22].

The pathophysiology for eosinopenia in COVID-19 is a matter of controversial, but is likely multifactorial and related to the migration of eosinophils to the inflammatory site, inhibition of eosinophil mobilization from the bone marrow, blockade of eosinophilopoiesis, reduced expression of chemokine receptors/adhesion molecules, and/or direct eosinophil apoptosis during the acute phase of inflammation [22 & 23].

The Basophil count decrease in group II, with more decrease at group III; may be explained by the following:

In previous study, basophils leave the circulation and migrate to inflammatory sites during allergic inflammation and infection, enhancing immunological memory responses by binding antigens on their surface [24].

Rodriguez *et al.* demonstrated that basophils are depleted during acute and severe COVID-19, thus suggesting that the degree of basophil depletion may influence the efficacy of IgG responses to SARS-CoV-2 [25].

Platelets count had significant decrease in group II (thrombocytopenia), with more significant decrease at group III, which might be discussed as the following:

Platelet number reflected a serious parameter in weighing the severity of COVID-19 illness, just like multi-organ dysfunction syndrome. Thrombocytopenia in COVID-19 viral infection designates consumption coagulopathy, plus, it correlates with the disease severity. Besides, a severe thrombocytopenia is associated with high mortality rate [26].

Neutrophil-lymphocyte ratio had increase in group II, with more increase at group III, which might be discussed as the following:

The results of this study showed that the neutrophil count in group II of pregnant women was higher than that in those within group III, and it is well known that as the disease progressed, the neutrophil count increased, especially among severe patients [27]. Nevertheless, neutrophilia could be a predictor of poor outcome of illness or a high viral load exposure, so, may indicate that the patient will require more supportive treatment [28-30]. Neutrophilia may be related to cytokine storms induced by virus invasion [31].

Platelets-lymphocyte ratio had increase in group II, with more increase at group III, which might be discussed as the following:

Both thrombocytopenia and lymphopenia were regarded as the most prominent laboratory finding in COVID 19 patients, being having a positive relation with the severity of clinical course [32]. Also, it was reported that thrombocytopenia was closely related to prognosis of the illness and a decrease in the platelet count, especially a gradual decrease, was a marker of aggravation of illness state and suggested that appropriate emergency measures should be taken immediately to prevent the disease from getting worse [33].

Hemoglobin level in g/dl was noticed to have a little decrease at group II, whilst it had more decrease at group III, which could be due to the next details:

The hemoglobin level is being to be changed consistent with the severity of COVID 19 infection and occurrence of any complication that is because COVID-19 may induces anemic hypoxia that leads to low hemoglobin level, which is turning into more inferior in case of increasing sharpness of the infection and existence of any complication (34 &35), hence, in conclusion: those findings of the current work might give an idea; that the pregnant women at group II who were already taking anticoagulant medications for treating another conditions during their pregnancies, concomitantly before and during COVID-19 course of infection, had a reduced illness than those at group III of the affected pregnant women who were not taking any anticoagulant medications during their pregnancies, before their COVID-19 course of infection..

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