



Hematological Changes, Serum Interferon Gamma and Interleukin-4 Alterations in Normal Pregnancy and Preeclampsia

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Abstract

Background: Various hematological and immunological changes can occur in pregnancy which could be beneficial for the growth of the fetus and the maintenance of the pregnancy although some of these changes could be hazardous to the fetus and can cause complications during pregnancy. Thus, this study was conducted to investigate the hematological and immunological changes in normal pregnancy and preeclampsia (PE).

Materials and Methods: To this end, hematological and immunological changes were evaluated in 62 normal pregnant women and 56 pregnant women with PE. Moreover, 58 healthy non-pregnant women were studied as the control group. The study was done between December 1, 2018 to May 1, 2019 in Chwarbakh Private Clinic and Shorsh Teaching Hospital. The venous peripheral blood from the antecubital vein was used in this study.

Results: The results revealed a significant increase in the number of granulocytes, monocytes, and mean platelet (PLT) volume in both normal pregnant women and PE patients in comparison to normal (non-pregnant) controls ($P < 0.01$). In addition, there was a significant correlation between a reduction in their hematocrit (HCT), PLT, and lymphocytes ($P < 0.01$). With regard to immunological changes, a significant increase was also observed in the serum interleukin-4 (IL-4) levels in both normal pregnancy and preeclamptic patients when compared to non-pregnant controls ($P < 0.01$), but gamma interferon was not significantly different. Conversely, there were no significant associations between the serum level of antiphospholipid antibodies and anticardiolipin antibodies in the study groups except for antiphospholipid antibodies which were significantly lower in the third trimester of pregnancy in the preeclamptic patients ($P < 0.05$).

Conclusion: In general, significant changes in hematological and immunological parameters were observed in both normal pregnant and PE patients although further studies are required to include more immunological parameters.

Keywords: Hematological changes, Interleukin-4, Pregnancy, Preeclampsia

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Introduction

Pregnancy, also known as gestation or gravidity, is a natural process following copulation in women and associated with various somatic, metabolic, and physiological changes. It starts with the formation of the embryo and subsequent implantation of the embryo in the uterus which develops into a fetus (1) and the full-term pregnancy takes about 38 to 42 weeks. Maternal changes occurring during pregnancy aim to accommodate and provide both the needs of the mother and fetus for a successful pregnancy (2, 3) and include hematological and immunological changes. The

major hematological changes encompass alterations in erythrogram, leukogram, and thrombogram (4). In addition, immunological changes accompanied a normal pregnancy include variations in cytokine production, different cells, and antibody production (5).

Regarding the hematological changes in a normal pregnancy, many changes (e.g., anemia, leukocytosis, monocytosis, and thrombocytopenia) are reported for providing optimal hematopoiesis and ensuring adequate blood supply to the growing fetus and the enlarged uterus and its contents, along with safeguarding against bleeding at delivery (4). As regards immunological changes, some

variations are found in cytokine release by different cells of a pregnant woman, including an increase in interleukin (IL)-4, IL-5, IL-9, IL-10, and IL-13 (6). According to Szarka et al (7) and Sykes et al (8) studies, these cytokines are produced by type 2 helper cells, which provide optimal help for humoral immune responses and are regarded as anti-inflammatory cytokines. The increase in Th2 cytokines is probably caused by a reduction in type 1 (Th1) cytokines which are considered as proinflammatory cytokines such as IL-1, IL-6, gamma interferon, and tumor necrosis factor (TNF). Abnormal hematological and immunological responses during pregnancy may cause several complications observed in pregnancy such as preeclampsia (PE) which is a multisystem disorder associated with an increase in the maternal blood pressure and changes in the kidneys causing proteinuria and sometimes glycosuria (9).

PE affects about 5% of all pregnancies and is a widespread complication of pregnancy (9) that has serious consequences dangerous to both the mother and fetus. Further, it is characterized by the development of hypertension and proteinuria and frequently causes pre-term delivery and growth retardation (10). Furthermore, pregnancy-induced hypertension including PE and eclampsia is presented with high blood pressure (> 140/90 mm Hg) with persistent proteinuria over 300 mg proteins/24 hours. Moreover, PE first appears after 20 weeks of gestation and edema, although it is not a diagnostic criterion, and is frequently present (9). In PE, the hematological changes can be categorized into 3 major groups as follows.

The first changes related to the platelet (PLT) number and function, PLT dysfunction, and thrombocytopenia are observed in about 50% of patients with PE and the severity of these anomalies is proportional to the severity of clinical manifestation and may even precede the clinical manifestation. Additionally, thrombocytopenia may be so severe that can endanger the life of the mother and the fetus. Low PLT count may also be associated with higher mean PLT volume (11, 12).

The second hematological changes are the ones in the erythrogram and appear as an alteration in the Hgb content. In addition, the increased hematocrit (HCT) can occur in patients with PE due to the increased permeability of the endothelium covering the blood vessels on rare occasion anemia and is related to hemodilution, iron deficiency, or bleeding.

Regarding immunological changes in PE, both natural (innate) and acquired (adaptive) types of the immune response are involved in the pathogenesis of the disease, and the exaggerated inflammatory response is observed in patients with PE. This is manifested by the excess production of proinflammatory cytokines secreted by type 1 (Th1) lymphocytes such as interferon-gamma (IFN γ), IL-1, TNF, and IL-2 (13) in addition to the exaggerated activation of neutrophils and monocytes with their

increased numbers in patients with PE. The observed hematological and immunological changes in patients with PE (14, 15) can have both genetic and environmental risk factors (16).

The exaggerated proinflammatory state in patients with PE is likely due to the high Th1/Th2 ratio and a reduction in Th2 cells (17, 18). The findings of a study revealed increased production of IL-2, IFN-g, and TNF a by peripheral blood mononuclear cells in PE and, interestingly, positive correlations between the mean blood pressure and concentrations of Th1 cytokines (18). With regard to changes in the antibody profile, it was shown that autoantibodies can involve in some pregnancy-associated complications such as PE, eclampsia, and abortion. An example of these antibodies includes antiphospholipid antibody which involves in a disease condition known as antiphospholipid antibody syndrome which is characterized by recurrent thrombosis and pregnancy morbidity. Further, it is serologically characterized by the presence of antiphospholipid antibodies in the serum which includes a group of antibodies such as anticardiolipin antibodies, anti-B2-glycoproteins, and lupus anticoagulant (19). Antiphospholipid antibodies react with a large number of phospholipids and form immune complexes with these phospholipids. Furthermore, antiphospholipid syndrome involves in many other disease conditions such as systemic lupus erythematosus, acquired thrombophilia, deep vein thrombosis, pulmonary embolism, strokes below the age of 50, myocardial infarction, recurrent abortion, PE, and eclampsia (20, 21). The severity of these diseases is related to the titers of those autoantibodies in the peripheral circulation (22). Considering the above-mentioned explanations, the present study investigated hematological and immunological changes in normal pregnancy and PE.

Material and Methods

The samples were collected at the laboratory of a maternity hospital in Sulaimani, Kurdistan, Iraq during the 1st of December 2018 to the 1st of May 2019. Moreover, the investigation was performed in the Chwarbakh Private Health Laboratory and Shorsh Teaching Hospital, followed by documenting patients' information.

Individuals of the Study

This study involved 56 pregnant women with PE, 62 normal pregnant women, and 58 healthy non-pregnant controls who were all in the age range of 20-40 years.

Specimens Used in the Study

Six milliliters of venous blood samples were drawn from the antecubital vein of each participant by a disposable syringe using the venipuncture technique. Additionally, 2 mL of the blood was collected in an ethylenediaminetetraacetic acid tube for the complete blood count (CBC). The other

four milliliters of blood were collected in a clot activator gel tube, allowed to clot at room temperature, and then centrifuged at 3500 rounds per minute for 10 minutes, followed by separating the sera. Finally, the obtained sera were dispensed into a plain tube and kept in a freezer (70°C) until tested for immunological tests.

Hematological Analysis

Sysmex KX-21N, an automated 3-part differential hematology analyzer (ColterSwelab Alfa Plus Systems SE-163 53 Spånga, Sweden) was used for the hematological analysis of the CBC. This system measures CBC, white blood cell (WBC) count, red blood cell (RBC) count, Hgb count, pack cell volume (PCV), PLT count, lymphocytes, neutrophils, and RBC indices, namely, mean cell volume (MCV), mean cell Hgb (MCH), and mean cell Hgb concentration (MCHC) count. Eventually, the standardization, calibration of the instrument, and processing of the samples were done according to the manufacturer's instructions.

Immunological Analysis

In this regard, the enzyme-linked immunosorbent assay (ELISA) was performed using the device (Chromate principle ELISA model 4300, USA). In addition, the ELISA kit for the measurement of cytokine and antibody levels was supplied by Elabscience, China. The test was performed according to the manufacturer's instructions, which was a double sandwich ELISA technique with a sensitivity of <9.375 pg/mL.

Statistical Analysis

Data were collected and coded and then reviewed and analyzed using the Statistical Package for Social sciences (SPSS, version 22). Descriptive statistics such as frequency and percentage were calculated and the student *t* test measures of central tendency and dispersion around

the mean were used to describe continuous variables. The $P < 0.05$ was considered significant, which was obtained for the continuous variable using the independent samples test for mean comparison.

Results

The laboratory findings of the participants showed the leukogram of normal control, normal pregnancy, and PE patients. The WBC significantly increased in normal pregnancy ($P < 0.008$) and PE ($P < 0.001$). Monocytes also significantly increased in normal pregnancy ($P < 0.002$) and PE ($P < 0.003$). However, lymphocyte significantly decreased in PE ($P < 0.024$), the details of which are provided in Table 1.

The results indicated that granulocyte significantly increased in normal pregnancy ($P < 0.001$) and PE ($P < 0.001$).

On the other hand, erythrogram in all three groups showed that the RBC number significantly decreased in normal pregnancy ($P < 0.001$). Similarly, Hgb concentration ($P < 0.017$), as well as Hgb ($P < 0.001$) and HCT ($P < 0.04$) decreased significantly in normal pregnancy. However, MCV, $P < 0.003$) and MCH demonstrated a significant increase ($P < 0.012$). In Thrombogram in normal control, normal pregnancy, and PE. Based on the results, there was a significant reduction in the PLT count in normal pregnancy ($P < 0.001$) and PE ($P < 0.001$) while mean PLT volume increased significantly in normal pregnancy ($P < 0.009$) and PE ($P < 0.002$), related data are presented in Table 2.

Leukogram showed differences among different stages of pregnancy (i.e., 1st, 2nd, and 3rd trimester) in normal pregnancy. Based on the data in Table 3, WBC represented a significant increase in the 1st and 3rd trimester in normal pregnant ($P < 0.02$).

In addition, erythrogram differences among different stages of pregnancy indicated a significant decrease in

Table 1. Leukogram in Normal Control, Normal Pregnancy, and Preeclampsia Patient

	WBC	MID	LYM	GRAN
Normal control	7.819±3.1248	0.460±0.1580	2.351±1.6278	4.946±2.0380
Normal pregnancy	9.106±1.9722**	0.573±0.2334**	1.969±0.4696	6.442±1.9575***
Preeclampsia	9.991±3.6160***	0.610±0.3401**	1.828±0.6017*	7.553±3.1958***

Note. WBC: white blood cell; MID: LYM: Lymphocyte; GRAN: Granulocyte; *** $P < 0.001$, ** $P < 0.01$, and * $P < 0.05$ represent very highly, highly, and significant differences, respectively.

Table 2. Erythrogram in Normal Control, Normal Pregnancy, and Preeclampsia

	RBC Mean ± SD	Hgb (g/dL) Mean ± SD	HCT Mean ± SD	MCV (fl) Mean ± SD	MCH (pg) Mean ± SD	MCHC (g/dL) Mean ± SD
Normal control	4.70±0.375	12.81±1.49	38.50±3.99	82.03±7.15	27.35±2.85	33.25±1.05
Normal pregnant	***4.32±0.50	*12.20±1.31	*36.94±4.20	**85.70±5.90	*28.41±2.65	33.92±6.60
Preeclampsia	4.54±1.62	12.73±5.08	***34.04±7.86	*81.92±9.59	28.94±8.65	34.42±6.44

Note. RBC: Red blood cell; SD: Standard deviation; Hgb: Hemoglobin; HCT: Hematocrit; MCV: Mean cell volume; MCH: Mean cell hemoglobin; MCHC: Mean cell hemoglobin concentration; *** $P < 0.001$, ** $P < 0.01$, and * $P < 0.05$ very highly significant different. highly significantly different. significant different.

Table 3. Leukogram in the 1st, 2nd, and 3rd Trimester in a Normal Pregnancy

	Group	Mean ± SD
WBC	First trimester	7.05±1.02*
	Second trimester	8.81±1.78
	Third trimester	9.40±2.03*
GRAN	First trimester	5.100±1.3880
	Second trimester	6.205±1.4842
	Third trimester	6.814±1.9780
MID	First trimester	0.525±0.1500
	Second trimester	0.621±0.2879
	Third trimester	0.553±0.2171
LYM	First trimester	1.675±0.2986
	Second trimester	1.984±0.4233
	Third trimester	2.003±0.5185

Note. WBC: White blood cell; GRAN: Granulocyte; MID : Monocytes ; LYM: Lymphocyte; * $P < 0.05$ indicates a significant difference.

MCH and MCV in the 2nd and 3rd trimesters in normal pregnancy ($P < 0.005$). Table 4 presents the related data in this regard.

The thrombogram in the 1st, 2nd, and 3rd trimester in normal pregnancy demonstrated no significant difference between the parameters while in PE, PLT increased significantly in the 1st and 3rd trimester ($P < 0.045$).

Statistical analysis (Table 5) showed leukogram in different trimesters in patients with PE, indicating a significant increase in granulocyte count in the 1st, 2nd ($P < 0.007$), and 3rd trimesters ($P < 0.045$) of PE. Monocytes also increased significantly in the 1st and 2nd ($P < 0.028$) and 3rd trimesters ($P < 0.001$). Finally, the total WBC count significantly increased in all stages of pregnancy as well ($P < 0.05$).

Based on data (Table 6) respecting erythrogram changes in different trimesters in preeclamptic patients, a significant decrease was found in the MCHC in the 1st and 3rd stages of pregnancy ($P < 0.003$).

Data analysis (Table 7) represents the amount of APAAb, ACAIgM, ACAIgG, INF-gamma, and IL-4 in the 1st, 2nd, and 3rd trimester in normal pregnancy. The results indicated no significant difference between the parameters and IL-4 significantly increased in normal pregnancy ($P < 0.001$) and PE ($P < 0.004$).

Regarding immunological changes in different stages of pregnancy, there were no significant changes except for

antiphospholipid antibody (APA Ab), in the 2nd and 3rd trimesters of pregnancy ($P < 0.035$).

Discussion

In general, the results of this study showed that there was a considerable increase in the metabolic requirements, as well as modifications of the hormonal balance during pregnancy. These changes included various hematological parameters. The present study measured changes occurring in the hematological parameters (i.e., erythrogram, leukogram, and thrombogram) and some immunological changes encompassing IL-4, interferon (INF)-gamma, APA Ab, anticardiolipin antibodies (ACA) IgM, and ACA IgG, in healthy pregnant woman, patients with PE, and in non-pregnant normal controls in Sulaimani, Kurdistan, Iraq. A follow-up study of the above-mentioned hematological and immunological parameters occurring in different trimesters of pregnancy was performed as well. Based on the findings of a study on breast cancer patients and normal individuals, no change was observed in the IFN- γ level despite the decrease in the percentage of CD4+ lymphocytes in patients (due to the activation of the compensative hemostatic system and an increase in IL-12). It seems that an increase in serum IL-12 levels correlates with disease progression. However, the serum IFN- γ level has no effect on disease progression, and as a whole, no prominent failure was recorded in the cellular immune response of breast cancer patients as compared to normal individuals (23).

Based on the results of the current research, changes in the leukocyte were most prominent in the 3rd trimester of pregnancy, which is in line with the findings of other researchers who demonstrated a progressive increase in leukocytes with the gestational age (24-27). Neutrophil was the main type of leukocyte that increased in this study (Table 2), which is similar to the findings of some other studies (24-27). Regarding the lymphocyte, the mean value of the lymphocyte numbers did not significantly change for pregnant women compared with non-pregnant women (Table 2). This contradicts the findings of Bakrim et al (24) and Örgül et al (28) that revealed a decrease in the number of lymphocytes. They referred this decrease to hormonal changes accompanying pregnancy which could have a negative impact on the lymphocyte. In the present study, a significant increase was found in the monocyte count in pregnant women compared with non-

Table 4. Erythrogram in the 1st, 2nd, and 3rd Trimester in a Normal Pregnancy

	MCHC Mean ± SD	MCH Mean ± SD	MCV Mean ± SD	HCT Mean ± SD	Hgb Mean ± SD	RBC Mean ± SD
1 st trimester	33.25±1.46	27.55±3.41	82.80±8.18	36.42±4.75	12.10±1.64	4.40±0.26
2 nd trimester	33.24±1.02	**29.52±1.02	**88.83±3.71	36.96±2.80	12.25±0.75	4.16±0.36
3 rd trimester	34.34±8.40	**27.92±3.02	**84.39±6.09	37.11±4.78	12.22±1.51	4.40±0.56

Note. MCHC: Mean cell hemoglobin concentration; MCH: Mean cell hemoglobin; SD: Standard deviation; MCV: Mean cell volume; HCT: Hematocrit; Hgb: Hemoglobin; RBC: Red blood cell; ** $P < 0.01$ highly significantly different.

Table 5. Leukogram in 1st, 2nd, and 3rd Trimester in Preeclampsia

	Group	Mean ± SD
WBC	First trimester	4.15±3.75**
	Second trimester	8.69±1.83**
	Third trimester	10.82±3.90**
GRAN	First trimester	3.000±2.8284**
	Second trimester	6.529±1.4378**
	Third trimester	8.233±3.4934*
MID	First trimester	0.250±0.2121*
	Second trimester	0.465±0.1115***
	Third trimester	0.692±0.3793***
LYM	First trimester	0.900±0.7071
	Second trimester	1.659±0.5646
	Third trimester	1.949±0.5679

Note. SD: standard deviation; WBC: white blood cell; GRAN: Granulocyte; MID: Monocytes; LYM: Lymphocyte; ****P*<0.001, ***P*<0.01, and **P*<0.05 denote a very high, high, and significant difference, respectively.

pregnant women (Table 2), which was consistent with the results of Bakrim et al (24) and Okpokam et al (29). This increase in the number of monocytes during pregnancy could be advantageous because some cytokines released by monocytes may help the growth of the fetus and continuation of pregnancy, including IL-4. Furthermore, monocytes can have a suppressor function and suppress unwanted immunological reactions that risk pregnancy (30).

As regards erythrogram changes, the findings (Table 3) demonstrated that the concentrations of Hgb were significantly lower for pregnant women (12.20 ± 1.31 g/dL) in comparison to non-pregnant women (12.81 ± 1.45 g/dL). This is in agreement with the results of the study of Bakrim et al (24), indicating that the Hgb concentration was significantly lower for pregnant women compared to the control group (non-pregnant women). The evaluation of hematological changes

during different stages of pregnancy demonstrated that the changes in the 1st and 2nd trimester in normal pregnancy were not significantly different (Table 6). The changes in hematological parameters were similar and not significant for the 1st and 3rd trimester of pregnancy (Table 6). However, WBC counts increased significantly between the 2nd and 3rd trimesters. On the other hand, MCHC and MCV decreased significantly, which is in line with the results of Bakrim et al (24). Contrarily, MCH and MCV significantly increased (*P*<0.03 & *P*<0.003) in our study (Table 3) when comparing pregnant women with controls, which is similar to the findings of the above-mentioned study. Likewise, Geetanjali et al (23) revealed a significant decrease in the Hgb concentration in normal pregnancy in comparison to controls, which is consistent with the results of our study. However, they found significant changes in different phases of pregnancy, which contradicts our results since the present study failed to show the difference between 1st and 2nd, 1st and 3rd, as well as 2nd and 3rd. These discrepancies could be due to differences in the operating machines reading the results or the laboratory technical procedures that were used for measuring those parameters. The reduction in Hgb concentration for pregnant women can be related to the hemodilution resulted from a quicker increase in the plasma volume compared to the erythrocyte mass (31). On the other hand, it could be due to an increase in the demand for essential vitamins (e.g., folic acid, vitamin B12, and vitamin C) regarding producing RBCs in addition to an increase in the iron demand for fetal hematopoiesis (32). These physiological changes occur in all pregnant women to compensate for the needs associated with fetal growth and the mother’s requirement (31).

Regarding the changes in the mean values of the HCT or PCV, a significant decrease was found in pregnant women compared to non-pregnant women (Table 3), which is similar to those of Geetanjali et al (23). Similarly, Kumar Dhariwal et al (33) noticed a decrease in the rate

Table 6. Erythrogram in the 1st, 2nd, and 3rd Trimesters in Preeclampsia

	MCHC Mean ±SD	MCH Mean ±SD	MCV Mean ±SD	HCT Mean ±SD	Hgb Mean ±SD	RBC Mean ±SD
1 st trimester	35.60±1.98**	27.85±2.19	78.40±10.46	22.60±20.79	7.80±6.93	2.73±2.28
2 nd trimester	36.82±11.86	28.12±3.22	82.64±8.00	32.76±8.83	13.29±6.15	4.72±1.94
3 rd trimester	33.37±0.93**	29.43±10.60	81.63±10.59	35.97±4.09	12.07±1.21	4.37±0.435

Note. MCHC: Mean cell hemoglobin concentration; MCH: Mean cell hemoglobin; SD: Standard deviation; MCV: Mean cell volume; HCT: Hematocrit; Hgb: Hemoglobin; RBC: Red blood cell; ***P*<0.01 indicates a highly significant difference.

Table 7. APA Ab, ACA IgM, ACA IgG, INF-gamma, and IL-4 in the 1st, 2nd, and 3rd Trimester in a Normal Pregnancy

	APAb Mean±SD	ACA IgM	ACA IgG	INF-gamma	IL4
1 st trimester	20.00±14.39	49.25±94.61	42.55±85.10	0.00±0.00	49.55±76.46
2 nd trimester	42.38±39.98	21.32±64.04	4.72±17.28	1.83±7.13	14.88±22.10
3 rd trimester	29.99±25.62	1.05±2.81	1.01±3.49	0.13±0.50	12.95±5.53

Note. APA: Antiphospholipid antibody; ACA: Anticardiolipin antibodies; INF: Interferon; IL: Interleukin; SD: Standard deviation.

of RBC and the HCT with gestational age. Contrarily, no significant difference was observed between the trimesters of pregnancy in the current study, which disagrees with the results of Mohamed et al (32). They showed a progressive decrease in RBC numbers in relation to the trimesters of pregnancy. In addition, Geetanjali et al (23) reported a decrease in HCT in succeeding trimesters. The reduction in the rate of the HCT accompanied by a decrease in the number of the RBC during pregnancy could be associated with an increase in the plasma volume during pregnancy causing a hemodilution or due to hormonal changes which may result in an increase in fluid retention and iron deficiency (33-35).

In our study, the mean value of the PLT number was significantly lower in pregnant women compared to non-pregnant women (Table 4), which corroborates with the results of Bakrim et al (24) and Ifeanyi et al (36). This reduction in the number of PLT could prevent spontaneous intravascular thrombosis in the placenta which may endanger the continuation of the pregnancy although profound thrombocytopenia increases the risk of bleeding and abortion (37).

According to our findings, a significant increase was found in the serum IL-4 level in normal pregnant woman while no significant changes occurred in the level of gamma IFN which is regarded as an inflammatory marker. Normal pregnancy is characterized by a shift toward Th2-type immunity in which IL-4 plays an important role including the inhibition of cytotoxic Th1 immune responses such as gamma IFN production which could be harmful to the fetus (7, 38). Based on the results of different studies, several genetic, behavioral, environmental, and technical factors are probably involved in the variations (18, 25, 39).

The findings of our study on patients with PE revealed changes in hematological and immunological parameters in comparison to normal controls. In PE condition, there was a significant increase in the number of WBC and mean PLT volume whereas a significant decrease in the HCT and PLT number. The results of the study by Ramos et al (40) regarding leukocytosis and thrombocytopenia were similar to those of our study. They found a significant increase in mean HCT values in preeclamptic compared to normal pregnant controls (41). In the current study, a significant decrease was observed when comparing the changes in HCT and MCV in patients with PE and normal pregnant woman. The changes in PCV during normal pregnancy could be caused by an increase in maternal erythropoietin production, and to a lesser extent, by an increase in the plasma volume resulting in this physiological change in PCV which may be attributed to an increased need for oxygen requirement due to increased metabolic activity during pregnancy (23).

With regard to immunological changes, no significant differences were found in APA Ab, ACA IgM, ACA IgG, and INF-gamma levels when comparing pre-eclamptic

patients with normal controls. However, there was a highly significant increase in the serum IL-4 levels in preeclamptic patients (Table 7). Some studies done on a number of cytokine level profiles in PE found an increase in the proinflammatory cytokines such as IFN- γ , IL-1, and IL-6 which could involve in the pathogenesis of the disease (42-46).

Considering autoantibodies, the comparison between normal pregnant women and preeclamptic patients represented no significant difference in APA Ab, ACA IgM, ACA IgG, INF-gamma, and IL-4 (Table 7). Further, there was no difference between the trimesters of pregnancy except for APA Ab levels which increased significantly in the 2nd trimesters in comparison to 3rd trimesters in PE (Table 7). However, other studies reported an increase in the level of APA Ab in the 3rd trimester of pregnancy in preeclamptic patients (47, 48). Based on previous evidence, no association was found between APA Ab and PE (48).

Regarding autoantibodies, the results of our study demonstrated no difference in the level of anticardiolipin (IgG, IgM) and antiphospholipid antibodies in preeclamptic patients compared to normal pregnant women and normal non-pregnant control tab11, which contradicts the findings of Sharmin Khanm et al (49), indicating a significantly higher level of anticardiolipin IgM antibody in preeclamptic woman. Furthermore, Salehi et al (50) found elevated levels of IgG and IgM anticardiolipin and IgG antiphospholipid antibodies in preeclamptic patients although they observed no significant change in the level of IgM antiphospholipid antibody comparatively. Many studies have focused on the role of the anticardiolipin antibody as a risk factor for PE in women with no evidence of previous autoimmune diseases for the past decades, mainly cohort and case-control studies including Briones-Garduño et al (51).

Some of these studies such as Mello et al (52), Pereira et al (53), Ferrer-Oliveras et al (54), and Kestlerová et al (55) demonstrated a positive relationship between anticardiolipin antibodies and PE. They postulated that the produced anticardiolipin IgM antibody during the acute state of PE causes vascular changes and increases the prothrombotic state which is responsible for maternal and neonatal complications. In another study, Briones-Garduño et al (51) found that changes in the systolic and diastolic blood pressure correlate with the level of anticardiolipin antibody. However, other similar studies (56-60) could not find any increase or relationship between anticardiolipin antibody and PE, which is in line with our results.

Conclusions

According to the obtained results, hematological parameters such as granulocytes, monocytes, and the mean PLT volume significantly increased in both normal pregnant women and PE patients in comparison to normal

non-pregnant controls. However, a significant reduction was observed in their HCT, PLT, and lymphocytes. On the other hand, some immunological parameters (e.g., IL-4 levels) demonstrated a significant increase in both normal pregnancy and preeclamptic patients when compared to non-pregnant controls although gamma interferon was not significantly different.

Conflict of Interest Disclosure

The authors declare that they have no competing interests.

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Ethical Statement

The current study was carried out according to the standard clinical ethics guideline and was approved by the Ethics Committee of the University of Sulaimani (4431/19/07).

Author's Contribution

SAM substantially contributed to designing the study, collecting the data, along with writing and drafting the manuscript. BMM also substantially contributed to designing and supervising the study and writing the draft of the manuscript.

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Informed Consent

Written consent was obtained from the target patients after they were provided with explanations about the study method and objectives and assured of data confidentiality and their freedom to quit the study.

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