Changes in hematological and coagulation parameters in women with pregnancy induced hypertension and pre-eclampsia: Case control study

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Abstract

Background: It has been stated that hypertension as a disorder can complicate up to 10 % of all gestations and is broadly including pregnancy related hypertension and preexisting one. It is associated with significant mortality and morbidity for mothers and babies. Poor placental circulation has been proposed to result from some form of endothelial dysfunction with resultant induction of an inflammatory response and oxidative stress. The interplay between these changes may be mirrored by changes in hematological parameters and coagulative parameters as stated by previous studies

Aim of the study: the aim of this study was to assess changes in hematological parameters in association with pregnancy induced hypertension and pre-eclampsia in a sample of Iraqi pregnant women.

Patients and methods: The current study was planned to be a case control study. The study started on April the 15th 2020 and ended at February the 3rd 2021. The study included two major groups. The first group included women diagnosed with pregnancy induced hypertension (n = 60) who were sub-classified into 30 women with hypertension and 30 women with eclampsia. The second group included 30 pregnant women with normal blood pressure. Those women were attending the obstetric department at Al-Imamein Al-Kadhimaein Medical City, Baghdad, Iraq.

Results: hemoglobin and hematocrit levels were significantly lower in women with pregnancy induced hypertension than in control group ($p < 0.05$). WBC count and ANC were significantly higher in women with pregnancy induced hypertension than in control group ($p < 0.05$). Platelet count was significantly lower in women with pregnancy induced hypertension than in control group ($p < 0.05$). Platelet volume was significantly higher in patients with pre-eclampsia in comparison with control group and pregnancy induced hypertension subgroup. PT and PTT were significantly higher in women with pregnancy induced hypertension than in control group ($p < 0.05$) and there was no significant difference between pregnancy induced hypertension pre-eclampsia subgroups ($p > 0.05$).

Conclusion: anemia, leukocytosis, thrombocytopenia and prolonged PT and PTT are the main features in association with pregnancy induced hypertension and that the most acceptable explanation is the presence of endothelial dysfunction with subsequent inflammation and induction of coagulation.

Key words: hematological, coagulation, pregnancy induced hypertension, pre-eclampsia, Iraq

Introduction

In pregnant women with previously normal blood pressure, the rise of systolic and or diastolic blood pressure after 20 weeks gestation is known as pregnancy induced hypertension (1, 2). The acceptable defining levels of systolic and diastolic blood pressure are ≥ 140 mmHg and ≥ 90 mmHg, respectively, in order to categorize pregnant women as having pregnancy induced hypertension provided that two measures at separate occasions have been carried out (3-5). The general categorization of pregnancy related rise in the blood pressure includes pregnancy (gestational) hypertension, pre-eclampsia and eclampsia (1, 2). The main features in association with pregnancy induced hypertension are pathologic edema, high blood pressure and proteinuria (6, 7).

The general estimation for the prevalence rate of hypertension in women with the reproductive age is around (7.7 %) (8). It has been stated that hypertension as a disorder can complicate up to 10 % of all gestations and is broadly including pregnancy related hypertension and preexisting one. It is associated with significant mortality and morbidity for mothers and babies (9).

The physiological changes during pregnancy favor reduction in blood pressure during first trimester. These changes are in the form of increased cardiac output, increased blood volume and generalized vasodilatation (10). During third trimester, blood pressure usually returns to normal. One of proposed mechanism in association with pre-eclampsia and hypertensive disorders in pregnancy is augmentation of inflammatory response as well a hypercoagulable state (10). Poor placental circulation has been proposed to result from some form of endothelial dysfunction with resultant induction of an inflammatory response and oxidative stress (5). The interplay between these changes may be mirrored by changes in hematological parameters and coagulative parameters as stated by previous studies (11, 12). However, the exact interaction among inflammation, immune system, hematological parameters and cardiovascular system are not fully understood. In addition, little research work has been allocated to changes in hematological parameters in association with hypertensive pregnancy disorders in Iraq. Therefore, because of lack of consensus about the exact role of hematological parameters in the pathogenesis of pregnancy induced hypertension and rarity of national Iraqi studies with regard, we were justified to plan and conduct the current study aiming at disclosing some aspect of this interaction.

Patients and methods

Study design: The current study was planned to be a case control study. The study started on April the 15th 2020 and ended at February the 3rd 2021. The study included two major groups. The first group included women diagnosed with pregnancy induced hypertension (n = 60) who were sub-classified into 30 women with hypertension and 30 women with eclampsia. The second group included 30 pregnant women with normal blood pressure. Those women were attending the obstetric department at Al-Imamein Al-Kadhimaein Medical City, Baghdad, Iraq.

Data collection: When either patients or control member met the inclusion criteria, blood sample was withdrawn soon as possible. Gestational hypertension was defined as systolic blood pressure equals 140 mmHg or more and / or diastolic blood pressure equals 90 mmHg or more in the absence of proteinuria. Pre-eclampsia and eclampsia were defined when there hypertension, proteinuria and other defining features (3-5). The main exclusion criteria were evidence of infection, blood transfusion and any chronic medical illness.

A questionnaire form was prepared according to literature and clinical experience and included age, gestational age, residency, educational level, parity, gravidity, abortion.

From each participant 5 ml of venous blood was withdrawn and transferred into an EDTA tube and the complete blood count was done using "Abbott Cell dyne 3700". Blood sample for purpose of PT and PTT was transferred into a blue cap tube (vacuum tube) with sodium citrate (32.06 mg/ml, final concentration of 3.8 %) with a 9 to 1 ratio volume. Tests of coagulation were done using Sysmex CA 500 machine.

Ethical consideration: The ethical approval for the study was issued by the ethical approval consideration of Al-Karkh health directorate, the formal representative of Iraqi ministry of health. A verbal consent was obtained from every participant after full illustration of the aim and the procedures of the study.

Statistical analysis: Data were transferred into two statistical software programs, the statistical package for social sciences (SPSS) version 16.0 (IBM, Chicago, USA) and Microsoft Office Excel 2007. Qualitative data were expressed as number and percentage, whereas, quantitative data were expressed as mean, standard deviation and range. Independent samples student *t*-test was used to compare mean values between study and control groups. Mann Whitney U test was used instead of *t*-test in case of comparing variables that are not normally distributed. Chi-square test was used to study difference in proportion among groups. One way ANOVA and post-hoc LSD test was used to study differences in means among groups. The level of significance was chosen at $p \leq 0.05$, while the level of high significance was chosen at $p \leq 0.01$.

Results

The sociodemographic characteristics of pregnant women enrolled in the current study are shown in table 1. There was no significant difference in mean age and mean gestational age between control group (non-hypertensive pregnant women) and women with pregnancy induced hypertension ($p > 0.05$). There was also no significant difference in the frequency distribution of woman according to residency, level of education and occupation between the two study groups ($p > 0.05$). In addition, there was no significant difference in gravidity, parity and abortion between study groups ($p > 0.05$).

Table 1: Sociodemographic characteristics of pregnant women enrolled in the present study

Characteristic	Control group *n* = 30	Hypertensive group *n* = 60	*p*
Age (years)			
Mean ±SD	28.70 ±6.07	27.30 ±6.23	0.215 I NS
Range	18-44	18-39	
Residency			
Urban	21 (70.0 %)	47 (78.3 %)	0.386 C NS
Rural	9 (30.0 %)	13 (21.7 %)	
Level of education			
Illiterate	5 (16.7 %)	9 (15.0 %)	0.698 C NS
Primary and secondary	18 (60.0 %)	41 (68.3 %)	

University	7 (23.3 %)	10 (16.7 %)	
Occupation			
Employee	11 (36.7 %)	19 (31.7 %)	0.635 C NS
Housewife	19 (63.3 %)	41 (68.3 %)	
Gestational age			
Mean ±SD	24.13 ±2.21	23.90 ±2.06	0.623 I NS
Range	21-29	21-28	
Gravidity			
Median (IQR)	3 (2)	3 (1)	0.519 M NS
Range	1 (6)	1 (5)	
Parity			
Median (IQR)	1 (3)	1 (2)	0.621 M NS
Range	0 (5)	0 (3)	
Abortion			
Median (IQR)	0 (0)	0 (0)	0.872 M NS
Range	0 (3)	0 (3)	

n: number of cases; **SD**: standard deviation; **IQR**: inter-quartile range; **I**: independent samples student t-test; **C**: Chi-square test; **M**: Mann Whitney U test; **NS**: not significant at $p > 0.05$

Hematological parameters of pregnant women enrolled in the present study are shown in table 2. In this table the group of women with pregnancy induced hypertension were sub-grouped into, women with pregnancy induced hypertension (n = 30) and women with pre-eclampsia (n = 30). Both mean hemoglobin and hematocrit levels were significantly lower in women with pregnancy induced hypertension than in control group ($p < 0.05$) and there was no significant difference between pregnancy induced hypertension pre-eclampsia subgroups ($p > 0.05$). Both mean WBC count and absolute neutrophil count (ANC) were significantly higher in women with pregnancy induced hypertension than in control group ($p < 0.05$) and there was no significant difference between pregnancy induced hypertension pre-eclampsia subgroups ($p > 0.05$).

Mean platelet count was significantly lower in women with pregnancy induced hypertension than in control group ($p < 0.05$) and there was no significant difference between pregnancy induced hypertension pre-eclampsia subgroups ($p > 0.05$). Mean platelet volume was significantly higher in patients with pre-eclampsia in comparison with control group and pregnancy induced hypertension subgroup.

Both mean Prothrombin time (PT) and partial thromboplastin time (PTT) were significantly higher in women with pregnancy induced hypertension than in control group ($p < 0.05$) and there was no significant difference between pregnancy induced hypertension pre-eclampsia subgroups ($p > 0.05$).

Table 2: Hematological parameters of pregnant women enrolled in the present study

Characteristic	Control *n* = 30	Pregnancy induced hypertension *n* = 30	Pre-eclampsia *n* = 30	*p*
Hb (g/dl)				
Mean ±SD	12.18 ±2.13 A	11.69 ±1.44 B	11.17 ±0.78 B	0.048 O S
Range	4.2 -14.4	8.6-15.1	9.8-12.3	
HCT (%)				
Mean ±SD	38.53 ±6.40 A	36.17 ±4.18 B	34.85 ±2.18 B	0.009 O HS
Range	14.6 -45.2	26.8-46.5	30.5-38.2	
WBC X10^9/L				
Mean ±SD	7.30 ±2.25 B	10.05 ±2.27 A	10.27 ±2.35 A	< 0.001 O HS
Range	3 -11	4.8-14	5.38-17.1	
ANC X10^9/L				
Mean ±SD	4.89 ±1.50 B	6.36 ±2.94 A	6.11 ±2.63 A	0.049 O S
Range	2.01 - 7.37	2.1-11.4	1.7-13.52	
Platelet X10^9/L	a	b	b	
Mean ±SD	300.73 ±109.46	222.03 ±46.69	212.50 ±79.75	< 0.001 O HS
Range	115 -487	112-322	68-326	
MPV (fl)				
Mean ±SD	9.29 ±1.50 B	8.91 ±1.82 B	10.80 ±2.25 A	< 0.001 O HS
Range	7.08 -13.18	6.4-12.8	7.1-17.1	
PT (seconds)				
Mean ±SD	11.57 ±0.94 B	12.37 ±0.99 A	12.92 ±0.90 A	< 0.001 O HS
Range	10.08 -13.64	10.2-15.5	11.5-14.9	
PTT (seconds)				
Mean ±SD	31.75 ±2.68 B	32.14 ±2.55 A	32.36 ±1.64 A	0.019 O S
Range	22.66 -35.48	27.3-35.7	29.6-35.4	

n: number of cases; **SD**: standard deviation; **Hb**: hemoglobin; **HCT**: hematocrit; **WBC**: white blood cell count; **ANC**: absolute neutrophil count; **MPV**: mean platelet volume; **PT**: Prothrombin time; **PTT**; partial thromboplastin time; **O**: one Way ANOVA; **S**: significant at $p \leq 0.05$; **HS**: highly significant at $p \leq 0.01$; Capital letter (**A, B** and **C**) were used to indicate the level of significance following **post hoc LSD** test so that similar letters indicate no significant difference whereas different letters indicate significant difference; letter **A** indicates the highest value followed by **B** then by **C**.

Discussion

The mortality and morbidity to the mother and to the fetus in association with pregnancy induced hypertension and pre-eclampsia are well recognized obstetric complications worldwide (13, 14). In this study we tried to figure out hematological changes in a sample of Iraqi pregnant women diagnosed with pregnancy induced hypertension and pre-eclampsia and compare these changes with hematological parameters in a control group comprising pregnant women with comparable age and gestational age and are known to be normotensive. We tried our best to make statistical adjustment between study group and control group with respect to sociodemographic characteristics in order to avoid any bias in the results which can be contributed to some confounding sociodemographic factors.

In the current study we found significantly lower hemoglobin level and hematocrit levels in association with pregnancy induced hypertension and the anemia appear to be associated more with pre-eclampsia than with just pregnancy induced rising blood pressure. Indeed, this observation is in agreement with that reported by Mtali *et al* (11) but it is inconsistent with that of and Ekun *et al* (15). In one previous study (11) there was significant negative correlation between hemoglobin level and serum IL-6 level and based on this observation they suggested that the reduced iron absorption caused by hepcidin, induced by IL-6, is the explanation for anemia in association with pregnancy induced hypertension. On the other hand, it can be suggested that anemia is a risk factor rather than being an outcome of pregnancy induced hypertension. Ali *et al* (16) and Rohilla *et al* (17) have reported anemia to be a risk factor for pregnancy induced hypertension and pre-eclampsia. The lack of anti-oxidants and micronutrients in under-nuritioned pregnant women was suggested to cause inflammation and subsequently pregnancy induced hypertension (16). Therefore, the association between anemia and pregnancy induced hypertension appears to be complicated and bi-directional and further research work is needed in order to reach a clear consensus about this association.

In the current study WBC and ANC counts were significantly associated with pregnancy induced hypertension. This observation was shared by previous authors (11, 15, 18). Increased neutrophil count indicates an inflammatory state and this inflammatory state can explain some aspects of the pathogenesis of pre-eclampsia and pregnancy induced hypertension. Mtali *et al* (11) suggested that leukocytosis is the result of rising IL-6. Some authors attributed the rise in leukocyte in pregnancy to be due to steroid rise in association with stress (18). However, we prefer that inflammatory response is the cause of this rise in leukocyte count and that inflammation has resulted from some form of endothelial dysfunction as suggested by previous studies (11, 19, 20).

In the current study we found significantly reduced platelet count and increase in PT and PTT in association with pregnancy induced hypertension. This observation is in agreement with pervious authors (11, 21). Endothelial injury and tissue factors release and activation of coagulation is the main proposed pathogenesis by previous literature (21).

Conclusion: Collectively we can put the following picture: anemia, leukocytosis, thrombocytopenia and prolonged PT and PTT are the main features in association with pregnancy induced hypertension and that the most acceptable explanation is the presence of endothelial dysfunction with subsequent inflammation and induction of coagulation.

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