An Evaluation Study of von Willebrand Factor and Other Hematological Parameters of Preeclamptic Patients in Babylon Province

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الخلاصة:

هدف الدراسة:

لمعرفة دور بعض معايير الدم في المساهمة في التشخيص المبكر لمرض ما قبل الشنج.

المرضى وطرق البحث:

أجريت هذه الدراسة في مستشفى الأمومة والطفولة التعليمي في بابل للفترة من تشرين الأول ٢٠٠٩ ولغاية مايس ٢٠١٠ وشملت الدراسة ٧٠ امرأة (٤٥ امرأة حاملة مصابة بداء ما قبل الشنج و١٥ امرأة حاملة طبيعية و١٠ نساء غير حوامل). حيث تم أجراء الفحوصات التالية للمشاركين في الدراسة : مستوى عامل ڤون ويلبراند، مستوى عامل مولد الليفين Plasma fibrinogen، حجم كريات الدم المرصوصة PCV، وتعداد الصفيحات الدموية في البلازما.

النتائج :

أظهرت نتائج الدراسة أن التوزيع الجغرافي السائد في مرضى ما قبل الشنج كان في المناطق الريفية أكثر مما هو عليه في المدن، معظم المريضات (60%) يمثلن الأعمار 35 < و 20 > سنة. (58%) من المريضات لديهن تاريخ عائلي للمرض. (62%) من المريضات هن من ذوات الحمل الأول. وأوضحت الدراسة بأن عامل الـڤون ويلبراند ازداد ازدياداً معنوياً ($P < 0.01$) في بلازما النساء المصابات مقارنة مع النساء الحوامل غير المصابات، وازداد ازدياداً معنوياً عالياً ($P < 0.001$) بالمقارنة مع غير الحوامل من مجموعتي السيطرة.وأظهرت الدراسة زيادة معنوية عالية ($P < 0.001$) في مستوى مولد الليفين في بلازما النساء المصابات بداء ما قبل الشنج مقارنة بمجموعتي السيطرة، وأن حجم كريات الدم المرصوصة أبدى ارتفاعاً معنوياً ملحوظاً ($P < 0.05$) في مجموعة المرضى مقارنة بمجموعتي السيطرة. في حين أظهرت الدراسة أن تعداد الصفيحات الدموية قد انخفض بمقدار معنوي عالي ($P < 0.001$) في النساء المصابات مقارنة بمجموعتي السيطرة من الحوامل وغير الحوامل.

الاستنتاج :

يستنتج من الدراسة الحالية أن هناك بعض المتغيرات والعوامل التي يجب إضافتها وبشكل دوري للفحوصات الكلاسيكية الروتينية خلال فترة الحمل وهذه تشكل كل من عامل الـڤون ويلبراند، تعداد الصفيحات الدموية، مولد الليفين وغيرها من المتغيرات المدروسة الاخرى والتي تعطي دليل تشخيصي مبكر لحدوث داء ما قبل الشنج ومن ثم إعطاء العناية الخاصة والانتباه للمريضات قبل تردي حالتهن المرضية.

Abstract

Aim: The aim of the study was to evaluate the role of some hematological parameters in early diagnosis of preeclampsia.

Patients and methods: The study was conducted in Maternity and Pediatrics Teaching Hospital in Hilla city during the period from November 2009 to May 2010. Seventy women(45 preeclamptic pregnant women as patients,15 healthy pregnant women and 10 healthy nonpregnant women as control groups) at the age of reproduction were included in this study**.** For every subjects participate in this study the following parameters were measured; the level of vWF, fibrinogen, packed cell volume and platelets count.

Results

preeclampsia was (60%) more common in PE of > 35 and < 20 years. While, the remainder (40%) in PE of < 35 and > 20 years.PE seems more frequent (62%) in primigravida than of (38%) in multigravida.Our data confirm that percentage of PE in pregnant women lived in rural areas (60%) more than urban areas (40%).Parameter of family history show that 26 out of 45 (58%) had have family history, while 19 out of 45 (42%) hadn't have PE family history. Hematological investigate results observe high

significant increase in vWF concentration in PE patient group compare with non pregnant group. As well as, to significant increase in fibrinogen levels in PE group than in non pregnant and pregnant control groups.Also, obtained data detect significant increase in PCV ratio in PE group than in the two control groups.Finally, the platelets count show highly significant decrease ($P < 0.001$) in PE group than in those two control groups. In addition to present of significant differences between the two control groups**.**

Conclusion We conclude from this study that there are some parameters may be give an early diagnostic evidence for occurrence of preeclampsia .

Introduction

Preeclampsia is a pregnancy-specific syndrome characterized by new-onset hypertension and proteinuria, occurring usually after 20 weeks' gestation and is classified into mild and severe types. Although the etiology remains unknown, placental hypoperfusion and diffuse endothelial cell injury are considered to be the central pathologic events. In the United States, t is believed to be responsible for 15% of premature deliveries [(1)] and 17.6% of maternal deaths [(2)].The Possible Causes of preeclampsia may include: Insufficient blood flow to the uterus ,Damage to the blood vessels ,A problem with the immune system ,Poor diet and Gene and air pollution [(3;4;5)] .The risk factors for preeclampsia include: Pregnancy-associated factors, Maternal-specific factors and Paternal-specific factors [(6; 7 ; 8 ; 9)].

Endothelium-derived relaxing and contracting factors have an important regulatory role in maintaining vascular resistance and blood pressure. An imbalance between factors promoting angiogenesis (vascular endothelial growth factor [VEGF], placental growth factor [PlGF] and antagonizing factors (such as soluble fms-like tyrosine kinase 1 [sFlt1] and soluble endoglin) has been proposed to have a major role in the pathogenesis of preeclampsia [(10)]. The increased circulating blood volume and cardiac output of normal pregnancy results in increased renal blood flow and glomerular filtration rates (GFRs). Women with preeclampsia have markedly decreased renal blood flow and GFRs [(11)]. Renal biopsies of these women show a constellation of lesions, termed glomerular capillary endotheliosis. Some consider glomerular capillary endothelial swelling that is accompanied by deposits of fibrinogen degradation products within and under the endothelial cells as pathognomonic of the disease. The presence of proteinuria differentiates preeclampsia from gestational hypertension, these lesions resolve within a month of delivery [(12)].

von Willebrand Factor (vWF) is a multimeric plasma protein that mediates platelet adhesion as well as platelet aggregation at sites of vascular injury and acts as a carrier of factor VIII. Although acquired or inherited vWF deficiency is associated with a bleeding tendency, there is increasing evidence that vWF has a pivotal role in thrombogenesis [(13)].

Fibrinogen is a protein produced by the liver. This protein helps stop bleeding by helping blood clots to form [(14)]. .A study by Williams *et al*[(15)]has shown a novel increase in fibrinogen concentration in pregnant women with preeclampsia compared with values obtained from women with normal or non-preeclampsia complicated pregnancies.

Materials and Methods

The study was conducted in Maternity and Pediatrics Teaching Hospital in Hilla city during the period from November 2009 to May 2010. Seventy women(45 preeclamptic pregnant women as patients,15 healthy pregnant women and 10 healthy nonpregnant women as control groups) at the age of reproduction were included in this study, those women were not smokers, not alcoholics and not suffering from any other serious systemic illnesses like diabetes mellitus, cardiac diseases, renal diseases and hepatic diseases. The history taking includes: name, age, weight, address ,occupation, number of delivery, number of abortion, previous history of preeclampsia and family history of preeclampsia.

Five ml of blood was collected from an antecubital vein of every participant. 2 ml of blood was put into first tube which contains EDTA as anticoagulant for hematological studies and 2 ml of blood put in second tube was used to prepare platelet poor plasma (ppp) ,by taking of 1.8 ml of blood (9 volumes)then added to 0.2 ml of 109 mmol/L of trisodium citrate solution (1 volume) to be used for determination of vWF . The ppp was prepared by centrifugation of the blood sample at 4000 rpm for 15 minutes [16] .

Determination of vWF concentration is done according to the procedure recommended by the company (Biomerieux ,France)[17]. The VIDAS vWF test is calibrated against the WHO International Standard and vWF concentrations are expressed as a % . Microhematocrit method was used to determine PCV, and platelets count is done manually [31].The plasma fibrinogen concentration is done according to the procedure recommended by the company (Biomerieux ,France) that depends on the clot based method of Clauss for estimating the functional (clotable) fibrinogen level[16].

Data are expressed as mean ± standard deviation. Comparisons of the variable data were considered using un- paired Student's t-test. Statistical analysis was performed with SPSS 18 for Windows (SPSS Corporation, Chicago, Illinois).

The Results

In preeclamptic group, 27 out of 45(60%) represent age > 35 and < 20 years while 18 out of 45 (40%) represent age < 35 and > 20 years.The percentage of patients with preeclampsia lived in rural areas(60%) more than urban areas (40%). Twenty six patients out of 45 (58%) had a family history of preeclampsia, while 19 patients out of 45(42%) had no family history of preeclampsia.Twenty eight patients out of 45 (62%) were primigravida while,17 patients out of 45(38%) were multigravida. Results of hematological tests show there is a highly significant increase in vWF concentration in preeclamptic group than in non pregnant group($p< 0.001$) and there is significant increase in preeclamptic group than in pregnant group($p<0.01$). Also there is significant increase in pregnant group than in non pregnant group($p< 0.01$) as shown in Table(1).

Table (1) Comparison (Mean ± S.D.) between preeclamptic women and two control groups in vWF concentrations

Groups	NO.	vWF% (Mean ± S. D)	P. value
preeclamptic	45	374.488±137.286	0.001<P
Control (Pregnants)	15	264.200 ± 83.759	
preeclamptic	45	374.488 ± 137.286	0.001<P
Control Nonpregnant)(	10	111.000 ± 26.587	
Pregnants	15	264.200 ± 83.759	0.01 <P
Nonpregnant	10	111.000 ± 26.587	

Fibrinogen levels show highly significant increase in preeclamptic group than in nonpregnant group($p< 0.001$) and there is significant increase in preeclamptic group than in pregnant group($p<0.05$). Also there is significant increase in pregnant group than in nonpregnant group($p<0.01$)} as shown in Table(2).

Table (2) Comparison(Mean ± SD) between preeclamptic women and two control groups in plasma fibrinogen levels

Groups	No.	Plasma fibrinogen g/L (Mean ± S. D)	P- value
Preeclamptic	45	4.720 ±1.108	0.05 <P
Control (Pregnants)	15	4.013 ±1.041	
Preeclamptic	45	4.720 ±1.108	0.001 <P
Control (Nonpregnant)	10	2.850 ±0.797	
Pregnants	15	4.013 ±1.041	0.01 <P
Nonpregnant	10	2.850 ±0.797	

The PCV ratio show significant increase in preeclamptic group than the two control groups ($p< 0.01$),while there is insignificant difference between the two control groups ($p>0.05$), as shown in Table(3)

Table (3) Comparison(Mean ± SD) between preeclamptic women and two control groups in Packed cell volume concentration

Groups	No.	Packed cell volume % (Mean ± St. D)	P- value
Preeclamptic	45	0.415 ± 0.069	P < 0.01
Control (Pregnants)	15	0.368 ± 0.033	
Preeclamptic	45	0.415±0.069	P < 0.01
Control (Nonpregnant)	10	0.363 ± 0.026	
Pregnants	15	0.368 ± 0.033	P > 0.05
Nonpregnant	10	0.363 ± 0.026	

Platelets count show a highly significant decrease in preeclamptic group than in two control groups ($p< 0.001$), also there is significant differences between the two control groups {significant decrease in pregnant group than in nonpregnant group($p< 0.05$)} as shown in Table(4)

Table (4) Comparison (Mean ± SD) between preeclamptic women and two control groups in platelets count

Groups	No.	platelets count x 10^9/L (Mean ± S.D)	P- value
Preeclamptic	45	194.8667 ± 38.89999	0.001 <P
Control (Pregnants)	15	269.6667 ± 99.60541	
Preeclamptic	45	194.8667 ± 38.89999	0.001 <P
Control (Nonpregnant)	10	319.8000 ± 80.22441	
Pregnants	15	269.6667 ± 99.60541	0.05 < P
Nonpregnant	10	319.8000 ± 80.22441	

Discussion

The studied age groups of preeclamptic patients in our study showed that about 60% of the patients group ages were >35 and < 20 years , which is the more common age for PE and this result was in agreement with other study Wagner, 2004whofound that age greater than 35 years and age less than 20 years is one of the maternal specific risk factor that causes PE[6]. From history , it has been found that more patients are inhabited in rural areas than urban areas and this will agree with Moore (2008) outcome, who found that social factors—including living in a rural county—may also increase the risk of preeclampsia and the reason for this increased risk is unclear, but may possibly be associated with family poverty, type and quality of diet, difficulties of life style and social deprivation[18].The results show that about 58% of the patients in our study had family history of PE ,while patients without family history of PE reach to 42% (and this percentage will go parallel with the study of Barton , *et al*. (2008), who found that a personal or family history of preeclampsia increases the risk of developing the condition[19]. Our result show that PE is more frequent in primigravida 28/45 (62%) than in multigravida 17/45 (38%)and this is in agreement with Campbell and Lees, (2000)[20].Some studies suggested differences in immunological responses in the aetiology of pre-eclampsia in primiparous vs. multiparous women. Other recent study indicated that the differences in angiogenic factor profile may explain the elevated pre-eclampsia risk in the first pregnancies[21].

From the preeclamptic hematological assessment the obtained data indicate that the level of vWF in plasma of preeclamptic group was significantly increased ($p<0.01$) when compared with control pregnant group, while there is a highly significant increase($p<0.001$) in preeclamptic group than nonpregnant control group as shown in Table (1) , the concluded data of the present study go together with the results of other studies [22;23] who found that vWF is higher significantly in preeclamptic women than in healthy pregnant and non-pregnant women. And this increment in the level of vWF in preeclamptic women may be atrributed to the endothelial dysfunction(the endothelial cells is the main site of vWF) which were caused mainly from decreased placental perfusion which lead to fetoplacental ischemia, and finally promote generalized maternal vascular endothelium dysfunction [2].

Some studies suggest that hypoxia resulting from inadequate perfusion upregulates sFlt-1, a VEGF and PlGF antagonist, leading to a damaged maternal endothelium and restriction of placental growth[24].

The mechanism of action of estrogen may be related to the increase production of vWF through a direct effect on endothelial cells[25]. Also, vWF is an acute phase reactant and its levels elevated during pregnancy [26].

During this study, the concentration of fibrinogen shows significant differences when compared between three studied groups leading for highly significant increase in preeclamptic group than nonpregnant control group ($p<0.001$) and significant increase ($p<0.05$)in PE group than pregnant control group (Table 2), and this result goes together with other scientific research of Williams *et al*., (2007) who shows a novel increase in fibrinogen concentration in preeclamptic women when compared with values obtained from women with normal pregnancy and with nonpregnant women [15]. This increase may contribute to the hypercoagulability seen in preeclampsia.

The significant increase in pregnant group when compared with nonpregnant group ($p<0.01$) is in agreement with the results of study by Iacoviello *et al* .,(1998) who found that the increase concentrations are associated with pregnancy [27].This increase in the

concentration of plasma fibrinogen may be explained by hormonal changes or increase activation of the clotting system at delivery [28].

The results from Table (3) show that there was a significant increase ($p<0.01$) in the level of Packed cell volume in preeclamptic group than the two control groups. This increase was due to the hemoconcentration, (as a result of diminished plasma volume) which is a common feature in PE.

The hemoconcentration may be as a result of vasoconstriction which caused by a decrease in production of nitric oxide (NO) [29] and/or increase in plasma endothelin concentrations which appear to be elevated in PE [30]. The hematocrit increases as the severity of preeclampsia increases [31]. On the other hand, there is insignificant difference between pregnants group and nonpregnant group which may be dependent on the medical personal education and enrolled program of tonics medication for pregnant women, especially at the last decade.

In preeclamptic group there was a highly significantly decrement in the mean of platelets count than that of two control groups ($p< 0.001$), although it was still within the normal range(Table 4). This may be firstly due to intra vascular coagulation induced by thromboplastin from placenta and platelets adherence at sites of vascular discontinuity [32]. Whereas, the second explanation is that thrombocytopenia in PE is the most common hemostatic abnormality and is caused by platelet consumption. Immune mechanisms or severe vasospasm with resultant endothelial damage may contribute to the thrombocytopenia in some patients with PE [33]. Our results regarding platelets count in preeclamptic group were consistent with those obtained by other study[34,35].

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