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Original article

Urinary Protein and Creatinine Levels of Different Haptoglobin Phenotypes among a Nigerian Pre-eclamptic Population

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ABSTRACT

Background and aim. *Proteinuria is a major component of preeclampsia whose pathophysiology is not fully understood. The aim of this study was to determine the urinary protein and creatinine levels of different haptoglobin phenotypes among pre-eclamptic population in Ekiti State, Nigeria.* ***Methods.*** *A total number of 92 subjects comprising of 28 (30.43%) pregnant women diagnosed of pre-eclampsia, 34 (36.96%) pregnant women without pre-eclampsia and 30 (32.61%) non-pregnant women of child bearing age without pre-eclampsia used as control subjects. Urinary protein was determined using 25% sulphosalicylic acid, urinary creatinine was determined using Jaffe slot's method and haptoglobin phenotypes was determined using protein electrophoresis method of polyacrylamide gel and determined using specific peroxidase staining. The results were presented in tables and charts as mean ± standard deviation. Statistical analysis was done using the Student's t-test using SPSS software. A p-value<0.05 was considered significant.* ***Results.*** *The results obtained showed that in pregnant women with pre-eclampsia, BMI, SBP, DBP, urinary (mg/creatinine) were significantly higher compared to both non-pre-eclamptic pregnant women and control (p<0.05). BMI, SBP, DBP and urinary protein (mg/creatinine) was significantly higher (p<0.05) in pre-eclamptic women with the Hp 2 allele (Hp 2-2 and Hp 2-1). Hp 2 allele which has a lower scavenging effect was higher in pre-eclamptic subjects.* ***Conclusion.*** *In conclusion, haptoglobin 2 and increased urinary protein appears to be higher in pre-eclampsia. Therefore, this research deduced that the Hp 2 allele could be a determining factor in development of pre-eclampsia.*

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INTRODUCTION

Pregnancy also known as gestation is a period when one or more offspring develops in a woman [1]. Pre-eclampsia can be defined as occurrence of hypertension and significant proteinuria in previously healthy woman on or after the 20th week of gestation [2]. Pre-eclampsia is the onset of hypertension where the systolic pressure is greater than 140 mmHg and diastolic pressure is greater than 90 mmHg and occurrence of proteinuria at early stage or late stage during pregnancy [3]. The pathophysiology of pre-eclampsia is based on vasoconstriction that leads to hypertension, platelet activation with intravascular coagulation, endothelial dysfunction and maternal plasma volume contraction. The various signs and symptoms of pre-eclampsia includes new onset of hypertension, new onset of proteinuria, nausea, vomiting, headache and epigastric abdominal pain [4]. The risk factors of pre-eclampsia are smoking, obesity, chronic

kidney disease, multiple gestation and family history. Pre-eclampsia can affect mother and foetus. The effects of pre-eclampsia on mothers are pulmonary edema, liver rupture, seizures, retina vasospasm, temporary blindness, brain ischemia. The effects of pre-eclampsia on foetus are placental perfusion, intrauterine growth restriction, premature delivery, oligohydramnios [5].

Hypertension is associated with pre-eclampsia developed during pregnancy. Gestational hypertension occurs when there is new onset of proteinuria that causes pre-eclampsia. Chronic hypertension is when hypertension occurs before 4th week of pregnancy. When a woman has chronic hypertension, it manifests signs and symptoms of pre-eclampsia, and it is known as superimposed pre-eclampsia [6]. Hypertension during pregnancy is common in the first, second and third trimester. Hypertension occurs when placenta starts releasing pro-inflammatory proteins which gets into the mother's circulation and enters the endothelial cell to become dysfunctional which leads to vasoconstriction causing the kidney to retain more salts and causes hypertension [7].

The haptoglobins are reserved protein present in all humans. The haptoglobins are a group of plasma glycoprotein which is expressed mostly in the liver. The haptoglobins bind haemoglobin with a very high affinity to prevent loss of iron and kidney damage due to the oxidative activity of the haemolysis intravascularly [8]. The haptoglobins are involved in various processes and serves as a biomarker for several diseases. The haptoglobins have immunoregulatory properties and participate in inhibition of nitric oxide. The haptoglobin genes of humans are characterized by molecular differences due to genetic polymorphism. The haptoglobins are synthesized mainly in the lungs and liver and moves into the blood plasma [9]. The haptoglobin genes are highly polymorphic in humans with strong evidence of functionally distinct biochemical phenotypes. In all human populations, three major haptoglobin phenotypes are present; Hp 1-1, Hp 2-1, and Hp 2-2 respectively. Haptoglobins polymorphism has important biological and clinical significance [10].

Urinary protein is the quantification of proteinuria. The urinary protein concentration is determined from individual measurements of urinary protein and urinary creatinine concentration [11]. Non-significant protein in urine is called Tamm–Horsfall protein (THP). Protein found in urine is due to autoimmunity in the kidney which will likely cause nephrotic syndrome. Glomerular filtration barrier (GFB) consists of glomerular endothelial cells, the glomerular basement membrane and podocyte. Podocyte is the key structure within the nephron that prevents filtration of serum proteins into the urine [12]. Podocyte is a major part of glomerular filtration barrier, a structure that prevents filtration of large proteins into urine [13].

The kidneys play a vital role in the excretion of waste products and toxins such as urea, creatinine, regulation of extracellular fluid volume, serum osmolality and electrolyte concentrations, as well as the production of hormones like erythropoietin and 1,25-dihydroxy vitamin D and rennin [14]. The functional unit of the kidney is the nephron, which consists of the glomerulus, proximal and distal tubules, and collecting duct [15]. Assessment of renal function is important in the management of patients with kidney disease or pathologies affecting renal function. Tests of renal function have utility in identifying the presence of renal disease, monitoring the response of kidneys to treatment, and determining the progression of renal disease [14]. The association of hypertension with significant protein in the urine constitute preeclampsia. Significant proteinuria is the presence of 300 mg of protein in the urine collected over 24 hours or 30 mg/mmol on spot protein: Creatinine ratio. The phenotype haptoglobin predicts cardiovascular disease risk and treatment response to certain disease conditions. This study was carried out to determine the urinary protein and creatinine levels of different haptoglobin phenotypes among pre-eclamptic population in Ekiti State, Nigeria.

METHODS

Study Design

The study was a case control design using stratified random sampling method. Stratification was based on age range. The subjects used for this study were pregnant women attending antenatal clinic at Federal Teaching Hospital, Ido-Ekiti, Ekiti State.

Study Area

The study was carried out in Federal Teaching Hospital, Ido-Ekiti, Ekiti State. The state is mainly an upland zone, rising over 250 meters above sea level. Its coordinates are 7° 40'5° 15E.

Sample Size

The minimum sample size (N) was calculated by using alternate single proportion formula. Allowance for error of 0.05 at 95% confidence interval (Z) [16].

$N=Z_{1-\alpha}/_2{}^2\, P/d^2$

Where $Z_{1-\alpha}/_2 = 1.96$ at 95% confidence interval

N = minimum sample size
D = allowance for error =0.05
P = estimated prevalence of pre-eclampsia in Nigeria at 3% (0.03) [17]
$N = (1.96/0.05)^2 \times 0.03 = 46$
Sample size = 46
Therefore, a total of 46 subjects were used for this research consisting of 17 subjects newly diagnosed with pre-eclampsia, 20 subjects without pre-eclampsia and 15 subjects who were non-pregnant women (control).

Inclusion Criteria
Pregnant women with pre-eclampsia attending antenatal clinic at Federal Teaching Hospital Ido-Ekiti (FETHI), Ekiti State, those being managed for pre-eclampsia, those without pre-eclampsia who gave their consent were included the study. Women of childbearing age who were not pregnant were recruited as control subjects.

Exclusion Criteria
Women who were pregnant below the age 18, pregnant women who were not in FETHI, women who were diagnosed to have chronic hypertension before the onset of pregnancy or before 20th week of pregnancy, those with other underlying health conditions and those who did not give their consent were excluded from the study.

Ethical Clearance
Ethical approval was sought from the Ethics and Research Committee of Federal Teaching Hospital Ido, Ido-Ekiti, Ekiti State. Informed consent was obtained from each participant who participated in the study.

Sample Collection
Venous blood was collected from sterilized cubital fossa using 22G needle and syringe. The blood sample was put into a plain bottle and allowed to stand for one hour, after which it was centrifuged at 12000 rpm for 5 minutes and serum was separated and put into another plain bottle. The serum was stored at temperature of -20 degree Celsius for a maximum of 21 days before been assayed for haptoglobin characterization. For the urine sample collection, mid-stream urine was taken and stored for 6 days and assayed for urinary protein (mg/creatinine).

Analytical Methods
Body Mass Index (BMI) expressed in Kg/m^2 was derived from the measurement of height and weight using the formula below.[18] Height and weight was obtained using a metre gauge and a bathroom scale respectively.

$$BMI = \frac{\text{Weight (kg)}}{\text{Height (m}^2\text{)}}$$

Blood Pressure: Blood pressure was determined using a digital sphygmomanometer.
Estimation of urinary protein was determined using 25% sulphosalicylic acid.
Principle: Sulphosalicylic acid is an anionic precipitant and therefore the neutralization of protein cation results in the precipitation of the protein.
Estimation of urinary creatinine was determined using Jaffe slot's method.
Principle: Creatinine in serum or urine is determined by Jaffe's reaction where creatinine produces quantitatively an orange colour with picric acid in alkaline medium. After incubation for 15 minutes at room temperature for colour development, the intensity of the colour produced is measured at 520nm.
Haptoglobulins: Characterization of serum haptoglobin phenotypes was determined using protein electrophoresis method of polyacrylamide gel and determined using specific peroxidase staining.[19]
Principle: When proteins are separated by electrophoresis through a gel matrix, smaller proteins migrate faster due to less resistance from the gel matrix.

Statistical Analysis
The result obtained was presented as mean ± standard deviation using tables. Data analysis was done using SPSS (version 21.0). Statistical significance was determined using the Student's t-test and One-way Analysis of Variance (ANOVA) and a p-value less than 0.05 was considered significant.

RESULTS

Figure 1 showed the distribution of all subjects under examination. From the four-six (92) subjects recruited for this study, 28 (30.43%) subjects were pregnant women diagnosed of pre-eclampsia, 34 (36.96%) were pregnant women without pre-eclampsia and 30 (32.61%) of the subjects were non-pregnant women without pre-eclampsia used as control subjects.

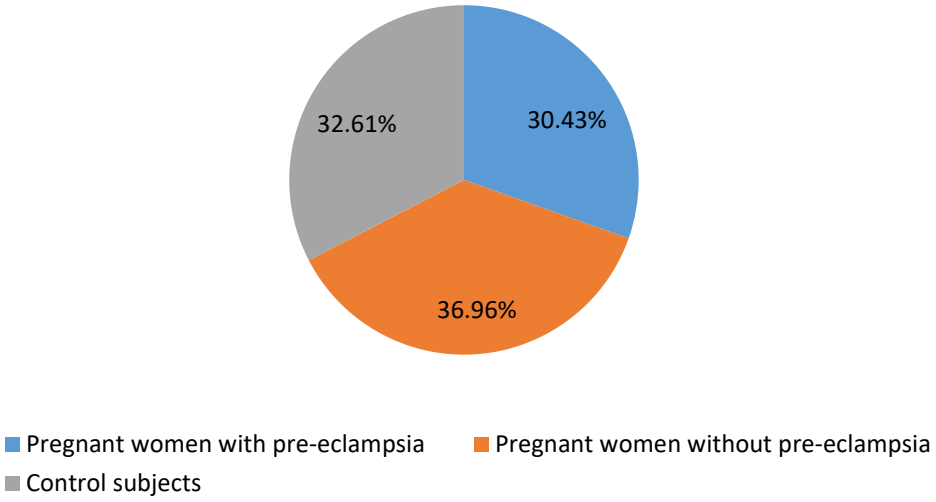

Figure 1. Distribution of all subjects under study

Table 1 showed the BMI, Blood pressure and Urinary protein of the subjects compared with control. From the results obtained, the Body mass index (kg/m^2), systolic blood pressure (mmHg), diastolic blood pressure (mmHg) and urinary protein (mg/creatinine) were significantly higher ($p<0.05$) in subjects with pre-eclampsia compared to control. Similarly, BMI (Kg/m^2), systolic blood pressure (mmHg), diastolic blood pressure (mmHg) and urinary protein (mg/creatinine) were significantly higher ($p<0.05$) in subjects without pre-eclampsia compared to control. Furthermore, the BMI (kg/m^2), systolic blood pressure (mmHg), diastolic blood pressure (mmHg) and urinary protein (mg/creatinine) were significantly higher ($p<0.05$) in pregnant women with pre-eclampsia compared pregnant women without pre-eclampsia.

Table 1. BMI, Blood pressure and Urinary protein of the subjects compared with control

Group	Pre-eclampsia	Non pre-eclampsia	Control	P value for pre-eclampsia vs control	P value for non-pre-eclampsia vs control	P value for pre-eclampsia vs non pre-eclampsia
BMI (Kg/m^2)	2.3±2.31	130±4.11	21.23±1.69	0.0254	<0.0001***	<0.0001***
SBP (mm Hg)	143±5.35	84.48±3.60	115.78±4.41	<0.0001***	<0.0001***	<0.0001***
DBP (mm Hg)	90±4.58	22.25±2.05	74.53±3.41	<0.0001***	<0.0001***	<0.0001***
UPR (mm Hg)	89±13.17	20.17±13.60	30.11±7.80	<0.0001***	<0.0001***	<0.0001***

**Values are significant at p<0.05; **Values are significant p<0.005, ***Values are significant p<0.0001*
***Keys**: BMI - Body mass index, SBP – Systolic blood pressure, DBP – Diastolic blood pressure, UPR – Urinary proteins*

Table 2 showed the correlation of urinary protein with other parameters in pregnant women with pre-eclampsia. The correlation of urinary protein (mg/creatinine) level with other parameters for pregnant women with pre-eclampsia indicates that there was a positive correlation with body mass index, systolic blood pressure and diastolic blood pressure respectively.

Table 2. Correlation of Urinary protein with other parameters in pregnant women with pre-eclampsia

Parameters	r	P value
BMI (kg/m^2)	0.234	0.421
SBP (mmHg)	0.504	0.066
DBP (mmHg)	-0.044	0.881

**Values are significant at p<0.05*

***Keys**: BMI - Body mass index, SBP – Systolic blood pressure, DBP – Diastolic blood pressure*

Table 3 showed the correlation of urinary protein with other parameters in pregnant women without pre-eclampsia. The correlation of urinary protein (mg/creatinine) level with other parameters for pregnant women without pre-eclampsia showed that there was a negative correlation in body mass index and a positive correlation in systolic blood pressure and diastolic blood pressure respectively.

Table 3. Correlation of Urinary protein with other parameters in pregnant women without pre-eclampsia

Parameters	r	p-value
BMI (kg/m^2)	0.297	-0.247
SBP (mmHg)	0.297	0.247
DBP (mmHg)	0.297	0.247

**Values are significant at p<0.05*

***Keys**: BMI - Body mass index, SBP – Systolic blood pressure, DBP – Diastolic blood pressure*

Table 4 showed the Haptoglobin phenotypes in pregnant women with pre-eclampsia and pregnant women without pre-eclampsia. The results obtained showed that in pregnant women with pre-eclampsia, haptoglobin 2-2 (46.1%) has highest frequency compared haptoglobin 1-1 (15.4%) and haptoglobin 2-1 (38.5%). In pregnant women without pre-eclampsia, haptoglobin 1-1 (52.9%) has the highest frequency compared haptoglobin 2-1 (36.39%) and haptoglobin 2-2 (11.8%) respectively. The findings showed that haptoglobin phenotype 2-2 increases the likelihood of a pregnant woman to have pre-eclampsia.

Table 4. Haptoglobin phenotypes in pregnant women with pre-eclampsia and pregnant women without pre-eclampsia

Group	Frequency (%)		
	Hp 1-1	Hp 2-1	Hp 2-2
PW with Pre-eclampsia (n=14)	15.4% (2/13)	38.5% (5/13)	46.1% (6/13)
PW without pre-eclampsia (n=17)	52.9% (9/17)	36.3% (6/17)	11.8% (2/17)
Control (n=15)	57.1% (8/14)	28.6% (4/14)	14.3% (2/14)

Keys: PW – Pregnant women; % - Percentage

Figure 2 showed the comparison between body mass index and urinary protein of pregnant women with pre-eclampsia with respect to haptoglobin phenotypes. From the results obtained, in body mass index and urinary protein, Hp 2-2 was higher, Hp 2-1 was intermediate and Hp 1-1 was lowest in pregnant women with pre-eclampsia.

Figure 3 showed the comparison between systolic blood pressure and diastolic blood pressure in pregnant women with pre-eclampsia with respect to haptoglobin phenotypes. From the results obtained, in systolic blood pressure and diastolic blood pressure of pregnant women with pre-eclampsia, Hp 2-2 was higher, Hp 2-1 was intermediate and Hp 1-1 was the lowest.

Figure 4 showed the comparison of systolic blood pressure and diastolic blood pressure in pregnant women without pre-eclampsia with respect to their haptoglobin phenotypes. From the results obtained, in systolic blood pressure and diastolic blood pressure, Hp 2-2 was

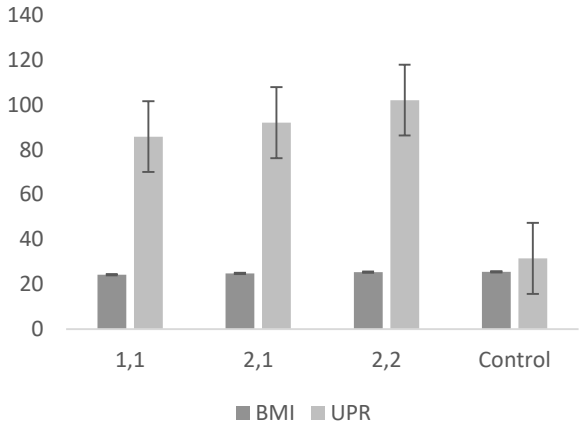

Figure 3. BMI and urinary proteins in pregnant women with pre-eclampsia with respect to their haptoglobulin phenotypes
Keys: BMI = Body mass index, UPR = Urinary protein

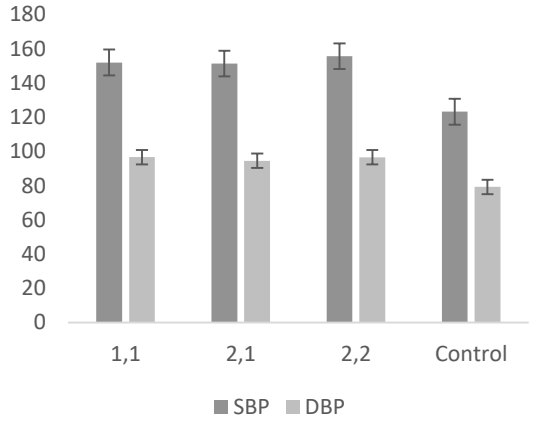

Figure 4. A chart comparing SBP and DBP in pregnant women with pre-eclampsia with respect to their haptoglobin phenotypes
**Values are significantly increase in parameters when compared at p<0.05*
Keys: SBP = Systolic blood pressure, DBP = Diastolic blood pressure

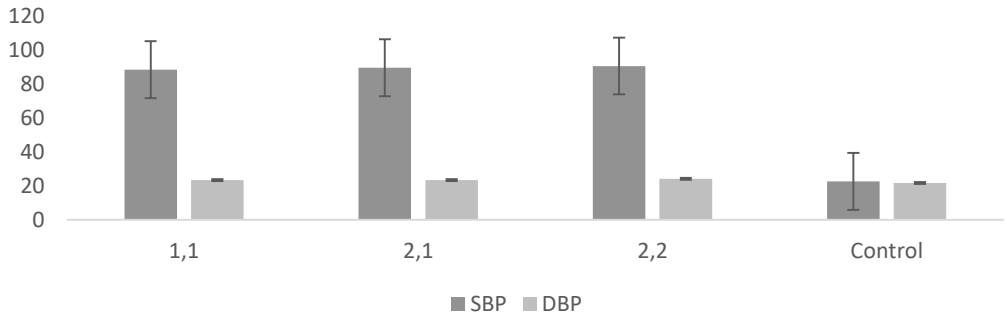

Figure 5. A chart comparing SBP and DBP in pregnant women without pre-eclampsia with respect to their haptoglobin phenotypes
Keys: SBP = Systolic blood pressure, DBP = Diastolic blood pressure

DISCUSSION

Pre–eclampsia is a type of hypertensive disorder and can be defined as the new onset of elevated blood pressure and proteinuria during gestation. Pre-eclampsia occurs in 10-15% pregnancy worldwide. The pathophysiology of pre-eclampsia is based on the vasoconstriction, platelet activation with intravascular coagulation, endothelial dysfunction, and maternal plasma volume contraction [1]. As the development of hypertension has been associated with reduced

antioxidants status and possibly to the possession of some haptoglobin phenotypes [20]. This study was carried out to determine the urinary protein and creatinine levels of different haptoglobin phenotypes among pre-eclamptic population in Ekiti State, Nigeria.

In this study, BMI was significantly higher in both pregnant women with pre-eclampsia and pregnant women without pre-eclampsia compared to control, while BMI was significantly higher in pregnant women with pre-eclampsia compared to pregnant women without pre-eclampsia. The results of this study is in agreement with previous study by Motedayen *et al.* [21] who revealed that there is a significant relationship between BMI and the risk of preeclampsia, so it can be said that BMI may be one of the ways to diagnose preeclampsia. Most observational studies demonstrate a consistently strong positive association between maternal pregnancy body mass index and the risk of preeclampsia. Increasing obesity in developed countries is likely to increase the occurrence of preeclampsia [22]. Consideration should be given to the potential benefits of pre-pregnancy weight reduction programs. With respect to age, BMI was significantly higher in pregnant women with pre-eclampsia in age group 31-40 years compared to control and significantly higher in pregnant women without pre-eclampsia in age group 20-30 years. These findings are not astonishing as obesity has been known to be a risk factor for the development of pre-eclampsia. This finding is in agreement with previous research by Lisonkova & Joseph [23] and Rasmussen *et al*. [24] who reported significantly higher BMI in pregnant women with preeclampsia with respect to age. Congruent with the role of obesity as a risk factor for pre-eclampsia, sedentary lifestyle and sugary food consumption also represents major risk factors of pre-eclampsia in that both contribute to an increase in gestational weight gain.

In this research, SBP and DBP was significantly higher ($p<0.05$) in both pregnant women with pre-eclampsia and pregnant women without pre-eclampsia when compared to control. Furthermore, blood pressure was significantly higher ($p<0.05$) in pregnant women with pre-eclampsia compared to pregnant women without pre-eclampsia. This finding agrees with Qureshi *et al.* [35] who reported that blood pressure was significantly higher in pre-eclamptic and non-pre-eclamptic subjects compared to control. In normal pregnancy, blood volume tends to increase causing a rise in blood pressure [26]. The decrease in uterine placenta blood flow causes blood pressure to flow leading to increase in malignant ways [27]. The causes of pregnancy-induced hypertension and the risk factors associated with it are largely unknown. Apart from nulliparity and previous history of preeclampsia in multiparas, few other risks are universally agreed upon. There are many attributes that have been reported to be related to preeclampsia: maternal age, familial aggregation, race, smoking, socioeconomic level, diet, season and climate, quite apart from the geographical area [28].

The haptoglobins are an abundant human plasma protein that tightly binds haemoglobin during haemolysis and they have reactive oxygen species (ROS) scavenging property.[29] The haptoglobins are acute phase proteins which supports the immune response and protects tissues from free radicals [30]. In this study, Hp 2-2 was predominant (46.1%) in pregnant women with pre-eclampsia, while Hp 1-1 had the lowest incidence (15.4%), with Hp 2-1 being the intermediate (38.5%) compared to control. The findings is in tandem with previous study by Weissgerber *et al.* [31] where haptoglobin phenotypes were associated with pre-eclampsia and its relationship between haptoglobins, kidney disease (proteinuria), and development of hypertension were recorded [31]. Hp 2-2 allele was found in pregnant women with pre-eclampsia, a finding similar to previous study [32]. Haptoglobin phenotype 2-2 is a very large molecule and cannot enter cells and come out readily so therefore reactive oxygen species increase. As reactive oxygen species build up, one kidney works for two persons (mother and foetus) during pregnancy. The other causes of increased blood pressure can be due to release of pro-inflammatory proteins and retention of salt in the kidney which causes vasoconstriction [1].

Urinary protein (mg/creatinine) is the quantification of proteinuria. The urinary protein concentration is determined from individual measurements of urinary protein and urinary creatinine concentration [33]. In this study, urinary (mg/creatinine) was higher in pregnant women with pre-eclampsia and pregnant women without pre-eclampsia when compared to control ($p<0.0001$). Urinary protein was also significantly higher in pregnant women with pre-eclampsia in age group 31-40 years compared to pregnant women without pre-eclampsia in age group 31-40 years. This finding is in consonant with previous report by Demirci *et al.* [34] who reported proteinuria as a major component of preeclampsia with increased urinary protein (mg/creatinine) concentration in pregnant women with pre-eclampsia compared with control.Preeclampsia manifested on a high rate hypertension and proteinuria. The increase in urinary protein seen in pregnant women with pre-eclampsia can be explained in terms of nephrotic syndrome of pregnancy [35]. Nephrotic syndrome is usually because of autoimmunity. Pregnancy itself is also a graft (most times non-self) which is not totally rejected, the result on the kidney is an enlargement of the glomerular pores, allowing large proteins to pass into the urine [36].

CONCLUSION

From this research, haptoglobin characterization and urinary protein (mg/creatinine) estimation during pregnancy is a hallmark of pre-eclampsia. It was also found that pregnant women in their second and third trimester had pre-eclampsia and the Hp 2-2 allele has reactive oxygen species (ROS) scavenging property which is higher in pregnant women with pre-eclampsia compared with pregnant women without pre-eclampsia. Haptoglobin characterization is a more efficient diagnostic tool than urinary protein comparing the specificity and sensitivity of both markers in early detection of pregnancy. Haptoglobin characterization is recommended as major step in prevention of severe pre-eclampsia. Though it is extremely expensive, it provides better clinical outcome.

Conflict of Interest

There are no financial, personal, or professional conflicts of interest to declare.

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مستويات البروتينات البولية والكرياتينين لأنماط ظاهرية مختلفة للهابتوغلوبين بين السكان النيجيريين الذين يعانون من حالة ما قبل الإصابة بالسرطان

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المستخلص

الخلفية والهدف. تعتبر البِيلَة البروتينية مكونًا رئيسيًا لمقدمات الارتعاج التي لا تُفهم الفيزيولوجيا المرضية بشكل كامل. كان الهدف من هذه الدراسة هو تحديد مستويات البروتين والكرياتينين في المسالك البولية للأنماط الظاهرية المختلفة للهبتوجلوبين بين السكان الذين يعانون من مرحلة ما قبل التشنج في ولاية إيكيتي ، نيجيريا. **طُرق الدراسة**. إجمالي عدد 92 شخصًا يتألفون من 28 (30.43٪) من النساء الحوامل المصابات بمقدمات الارتعاج ، و 34 (36.96٪) من النساء الحوامل المصابات بتسمم الحمل ، و 30 (32.61٪) من النساء غير الحوامل في سن الإنجاب دون تسمم الحمل. تستخدم كمواضيع تحكم. تم تحديد البروتين البولي باستخدام 25٪ من حمض السلفوساليسيليك ، وتم تحديد الكرياتينين البولي باستخدام طريقة Jaffe slot ، وتم تحديد الأنماط الظاهرية للهبتوجلوبين باستخدام طريقة الفصل الكهربائي للبروتين من هلام بولي أكريلاميد وتم تحديده باستخدام تلطيخ بيروكسيداز معين. تم عرض النتائج في جداول ورسوم بيانية يعني ± الانحراف المعياري. تم إجراء التحليل الإحصائي باستخدام اختبار الطالب باستخدام برنامج .SPSS اعتبرت قيمة p <0.05مهمة. **النتائج**. أظهرت النتائج التي تم الحصول عليها أنه في النساء الحوامل المصابات بمقدمات الارتعاج ، مؤشر كتلة الجسم ، مؤشر كتلة الجسم ، مؤشر ضغط الدم ، DBP، البول (ملجم / كرياتينين) كانت أعلى بشكل ملحوظ مقارنة بكل من النساء الحوامل غير المصابات بالارتعاج .(P <0.05) كان مؤشر كتلة الجسم و SBP و DBP والبروتين البولي (ملغم / كرياتينين) أعلى بشكل ملحوظ (p <0.05) في النساء اللاتي تعرضن للتشنج مع أليل Hp 2 (Hp 2-2)و .(Hp 2-1 كان أليل Hp 2 الذي له تأثير كسح أقل أعلى في موضوعات ما قبل التشنج. **الخاتمة**. في الختام ، يبدو أن هابتوغلوبين 2 وزيادة البروتين في المسالك البولية يكون أعلى في مقدمات الارتعاج. لذلك ، استنتج هذا البحث أن أليل Hp 2 يمكن أن يكون عاملاً حاسماً في تطور مقدمات الارتعاج.

الكلمات الدالة. بيلة بروتينية ، الحمل ، تسمم الحمل ، ارتفاع ضغط الدم ، هابتوغلوبين.