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ASSESSMENT OF C-REACTIVE PROTEIN LEVELS IN NORMOTENSIVE AND HYPERTENSIVE PREGNANT SUBJECTS IN PORT HARCOURT, NIGERIA

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ABSTRACT

Background: C-reactive protein (CRP) is a blood test marker for inflammation in the body whose levels rise in response to inflammation. The elevation has been linked to atherosclerosis. Because of the inflammatory component of atherosclerosis, elevated CRP levels have been linked with cardiovascular disease. **Objective:** To evaluate some cardiovascular disease risk status such as C-reactive protein in pregnant Normotensive and hypertensive pregnant women and compare it with the corresponding levels in non-pregnant normotensive women. **Method:** This study was conducted in the Department of Medical Laboratory Science, Rivers State University, Port Harcourt. Nigeria. A total of 300 women were registered for the study after taking informed conscent. 100 of them were pregnant hypertensives, 100 were pregnant normotensives and 100 non pregnant normotensives as control. All relevant information was recorded on a predesigned questionnaire. HsCRP levels were measured in the 200 normotensive and hypertensive pregnant women, including systolic and diastolic blood pressure, and BMI: and compared with that of the control. BMI was calculated as weight in kg divided by the square of height in metres. **Result:** Mean values of HsCRP between the two case groups and control were significant at $p<0.05$. Age, BMI, Systolic and Diastolic blood pressures were also significant at $p< 0.05$. BMI, Systolic and diastolic, and HsCRP were statistically significant when HPW were compared with NPW: Age, BMI, Systolic, diastolic and HsCRP were significant when HPW were compared with NNPW. Only BMI was significant when NPW was compared with NNPW. HsCRP was not significant .90% of HPW at 38.72±6.56, 14 % of NPW at 36.16±12.74, and 2% of NNPW at 31.38±0.88kg/m^2 were obese. 58% of NPW at 27.24±1.34, 31% of NNPW at 26.78±1.40 and 10% of HPW at 27.41±1.14kg/m^2 were overweight. 2% of NNPW at 17.20±1.23 were deficient, others were normal. HPW had the highest percentage of HsCRP for increased risk (62%) at 8.32±8.09, and the least percentage for low risk (7%) at 0.61±0.34mg/l. NNPW had the highest percentage for low risk(42%) at 0. 40±0.24mg/l and almost half of HPW for increased risk (32%) at 7.0±3.33mg/l. NPW had same percentage for high risk and low risk, (36%) at 7.03±4.51 and 0.31±0.33mg/l. 28% was recorded for moderate risk at 2.19±0.53mg/l using the different risk group categories. **Conclusion:** C-reactive protein as a marker of inflammation was elevated in normal pregnancy and further increased in hypertensive pregnant state.

KEYWORDS: C -reactive protein, Normotensive, Hypertensive, Pregnant women.

INTRODUCTION

Heart disease remains the leading cause of death in women globally (Brown et al., 2013). Evaluation of cardiovascular disease (CVD) risk factors and preventive measures in women need to exceed the established CVD risk factor screening to include pregnancy states. (Roberts and Hubel, 2010). There is increasing evidence that hypertension in pregnancy is an independent under-recognized risk factor for CVD.Researchers have continued to say that hypertensive pregnant women are at greater risk of cardiovascular and cerebrovascular events years after their pregnancies compared to normotensive pregnant women (Smith et al., 2001). The likely mechanism for this association is that hypertensive disorders of pregnancy and CVD share several common risk factors, such as obesity, diabetes, and renal disease that contribute to endothelial dysfunction and lead to hypertension in pregnancy and CVD at different times in a womans life; hypertension in pregnancy itself could modify the future risk of CVD by inducing long-term metabolic and vascular changes.(Garovic and Hayman, 2007). Women with a history of pre-eclampsia are at greater risk for CVD after pregnancy for reasons that remain unclear. Studies have shown that inflammation,

dyslipidemia, and insulin resistance are associated with increased risk of pre-eclampsia (Hubel et al, 2008). Irrespective of the underlying mechanism of association, a biomarker that might identify women at increased CVD risk among those with hypertensive pregnancies may contribute positively to their clinical management (Brown et al, 2013). C - reactive protein has been shown to be a sensitive marker of tissue damage and inflammation (Tuomisto et al, 2006). Pre eclampsia is a multisystem disorder affecting the central nervous system, kidney,liver and coagulation system(Reslan and Khalil(2010)., leading to organ damage (Roberts,1998).The increased levels of CRP above the reference limits for the healthy pregnant population is an indication of some form of organ dysfunction (Stillman and Karumanchi,2007). There is a significant relationship between CRP and increasing blood pressure indicating that inflammation is involved in tissue damage which occurs in preeclampsia (Udenze et al, 2015). Inflammation itself has recently been reported to induce endothelial damage (Koenig and Pepys (2002). Moreso, since inflammation is believed to have a role in the pathogenesis of cardiovascular events, measurement of markers of inflammation has been proposed as an improvement method used in the prediction of the risks of these events (Ridker, 2007). C-reactive protein is a marker of systemic inflammation that has been associated with increased risk of incident myocardial infarction and stroke (Ridker and Hennekens, 2000). Inflammation is thought to play a role in the development of hypertension, and higher CRP levels are found in individuals with elevated blood pressue (Bermudez et al, 2002). Higher levels of C-reactive protein may increase BP by reducing nitric oxide production in endothelial cells(Venugopal et al, 2002); resulting in vasoconstriction and increased production of endothelin 1(Lau et al, 2005).Inflammation has been shown to correlate with endothelial dysfunction (Yudkin et al, (1999), and relate to the angiotensin system(Brasier et al 2002). Clinical data linking inflammation with incident hypertension are scarce (Yudkin et al, 1999. This work is aimed at assessing C-reactive protein levels in normotensive and hypertensive pregnant women in Port Harcourt, Nigeria.

MATERIALS AND METHODS

This study was conducted jointly by the Department of Medical Laboratory science, RSU, Ekoistic and Biotek laboratories in Port Harcourt. 300 women were enrolled in our study after informed oral and written consent. The study subjects were divided into three groups. 100 Hypertensive pregnant women (HPW), 100 Normotensive pregnant women (NPW) attending antenatal clinic at the Braitwaite Memorial Specialist Hospital; and 100 Normotensive Non Pregnant Women as control.The control group were healthy women between 18 and 30 years. All participants were nonsmokers, non-alcoholics and there was no positive family history of CAD in the women. Hypertension was defined as BP≥140/90mmHg on several occasions. Anthropometric assessment was done, using a meter rule and a weighing balance, which included Height (meters), Weight (kilograms) and calculation of Body Mass Index (BMI) as weight (kg)/Height (m^2). A detailed history of clinical examination was recorded for all participants. 2ml of peripheral venous blood was collected from anticubital vein using a dry, disposable syringe under sterile conditions in a sterile plain bottle. Serum was separated by centrifugation at 3000rpm for 15minutes, stored in refrigerator until ready for use; and assayed for HsCRP. The test was carried out in a semi-automated clinical chemistry auto analyzer (MAP LAB PLUS). Using bio check hsC-Reactive protein concentration in Human Serum; Serial No 6128, code RM2060-8 Biochemical System International.

RESULTS

Table 1: Anthropometric and biochemical indices among the study groups.

Parameter	NNPW (n=100)	NPW (n=100)	HPW (n=100)	Fvalue	Pvalue
Age (yrs)	28.68± 6.60	30.25± 9.74	32.70 ± 5.30	11.93	<0.001
BMI (Kg/m^2)	23.74± 2.85	27.36± 1.46	37.59 ± 7.10	136.44	<0.001
Systolic (mm/Hg)	100.80±3.94	104.10±5.48	153.40±19.24	306.40	<0.001
Diastolic(mm/Hg)	70.20± 1.41	66.80± 6.20	96.10±14.35	194.70	<0.001
HsCRP (mg/l)	2.90 ± 3.53	3.45 ± 4.14	5.88 ± 7.17	20.97	<0.001

Table 2: The ANOVA Post-Hoc findings within the study group.

Parameters	NNPW vs NPW (P. Value)	NNPW VS HPW(P-Value)	NPW VS HPW(P-Value)
Age	0.136	<0.001	0.010
BMI	<0.001	<0.001	<0.001
Systolic	0.311	<0.001	<0.001
Diastolic	0.100	<0.001	<0.001
CRP	0.217	<0.001	<0.001

Table 3: Pearson's classification of Risk with CRP.

	Low (0-1)mg/L	Moderate (1-3)mg/L	High > 3mg/L
NNPW	0.40±0.24 (42%)	1.70±0.50 (26%)	7.00 ±3.33 (32%)
NPW	0.31±0.33 (36%)	2.19± 0.53 (28%)	7.03 ±4.51 (36%)
HPW	0.61±0.34 (7%)	1.98± 0.56 (31%)	8.32 ±8.09 (62%)

Table 4: Risk profile of subjects using BMI.

	Deficient	Normal	Over weight	Obese
	<18.50Kg/m^2	18.50-24.50Kg/m^2	25- 29.50Kg/m^2	>30Kg/m^2
NNPW	17.20±1.23 (2%)	22.33±1.45 (65%)	26.78±1.40 (31%)	31.38±0.88 (2%)
NPW	-	23.20±0.98 (28%)	27.24±1.34 (58%)	36.16±12.74 (14%)
HPW	-	-	27.41±1.14 (10%)	38.72±6.56 (90%)

A total of 300 women were categorized as 100 Normotensive pregnant women (NPW), 100 Hypertensive pregnant Women (HPW) and 100 Normotensive Non Pregnant Women (NNPW).Anthropometric parameters (Age, BMI, Systolic and Diastolic Blood Pressures) and HsCRP mean and standard deviation are shown in Table 1. The three categories of women differed significantly in mean values for Age, BMI, Systolic and Diastolic Blood Pressures and HsCRP at P<0.05. Table 2 , uses the ANOVA Post –Hoc findings to differentiate between two groups.There was a significant difference between NNPW and HPW at p<0.05, No significant difference was recorded between NPW&HPW, and NNPW & NPW for Age. There was a significant difference among the three groups compared for BMI. No significant difference was recorded for systolic among the NNPW & NPW; but for NNPW&HPW and NPW& HPW at p<0.05. Diastolic was not significant for NNPW&NPW, But significant at p<0.05 for NNPW&HPW and NPW&HPW. HsCRP was significant at p<0.05 for NNPW&HPW and NPW&HPW; but not significant for NNPW &NPW. Table 3 shows the classification of risks with CRP using pearsons, 62% of HPW were classified under high risk at 8.32±8.09, 36% NPW at 7.03±4.51, and 32%of NNPW at 7.0±3.33mg/l. The highest percentage for low risk was for NNPW (42%) at 0.4±0.24, NPW (36%) at 0.31±0.33 and HPW (7%) at 0.61±0.34mg/l. The rest were classified as moderate. Table 4, shows the risk profile of subjects using BMI. 90% of HPW were obese at 38.72±6.56, 14% of NPW at 36.16±12.74 and 2% of NNPW at 31.38±0.88kg/m^2. Also, 58% of NPW were overweight at 27.24±1.34, 31% of NNPW were overweight at 26.78±1.40 and 10% of HPW at 27.41±1.14. Non was recorded for normal and deficient in HPW: and non was recorded for deficient in NPW. The highest percentage (65%) at 22.33±1.45kg/m^2 normal were for NNPW.

DISCUSSION

Our results indicate that hypertensive pregnant women are associated with elevated CRP levels and BMI .According to Garovic et al.,2010, hypertensive pregnant women had a 1.9 fold increased risk of having a subsequent diagnosis of hypertension and a 2.1 fold increased risk of stroke in later life, compared with women who had a history of normal blood pressure in pregnancy.Among the women in this study, CRP levels were twice increased in HPW compared with NPW and NNPW.This agrees with Brown et al., 2013 that there may be a role for the measurement of CRP in conjunction with blood pressure and modifiable CVD risk factors even if, timing of such screening is not yet established. There was also a correlation between CRP and BMI in this work. The highest percentage (90%) of HPW were obese and the highest percentage (62%) of HPW were categorized under high risk. This implies that CRP is a sure guide for at risk women for CVD disease; moreso, obesity on its own being a modifiable risk factor for cardiovascular disease. Our results indicate that CRP is an inflammatory marker, and shows an inducement of inflammation in pregnancy. Hypertension in the pregnant women made inflammation more in HPW.This agrees with Kaptoge et al.,2010 that inflammatory state may be one of the shared mechanisms leading to hypertensive pregnancy disorders and CVD at different times in a womans life. According to Von Versen-Hoeynek et al., 2009, CRP levels are elevated even in normal human pregnancy as was seen in this work, and further increased in preeclamptic pregnancies as early as 13 weeks gestation as was also seen in this work even if gestation period was not specified. Sesso et al., 2003 and Qui, et al.,2004 link elevated CRP levels to increased risk for the development of hypertension,CVD, ischemic stroke and vascular mortality as shown in our findings. This agrees with Ridker et al., 2000 that CRP seems to have a prognostic role for CVD in women. This means that CRP may be useful for CVD risk assessment in assymptomatic intermediate- risk women 60 years of age or younger.(Collaboration CRPCHDG,2011). This work agrees with Keavney, 2011 and Brown et al., 2013 that CRP could be applied as a biomarker of the severity of atheromatous disease and identifying individuals at risk for CVD. Brown et al., 2013 in their findings gave evidence that a history of hypertension in pregnancy is associated with elevated CRP levels later in life, suggesting that the inflammatory response may persist years after the hypertensive pregnancies; But our study gives evidence that hypertension in pregnancy is associated with elevated CRP levels immediately.

CONCLUSION

Hypertension in pregnancy is associated with elevated CRP levels, BMI and obesity could predispose to Cardiovascular disease later in life.

RECOMMENDATION

C - reactive protein should be recommended as a screening test for all women of child bearing age, as a prognosis for cardiovascular risk.

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