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A comparative study of physiological and hematological profile of preeclampsia in relation to body mass index

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ABSTRACT

Preeclampsia (PE) is a major cause for maternal morbidity and mortality globally. Studies showed that body mass index (BMI) is one of the risk factors of PE. In this study, the BMI and physiological and hematological profile was associated to predict the severity of preeclampsia, so that proper counseling and antenatal care could be given for good pregnancy outcome. The study was carried out on 100 healthy normotensive pregnant and 100 diagnosed preeclamptic women. Healthy pregnant and PE were categorized into three groups based on BMI, on WHO criteria. BMI group 1 (<25 Kg/m^2) considered as normal, group 2 (25 – 30 Kg/m^2) as over-weight and group 3 (>30 Kg/m^2) obese. Systolic blood pressure (SBP), diastolic blood pressure (DBP), hemoglobin (Hb), white blood corpuscles (WBC), red blood corpuscles (RBC) and platelets were compared in control and PE groups. Then the respective control groups were compared with PE groups. The prevalence of overweight was more in PE groups when compared to normotensive pregnancy (P=0.004). Statistically, a significant difference was not observed in BMI group1, group 2 and group 3 of control and in PE in relation to SBP, DBP, Hb, WBC, RBC and platelets. But a statistically significant difference was observed when respective control groups were compared with PE (P<0.005). BMI does not have any statistically significant association with SBP, DBP, Hb, WBC, RBC and platelets. BMI could not be considered as a predictor or severity of preeclampsia.

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INTRODUCTION

Preeclampsia (PE) is a pregnancy-associated disorder of humans, with the development of hypertension, proteinuria, after 20 weeks of gestation in women without any history of medical problems. PE occurs in about 2–8% of pregnancies (Moodley, 2004). PE is the common medical complication of pregnancy and the prevalence of PE is on rise alarmingly. Significant maternal mortality and morbidity are consociated with PE, accounting for about 50,000 deaths worldwide annually (Duley, 2009). Both mother and foetus affected by this disorder. Women with PE develops microangiopathy,

which affects the major organs like kidney, liver and brain, leads to acute renal failure, liver ailments, low platelets count, haemolytic anaemia, visual impairment, stroke, convulsion, placental abruption and maternal death. In PE, there is intrauterine growth restriction, results in foetus prematurity. Women suffered from PE are at high risk of developing health complication in future (Bellamy *et al.*, 2007).

The major contributing factors for PE are multifetal pregnancy, nulliparity, previous history of preeclampsia, obesity, diabetes mellitus, systemic lupus erythematosus, first pregnancy after the age of 35 years, smoking and African American race. The relationship between these contributing factors and the occurrence of PE is not very well understood. The role of ethnicity suggests, there may be a substantial role of genetic factors in the development of PE. Various theories on the etiology of PE indicate that the disorder is characterized by endothelial dysfunction, unusual maternal response to inflammation, improper hemodynamic status and derange immunity (Maynard and Karumanchi, 2011). The exact cause that amalgamates the deranged immune, inflammatory and vascular responses remains to be elucidated.

The eminent features of PE are, development of the ischemic and hypoxic placenta, oxidative stress, results in endothelial dysfunction. The precise triggers that lead to endothelial dysfunction are the imbalance in the synthesis of pro and antiangiogenic growth factors by the diseased placenta and their inappropriate released into the maternal circulation. Studies are indicating that ischemic placenta synthesizes more antiangiogenic growth factors like soluble Fms-like tyrosine kinase 1 (sFlt1) and soluble endoglin, which intern inhibits the formation of proangiogenic factors like placental growth factor (PlGF), vascular endothelial growth factor (VEGF). The perfuse placenta and also the mononuclear cells are the major source of sFlt1 in preeclampsia (Hui *et al.*, 2012). The abundance of sFlt-1 reduces the synthesis of nitric oxide (NO) by inhibiting the binding of VEGF onto its receptor, results in reduction of phosphorylation of endothelial nitric oxide synthase (eNOS). Less bioavailability of NO triggers the improper angiogenesis and reduced vasodilation, resulting in vascular endothelial dysfunction. Along with high BP, proteinuria, edema, PE, also clinically manifested as hemolysis, thrombocytopenia, raised level of liver enzymes, unifying the HELLP syndrome (Gélinas *et al.*, 2002).

Preeclampsia is an idiopathic disorder and it is speculated that the occurrence may increase in obesity and overweight. One of the major attributing factors of PE and cardiovascular disease is high body mass index (BMI) (Bodnar *et al.*, 2007). Worldwide prevalence of obesity is increasing at an alarming rate. Globally, obesity is the major concern for women of reproductive age and one of the predisposing factor for adverse pregnancy. Excessive gestational weight gain may have an association with adverse birth and pregnancy outcomes (Chung *et al.*, 2013). Among European women, the prevalence of obesity ranges from 10–25%. A study suggests that women with normal weight, less prone to develop PE than overweight women (Knight *et al.*, 2010). Whether obesity and overweight is the early or late-onset attributing factor for PE, is not clearly understood, studies are showing contradictory findings. Very few studies with diverging results available regarding the role of BMI on PE separately. The relationship between gestational BMI and preeclampsia is still inconclusive and also whether maternal weight could predict the severity after preeclampsia has already developed is still not clear.

Systolic and diastolic blood pressure have been shown to correlate with increased cardiovascular complications (Glynn *et al.*, 1995). Diabetes mellitus, family history and high body fat levels are the predisposing factors for hypertension (Rajakumar *et al.*, 2012; Priyadarshini *et al.*, 2019). Obesity was shown to be an important risk factor for cardiovascular ailment and an indirect risk factor because of its effect on hypertension. Not much data is available regarding the relationship between the BMI and blood pressure and hematological parameters, particularly in PE. Studies are not available in India regarding the association between physiological and hematological parameters with BMI. The knowledge of the effect of obesity on hypertension is very important as it is a modifiable risk factor. The study of the hematological profile is also important to predict the severity of PE. The present study was undertaken to see the association between BMI and physiological and hematological profile to predict the risk or severity of preeclampsia.

MATERIALS AND METHODS

Study Group

One hundred diagnosed preeclamptic pregnant women and one hundred healthy normal pregnant women without any complications were the participants of this study. For both normotensive and PE women, gestational age was 30 to 31 weeks. The maternal age was 25 to 30 years. Based on BMI, healthy pregnant and preeclampsia (PE) were categorized into three groups, as per WHO guidelines. Group 1, normal (BMI < 25 kg/m^2), group 2, over-

Table 1: Age distribution data in normal healthy pregnant (control) and preeclampsia (PE)women.

Group	BMI Category	Total Numbers(n)	Median	25%	75%
Normal Healthy Pregnant women(Control)	Group 1	21	31	30	32
	Group 2	38	30	29	31
	Group 3	41	30	29	32
Preeclampsia(PE)	Group 1	06	31	30.75	32.3
	Group 2	37	30	29.50	31.5
	Group 3	57	30	29	31

The median values among the different groups are calculated by Kruskal-Wallis one way analysis of variance on ranks, where H= 10.148 and P=0.071.

Table 2: BMI categorization in normal healthy pregnant (control) and preeclampsia (PE)women.

BMI Category	Group	BMI Range	Numbers	Percentage (%)
Group 1	Normal healthy Pregnant women(Control)	<25	21	21%
Group 2		25 - 29	38	38%
Group 3		>30	41	41%
Group 1	Preeclampsia(PE)	<25	06	06%
Group 2		25 - 29	37	37%
Group 3		>30	57	57%

Chi-square = 10.959 and P = 0.004.

weight (BMI 25 – 30 Kg/m^2) and group 3, obese (BMI > 30 Kg/m^2) (WHO Obesity, 2000).

Diagnosis of preeclampsia

According to American College of Obstetricians and Gynaecologist (ACOG Practice Bulletin, 2002), diagnosis of PE was made by an increasing of SBP more than 140 mmHg and DBP more than 90 mmHg, measured on two separate times at two hours apart, with proteinuria, characterized by excretion of protein greater than 0.3gm in 24 hours or 1+ proteinuria by dipstick analysis. All the preeclamptic women were fully normal or without having any medical complications such as hypertension, renal disorder and proteinuria, before 20 weeks of pregnancy (inclusion criteria). Women with PE, included in this study, on their admission to the Department of Obstetrics and Gynaecology, College of Medicine and JNM Hospital, (Kalyani, Nadia) after the confirmation of diagnosis.

100 normal healthy pregnant women with singleton pregnancy, without any systematic illness like cardiovascular disease, endocrinological disorder, diabetes mellitus and hypertension were included in this study during their routine visit. Women had a history of smoking, alcohol intake and multiple pregnancies were excluded from the study. Arterial blood pressure for the control group was never exceeded 135/85mmHg.

Measurements

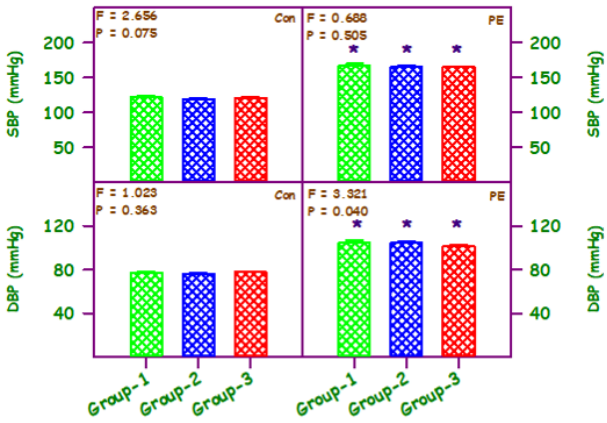

Figure 1: Comparisonof systolic blood pressure (SBP) and diastolic blood pressure (DBP) in normal pregnant (Con) and preeclampsia (PE) in group 1, group 2, and group 3.*Statistically significant from the respective normal pregnant.

Height was measured by a measuring tape with barefoot to the nearest 0.5 cm. For the weighing measurement, a portable electronic battery operated weighing scale (Tanita Corporation of America Inc., USA) was used. Weight in kilograms was recorded by taking the necessary precaution to ensure accuracy. The weighing machine was standardized by a 10 kg weight. BMI was calculated by using the definition, weight in kilograms divided by height in m^2. Three categories of BMI were spec-

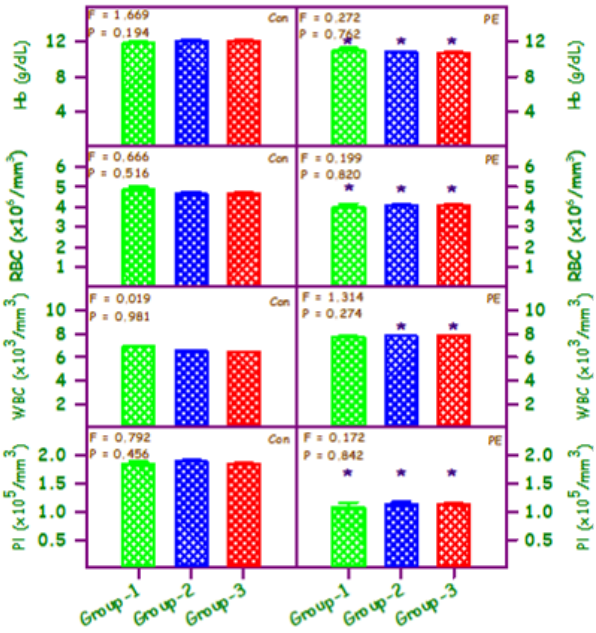

Figure 2: Comparison of hemoglobin (Hb), red blood corpuscles (RBC), white blood corpuscles (WBC)and platelets (Pl) in normal pregnant (Con) and pre-eclampsia (PE), in Group1,Group 2 and Group 3. *Statistically significant from the respective normal pregnant.

ified as normal (<25 kg/m^2), over-weight (25 – 30Kg/m^2) and Obese (> 30 Kg/m^2) as per the guideline of WHO. For the measurement of blood pressure, each participant was asked to sit for 15 minutes with legs unfolded, back supported, feet rest on the floor. The left arm of the participant was placed on the table facing the palm upward and then appropriate size cuff was wrapped on the left arm, 1 – 2 cm above the elbow joint and SBP and DBP were recorded with the help of a stethoscope. Hypertension was categorized following the guideline.

Hematological parameters

For hematological profile, 2mL of the venous blood sample was collected in the EDTA-K2 vacutainer from the preeclamptic women after their diagnosis and before administering any medicine and from the healthy pregnant women during their normal routine checkups. Hemoglobin (Hb), red blood cell (RBC), white blood cell (WBC) and platelets were measured using an automated quantitative hematology analyzer (Sysmex, XP 300 cell counter, Japan).

Ethical issues

Prior approval was obtained for this investigation from the Institutional Ethics Committee of College of Medicine and Jawaharlal Nehru Memorial Hospital, (No.F24/Pr/CMJNMH/IEC/14/93/(5), dated 23 April 2015). A participant information sheet was prepared in two languages (English and Bengali) about the investigation. Signed consent was taken from every individual participant and privacy was asserted. The duration of the study was from May 2015 to January 2018.

Statistical analysis

Data were represented as mean ± SEM. One way analysis of variance (ANOVA) was used to test differences between the 3 independent BMI groups of control and preeclampsia, with Student Newman Keul's multiple comparison tests. Unpaired 't' test was done for comparison, between the respective BMI groups of control and preeclampsia. A probability of 0.05 or less considered as statistically significant. The age was analyzed by Kruskal-Wallis one way analysis of variance on ranks. BMI association between control and preeclampsia group was done by the Chi-square test. SigmaPlot 13 (systat software, USA) was used for statistical analysis and graph plotting

RESULTS AND DISCUSSION

The median age of BMI category of control group1, group 2 and group 3 were 31, 30, 30 respectively and preeclampsia group1, 2 and 3 were 31, 30 and 30, respectively. The median was statistically not significant between the groups (P= 0.071) (Table 1).

The number of women in control group 1, group 2 and group 3 were 21, 38, 41 respectively and in preeclampsia group 1 group 2 and group 3 were 6, 37, 57 respectively. The prevalence of underweight in the control group (BMI less than 18.5 kg/ m^2) was 0%. The prevalence of underweight BMI in the preeclampsia group also was 0%. When the prevalence of BMI category of control and preeclampsia was analyzed by the Chi-square test, it was statistically significant (P=0.004) (Table 2).

The mean value of SBP for control groups were 122.1, 119.1, 121.0 mmHg respectively. It was statistically non-significant (P= 0.075). The mean value of SBP in PE groups were 167.3, 166.0, 164.7 mmHg respectively. Statistically, no significant difference was observed (P= 0.505). There was 37%, 39.4% and 36.2% increase of SBP in PE when respective control groups were compared with PE groups (P<0.001) (Figure 1).

The mean value of control group1, group 2 and group 3 of diastolic blood pressure (DBP) were 77.4, 76.4, 77.6 mmHg respectively. It was not found to be statistically significant (P= 0.363). The mean value of DBP in PE group1, group 2 and group 3 were 105.2, 104.7, 102.0 mmHg respectively. It was also not found to be statistically significant (P= 0.040). Respective control groups, when compared with PE

groups, there was 35.8%, 37% and 31.4% increase of DBP in PE (P<0.001) (Figure 1).

The mean value of Hb in control groups were 11.8, 12.1, 12.0 gm/dL respectively. It was statistically not significant (P= 0.194). The mean value of Hb in PE groups were 10.9, 10.7, 10.6 gm/dL respectively. It was also statistically not significant (P= 0.762). When respective control groups were compared with PE, there was 7.6%, 11.6 % and 11.7 % decrease of Hb in PE (P<0.001) (Figure 2).

The mean value of WBC in control groups, were 6.914, 6.517, 6.453 ($x10^3/mm^3$), respectively. No statistically significant difference was observed (P= 0.274). The mean value of WBC in PE groups were 7.728, 7.779, 7.828 ($x10^3/mm^3$) respectively. It was also not statistically significant (P= 0.981). Respective control groups, when compared with PE, groups 2 and 3, showed a significant increase in PE (P<0.001), but group 1 was statistically not significant (P= 0.258). There was 11.8%, 19.4% and 21.3 % increase of WBC in PE (Figure 2).

The mean value of RBC in control groups, were 4.84, 4.65, 4.66 ($x10^6/mm^3$) respectively. It was statistically not significant (P= 0.516). The mean value of RBC in PE groups were 3.98, 4.09, 4.07($x10^6/mm^3$) respectively. It was also statistically non-significant (P= 0.820). When respective control groups were compared with PE groups, there was 17.8%, 12.0 %, and 12.7 % decrease of RBC in PE (P<0.001) (Figure 2).

The mean value of platelet in control groups were 1.856, 1.890, 1.853 ($x10^5/mm^3$) respectively. No statistically significant observation was made (P= 0.456). The mean value of platelet in PE groups, were 1.081, 1.133, 1.134 ($x10^5/mm^3$) respectively. It was also statistically not significant (P= 0.842). When respective control groups were compared with PE groups, there was 41.8%, 40.0 % and 38.8 % decrease of platelet in PE (P<0.001) (Figure 2).

BMI proposed to be one of the clinical predictor for the development of preeclampsia, but the data is limited. Obesity during pregnancy has been on the rise. Reports are stating that more than 20% of pregnant women fall into the obesity criteria. Maternal obesity is one of the important contributing factor for preeclampsia. The relationship between BMI and obesity may predict, those are having a risk of developing PE during pregnancy (TE O'Brien, Ray JG, Chan WS, 2003). Chi-square analysis showed, preeclampsia is associated with over-weight women (P<0.001). This finding is in accordance with the earlier studies. Studies showed that maternal pregnancy BMI is correlated positively for the progression of PE and an increase of BMI may increase the occurrence of PE (Belogolovkin *et al.*, 2007; Bodnar *et al.*, 2005).

One study suggested that obese children are more likely to develop hypertension (Falkner *et al.*, 2006). A study from China reported that people with overweight and obesity have a strong correlation with SBP and DBP, and found that children between 7 - 15 years and adolescents are at risk of developing hypertension (Wang *et al.*, 2004). Another study identified that BMI is significantly related to SBP and DBP in adolescents (Chorin *et al.*, 2015). Very few studies are available on the effect of BMI on blood pressure, especially with PE. In the present study, no association was observed between BMI and blood pressure either in control or in PE groups during pregnancy. Statistically, significant variation was observed in systolic and diastolic blood pressure, when respective control groups were compared with PE groups (P<0.001). These findings are in accordance with the other studies (Roberts *et al.*, 2003; Brennan *et al.*, 2014).

Abnormal placental development in PE leads to reduction of uterine perfusion pressure (RUPP) in the placenta, results in placental ischemia or hypoxia. Ischemic placenta synthesizes various biomolecules like cytokines, hypoxia-inducible factors, free radicals, angiotensin II (Mistry *et al.*, 2013). Improper placentation also responsible for an imbalance in the formation of pro and antiangiogenic factors, like VEGF, PLGF and sFlt -1, sEng, the net effect is, reduced synthesis of NO and vasoconstriction of spiral arteries (Bai *et al.*, 2013; Siddiqui *et al.*, 2013).Another biomolecule, asymmetric dimethylarginine (ADMA), found more in the maternal circulation of PE, reversibly inhibits the eNOS which further reduces the NO biosynthesis. Decreased NO bioavailability leads to vascular endothelial dysfunction and vasoconstriction, generalized endothelial cell (EC) dysfunction, renal glomerular endotheliosis and decrease in renal plasma flow, leading to hypertension (Ehsanipoor *et al.*, 2013).

The present study showed no association between BMI and Hb, RBC, WBC and platelets in control and PE groups, but statistically significant increase of WBC and decrease of Hb, RBC and platelet was observed when respective control groups were compared with PE groups. Low platelet, RBC and Hb and high WBC are in accordance with other studies (Sitotaw *et al.*, 2018; Sibai BM, 2004). Inadequate placentation in PE induces over expression of major histocompatibility complex (MHC), natural killer (NK) cells, integrins and matrix metalloproteinases (MMPs) which is responsible for shal-

low invasion of trophoblastic cells, poor remodeling of extracellular matrix (ECM) and spiral arteries, resulting in imbalance in angiogenic and antiangiogenic state and oxidative stress, which leads to endotheliosis and progression to HELLP syndrome (Hemolysis, elevated liver enzymes and low platelet count) (Vaught *et al.*, 2016).

CONCLUSIONS

Though BMI has been shown to be an important factor in cardiovascular disease, type 2 diabetes mellitus and in chronic kidney disease. In this study, there was no association between BMI and systolic and diastolic blood pressure, hemoglobin, red blood corpuscles, white blood corpuscles and platelets in PE. Overweight and obesity are more common in pregnant women and BMI does not have any additional adverse effect on physiological and hematological profile during pregnancy.

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