

# Obesity and preeclampsia: Role of fibrinogen and C-reactive protein

BABAH OA, OLUWOLE AA, AYANBODE OS<sup>1</sup>, OHAZURIKE EO<sup>1</sup>

Department of Obstetrics and Gynaecology, Faculty of Clinical Sciences, College of Medicine, University of Lagos/Lagos University Teaching Hospital, <sup>1</sup>Department of Obstetrics and Gynaecology, Lagos University Teaching Hospital, Idi-araba, Lagos, Nigeria

## ABSTRACT

**Objective:** This study aimed at ascertaining the relationship between obesity and preeclampsia and the role of fibrinogen and C-reactive protein (CRP).

**Study design:** This was a case-control study involving 200 pregnant women, 100 of whom were healthy pregnant women, and 100 preeclamptic women, matched for age, parity, and gestational age. Information about their sociodemographic characteristics was obtained and body mass index (BMI) calculated using their height and weight at recruitment. Their plasma fibrinogen and CRP levels were assayed using enzyme-linked immunosorbent assay (ELISA) technique. All data collected were subjected to statistical analysis using Epi Info.

**Results:** The mean ( $\pm$ SD) age of subjects was  $31.1 \pm 4.51$  years. The preeclamptic subjects were found to have higher BMI ( $30.04 \pm 6.06$  kg/m<sup>2</sup>) compared to the normotensive pregnant women ( $28.08 \pm 2.97$  kg/m<sup>2</sup>). However, this was not statistically significant. Using mean arterial blood pressure as an indicator of disease severity, with a cut-off of 125 mmHg, it was found that severe preeclampsics had higher BMI ( $30.18 \pm 6.49$  kg/m<sup>2</sup>) compared to women with mild form of the disease ( $29.83 \pm 5.48$  kg/m<sup>2</sup>) but this difference was not statistically significant ( $P = 0.2131$ ). There was also statistically significant association between BMI and high-sensitivity C-reactive protein (hsCRP) ( $P = 0.0000$ ), and between BMI and plasma fibrinogen levels ( $P = 0.0000$ ).

**Conclusion:** It can thus be inferred from this study that obesity elicits inflammatory response which might predispose to the development of preeclampsia. Lifestyle modifications such as dietary control, exercise, and pre-pregnancy weight reduction may help in reducing the incidence of preeclampsia.

**Key words:** C-reactive protein; obesity; pre-eclampsia; plasma fibrinogen; severity of the disease.

## Introduction

Preeclampsia is a multisystemic disorder characterized by hypertension in previously normotensive pregnant woman with associated proteinuria, occurring after 20 weeks gestation.<sup>[1]</sup> It is a common cardiovascular complication that may arise in pregnancy, and poses danger to both mother and baby. Its etiology is unknown but many postulations have been made overtime. The worldwide prevalence of preeclampsia is 2–8%.<sup>[2]</sup>

Obesity is defined as body mass index (BMI) of 30 kg/m<sup>2</sup> or more. The prevalence of obesity varies from country to country. According to the World Health Organization (WHO), the prevalence of overweight and obese women combined (BMI of  $\geq 25$  kg/m<sup>2</sup>) is 77% in the United States, 73% in Mexico, 37% in France, 32% in China, and 18% in India.<sup>[3]</sup> In Nigeria,

**Address for correspondence:** Dr. Ochuwa A Babah, Department of Obstetrics and Gynaecology, Lagos University Teaching Hospital, PMB 12003, Surulere, Lagos, Nigeria. E-mail: ochuwab@yahoo.co.uk

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the prevalence of overweight and obese women has been estimated to be 20.3–35.1% and 8.1–22.2% respectively.<sup>[4]</sup> Obesity has been found to be a risk factor in many medical conditions, of which cardiovascular disease is one.<sup>[5,6]</sup>

Several studies conducted have identified preeclampsia as an inflammatory condition. A number of inflammatory markers, e.g., C-reactive protein (CRP), IL-6, fibrinogen, TNF $\alpha$ , etc., have been found to be elevated in patients with preeclampsia.<sup>[7-9]</sup> More recently, an association has been established between obesity and levels of inflammatory markers, suggesting that obesity is an inflammatory disease or predisposes to various adverse medical conditions by causing inflammation.<sup>[6,10-12]</sup> It is known that obesity is associated with elevated serum leptin level. In a study by El-Mekhzangy *et al.*, it was found that serum leptin level is significantly higher in preeclampsia when compared with normotensive pregnant women and this is thought to be a contributory factor to the endothelial dysfunction involved in the pathogenesis of preeclampsia.<sup>[13]</sup> If this be the case, then is there any association between obesity and preeclampsia?

In some studies, most of which were conducted in developed countries, it has been established that there is a three-fold increase in the risk of an obese pregnant woman developing preeclampsia.<sup>[14]</sup> It therefore follows that there is a possibility that obesity elicits chronic inflammation in the vascular system and this might serve as a trigger for the development of preeclampsia.

Researches are still on-going worldwide to establish the cause of preeclampsia and to identify modifiable factors that may be adjusted to prevent its occurrence. The most popular of these has remained the use of low dose aspirin, which has been found to be useful in minimizing the risk of development of preeclampsia if commenced early in pregnancy.

Obesity, as we know is a modifiable condition. So, if we are able to establish a clear-cut association between obesity and preeclampsia, it might be easier for us to institute strategies to prevent its occurrence, considering the huge burden the disease poses in obstetric practice.

### Objectives

- To ascertain if there is any association between obesity and preeclampsia
- To assess if there is a relationship between obesity, preeclampsia and levels of inflammatory markers (CRP and fibrinogen).

## Materials and Methods

### Design

Case-control study.

### Setting

Conducted at the Lagos University Teaching Hospital, Surulere, Lagos following ethical approval by the Health Research and Ethics Committee (HREC).

### Study population

This comprised 100 normotensive pregnant women and 100 preeclamptic women, matched for age, parity, and gestational age.

### Exclusion criteria

- Those in labor at the time of admission
- Those with congenital fetal anomaly
- Those with history of membrane rupture
- Women with chronic medical disorders such as renal disease, diabetes mellitus, human immunodeficiency virus infection, or other symptomatic infections
- Those with multiple gestations
- Those transfused with blood in the last 1 month
- Those who have had steroid in the last 24 hours.

### Data/sample collection

Information about their sociodemographic characteristics was obtained. BMI calculated using their height and weight at recruitment. Their plasma fibrinogen and CRP levels were assayed using enzyme-linked immunosorbent assay (ELISA) technique.

### Data management

The data collected was analyzed using the Epi Info. Chi-square and Kruskal-Wallis were used to test for statistical significance where applicable. A *P* value <0.05 was considered to be statistically significant.

## Results

### Clinical profile of patients

The mean age  $\pm$  S.D. of subjects was 31.1  $\pm$  4.46 years for the preeclamptic women and 31.1  $\pm$  4.50 years for the control group (*P* = 0.9345) [Table 1].

### Association between obesity and preeclampsia

Preeclamptics have higher BMI (30.04  $\pm$  6.06 kg/m<sup>2</sup>) than normotensive pregnant women (28.08  $\pm$  2.97 kg/m<sup>2</sup>). However, this was not statistically significant. Using mean arterial blood pressure (MAP) as an indicator of disease severity, with a cut off of 125 mmHg, it was found that severe

preeclampsia had higher BMI ( $30.18 \pm 6.49 \text{ kg/m}^2$ ) compared to women with mild form of the disease ( $29.83 \pm 5.48 \text{ kg/m}^2$ ),  $P = 0.2131$  [Figure 1].

### Association between obesity and markers of inflammation

There was statistically significant association between BMI and hsCRP ( $P = 0.0000$ ). There was statistically significant association BMI and plasma fibrinogen levels ( $P = 0.0000$ ).

### Levels of inflammatory markers in preeclamptic and normotensive pregnant women

The hsCRP level is higher in preeclampsia compared to normotensive pregnant women, median values of 5.70 mg/L and 4.35 mg/L respectively ( $P = 0.0453$ ). The hsCRP level is higher in women with severe preeclampsia compared to those with mild form of the disease, median values of 5.80 mg/L and 5.60 mg/L respectively [Table 1]. A large proportion of subjects with high levels of hsCRP and plasma fibrinogen are overweight and obese [Figures 2 and 3].

Plasma fibrinogen level is higher in preeclampsia compared to normotensive pregnant women, median values of 97.7 mg/dl and 52.9 mg/dl respectively ( $P = 0.0021$ ). Plasma fibrinogen level is higher in women with severe preeclampsia compared to those with mild form of the

disease, median values of 86.0 mg/dl and 101.2 mg/dl respectively.

### Discussion

Preeclamptic women in this study were found to have higher BMI. Similar observation was made in Southeastern Nigeria.<sup>[15]</sup> This finding is not surprising as obesity for a long time has been linked with various chronic diseases such as metabolic syndrome, cardiovascular diseases, diabetes, hypertension, non-alcoholic liver cirrhosis, and some cancers.<sup>[6]</sup>

Women with severe preeclampsia were also observed to be weightier than those with mild form of the disease. Considering the fact that obesity was adjudged to be a possible inflammatory trigger in a number of studies;<sup>[8,12,15]</sup> it therefore follows that the difference in BMI based on disease severity might be related to the degree of inflammation, thereby buttressing the fact that obesity is a possible trigger of inflammation. This assumption is further supported by the finding of higher levels of the inflammatory markers, CRP, and plasma fibrinogen in women with severe preeclampsia compared to women with mild form of the disease in this study.

There is a greater expression of inflammatory markers in preeclampsia compared to normotensive pregnant women, as hsCRP and fibrinogen levels were found to be

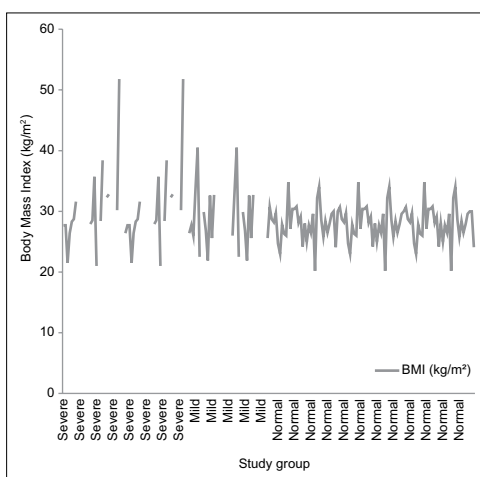


Figure 1: Association between body mass index (BMI) and pre-eclamptic and normotensive pregnant women

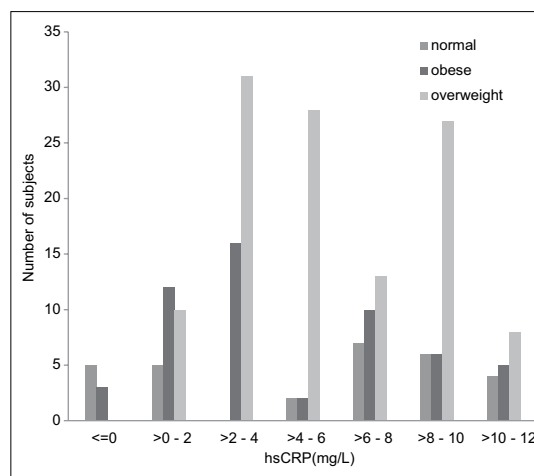
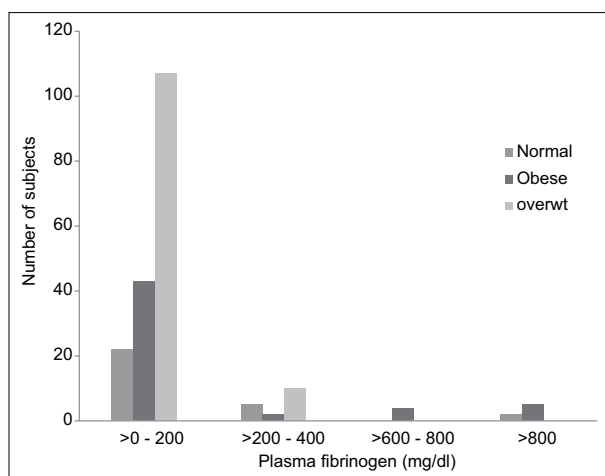


Figure 2: Distribution of subjects by BMI and hsCRP levels

Table 1: Distribution of subjects by age and level of inflammatory markers

	Mild pre-eclampsia $n=37$	Severe pre-eclampsia $n=63$	Control $n=100$	$P$
Maternal age (years)		32 (19-42)	31 (22-40)	0.9345
Plasma fibrinogen (mg/dl)		97.7 (20.1-623.9)	52.9 (20.8-848.5)	0.0021
Plasma fibrinogen (mg/dl)	86.0 (20.1-623.9)		101.2 (24.5-306.6)	0.5551
hsCRP (mg/L)		5.70 (-0.2-12.0)	4.35 (0.0-10.6)	0.0453
hsCRP (mg/L)	5.60 (0.1-12.0)		5.80 (-0.2-11.3)	0.9118

Data of cases are presented as median (range), 95% confidence interval.  $P < 0.05$  is considered to be statistically significant.



**Figure 3: Distribution of subjects by BMI and fibrinogen levels**

significantly higher in the preeclamptics. Similar findings have been reported previously in several other studies.<sup>[15-17]</sup> Statistically, significant associations were found between obesity and hsCRP and plasma fibrinogen levels. Veigas *et al.* also reported a strong association between BMI, waist circumference and fat mass, and CRP and fibrinogen levels.<sup>[18]</sup> This further buttresses the fact that obesity is a trigger of inflammation.

In obesity, it has been found that the production of IL-6 in human adipose tissue increases and it may induce CRP synthesis in the liver, which in turn may promote onset of cardiovascular complications and insulin resistance.<sup>[11]</sup> Obesity may thus be considered a subclinical inflammatory condition.

Considering the prevalence of obesity worldwide, it becomes important to employ strategies to minimize obesity in the pre-pregnancy period with the hope of reducing the incidence and/or the severity of preeclampsia. Strategies that may be employed to reduce excess weight gain include dietary modifications and regular exercises. This calls for persistent health education of our women on the risk associated with obesity even in pregnancy and the need to embark on pre-pregnancy weight reduction in order to avert complications like preeclampsia and other forms hypertensive disorders in pregnancy. By so doing we may be able to reduce maternal mortality rate as preeclampsia till date has remained one of the leading causes of maternal deaths and fetal wastages.

## Conclusion

It can thus be inferred from this study that obesity elicits inflammatory response which might predispose to the development of preeclampsia. Lifestyle modifications such as

dietary control, exercise, and pre-pregnancy weight reduction may help in reducing the incidence of preeclampsia.

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Nil.

## Conflicts of interest

There are no conflicts of interest.

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