ORIGINAL ARTICLES

MATERNAL BODY MASS INDEX AND THE RISK OF HYPERTENSIVE DISEASE IN PREGNANCY - A STUDY OF AN URBAN POPULATION OF GHANA

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Abstract

Background: Hypertensive disease in pregnancy accounts for about 10-15% of maternal deaths in sub-Saharan Africa and Asia. The relationship between maternal BMI and Hypertensive disease in pregnancy has received limited attention especially in these low-and middle-income settings. This study aimed to quantitatively describe the relationship between maternal BMI in the first half of pregnancy and the risk of developing hypertensive disease later in pregnancy.

Methodology: A prospective cohort of pregnant women attending antenatal clinic at 37 Military Hospital, Accra between 15 June 2015 and 22nd March 2016 was conducted. A total of 196 consenting expectant mothers in the first half of pregnancy who met the inclusion criteria were recruited based on their BMI classification as normal or abnormal. They were followed up at regular antenatal visits till delivery. At these visits, repeated

measurements of weight and blood pressure were taken. Univariate and multivariate statistical analysis taking into account the other risk factors for hypertensive disease in pregnancy was performed. Level of significance was set at p<0.05.

Results: Maternal BMI in the first half of pregnancy was significantly associated with developing hypertensive disease in pregnancy in second half of pregnancy. About 10 % of normal BMI mothers and 14% of abnormal BMI mothers developed hypertensive disease respectively. An increase in BMI within each BMI category was associated with an increased risk of developing Hypertensive disease in pregnancy.

Conclusion: Promoting a healthy maternal BMI in the first half of pregnancy may help reduce the risk of hypertensive disease later in pregnancy.

Keywords : hypertension, pregnancy, body mass index

Introduction

Background to the study

All over the world, pregnancy is usually a time when most couples share a lot of joy as they go through the various stages of this new state awaiting the arrival of the new family member. The joy of motherhood is the expectation of every pregnant woman and all expectant couples.

However, in most developing countries, the unacceptably high rates of maternal mortality makes couples envisage pregnancy with great uncertainty. Globally an estimated 289 000 women died during and following pregnancy and childbirth in 2013 alone and almost all these maternal deaths occurred in developing countries with sub-Saharan Africa accounting for more than half of these deaths¹. In Ghana, maternal mortality was measured at 350 per 100,000 live births in 2010¹ and this is far greater than recent average maternal

Corresponding Author: Dr. Charles J Buckman Department of Obstetrics and Gynaecology 37 Military Hospital, Accra, Ghana Tel: +233 244381228 E-mail: <u>nanabuckman@gmail.com</u> Conflict of Interest : none declared mortality ratio of 230 per 100,000 live births in developing countries¹ indicating that there is the need for continued concerted efforts to further reduce maternal mortality in Ghana. In these low-resource settings, it is well established that complications of hypertensive disease in pregnancy is one of the top 4 leading causes of maternal deaths¹. Hypertensive disease in pregnancy however, complicates about 10% of all pregnancies², and in sub- Saharan Africa and Asia, contributes to 10-15% of maternal mortality³.

Obesity and overweight on the other hand have also been identified as risk factors for various obstetric complications including Hypertensive disease in pregnancy^{4,5}. However, the risk of developing hypertensive disease in pregnancy in the various BMI categories continues to be a subject area for research.

Significance of the study

A study to quantify the risk of developing hypertensive disease in the various BMI categories in a developing country like Ghana is imperative. This is because of the high prevalence of obesity among females in Ghana, and more so a higher prevalence in Greater Accra Region which is the subject region of the study. This is of immense public health value since the ramifications are huge and with advocacy and education, maternal mortality reduction, which is the fifth Millennium Development Goal of the WHO, could be supported.

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Aim of the study

To determine and quantify the relationship between maternal body mass index in the first half of pregnancy and the risk developing hypertensive disease in pregnancy in the second half of pregnancy.

Objectives and Hypothesis

Objectives of the study

The specific objectives of this study include

- 1. To describe the socio-demographic characteristics of expectant mothers seeking antenatal care in an urban area.
- 2. To determine the prevalence of obesity disease amongst expectant mothers attending antenatal clinic at the Military hospital.
- 3. To determine the prevalence of hypertensive disease in pregnancy amongst expectant mothers attending antenatal clinic at the Military hospital.
- 4. To determine and quantify the risk of Body Mass Index on hypertensive disease in pregnancy whilst controlling for other important confounders.

Hypothesis

Null hypothesis:

HO: 1. Having a BMI greater than 25 at the booking visit has no effect on the risk of developing Hypertensive disease in pregnancy.

HO: 2. Increased maternal weight gain in each BMI category has no effect on developing Hypertensive disease in pregnancy.

Alternate hypothesis:

H1: 1. Having a BMI greater than 25 at the booking visit increases the risk of developing Hypertensive disease in pregnancy.

H1: 2. Increase in weight gain within each BMI category increases the risk of developing hypertensive disease in pregnancy.

Methodology

Study design

This study was a prospective cohort study, which was conducted at the Department of Obstetrics and Gynaecology at the 37 Military Hospital, in Accra.

Study site and setting

The 37 Military Hospital situated in Accra, Ghana, is a tertiary hospital and a referral centre for the Greater Accra Region, and also a centre for postgraduate training in various disciplines including obstetrics and gynaecology. Although it is primarily a Military Hospital, it provides services to both military personnel and the general civilian population. It is also the second biggest hospital in the city situated almost at the centre of Accra, which is the capital city of Ghana. The hospital has a 600-bed capacity with the Obstetrics and Gynaecology Department having 58 Beds.

The city lies in the savannah belt between the Central and Volta regions with its population being essentially a melting pot of diverse ethnic groups with a dominance of the Ga–Adangbe tribe. The population in the city is about 5 million and the major occupation ranges from marketing goods and services, civil service and fishing. The educational levels of the populace are mainly secondary and tertiary levels for the white collar working population, but a large proportion who work in the informal sector have only basic education.

The antenatal clinic is held at the maternity outpatient department during the working week days of Mondays to Wednesdays and Fridays. Each of the four teams has a fixed day to run the antenatal clinic. Activities on each clinic day include booking of new patients; follow up of old patients, HIV counselling and testing and patient education. Thursdays are used to see patients reporting for the booking visit. At the booking visit the identification particulars of the patient and a full history are taken. Each patient undergoes a thorough physical examination including general examination, respiratory, cardiovascular and gastrointestinal systems, nervous system and musculoskeletal systems. The obstetric examination is done and this information and any subsequent information are recorded in specially designed patient hand-held "Maternal Health Record Book". Most other medical institutions in Ghana use these booklets.

At the booking visit, the patient is weighed, her height is measured and the urine is tested for proteins and sugar with a dipstick. Investigations requested for on the first visit are haemoglobin estimation and sickling test (if positive haemoglobin electrophoresis), blood group and rhesus factor, VDRL test, G6PD enzyme activity, urine for microscopy and biochemistry and stool for microscopy. Referred patients who had these tests done prior to referral do not have to routinely repeat them. Other tests or repeat tests are ordered as indicated.

Patients are seen monthly up to twenty-eight weeks gestation, then fortnightly until thirty-six weeks gestation and then weekly until delivery. In complicated pregnancies, patients are seen more frequently, or as the Obstetrician in charge may determine. Patients who require admission are admitted to the maternity lying-in wards.

Study period

From 15th June 2015 to 22nd March 2016

Sample size determination

The sample size calculation was done with the help of Epi-info 7 Statistical software. The sample size was calculated for an unmatched cohort using Fleiss method with the correction factor⁶ at a power of 80% and a 95% confidence interval to detect the minimum Odds ratio of 3.4 between normal and abnormal BMI mothers based on literature. Similarly, a prevalence rate of hypertension in pregnancy of 10% was adapted from literature. The calculated sample size for the study was 178. However, adding a 10% non-response/ attrition rate, a sample size of 196 was used with 98 participants in each category.

Inclusion criteria

All antenatal attendants with normal blood pressure and with BMI within 18.5-24.9 were classified as normal BMI, and BMI equal to or greater than 25 was classified as abnormal BMI.

Exclusion criteria

- Foetal complications including multiple pregnancy and molar pregnancy
- Anomaly scan showing any foetal anomaly
- Patients with chronic medical conditions for example pre-existing hypertension before 20 weeks, renal disease and diabetes mellitus.

Data collection: Tools and methods

The primary tool used for data collection in this study was a structured questionnaire, which was administered by the principal investigator, and five research assistants who were trained at the beginning of the study to ensure standardisation of reporting.

The questionnaire was pretested at the antenatal clinic of the military hospital over 4 working days to improve the quality of data collection. Another meeting was scheduled after the pretesting was done and this helped to address issues and questions that came up during the pretesting period.

The participants who fitted the inclusion criteria and gave their informed consent, were recruited between 12 and 17 weeks, and were seen 2 weeks afterwards with their laboratory results, so as to be enrolled in the study. The dating of the pregnancy was done using a first trimester ultrasound scan. The scales that were used were Seca electronic scales and the patients were made to remove their shoes and have minimal clothing on. For the BP check, the patient had to be seated, and the right arm was used with a mercury sphygmomanometer with appropriate cuff for each patient, placed at the level of the heart.

At the initial visit, the patients were recruited based on their BMI into two groups, and those that consented to participate were given their laboratory requests and were seen 2 weeks afterwards, to be enrolled in the study. At the enrolment visit, at less than 20 weeks of pregnancy, a personal history was obtained and demographic data was collected. Also the BMI and blood pressure of patients were taken. This was important, so that patients with chronic Hypertension can be identified and excluded. The two groups based on normal BMI and abnormal BMI were then be followed up by trained research staff at clinic visits scheduled every 4 weeks, after 20 weeks of gestation, then every 2 weeks after 28 weeks to 36 weeks, and weekly thereafter till delivery.

A standard mercury sphygmomanometer was used to measure blood pressure with the patients in a seated

position. Diastolic blood pressure was determined with the fifth Korotkoff sound unless the diastolic measurement approached zero, when the fourth sound was used. A mid-stream voided urine specimen was collected for measurement of protein by dipstick. A dipstick measurement indicating proteinuria of \geq 1+ (300 mg/l) in a clean-catch, midstream urine sample was considered as positive. A dipstick measurement of zero or trace in the confirmatory sample was considered negative. BMI was categorized as normal weight (BMI 18.0–24.9), overweight (BMI 25.0–29.9), and obese (BMI >30.0). The patients were categorised into normal BMI group (BMI 18.5–24.9), and abnormal BMI group (BMI equal to or greater than 25).

Pregnancy Induced Hypertension was diagnosed if the systolic blood pressure is equal to or greater than 140mmHg and the diastolic blood pressure is equal to or greater than 90mmHg at two different times at least 6 hours apart, in the second half of pregnancy. Preeclampsia was diagnosed if there was an increased blood pressure equal to or greater than 140/90 mmHg with proteinuria, which occurs in the second half of pregnancy, after 20 weeks of pregnancy in a known normotensive non-proteinuric woman. Proteinuria in this situation is more than 300mg in a 24hour urine sample or more than 1+ on urine dipstick measurement. 1+ denotes 300mg/l of urine protein. Eclampsia was diagnosed with the occurrence of convulsion in a preeclampsia patient in the absence of coincidental neurologic disease. After delivery, the needed data were extracted from patient's folders, admission and discharge books at the labour and recovery wards as well as from obstetric operation entry book. Babies sent to NICU were also noted.

The information that was extracted included:

- 1. The socio-demographic data such as age, occupation, education level, marital status, occupation, level of income.
- 2. Development of hypertensive disease in a previous pregnancy and length of stay with current partner.
- 3. The blood pressure and the weights as determined at each visit.
- 4. The mode of delivery and attendance at Neonatal intensive care unit

Pregnancies were not allowed to progress beyond 42 weeks. All those who develop Hypertension were treated according to standard treatment guidelines

Data analysis

Data was originally entered using SPSS version 16 and the ensuing dataset extracted into Stata-SE version 12.0 for extensive checks and data cleaning. A descriptive analysis was performed to show the proportion of expectant mothers in each BMI classification that developed hypertensive disease in pregnancy. A general descriptive analysis of the study participants was first performed and assessed parameters compared between normal BMI group and abnormal BMI group. Simple logistic regression models were built for of each of the independent (or exposure) variables and the dependent (or outcome) variable (hypertension in pregnancy) to understand the relationship between these variables and diabetes. The crude odds ratios (ORs) and P-values from Wald tests of these variables were noted.

Multivariate logistic regression was used to estimate the total effect of BMI at less than 20 weeks on the risk of hypertensive in pregnancy. BMI was modelled as a continuous variable rather than a categorical variable. This is because using BMI as a categorical variable assumes a constant risk within a category and a large jump in risk with the next category, which is usually not biologically plausible⁸. Variables that showed an association with the outcome variable were noted in the other of their strength of association and later included in the multivariate analysis. An explorative analysis of all independent variables that were associated with hypertension in pregnancy in the univariate logistic regression analysis (i.e. p-value<0.05) were treated as covariates and used to build a multivariate model using the backward fitting approach. The associated covariates in the univariate analysis were entered into a logistic regression model. The covariates used in the final model (multivariate) were based on literature on confounding factors that were likely to be independent risk factors for hypertensive disease in pregnancy. The factors that were strongly associated, having a p value < 0.05 therefore met the definition of confounding, and was added to the final model of a multivariate logistic regression. ORs were calculated to approximate risk ratios.

Ethical consideration

The Institutional Review Board of the 37 Military Hospital, Accra, approved the study. A written consent was obtained from all study participants after meeting the inclusion criteria.

Results

Out of the total of 196 respondents at the initial booking visit, one was lost to follow up and so was excluded from the analysis. A total of 195 respondents were obtained with 97 in the normal BMI group and 98 in the abnormal BMI group. Their baseline characteristics have been shown in Table 1.

Demographic characteristics

Majority (62/97) of the normal BMI group representing 63.92% were aged between 27 to 35 years with the minimum age for this BMI category being 19 years and the maximum being 39 years. There was a similar pattern for the abnormal BMI category with majority (69/97) in the age group of 27 to 35 years representing 70.41%, with the minimum age being 16 and the maximum age being 49 years as shown in Table 1. Majority (80/97) of the normal BMI group representing 82.47% were married whilst 68 (out of 98), also a majority, and representing 69.39% for the abnormal BMI category were married.

The level of income for the abnormal BMI category was higher with about 56 (out of 98), representing 57.14% earning 1000Gh or more whilst 32 (out of 97), representing 32.98% earned 1000 Gh cedis or more for the normal BMI category.

The level of income for the partners of respondents was higher for those with abnormal BMI, with 87 (out of 98), representing 88.77% of them earning 1000 Gh cedis or more and 62 (out of 97) representing 63.91% of the partners for the normal BMI group earning 1000 Gh cedis or more. 167 of the respondents out the 195 respondents had either secondary or tertiary education representing about 85.64%. 148 of the respondents, representing 75.90% were married.

BMI category characteristics

Majority (51/97) of the normal BMI group had tertiary education (52.58%) and 33 out of 97, representing 34.02% had secondary education. For the abnormal BMI category, 37 (out of 98), representing 37.76% had tertiary education and 46 (out of 98), representing 46.94% had secondary education as shown in Table 1. The mean weight at the booking visit for the normal BMI group was $58.33kg\pm 5.66$. The minimum weight in this group was 44kg and the maximum was 76. The mean weight at the booking visit for those in the abnormal BMI category was $82.80kg\pm 10.16$. The minimum weight in this group was 63 and the maximum weight was 129.

The mean measured height in the normal BMI category was 1.655m±0.057. The minimum height in this BMI category was 1.53m and the maximum was 1.83m. The mean measured height in the abnormal BMI category was 1.638m± 0.067. The minimum height in this BMI category was 1.53m and the maximum was 1.83m. Majority of the normal BMI group were nulliparous (48.45%) while 39.18% were primiparous. 39.80% of the abnormal BMI group were nulliparous whiles 33.67% were primiparous. Majority (56.70%) of the normal BMI group had stayed with their current partner for between 1 and 5 years with about 17.53% having stayed for less than 1 year with the current partner. Majority (77.55%) of the respondents in the abnormal BMI group had stayed with the current partner for between 1 and 5 years with 6.12% having stayed with their partners for less than 1 year. At the booking visit, the mean BMI for nulliparous women was 25.68 with a standard deviation of 5.52. The minimum BMI for nulliparous women was 15.41 and the maximum BMI was 41.64. Multiparous women had a higher BMI, with the mean BMI being 28.47 with a standard deviation of 6.35. The minimum BMI for multiparous women was 16.14 and the maximum was 42.97. The prevalence of obesity from the study sample was 21.03%, using the weight at the booking visit. This is further illustrated in Figure 2.

Unexposed/Normal BMI (%) Exposed/Abnormal BMI (%) N=97 N=98 Maternal Age (years) 14 (14.29) 16-26 23 (23.71) 14 (14.29) 27-35 62 (63.92) 69 (70.41) 36 0r older 12 (12.37) 15 (15.31)	
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27-35 62 (63.92) 69 (70.41) 36 Or older 12 (12.37) 15 (15.31)	
36 Or older 12 (12.37) 15 (15.31)	
Educational level of	
Respondents	
None 1 (1.03) 3 (3.06)	
Primary 12 (12.37) 12 (12.34)	
Secondary 33 (34.02) 46 (46.94)	
Tertiary 51 (52.58) 37 (37.76)	
Characteristic Exposure Status	
Unexposed/Normal BMI (%) Exposed/Abnormal BMI (%)	
N=97 N=98	
Respondents level of	
income*	
<500 18 (18.56) 11 (11.22)	
500-1000 32 (32.99) 26 (26.53)	
1000-1500 23 (23.71) 25 (25.51)	
1500-2000 4 (4.12) 19 (19.39)	
>2000 5 (5.15) 12 (12.24)	
Unemployed 15 (15.46) 5 (5.10)	
Income level of partner *	
<500 5 (5.15)	
500-1000 29 (29.90) 10 (10.20)	
1000-1500 26 (26.80) 30 (30.61)	
1500-2000 16 (16.49) 23 (23.47)	
>2000 20 (20.62) 34 (34.69)	
Unemployed 1 (1.04) 1 (1.03)	
Characteristic Exposure Status	
Unexposed/Normal BMI (%) Exposed/Abnormal BMI (%)	
N=97 N=98	
Marital Status*	
Unmarried $17(17.53)$ $30(30.61)$	
Married 80 (82.47) 68 (69.39)	
Hypertensive disease in	
$\mathbf{y}_{\mathbf{x}} = \mathbf{y}_{\mathbf{x}} = $	
$\begin{array}{c} 100 \\ Y_{20} \\ Y_{20} \\ \end{array} \qquad \qquad$	
1es 0 (0.23) / (7.14)	
$\begin{array}{c c} rainy \\ Nulliparous \\ 17 (18.45) \\ 20 (20.80) \\ 10 \\ 10 \\ 10 \\ 10 \\ 10 \\ 10 \\ 10 \\ $	
$\begin{array}{cccc} \text{Nulliparous} & 47 (40.45) & 59 (57.60) \\ \text{Driminarous} & 28 (20.18) & 23 (22.67) \\ \end{array}$	
Filmparous $56(39.16)$ $55(53.07)$ Multiparous $12(12.37)$ $26(26.53)$	
12 (12.57) 20 (20.55)	
current partner*	
Less than 1 year $17(1753)$ $6(612)$	
Loss that 1 year $17(17.57)$ $0(0.12)$ Between 1 and 5 years $55(5670)$ $76(7755)$	
Between 5 and 10 years $24(2474)$ 12 (12 24)	
More than 10 years $1 (1.03)$ $4 (4.08)$	

Table 1. Baseline characteristics and demography of respondents

*The following had a strong association with BMI classification,

Marital status P value 0.033 Respondent's level of income P value 0.001 Income of partner P value 0.002 Parity P value 0.044

Length of stay with current partner P value 0.002 **There was one non-respondent for this variable





BMI categories and hypertensive disease in pregnancy

4% of the normal BMI category had pre-eclampsia whilst 6% of abnormal BMI category had preeclampsia. 6 (6.25%) out of 96 of the normal BMI group said they had developed hypertensive disease in a previous pregnancy whilst 1 did not respond. 7 (7.14%) out of 98 in the abnormal BMI group said they had developed hypertensive disease in a previous pregnancy.



Figure 2: Pie chart showing BMI classification at the booking visit

9 women in the normal BMI group, representing 9.28% developed hypertensive disease in pregnancy whilst 14 representing 14.29% in the abnormal BMI group developed hypertensive disease in pregnancy. Also 4 women in the normal BMI category, representing 4.12% developed pre-eclampsia whilst 6 in the abnormal BMI category, representing 6.12% developed pre-eclampsia. The overall prevalence of Hypertensive disease in pregnancy was 11.79%. The overall prevalence of preeclampsia was 5.12%

Delivery and outcomes

A total of 16 of the 23 women who developed hypertensive disease had caesarean section representing 69.57%. A total of 6 women who were obese had caesarean section among the women that developed hypertensive disease in pregnancy representing about 26.09% of them.

A total of 13 of the babies delivered were sent to the neonatal Intensive Care Unit, representing 6.7% of respondent deliveries. The number of babies of

respondents with hypertensive disease in pregnancy that went to NICU was 6 representing 46.15% of the babies that has been sent to NICU. Two out of the 6 babies from the hypertensive women that were sent to NICU, were from mothers in the obese group, representing 15.38%.

Crude analysis

Parity, as well as the number of years of stay with the current partner were determined to be independent risk factors for the development of hypertensive disease in pregnancy with crude analysis, both having a p value less than 0.05.

Univariate Analysis

With univariate logistic regression, the age group, parity, length of stay with current partner, hypertensive disease in a previous pregnancy and the enrolment BMI, at less than 20 weeks were independent risk factors for the development of hypertensive disease in pregnancy, all having p values less than 0.05. This is shown in Table 2 below

 Table 2: Univariate Analysis of variables showing positive association with Hypertensive disease in Pregnancy

Characteristic	OR (95% CI)	P value
Enrolment BMI	1.0880(1.0068-1.1757)	0.0328
27-35 years	0.2057(0.0644-0.6568)	< 0.0001
36 years or older	2.5210(8108-7.8388)	
Parity	0.4946(0.3013-0.7191)	0.0182
Hypertensive disease in previous	5.6597(1.6729-19.1474)	0.0097
pregnancy		
Length of stay with partner	0.4645(0.3013-0.7190)	< 0.0001

For the age group, using univariate logistic regression, the age group between 16 to 26 years was compared with the age group between 27 to 35 years and 36 years or greater with the risk of developing hypertensive disease in pregnancy. The OR for the age group between 27 and 35 years was 0.206 (CI 0.064-0.657). The OR for the age group 36 years or greater was 2.5 (CI 0.811-7.839) as shown in Table 2. For the variable, hypertension in previous pregnancy, the OR of developing hypertensive disease in the index pregnancy was 5.660 (CI 1.673-19.147) as shown in Table 2.

From the enrolment, which was less than 20 weeks of gestation, to delivery 9.78% in the normal BMI group developed Hypertensive disease in pregnancy whilst 13.59% in the abnormal BMI group developed Hypertensive disease in pregnancy. This result however failed to reach significance with crude analysis at a P value of 0.41. However with the application of the univariate logistic regression, the p value of the enrolment BMI at pregnancy less than 20 weeks became 0.0328, which was strongly associated with the risk of developing hypertensive disease in pregnancy. The OR was 1.0880(CI 1.0068-1.1757).

The OR for BMI group 18-24.9 (normal weight) was 0.1084 (CI 0.0545-0.2157). The OR for BMI group 25-29.9 (overweight) was 0.5764 (CI 0.1180-2.8138). The OR for BMI group 30 or greater (obese) was 1.9415 (CI 0.7678-4.9095)

Multivariate Analysis

With the multivariate logistic regression, using the independent risk factors of age, hypertension in previous pregnancy, length of stay with current partner and parity, the p value was less than 0.001 showing a strong association between abnormal BMI at less than 20 weeks of gestation and the risk of developing Hypertensive disease in pregnancy which is shown in Table 3 below.

Table 3: Multivariate analysis showing the BMI at enrolment, and risk of developing hypertensive disease in pregnancy, controlling for confounding factors. n=194*

Characteristic	Unadjusted OR (95% CI)	Adjusted OR (95% CI)
Enrolment BMI	1.08(1.0068-1.1758)	1.1356(1.0292-1.2530)
27-35 years 36 years or	0.2057(0.0644-0.6568)	0.3076(0.0794-1.1916)
older	2.5210(0.8108-7.8389)	4.6661(1.0638-20.4667)
Parity	0.4946(0.2568-0.9526)	0.3637(0.1579-0.8373)
Hypertensive disease in previous pregnancy	5.6597(1.6729-19.1474)	10.3907(1.7037-63.3708)
Length of stay with partner	0.4655(0.3013-0.7190)	0.1540(0.0504-0.4709)

*There was one missing variable in the final model **Discussion**

The essence of this prospective cohort study was to determine the prevalence of obesity and hypertensive

disease in pregnancy, and to determine and quantify the effect of Body Mass Index on the risk of Hypertensive disease in pregnancy whilst controlling for other important confounders.

Socio-demographic characteristics of the study population

This study was done among an urban population in the city of Accra and so there might be certain differences even though the general socio-demographic characteristics reflect what pertains in the whole country of Ghana. According to the Ghana Demographic and Health Survey, 2008⁹, 21% of women in the reproductive age group had no formal at all whilst 4% had tertiary education. In the study population 2.05% had no formal education whilst 45.13% had had tertiary education. The difference can be explained by the fact that the 37 Military Hospital is located in the capital city of the country where schools, colleges and universities are easily accessible compared to other parts of the country.

Also, according to the Ghana Demographic and Health Survey, 2008⁹, 59% of women were married or in a union whilst it was 75.90% in the study population, largely reflecting the majority which pertains nationally.

Prevalence of Obesity

The prevalence of obesity from the study sample was 21.03%, using the weight at the booking visit. This was comparable to what was found by Yogev et al, 2009¹⁰ in the USA, which gave a prevalence of obesity among pregnant women to be between 18.5% and 38.3%. It is however slightly higher than the general prevalence of obesity in Accra found by Biritwum et al, 2005¹¹, which was 16%. This can be explained by the higher income earnings of the study population and the tendency for sedentary lifestyles leading to obesity.

Prevalence of Hypertensive disease in pregnancy

The overall prevalence of Hypertensive disease in pregnancy was 11.79%. The overall prevalence of preeclampsia was 5.12%. This corresponds to the worldwide prevalence of 10% for hypertensive disease in pregnancy and 2-8% for pre-eclampsia². The prevalence of preeclampsia also corresponds to a study done in Benin City, Nigeria, which was 5.6%, however the overall prevalence of Hypertensive disease in pregnancy was higher than that found in Benin City of $7.2\%^{12}$.

Delivery outcomes

A total of 16 of the 23 women who developed hypertensive disease had caesarean section representing 69.57%. This is comparable to what was found by Hall et al, 2000¹³ where 80% of them had caesarean section. This is because the core treatment in literature for hypertensive disease in pregnancy is delivery¹⁴ and sometimes has to be done preterm, with an unfavourable cervix so when induction of labour fails caesarean

section has to be done. Also a total of 6 obese women had caesarean section, which represents 26.09% of the 23 women who developed hypertensive disease in pregnancy. This is comparable to a meta-analysis by Poobalan et al (2008), which showed that 29.02% of obese women had caesarean section¹⁵. This high percentage is because obesity is an independent risk factor for a caresarean section¹⁵.

A total of 13 of the babies delivered were sent to the neonatal Intensive Care Unit, with the number of babies of respondents with hypertensive disease in pregnancy that went to NICU being 6 representing 46.15% of respondent deliveries that were sent to NICU. This is slightly higher than what was found by Hall et al, 2000¹³ where 40.7% of the babies born to early onset pre-eclamptics had been sent to NICU. This can be explained by the fact that our study included the whole spectrum of hypertensive disease in pregnancy. Also 2 of the women in the obese group had their babies sent to NICU representing 15.38%. This was comparable to what was found by Yogev et al (2005), in obese non-diabetic pregnant women who had 12.3% of their babies being sent to NICU¹⁶.

BMI categories and hypertensive disease in pregnancy

The results show that BMI before 20 weeks is a strong independent risk factor for the development of hypertensive disease in pregnancy. It also shows a strong association between increasing BMI at enrolment of the study, which was before 20 weeks and the risk of developing hypertensive disease in pregnancy. This corresponds to what was found by Bodnar et al, 2005¹⁷. The age group of 27 to 35 years was protective with an unadjusted OR of 0.2057(0.0644-0.6568). However age group 36 years or greater had an OR of 2.5210(0.8108-7.8389), showing a 2.5 times increased risk of developing hypertensive disease in pregnancy compared to age group 16 to 26 years. This therefore shows that the best time to have children is in this age group, to reduce the risk of hypertensive disease in pregnancy which is corroborated by published literature which shows that the extremes of age have an increased risk of developing hypertensive disease in pregnancy¹⁸.

The OR for hypertensive disease in a previous pregnancy was 5.6597(1.6729-19.1474), which shows a high risk 5 times of developing hypertension in pregnancy. This is corroborated by published studies by Duckitt, 2005^{18} who got an OR 7.19 (5.85-8.83) for developing pre-eclampsia, in a woman with a previous history of pre-eclampsia. This information is therefore very useful so that such patients can be labelled as high risk and be seen more frequently and be given more attention in the second half of pregnancy. The length of stay was also positively associated with a p value of <0.0001 with a negative association as shown in Table 2. This therefore shows that the shorter the time couples stay together before pregnancy, the higher the risk of developing hypertensive disease in pregnancy. This also

agrees with what Klonoff-Cohen et al, 1989¹⁹ found with logistic regression results suggest increasing risk of preeclampsia with decreasing amounts of sperm and seminal fluid exposure by a factor of 1.34 per quartile.

The BMI at enrolment in the study was positively associated with the risk of developing hypertensive disease in pregnancy. It shows that increasing BMI even within the normal BMI group leads to an increased risk of developing hypertensive disease in pregnancy. The OR from enrolment BMI was 1.08 (1.0068-1.1758), showing an 8% increase in risk for each unit of BMI increase which agrees with published literature¹⁷. Bodnar et al, 2005¹⁷ found a sharp rise in risk across most of the BMI distribution indicates that the risk of preeclampsia increases even within traditional BMI categories. For instance in the study by Bodnar et al, women with a BMI of 28 are 40% more likely to develop preeclampsia as women with a BMI of 25 (adjusted OR: 1.4; 95% confidence interval, 1.1-1.6), even though both are considered overweight by conventional cut off points.

The OR for BMI group 30 or greater (obese) was 1.9415 (CI 0.7678-4.9095) showing an increase in risk when obese compared to overweight was 0.5764 (CI 0.1180-2.8138) and normal weight which was 0.1084 (CI 0.0545-0.2157). The high OR for BMI group 30 or greater (obese) being 1.9415, gives almost double the risk for developing hypertensive disease in pregnancy. One author found a substantially increased risk of hypertensive disease in pregnancy with high BMI 26 to 34.9 and greater than 35^{20} . Women can therefore be advised to lose weight prior to getting pregnant to reduce the risk of developing hypertensive disease in pregnancy. There was an increased proportion of respondents developing hypertensive disease in pregnancy for the abnormal BMI group (14%), compared to 9% in the normal BMI group which agrees with published literature²¹.

The mechanisms underlying the BMI–preeclampsia relation have yet to be identified. Reduced placental perfusion, secondary to abnormal implantation and subsequent reduced placental vascularization, is the defining feature of preeclampsia²². However, it has been noted that not all women with reduced placental perfusion, develop preeclampsia. This paradox has led to the theory that preeclampsia is a two stage disorder with maternal-foetal interactions necessary to link the two stages²³.

Reduced placental perfusion is thought of as the first stage, while the second stage, the maternal syndrome, develops in a subgroup of women with certain genetic, environmental and behavioural characteristics as a response to factors produced by the poorly perfused placenta²³. In a suitable maternal environment, oxidative stress and subsequent endothelial activation and injury result, initiating the coagulation cascade and ensuing multisystem sequelae²⁴. Abnormal BMI (Overweight and obesity)

can be postulated as one such predisposing maternal characteristic¹⁷.

However on the causal pathway between abnormal BMI and Hypertensive disease in pregnancy, factors like parity, the number of years of stay with the partner, hypertensive disease in previous pregnancy were found to be independent risk factors for the development of hypertensive disease in pregnancy from our study and so had to be controlled for. This is corroborated by published literature^{25,14,19}. These factors therefore provide the appropriate maternal environment²⁴ for the development of hypertensive disease in pregnancy. The observed association between abnormal BMI in the first half of pregnancy and hypertensive disease in pregnancy may be confounded by the presence of chronic hypertension²⁶, diabetes mellitus²⁷, each of which are known risk factors for preeclampsia. These were therefore part of the exclusion criteria.

Conclusion

The study found an increased risk of developing Hypertensive disease in pregnancy with increase in BMI within each BMI category. There is also an increased risk (almost double) of developing hypertensive disease in pregnancy in obese pregnant women.

Limitations

The contribution of the baby's weight as pregnancy advanced to the maternal BMI could not be reasonably accounted for. For example, if the BMI was 26 and after delivery it dropped to 24 she was now of normal BMI.

Another limitation was that a history of hypertension in a previous pregnancy was self-reported. This was therefore subject to recall bias. However the strength of association was strong, which agreed with published data.

The other limitation was the generalizability of the findings as the sample was taken from patients only attending the 37 Military Hospital for antenatal care. This is a tertiary hospital and so overweight and obese pregnant women were likely to be referred to the hospital from primary care providers. The results however agreed with published literature so were quite representative.

Recommendations

Medical practitioners attending to obese pregnant women should monitor their blood pressures carefully, especially in the second trimester because they are at an increased risk of developing hypertensive disease in pregnancy. There should be adequate health education on overweight and obese women embarking on pregnancy to try to reduce their weight. Future studies should also confirm hypertensive disease in a previous pregnancy from medical records and not from recall of patients.

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References

- 1. WHO. Fact Sheet No 348 [Internet]. 2014 [cited 2014 Jul 3]. Available from: http://www.who.int/mediacentre/factsheets/fs348/e n/
- Duley L. The Global Impact of Pre-eclampsia and Eclampsia. *YSPER* [Internet]. Elsevier Inc.; 2009;33(3):130–7. Available from: http://dx.doi.org/10.1053/j.semperi.2009.02.010
- DULEY L. Maternal mortality associated with hypertensive disorders of pregnancy in Africa, Asia, Latin America and the Caribbean. *BJOG An Int J Obstet Gynaecol* [Internet]. 1992 Jul [cited 2016 Mar 28]; 99(7):547–53.Available from: http://doi.wiley.com/10.1111/j.1471-0528.1992.tb13818.x
- 4. Brien TEO, Ray JG, Chan W. Maternal Body Mass Index and the Risk of Preeclampsia: A Systematic Overview. *Epidemiology*. 2003;14:368–74.
- Leddy MA, Power ML, Schulkin J. The impact of maternal obesity on maternal and fetal health. *Rev Obstet Gynecol* [Internet]. 2008 Jan [cited 2015 Jun 19];1(4):170–8. Available from: http://www.pubmedcentral.nih.gov/articlerender.fc gi?artid=2621047&tool=pmcentrez&rendertype=a bstract
- 6. Fleiss JL, Levin B, Paik MC. Determining sample sizes needed to detect a difference between two proportions. Wiley Online Library; 2004.
- Edwards LE, Hellerstedt WL, Alton IR, Story M. Pregnancy complications and birth outcomes in obese and normal weight women: Effect of gestational weight change. *Obstet Gynecol*; 1996. 87:389–394.
- Greenland S. Avoiding power loss associated with categorization and ordinal scores in dose-response and trend analysis. *Epidemiology* [Internet]. 1995 [cited 2016 Mar 22]; Available from: http://journals.lww.com/epidem/Citation/1995/070 00/Avoiding_Power_Loss_Associated_with_Categ orization.25.aspx
- 9. Ghana Statistical Service, Accra, Ghana Ghana Health Service, Accra G. Ghana Demographic and Health Survey. 2008
- 10. Yogev Y, Catalano PM. Pregnancy and obesity. *Obstet Gynecol Clin North Am* [Internet]. Elsevier Ltd; 2009 Jun [cited 2014 May 28];36(2):285–300, viii. Available from: http://www.ncbi.nlm.nih.gov/pubmed/19501314
- 11. Biritwum RB, Gyapong J, Mensah G. The epidemiology of obesity in ghana. *Ghana Med J*. 2005;39:82–5.

- 12. Onyiriuka AN, Okolo AA. Perinatal outcome in patients with pre-eclampsia in Benin City, Nigeria. *Trop J Obstet Gynaecol. Society of Gynaecology and Obstetrics of Nigeria (SOGON)*; 2004;21:148–52.
- Hall DR, Odendaal HJ, Kirsten GF, Smith J, Grove D. Expectant management of early onset, severe pre-eclampsia: perinatal outcome. *BJOG An Int J Obstet Gynaecol* [Internet]. 2000 Oct [cited 2016 Apr 3];107:1258–64. Available from: http://doi.wiley.com/10.1111/j.1471-0528.2000.tb11617.x
- Cunningham F, Leveno K, Bloom S, Hauth J, Dwight J. Pregnancy Hypertension. In: Williams Obstetrics. 23rd ed. New York: McGraw Hill Medical; 2010. 706-746 p.
- 15. Poobalan AS, Aucott LS, Gurung T, Smith WCS, Bhattacharya S. Obesity as an independent risk factor for elective and emergency caesarean delivery in nulliparous women–systematic review and meta-analysis of cohort studies. *Obes Rev. Wiley Online Library*; 2009;10:28–35.
- Yogev Y, Langer O, Xenakis EMJ, Rosenn B. The association between glucose challenge test, obesity and pregnancy outcome in 6390 non-diabetic women. *J Matern Neonatal Med. Taylor & Francis*; 2005;17:29–34.
- Bodnar L, Ness R, Markovic N, Roberts J. The risk of preeclampsia rises with increasing prepregnancy body mass index. *Ann Epidemiol* [Internet]. 2005 [cited 2016 Mar 21]; Available from: http://www.sciencedirect.com/science/article/pii/S 1047279705000098
- Duckitt K, Harrington D. Risk factors for preeclampsia at antenatal booking: systematic review of controlled studies. *BMJ* [Internet]. 2005 Mar 12 [cited 2016 Jan 15];330(7491):565. Available from: http://www.bmj.com/content/330/7491/565.short
- Klonoff-Cohen HS, Savitz DA, Cefalo RC, McCann MF. An epidemiologic study of contraception and preeclampsia. *JAMA* [Internet]. 1989 Dec 8 [cited 2014 Jul 23];262(22):3143–7. Available from: http://www.ncbi.nlm.nih.gov/pubmed/2810672
- Sibai B, Ewell M, Levine R. Risk factors associated with preeclampsia in healthy nulliparous women. *Am J Obstet Gynecol* [Internet]. 1997 [cited 2016 Mar 21];

Available from: http://www.sciencedirect.com/science/article/pii/S 0002937897700048

- 21. Thadhani R. High body mass index and hypercholesterolemia: risk of hypertensive disorders of pregnancy,. *Obstet Gynecol* [Internet]. 1999 Oct [cited 2016 Mar 21];94(4):543–50. Available from: http://www.sciencedirect.com/science/article/pii/S 0029784499004007
- 22. Page E. The relation between hydatid moles, relative ischemia of the gravid uterus, and the placental origin of eclampsia. *Am J Obs Gynecol* [Internet]. 1939 [cited 2016 Mar 21]; Available from:

 $\label{eq:https://scholar.google.com/scholar?q=Page+E.+Th e+relation+between+hydatid+moles%2C+relative +ischemia+of+the+gravid+uterus%2C+and+the+p lacental+origin+of+eclampsia.+Am+J+Obstet+Gy necol.+1939%3B37%3A291%E2%80%93293&bt nG=&hl=en&as_sdt=0\%2C5\#0$

- 23. Roberts J, Cooper D. Pathogenesis and genetics of pre-eclampsia. *Lancet* [Internet]. 2001 [cited 2016 Mar 21]; Available from: http://www.sciencedirect.com/science/article/pii/S 0140673600035777
- 24. Surratt N. Severe Preeclampsia: Implications for Critical-Care Obstetric Nursing. *J Obstet Gynecol Neonatal Nurs* [Internet]. 1993 [cited 2016 Mar 21]; Available from: http://onlinelibrary.wiley.com/doi/10.1111/j.1552-6909.1993.tb01835.x/abstract
- 25. Kwawukume E. Hypertension in Pregnancy. In: Comprehensive Obstetrics in the tropics. Kwawukume E, Emuveyan E, editors. Accra: Asante & Hittscher Printing Press Ltd; 2002. 173-184 p.
- 26. Ray J, Burrows R. MOS HIP: McMaster outcome study of hypertension in pregnancy. *Early Hum Dev* [Internet]. 2001 [cited 2016 Mar 21]; Available from:http://www.sciencedirect.com/science/article/ pii/S0378378201001815
- 27. Ray J, Vermeulen M, Shapiro J, Kenshole A. Maternal and neonatal outcomes in pregestational and gestational diabetes mellitus, and the influence of maternal obesity and weight gain: the DEPOSIT study. *Qjm* [Internet]. 2001 [cited 2016 Mar 21]; Available from: http ://qjmed.oxfordjournals.org/content/94/7/347.short