

ORIGINAL ARTICLE

Putative risk factors of pregnancy-induced hypertension among Ghanaian pregnant women

W.K.B.A. Owiredu¹, L. Ahenkorah¹, C. A. Turpin², N. Amidu³ and E. F. Laing¹

¹Department of Molecular Medicine, ²Department of Obstetrics and Gynaecology, School of Medical Sciences, College of Health Sciences, Kwame Nkrumah University of Science and Technology, Kumasi, Ghana; ³Department of Medical Laboratory Science, School of Medicine and Health Sciences, University for Development Studies, Tamale, Ghana

Hypertensive pregnancy is an important cause of maternal mortality with several risk factors which can be related to regional and ethnic factors. Although there have been many studies worldwide on preeclampsia, not many have come from black Africa and for that matter Ghana. This study sought to identify some putative risk factors of Pregnancy-Induced Hypertension among Ghanaian pregnant women. A case-control study was conducted among pregnant women visiting Komfo Anokye Teaching Hospital (KATH), Kumasi, Ghana between November, 2006 and December, 2007 to determine the risk factors for Pregnancy-Induced Hypertension (PIH). Information on socio-demographic characteristics, medical history and previous obstetric history were obtained by face-to-face interviews and assessed through medical records. One hundred PIH women (thirty with preeclampsia (PE) and seventy with gestational hypertension (GH) and fifty normotensive pregnant women (controls) in the second half of pregnancy were recruited for the study. Advanced maternal age was a significant risk for developing PIH (PE+GH). Obesity increased the risk of PIH. Family history of hypertension increased the risk of developing PIH (*aOR* 6.8; 95% CI 2.3-19.6). Nulliparity was not a risk factor for PE (*cOR* 0.0; 95% CI 0.0–0.2) but was a risk factor for GH (*cOR* 3.0; 95% CI 1.2-7.4) from this study. Condom use in the male partner, contraceptive use in females, change of partner as well as placental hormonal imbalance were also associated with PIH. The findings of this study suggest that, besides maternal aberrations posing risk for PIH, change of partner and placental roles could also be linked to the aetiology of PIH. Furthermore, some risk factors for PIH are similar for both non-African populations as well as black Africans.

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INTRODUCTION

Over half a million women die each year of pregnancy-related causes. Ninety-nine (99%) percent of these deaths occur in the developing world (Verwoerd *et al.*, 2002) which includes Ghana. The most common cause of these maternal deaths are complications of pregnancy and child birth such as haemorrhage, sepsis, complications of unsafe abortions, hypertensive disorders of pregnancy and obstructed

labour (WHO, 1994). Maternal and perinatal morbidity and mortality are also major public health problems in developing countries like Ghana. A study conducted by Osei-Nketiah, (2001) in Ghana established that forty percent (40%) of maternal deaths are as a result of hypertensive pregnancy, antepartum haemorrhage and post partum haemorrhage. Hypertensive disorders of pregnancy remain a major cause of maternal and foetal morbidity and are of grave concern to healthcare professionals not only in Ghana but the world at large. Pregnancy-Induced Hypertension continues to be a major obstetric problem in present-day healthcare practice. It presents a great medical dilemma because it af-

Correspondence: W.K.B.A. Owiredu, Department of Molecular Medicine, School of Medical Sciences, Kwame Nkrumah University of Science and Technology, Kumasi, Ghana. E-mail: wkbaowiredu@yahoo.com

fects not only maternal health but also puts foetal development at risk (Ahenkorah *et al.*, 2008).

Pregnancy-Induced Hypertension is hypertension that develops as a consequence of pregnancy and regresses after delivery. Pregnancy-Induced Hypertension can be differentiated from chronic hypertension, which appears before 20 weeks gestation or usually continues for more than six weeks after delivery (ACOG, 1996). Gestational hypertension and PE (together referred to as PIH) are conditions of pregnancy characterized by increased blood pressure. Preeclampsia, according to the National High Blood Pressure Education Program of the USA, (National High Blood Pressure Education Group, 2000) is defined as hypertension developing after 20 weeks' gestation with proteinuria and/or oedema. Gestational hypertension on the other hand, is hypertension developing after 20 weeks' gestation without other signs of preeclampsia.

Pregnancy-Induced Hypertension is a known cause of premature delivery, intrauterine growth restriction (IUGR), placental abruption and foetal death, as well as maternal mortality and morbidity. Pregnancy-Induced Hypertension is one of the commonest pregnancy complications in Ghanaian hospitals today with a 7.03% incidence rate for preeclampsia being reported by Obed and Patience (2006).

To date, the aetiology of PIH remains unknown, however, a number of risk factors have been identified (Roberts and Lain, 2002; Zhang *et al.*, 1997). Primiparas are known to be at markedly greater risk of preeclampsia than multiparas. Preeclampsia is a complication in 25-30% of nulliparous pregnancies. It is more common in nulliparous than in multiparous women and as such the first pregnancy is a risk factor for preeclampsia (Serhal *et al.*, 2003). The use of barrier contraceptives, young maternal age, change of partner (Duckitt and Harrington, 2005; Skjaerven *et al.*, 2002; Trupin *et al.*, 1996), have all been reported to amplify the risk of PIH or preeclampsia, but these observations await corroboration or refutation most especially in the black African community.

Previous studies reported hypertension in pregnancy to be associated with an increased risk of preterm delivery (Hauth *et al.*, 2000; Sibai *et al.*, 1998). It is also known that the condition reverses after delivery of the placenta. As such, placental hormonal imbalance in hypertensive pregnant women has been studied (Bhansali and Eugere, 1992; Friedman *et al.*, 1991). Human placental lactogen and cortisol levels have been reported to be either unchanged or decreased (Garoff and Seppala, 1976; Salem *et al.*, 1983). It is therefore essential to identify patients with Pregnancy-Induced Hypertension in whom the foetus is at greatest risk. One approach to this is the assessment of the size and growth rate of the foetus by clinical or ultrasonic means. A second approach based on the fact that foetal morbidity and mortality can be largely attributed to placental dysfunction, is the measurement, in the maternal circulation of substances such as Human Placental Lactogen (hPL) produced by the fetoplacental unit (Letchworth and Chard, 1972a; Letchworth and Chard, 1972b).

Human placental lactogen is a member of a structurally and biologically overlapping family of polypeptide hormones (Corbacho *et al.*, 2002; Goffin *et al.*, 1996). They are known to play an important role in lactation, reproduction, osmoregulation, immunomodulation and growth of tissues and blood vessels (Corbacho *et al.*, 2002; Karabulut *et al.*, 2001). Human placental lactogen, due to its effect on blood vessels, has been implicated in the aetiology of PIH due to the fact that endothelial and vascular dysfunctions are associated with the disorder.

There is need for follow-up studies in the black populations in Africa and as such, studying the patterns of risk factors for PIH among Ghanaian women is essential since publications on this subject in Ghana are very scanty. This study, therefore, seeks to identify the relationship between some putative risk factors of PIH among Ghanaian pregnant women and to determine if placental hormonal imbalance is associated with PIH among Ghanaians with the aim of making inputs to available literature and also as a step to possibly finding in-

terventions for reducing the prevalence of this clinical condition, which is associated with a high maternal as well as perinatal morbidity and mortality worldwide.

MATERIALS AND METHODS

Subjects

This cross-sectional study was conducted at the Komfo Anokye Teaching Hospital in Kumasi, Ashanti Region of Ghana between November, 2006 and December, 2007. Women within the age group of 17- 45 years visiting the Obstetrics and Gynaecology Department of the Hospital were recruited for the study. One hundred pregnant women with Pregnancy-Induced Hypertension (seventy with gestational hypertension and thirty with preeclampsia) served as cases; and fifty normotensive pregnant women with uncomplicated pregnancy served as study control. Only one woman with PE declined to participate in the study. Most importantly, women with known renal disease, diabetes and hypertension prior to pregnancy or cardiovascular diseases were excluded from this study among both case and control participants. Women with a history of twin birth or who were carrying twin pregnancy as observed from their ultrasound scan were also excluded from the study.

Pregnancy-Induced Hypertension was diagnosed according to the criteria of the National High Blood Pressure Education Program Working Group for PIH as assessed by a single qualified Obstetrician/ Gynaecologist. Briefly, the presence of high blood pressure on two occasions six hours apart was considered GH while pregnant women who had proteinuria level of 2+ positive result on a dipstick (using early morning midstream urine), were considered as presenting with PE (Forest *et al.*, 2005). Finally, GH and PE were collectively considered as PIH. All the subjects were Ghanaians and their participation was voluntary and informed consent was obtained from each subject. The study was approved by the School of Medical Sciences and Komfo Anokye Teaching Hospital Committee on Human Research Publications and Ethics (CHRPE/ KNUST/KATH/15_03_08).

Each subject had a questionnaire-based interview, which was conducted privately and in person and lasted approximately 45 minutes. Information on maternal lifestyle factors such as smoking and alcohol consumption during pregnancy, demographic data, recent medical history, a complete obstetric history, contraceptive use, occupational factors, exercise and social data was obtained. Each participant reported the outcomes of all previous pregnancies as live births, stillbirths, spontaneous abortions or induced abortions. Information extracted from questionnaire included socio-demographic characteristics, medical and previous reproductive history as well as social information and lifestyle habits. The veracity of the information extracted from the questionnaire on reproductive history and socio-demography obtained during the interview was verified through a review of hospital records.

Exercise was defined as at least a conscious effort to stroll around participant's home for not less than 20-30 minutes daily. Change of partner was defined as a change in spouse at least four months before the participant's current pregnancy. Alcohol consumption related to alcohol intake in the months preceding pregnancy as well as during the current pregnancy.

Sample Collection and Preparation

Biochemical analysis

Fasting Blood Glucose (FBG) was determined using the glucose oxidase/peroxidase method (Trinder, 1969) and hPL was analyzed using Enzyme-Linked Immunoassay specific for hPL using a DRG® hPL Enzyme Immunoassay kit (DRG® Instruments, GmbH Germany) and results calculated from the standard curve. Human placental lactogen and fasting glucose were estimated between 29-31 weeks of gestation in all the participants.

Urinalysis

Early morning midstream urine was collected in plastic containers from the respondents and urine protein was analyzed using the dip-stick qualitative method (CYBOW™ DFI Co Ltd, Gimhae-City,

Republic of Korea). Proteinuria values of 0, 0.1, 0.3, 1 and 5 g L⁻¹ corresponded to qualitative dipstick testing attributes of negative, trace, +, ++ and +++ respectively.

Anthropometric variables

Subjects were weighed on a bathroom scale (Zhongshan Camry Electronic Co. Ltd, Guangdong, China) and their height measured with a wall-mounted ruler. BMI was calculated by dividing weight (kg) by height squared (m²) and obesity defined as BMI greater or equal to 30 kg m⁻².

Blood Pressure

Blood pressure was taken by trained personnel using a mercury sphygmomanometer and a stethoscope. Measurements were taken from the left upper arm after subjects had been sitting for >5 minutes in accordance with the recommendation of the American Heart Association (Kirkendall *et al.*, 1967). Duplicate measurements were taken with a 5 minute rest interval between measurements and the mean value was recorded to the nearest 2.0 mm Hg.

Statistical Analysis

Statistical analyses were performed using GraphPad Prism version 5.00 for windows (GraphPad software, San Diego California USA, www.graphpad.com). Continuous variables are expressed as their mean \pm SEM while categorical variable were expressed as proportion. Comparisons of the women with PIH (gestational hypertension and preeclampsia separately and combined) against the control group were carried out using, unpaired *t*-tests, χ^2 tests or fisher exact tests where appropriate. A level of $p < 0.05$ was considered as statistically significant.

SAS System for windows, version 6.12 was used to examine other putative risk factors for possible confounding effects on PIH. Abortion variables were similarly examined by analysis to estimate the risk on PIH (preeclampsia and gestational hypertension). We examined abortion by type; spontaneous or induced. Subjects were categorized by the type of abortion history, as follows: (a) women with no prior history of abortion (reference group), (b) women with prior

history of spontaneous abortion, (c) women with prior history of induced abortion. Crude odds ratios (*c*OR) and 95% confidence interval for PIH were calculated for all studied risk factors. Crude ORs were then adjusted by taking into account possible influence of other covariates, with the use of multiple logistic regression analysis to obtain adjusted (*a*OR). The *c*OR were adjusted for age, family history of hypertension, condom use, contraceptive use and change of partner. Three models were constructed one for each of the outcomes (GH, PE, and PIH). Variables with zero cells in some of the categories were not included in the models. Variables were entered into the model if $p < 0.05$ and a stepwise procedure was applied using the Cornfield exact method.

RESULTS

Clinical Characteristics

The demographic and clinical characteristics of the study population are as shown in Table 1. The mean value and the percentage prevalence of components of the metabolic syndrome were significantly increased in the entire studied group compared to the control group. The frequency distributions of the various putative risk factors are as shown in Table 2. As shown in Figure 1, the concentration of Human Placental Lactogen was significantly decreased when the PIH group was compared to the control group. The mean concentration of hPL was 4.9 ± 0.3 g L⁻¹ for the PIH subjects, 4.8 ± 0.4 g L⁻¹ for GH subjects, 4.4 ± 0.6 g L⁻¹ for PE subjects and that of the control group was 8.6 ± 1.1 g L⁻¹.

Putative Risk Factors

Pregnancy-Induced Hypertension

Women aged 24 years or less did not have a significantly increased risk of developing PIH compared to women between 25–29 years of age (*a*OR 2.2; 95% CI 0.6–7.6). However, women between 35–39 years of age had about 9 times increased risk of developing PIH compared to women between 25–29 years (95% CI 2.5–34.7). Nulliparity was not a significant risk factor for PIH from this study (*a*OR

Table 1: Demographics and clinical characteristics of Ghanaian pregnant women, 2006-2007

Parameters	Control	PIH	P value	GH	P value	PE	P value
<i>n</i>	50	100		70		30	
Maternal age (yrs)	30.9±0.7	31.8±0.6	0.004	32.4±0.7	0.000	30.4±1.3	0.280
GP (weeks)	31.0±0.9	30.4±0.8	0.110	29.4±0.7	0.220	30.7±1.0	0.100
Proteinuria (g L ⁻¹)	0.0±0.0	0.4±0.1	0.001	0.0±0.0	0.320	1.4±0.3	0.000
SBP (mmHg)	105.8±1.5	149.0±1.7	0.000	147.1±1.6	0.000	153.3±3.9	0.000
DBP (mmHg)	67.2±1.1	95.6±1.2	0.000	94.1±1.1	0.000	99.0±2.9	0.000
BMI (kg m ⁻²)	27.0±0.5	29.5±0.6	0.009	29.2±0.8	0.032	30.1± 0.9	0.001
Obesity	9(18.0%)	51(51.0%)	0.000	32(45.7%)	0.002	19(63.3%)	0.000
FBS (mmol L ⁻¹)	3.5±0.1	4.0±0.2	0.060	3.9±0.2	0.200	4.2±0.2	0.000
Diabetes	0(0.0%)	7(7.0%)	0.100	6(8.57%)	0.039	1(3.3%)	0.370

Continuous data are presented as mean ± SEM and categorical variable as number with percentage in parenthesis. GP = gestational age, PIH = pregnancy-induced hypertension subjects, PE = preeclampsia group, GH = gestational hypertension group, SBP = systolic blood pressure, DBP = diastolic blood pressure, BMI = body mass index and FBS = fasting blood sugar

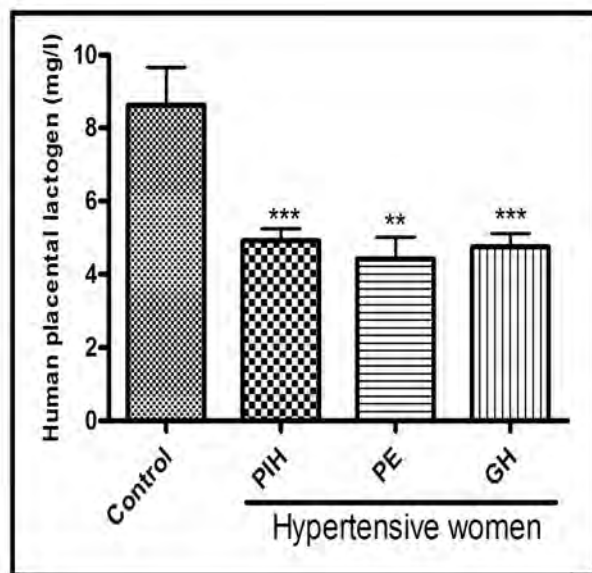


Figure 1: Distribution of human placental lactogen (hPL) in control and pregnancy-induced hypertension subjects (PIH). PE = preeclampsia group, GH = gestational hypertension group. Values are mean ± SEM and significantly different from control using unpaired *t*-test: **P < 0.01 and *P < 0.001**

1.8; 95% CI 0.8–4.0). Women who were obese were about 5 times at risk of developing PIH compared to the reference BMI group (95% CI 1.7-12.5). Marital status, the consumption of alcoholic beverages and educational attainment did not significantly influence the risk of developing PIH from this study (Table 3).

As shown in Table 4, lack of exercise and prior abortion did not pose any significant risk for the development of PIH from this study. However, women with a family history of hypertension were about 7 times at risk of developing PIH as compared to women without family history of hypertension (95% CI 2.3-19.6). Also, the risk of developing PIH was about 6 times among women whose partners used condom during coitus (95% CI 1.2-23.0), about 2 times among women who used contraceptives (95% CI 1.2-3.9) and about 2 times among women who changed sexual partners (95% CI 1.1-5.8) compared to women whose partners did not use condom, women who did not use contraceptives and women who did not change sexual partners respectively. Women with prior preterm delivery were not at risk of developing

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Table 2 - Distribution of the Risk Factors for Ghanaian pregnant women, 2006-2007

PARAMETERS	CG (50)	PIH (100)	GH (70)	PE(30)
Maternal Age (yrs)				
<25	8(16.0%)	11(11.0%)	7(10.0%)	4(13.3%)
25-29	19(38.0%)	17(17.0%)	9(12.9%)	8(26.7%)
30-34	17(34.0%)	35(35.0%)	26(37.1%)	9(30.0%)
35-39	4(8.0%)	28(28.0%)	22(31.4%)	6(20.0%)
40-44	2(4.0%)	9(9.0%)	6(8.6%)	3(10.0%)
Parity				
0	20(40.0%)	43(43.0%)	43(61.4%)	0(0.0%)
1+	30(60.0%)	57(57.0%)	27(38.6%)	30(100.0%)
Body Mass Index (BMI)				
< 19	0(0.0%)	4(4.0%)	3(4.3%)	1(3.3%)
19-24.9	14(28.0%)	17(17.0%)	13(18.6%)	4(13.3%)
25-29.9	27(54.0%)	28(28.0%)	22(31.4%)	6(20.0%)
≥ 30	9(18.0%)	51(51.0%)	32(45.7%)	19(63.3%)
Marital Status				
Single	2(4.0%)	8(8.0%)	4(5.7%)	4(13.3%)
Married	48(96.0%)	92(92.0%)	66(94.3%)	26(86.7%)
Alcohol Consumption				
Yes	15(30.0%)	42(42.0%)	28(40.0%)	14(46.7%)
No	35(70.0%)	58(58.0%)	42(60.0%)	16(53.3%)
Educational Background				
None at all	3(6.0%)	8(8.0%)	5(7.14%)	3(10.0%)
Basic	33(66.0%)	74(74.0%)	50(71.4%)	24(80.0%)
Secondary	7(14.0%)	12(12.0%)	9(12.9%)	3(10.0%)
Tertiary	7(14.0%)	6(6.0%)	6(8.6%)	0(0.0%)
Exercise				
Yes	28(56.0%)	45(45.0%)	31(44.3%)	14(46.7%)
No	22(44.0%)	55(55.0%)	39(55.7%)	16(53.3%)
Family history of hypertension				
Yes	5(10.0%)	38(38.0%)	26(37.1%)	12(40.0%)
No	45(90.0%)	62(62.0%)	44(62.9%)	18(60.0%)
Prior adverse birth outcome				
No prior adverse birth	47(94%)	93(93%)	70(100%)	24(80%)
Prior caesarian section	3(6%)	3(3%)	0(0%)	3(10%)
Prior preterm	0(0%)	5(5%)	0(0%)	5(16.7%)
Prior still birth	2(4%)	6(6%)	0(0%)	6(20%)
Prior abortion				
No prior abortion	32(64%)	62(62%)	52(74.3%)	8(26.7%)
Prior spontaneous abortion	17(34%)	31(31%)	14(20%)	17(56.7%)
Prior induced abortion	16(32%)	22(22%)	18(25.7%)	4(13.3%)
Condom Use				
Yes	2(4%)	19(19%)	12(17.1%)	7(23.3%)
No	48(96%)	81(81%)	58(82.9%)	23(76.7%)
Contraceptive Use				
Yes	13(26.0%)	37(37.0%)	25(35.7%)	12(40.0%)
No	37(74.0%)	63(63.0%)	45(64.3%)	18(60.0%)
Change of Partner				
Yes	10(20.0%)	37(37.0%)	21(30.0%)	16(53.3%)
No	40(80.0%)	63(63.0%)	49(70.0%)	14(46.7%)

PIH (cOR 0.0; 95% CI 0.0-0.4) (Table 4).

Gestational Hypertension

Women <25 years were not significantly at risk of GH when compared to women between 25–29 years of age (aOR 1.9; 95% CI 0.4-8.3). The risk of developing GH was about 4, 15, and 8 times higher among women in the age range 30-34 (95% CI 1.2-11.4), 35-39 (95% CI 3.6-63.2) and 40-44 (95% CI 1.0-55.0) respectively when compared to women between 25-29 years (Table 3). Nulliparity was a significant risk factor for GH (95% CI 1.2–7.4). However, pregnant women who were obese (i.e. BMI > 30 kg m⁻²) were about 4 times at risk of developing GH compared to women with normal BMI (19-24.9 kg m⁻²) (95% CI 1.3-10.9) (Table 3).

Pregnant women who did not engage in exercise and those with a prior history of adverse birth outcome as well as those with a history of abortion were not significantly at risk of developing GH when compared to their respective reference groups (Table 4). On the other hand, women with a family history of hypertension were significantly at risk of developing GH (95% CI 2.2-22.7). The risk of developing GH was about 4 times among women whose partners used condom during coitus (95% CI 1.1-2.1), about 2 times among women who used contraceptive (95% CI 1.1-2.6) and about 3 times among women who changed sexual partners (95% CI 1.1-8.0) when compared to women whose partners did not use condom, women who did not use contraceptives and women who did not change sexual partners respectively (Table 4).

Preeclampsia

The risk of developing PE significantly increased with maternal age, from 2 times among women 35-39 years old (95% CI 1.2-8.1) to about 3 times among women who were between 40-44 years old (95% CI 1.2-47.1) when compared to women who were between 25-29 years old. Women < 25 years were not significantly at risk of PE as compared to women between 25–29 years of age (95% CI 0.2-7.5) (Table 3). Nulliparity was not a significant risk factor for PE (cOR 0.0; 95% CI 0.0–0.2) from this study.

Obese women were about 7 times at risk of developing PE compared to the reference BMI group (95% CI 1.9-27.7). Marital status, the consumption of alcoholic beverages and educational status did not significantly influence the risk of developing PE from this study (Table 3).

Pregnant women with a family history of hypertension were about 10 times at risk of developing PE compared to those without a family history of hypertension (95% CI 2.2-42.6). Women with a prior history of spontaneous abortion were at about 4 times at risk of developing PE (95% CI 1.2-12.2) when compared to the reference group (Table 4). The risk of developing PE was about 5 times among women whose partners used condom during coitus (95% CI 1.3-33.0), about 3 times among women who used contraceptives (95% CI 1.2-16.1) and about 9 times among women who changed sexual partners (95% CI 2.4-30.3) when compared to women whose partners did not use condom, women who did not use contraceptives and women who did not change sexual partners respectively (Table 4).

DISCUSSION

Hypertension is regarded as a major public health problem (Cappuccio *et al.*, 2004). It is the most common medical complication of pregnancy, which occurs in 3% to 10% of pregnancies (Saudan *et al.*, 1998). Several epidemiological studies have indicated that a family history of chronic hypertension is an independent risk factor for preeclampsia (Eskenazi *et al.*, 1991; Kobashi *et al.*, 2001; Qiu *et al.*, 2003). This study has established a high risk for preeclampsia, gestational hypertension as well as PIH among women with a family history of hypertension indicating a familial inheritance.

Components of the metabolic syndrome increased significantly among the study population. The results of this study after adjusting for all other confounding risk factors indicates that advanced age posed a substantial risk factor for the development of PIH (GH+ PE). Although, nulliparity posed as risk for the development of GH, this risk was not observed for PIH and PE subjects. Obesity as as-

Table 3: Risk model of the putative socio-demographic risk factor for Ghanaian pregnant women, 2006-2007

PARAMETERS	PIH			GH			PE			
	cOR(95% CI)	P value	aOR(95% CI)	P value	cOR(95% CI)	aOR(95% CI)	P value	cOR(95% CI)	aOR(95% CI)	P value
Age (yrs)										
<25	1.5(0.5-4.7)	0.45	2.2(0.6-7.6)	0.20	1.8(0.5-6.5)	1.9(0.4-8.3)	0.35	1.2(0.3-4.8)	1.1(0.2-7.5)	0.82
25-29*	1	*	1	*	1	1	*	1	1	*
30-34	2.3(0.9-5.5)	0.06	2.7(1.0-7.0)	0.05	3.2(1.2-8.7)	3.7(1.2-11.4)	0.02	1.3(0.4-3.9)	0.8(0.2-3.4)	0.70
35-39	7.8(2.4-25.6)	0.001	9.2(2.5-34.7)	0.001	11.6(3.1-42.0)	15.1(3.6-63.2)	0.0001	3.6(0.8-15.3)	2.4(1.2-8.1)	0.04
40-44	5.0(1.0-26.6)	0.06	5.6(0.9-34.0)	0.06	6.3(1.1-32.9)	7.5(1.0-55.0)	0.03	3.6(0.6-21.6)	2.8(1.2-47.1)	0.04
Parity										
0	1.1(0.6-2.2)	0.86	1.8(0.8-4.0)	0.19	2.4(1.1-5.0)	3.0(1.2-7.4)	0.02	0.0(0.0-0.2)	§	§
1+*	1	*	1	*	1	1	*	1	§	§
Body Mass Index (BMI)										
< 19	undefined	§	§	§	undefined	§	§	undefined	§	§
19-24.9*	1	*	§	§	1	§	*	1	§	§
25-29.9	0.9(0.4-2.1)	0.82	§	§	0.9(0.3-2.2)	§	0.79	0.8(0.2-3.0)	§	§
≥ 30	4.7(1.7-12.5)	0.004	§	§	3.8(1.3-10.9)	§	0.01	7.4(1.9-27.7)	§	§
Marital Status										
Single	2.1(0.4-20.8)	0.36	3.5(0.6-21.3)	0.18	undefined	2.4(0.3-17.2)	*	3.7(0.6-21.5)	4.0(0.4-44.8)	0.27
Married*	1	*	1	*	1	1	*	1	1	*
Alc Consumption										
Yes	1.7(0.8-3.5)	0.15	1.1(0.5-2.6)	0.80	1.6(0.7-3.3)	1.3(0.5-3.4)	0.26	2.0(0.8-5.2)	1.3(0.4-4.3)	0.66
No*	1	*	1	*	1	1	*	1	1	*
Educational Background										
None at all	1.6(0.3-7.2)	0.59	2.8(0.5-17.5)	0.27	1.3(0.2-6.7)	1.2(0.1-10.4)	0.77	2.3(0.3-17.3)	§	§
Basic	1.3(0.5-3.5)	0.60	1.8(0.5-6.7)	0.36	1.2(0.4-3.3)	1.3(0.3-5.0)	0.76	1.7(0.4-6.6)	§	§
Secondary*	1	*	1	*	1	1	*	1	§	§
Tertiary	0.5(0.1-2.0)	0.34	0.5(0.2-4.9)	0.91	0.7(0.2-2.8)	1.7(0.3-9.2)	0.59	0.0(0.0-1.6)	§	§

*Reference group, CG = control group, PIH = pregnancy-induced hypertension subjects, PE = preeclampsia group, GH = gestational hypertension group, cOR = crude odds ratio, aOR = adjusted odds ratio and CI = confidence interval, §= variables with 0 cells not included in the multivariable model, Alc. = Alcohol

Table 4 - Risk model of the other putative risk factor for Ghanaian pregnant women, 2006-2007

PARAMETERS	PIH				GH				PE			
	cOR(95% CI)	P value	aOR(95% CI)	P value	cOR(95% CI)	P value	aOR(95% CI)	P value	cOR(95% CI)	P value	aOR(95% CI)	P value
Exercise												
Yes*	1	*	1	*	1	*	1	*	1	*	1	*
No	1.6(0.8-3.1)	0.20	1.3(0.6-2.9)	0.48	1.6(0.8-3.3)	0.21	1.4(0.6-3.4)	0.47	1.5(0.6-3.6)	0.42	1.0(0.3-3.3)	0.94
Family history of hypertension												
Yes	5.5(2.0-14.6)	0.0004	6.8(2.3-19.6)	0.001	5.3(1.9-14.6)	0.0008	7.0(2.2-22.7)	0.001	6.0(1.9-18.8)	0.002	9.7(2.2-42.6)	0.003
No*	1	*	1	*	1	*	1	*	1	*	1	*
Prior adverse birth outcome												
NPAB*	1	*	§	§	1	*	§	§	1	*	§	§
PCS	0.5(0.1-2.3)	0.41	§	§	0.0(0.0-0.8)	0.07	§	§	1.7(0.3-9.2)	0.66	§	§
PP	0.0(0.0-0.4)	0.005	§	§	undefined	§	§	§	undefined	§	§	§
PSB	1.5(0.3-7.5)	1.00	§	§	0.0(0.0-1.3)	0.17	§	§	6.0(1.1-32.0)	0.05	§	§
Prior abortion												
NPA*	1	*	1	*	1	*	1	*	1	*	1	*
PSA	0.9(0.5-1.9)	0.87	0.8(0.5-1.9)	1.00	0.5(0.2-1.2)	0.10	0.5(0.2-1.3)	0.16	4.0(1.5-11.0)	0.006	3.7(1.2-12.2)	0.02
PIA	0.7(0.3-1.5)	0.38	0.5(0.3-1.8)	0.49	0.7(0.3-1.5)	0.41	0.6(0.2-1.5)	0.51	1.0(0.3-3.7)	1	1.0(0.3-3.6)	1.00
Condom Use												
Yes	5.6(1.2-25.2)	0.01	5.8(1.2-23.0)	0.01	5.0(1.1-3.3)	0.04	3.8(1.1-2.1)	0.04	7.3(1.4-37.9)	0.01	4.5(1.3-33.0)	0.02
No*	1	*	1	*	1	*	1	*	1	*	1	*
Contraceptive Use												
Yes	1.7(0.7-3.5)	0.03	1.7(1.2-3.9)	0.03	1.6(0.8-3.5)	0.04	1.7(1.1-2.6)	0.04	1.9(0.7-5.0)	0.0411	3.4(1.2-16.1)	0.0391
No*	1	*	1	*	1	*	1	*	1	*	1	*
Change of Partner												
Yes	2.3(1.1-5.2)	0.03	2.3(1.1-5.8)	0.04	1.7(0.7-4.0)	0.22	2.6(1.1-8.0)	0.04	4.6(1.7-12.2)	0.002	8.5(2.4-30.3)	0.001
No*	1	*	1	*	1	*	1	*	1	*	1	*

*Reference group, CG = control group, PIH = pregnancy-induced hypertension subjects, PE = preclampsia group, GH = gestational hypertension group, cOR = crude odds ratio, aOR = adjusted odds ratio and CI = confidence interval. NPAB= No prior adverse birth, PCS= Prior caesarian section, PP= Prior Preterm, PSB= Prior still birth, NPA=No prior abortion, PSA=Prior spontaneous Abortion, PIA= Prior Induced abortion, §= variables with 0 cells not included in the multivariable model.

essed by BMI posed a significant risk factor for all three clinical conditions. Socio-economic status (SES) (evaluated by marital status and education) was not associated with PIH (including GH and PE). Alcohol consumption and lack of exercise during pregnancy did not significantly influence the risk of PIH, GH and PE. Although, history of prior adverse birth outcome and a history of prior abortion did not influence the risk of PIH and GH; an increased risk for PE was observed among women with prior preterm delivery and prior spontaneous abortion. Family history of hypertension significantly increased the risk for PIH, GH and PE; the use of contraceptives in either the male or the female partner as well as the change of sexual partner similarly, posed as risk factors for the development of the clinical conditions.

Some studies have reported increased risk of preeclampsia in younger women who are ≤ 21 years (Anorlu *et al.*, 2005; Sibai, 1990) and others have reported an association of increased risk of preeclampsia with women who are 35 years or older (Conde-Agudelo and Belizan, 2000; Sibai, 1990). This study found older mothers were at greater risk for the pathology. Indeed the relationship was not only observed for preeclampsia but also for GH. Stone *et al.*, (1995) and later Hartikainen *et al.*, (1998) have also demonstrated that older mothers were at increased risk of GH. The observed risk could be attributed to biological changes associated with maturity.

In this study, the risk of developing PIH, GH or PE positively associated with maternal obesity as measured by maternal Body Mass Index (BMI). This corroborates the findings of several studies where a strong association between increased maternal body mass and risk of preeclampsia has been reported (Anorlu *et al.*, 2005; Bodnar *et al.*, 2005; Eskenazi *et al.*, 1991; Villamor and Cnattingius, 2006). Obesity is associated with insulin resistance, dyslipidaemia, chronic inflammation and oxidative stress (Reilly and Rader, 2003), all of which have been demonstrated in women presenting with PIH (Ahenkorah *et al.*, 2008; Roberts and Lain, 2002; Turpin *et al.*,

2008). As a result of the strong relationship observed, the association between increasing changes in BMI and risk of PIH may support the theory that obesity-mediated inflammatory changes may play a role in the pathogenesis of PIH (Getahun *et al.*, 2007).

From this study, nulliparity was a risk factor for GH, as also reported by Hernandez-Diaz *et al.*, (2002). Preeclampsia is considered to be a disease largely associated with nulliparous women (Roberts and Redman, 1993). Serhal and Craft, (1987) also reported that first pregnancy is a risk factor for preeclampsia and its occurrence is more common in nulliparous than multiparous women (Eskenazi *et al.*, 1991; Roberts and Redman, 1993). Contrary to these and other reports, this study did not find nulliparity as a risk factor for women presenting with PE and PIH. The lack of association between nulliparity and risk of preeclampsia observed in this study is in agreement with the findings of Funai *et al.*, (2005). Although, the mechanism for this lack of association cannot be fully explained, Funai *et al.*, (2005) have proposed that, the degree to which preeclampsia would chiefly be a disease of nulliparity would depend on the fraction of patients seen who were nulliparous. Further research with emphasis on nulliparous women may be required to corroborate or refute this assertion.

Previous spontaneous abortion increased the risk for preeclampsia in this study. Contrary to this, Eras *et al.*, (2000) have reported that a history of abortion reduced the risk against both gestational hypertension and preeclampsia. Although, abortion reduced the risk for PIH and GH in this study, it however did not reach significant levels. In one of the few reported studies that evaluated the timing of abortion, Campbell *et al.*, (1985) showed and reported that late spontaneous abortion, defined as 13-27 weeks, conferred protection against preeclampsia in the subsequent pregnancy, whereas early spontaneous abortions did not. This might in part explain why spontaneous abortion (i.e. miscarriage) which usually occurs in the early weeks of pregnancy could not reduce the risk of preeclamp-

sia in this study.

Contraceptive use in either the male or the female partner as well as change of partner by the female partner positively associated with the risk of PIH, (PE and GH inclusive). Pregnancy-Induced Hypertension has long been considered to have an immunological basis. The results of several studies suggest that repeated exposure to the male partner's spermatozoa prior to conception reduces the risk of Pregnancy-Induced Hypertension in the first pregnancy (Marti and Herrmann, 1977). This implies that if extensive periods of cohabitation with the partner protects against Pregnancy-Induced Hypertension, it could be deduced that the mechanism may be related to the contact of spermatozoa with the female genital tract. This might explain the high risk observed in women whose spouses used condom as a means of contraception because the use of condom reduces or limits exposure of the female genital tract to the male partner's spermatozoa.

Similarly, women who used oral contraceptives prior to this study were not protected from Pregnancy-Induced Hypertension. From the face-to-face interview conducted in this study, most of the women used oral contraceptives. Oral contraceptives are known to act at different levels of the female reproductive tract, i.e. cervical mucus thickening, tubal motility, changes in endometrial lining (i.e. by decreasing the possibility of implantation, should conception occur) and ovulation suppression. However, in terms of exposure to spermatozoa, the main difference in a woman taking contraceptives is that the characteristics of cervical mucus may confine the semen to the vagina (Gratacos *et al.*, 1996). The non-protective effect of oral contraceptives might therefore be as a result of the reduced exposure to spermatozoa which is brought about by the effect of oral contraceptives on the female genital tract.

Various studies have reported paternity change as a risk factor for preeclampsia (Feeney and Scott, 1980; Li and Wi, 2000; Trupin *et al.*, 1996). This current study did not only find change of partner to be a strong risk factor for preeclampsia but also for gestational hypertension. Indeed, it is presumed that a

previous normal pregnancy is associated with a reduced risk of Pregnancy-Induced Hypertension, but other studies have reported that this protective effect is lost with the change of partner (Dekker, 2002; Robillard *et al.*, 1999; Robillard *et al.*, 1993). Lie *et al.*, (1998) have also reported on the existence of what they termed 'dangerous' father, where they established that men who fathered one preeclamptic pregnancy were nearly twice as likely to father a preeclamptic pregnancy in a different woman regardless of whether she had already had a preeclamptic pregnancy or not (Dekker, 2002; Lie *et al.*, 1998). Furthermore, it has been reported in some studies that multiparous women who have had a change of partner before the index pregnancy have an increased risk of preeclampsia (Eras *et al.*, 2000; Li and Wi, 2000). Therefore, preeclampsia might be a problem of primipaternity (Robillard *et al.*, 1999; Robillard *et al.*, 1993) rather than primigravidity as most studies suggest.

In assessing the levels of placental hormone hPL among Ghanaian women presenting with pregnancy-induced hypertension, decreased levels of hPL was observed in all the subject cases (PIH, PE, GH) with the least concentration noted among the PE subjects. The observed decrease in hPL level in this study is consistent with the findings of other studies (Bersinger *et al.*, 2002; Letchworth and Chard, 1972a; Westergaard *et al.*, 1984). Human placental lactogen levels are a valuable indicator of foetal well-being (Letchworth and Chard, 1972b), clinical signs of foetal growth retardation and very low hPL values seem to indicate high foetal risk (Lindberg and Nilsson, 1973) and appears to satisfy all the criteria of a good test of placental function (Genazzani *et al.*, 1971; Spellacy *et al.*, 1971).

The disclosure of information on abortion type, previous obstetric history and contraceptive use was obtained from personal interviews. Although verified with medical records, a drawback of the data is that, these matters bother on sexuality and thus considered personal and sensitive in this part of the world and as such, most women may not be forthcoming with accurate answers. Reporting errors would have resulted in non-differential mis-

classification that may have introduced a bias and thus potentially underestimate observed associations and thereby serving as a limiting factor to the outcomes of the study.

Another limitation of this study relates to the limited power to detect associations between previous adverse birth outcome and PIH, due to low numbers for some of the subtypes of previous adverse birth outcome. Further scientific enquiry may be required involving a larger sample size in order to corroborate or refute the findings in this report.

CONCLUSION

This study has shown that obesity, older women, family history of hypertension, contraceptive use are some significant risk factors for PIH among women in Ghana and possibly in other black African countries. Paternal and placental roles have also been observed in this cohort of Ghanaian subjects. These risk factors are not very different from what has been reported in studies conducted outside Ghana.

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COMPETING INTERESTS

The authors declare that they have no competing interests.

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