PREDICTORS OF PRE-ECLAMPSIA: A HOSPITAL BASED STUDY IN ACCRA, GHANA

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Abstract

Introduction: Pre-eclampsia is a medical condition which develops after 20 weeks of pregnancy, where blood pressure is elevated to 140/90mm/Hg or more, with significant amounts of protein in the urine. It is a pre-cursor of eclampsia and leads to increased morbidity and mortality in the affected mother and fetus or baby. The only cure for pre-eclampsia involves delivery of the placenta. Pre-eclampsia is asymptomatic and difficult to predict in the first trimester of pregnancy.

Methods: This was a case control study done at the Police Hospital in Accra, using secondary data which were antenatal clinic records from 1st January 2008 to 31st December 2010. We sought to determine the number of deliveries complicated with pre-eclampsia, the proportion of deliveries complicated by pre-eclampsia, and risk factors of pre-eclampsia.

Results: The proportion of deliveries complicated by pre-eclampsia was 2.5%. We found no association between pre-eclampsia and season of delivery, maternal blood group, history of previous abortions, maternal infections of syphilis, HIV and Hepatitis B. We found maternal age of 25 years and above, parity of one and systolic blood pressure of 130mm/Hg or more at booking were statistically significant predictors of pre-eclampsia.

Conclusion: These three variables could be used to select pregnant women in the first 20 weeks of pregnancy for focused surveillance, and as a tool for selecting women for early referral for specialist care. We however recommend larger studies with the addition of lifestyle variables in further studies.

Key Words: Pre-eclampsia, Eclampsia, Ghana, maternal death, Pre-cursor

Introduction

Pre-eclampsia (PE) is the pre-cursor of eclampsia, a pregnancy-specific syndrome characterized by new-onset hypertension and proteinuria, occurring usually after 20 weeks' gestation. It is associated with high maternal mortality and morbidity as well as risk of fetal perinatal death, preterm birth, and intrauterine growth restriction[1]. However it is asymptomatic and difficult to predict in the early stages of pregnancy. As a result, most cases are not detected early and are seen at health facilities in severe PE or eclampsia stage, which most of the time is difficult to treat or manage. The absence of screening tools makes diagnosis at an early stage of pregnancy in some antenatal clinic (ANC) settings difficult.

Although blood pressure (BP) elevation is the most visible sign of the disease, it involves generalized damage to the maternal endothelium, kidneys, and liver, with the release of vaso-constrictive factors being secondary to the original damage. There is currently no known treatment for pre-eclampsia and ultimate treatment involves delivery of the placenta[2].

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Pre-eclampsia is diagnosed when a pregnant woman develops high BP (two separate readings taken at least four hours apart of 140/90 mm/Hg or more). Also, laboratory values for PE include; proteinuria of >300 mg/24h, urine dipstick >1+, and protein/creatinine ratio >0.3[3]. A 24-hour urine protein analysis remains the criterion standard for proteinuria diagnosis. Alternatively, greater than 1+ protein on a dipstick analysis on a random sample is sufficient to make the diagnosis of proteinuria. A rise in baseline BP of 30mm/Hg systolic or 15mm/Hg diastolic, while not meeting the absolute criteria of 140/90mm/Hg is also considered important.

In the United States of America, PE is believed to be responsible for 15% of premature deliveries[4] and 17.6% of maternal deaths[5, 6]. In Ghana there was an estimated 11,166 cases of pre-eclampsia in 2003[7]. Despite its impact on maternal and child health, efforts to predict and prevent PE have been disappointing. Numerous strategies including the use of vitamin C and E supplementation have been shown to be of little benefit[8].

The Ghana Ministry of Health's five year Programme of work (POW) from 2002 to 2006, of reducing maternal mortality ratio (MMR) from 214 to 150 per 100,000 live births (figures based on health institutional data only) by 2006 was not achieved[9]. The rate of reduction in MMR is so low that Ghana is unlikely to achieve the Millennium Development Goal

5 which calls for a 75% reduction in the MMR of 1990, by 2015[10]. There is the need to develop a simple, low cost tool to identify women who are more likely to develop pre-eclampsia before the 20th week of pregnancy. This tool could be used in rural settings, clinics, and maternity homes and also serve as a guide for early referral to prevent progression to eclampsia, and thus reduce maternal morbidity and mortality from this cause.

Worldwide, approximately five to eight percent of pregnancies (over 6.6 million women) are affected by PE every year[11]. Over 90% of these occur in developing countries. In 2008, there were 953 institutional maternal deaths in Ghana, with 168 of these deaths due to eclampsia[12]. Since PE resolves postpartum, premature delivery of the baby may be essential to safeguard the mother's life. Up to a third of infants born of pre-eclamptic pregnancies are affected by intrauterine growth restriction[13].

Consequently, many of the infants born of pre-eclamptic pregnancies require costly support in special care baby units. The burden of pre-eclampsia on health care resources is therefore substantial.

As PE remains a serious and poorly understood complication of pregnancy, there is the need to identify epidemiological and clinical risk factors to predict it before it threatens the survival of both mother and fetus. The study of risk factors and the underlying evidence base can be used to assess risk of pre-eclampsia at antenatal booking[14].

Objectives

Our study objectives were:

- To determine the number of pre-eclampsia cases,
- To determine the proportion of deliveries complicated by pre-eclampsia,
- To determine risk factors of pre-eclampsia among pregnant women delivering at the Police Hospital

Methods

Study area

This study was conducted at the Police Hospital situated at Cantonments in the La Dade Kotopon Municipal Area in Accra in 2011. The Police Hospital was established for Police personnel and their dependents in 1976. However, since 1980, it has opened its doors to civilians as well and currently over 80% of out-patient attendees are civilians. In 2009, there were 1,638 deliveries. The following year however, there was a marginal decline of deliveries to 1,535. The department of Obstetrics and Gynaecology is headed by an experienced Consultant. Consistently, eclampsia has been one of the leading causes of maternal mortality in the hospital.

Study design

This was an unmatched case - control study, with the use of secondary data extracted from ANC cards and other available medical records to determine possible predictors of pre-eclampsia before the 20th week of pregnancy, with independent variables at the first visit or booking at the ANC.

Study population

The study population was pregnant women that delivered at the Police Hospital, from 1st January 2008 to 31st December, 2010.

Cases

A case was a pregnant woman with PE that delivered at the Police Hospital in Accra, from 1st January 2008 to 31st December 2010, irrespective of disease progression or outcome.

Controls

A control was a pregnant woman without PE that delivered at the Police Hospital, from 1st January 2008 to 31st December 2010.

Exclusion criteria

Pregnant woman that delivered with pre-existing hypertension, diabetes, renal disease, or previous history of PE were excluded from the study. Any pregnant woman, presenting at first visit at the ANC after the 20th week of gestation was also excluded from the study. Some controls were found to be having BPs higher than 130/90 on their first visit. However they were subsequently found not to be hypertensive. They were therefore not excluded from the study.

Sample size and sampling procedure

The sample size for the study was 200, with 100 cases and 100 controls. We used the Fleiss equation for analytic studies to calculate the sample size.

Selection of cases and controls

We found 115 women that delivered with complications of PE over the three year period, out of which 103 fit our case definition. 100 of the 103 were selected as cases by simple random sampling. In selecting the controls, a total number of 4,637 records arranged according to their dates of first ANC attendance for the three year period was obtained. This number was divided by 100, which was the sample size of controls. Every 46th record was thus selected to be part of the study. The selection of the first ANC card was done by cutting 46 identical pieces of paper, and then numbering them from 1 to 46. They were then folded identically and put in a bowl and thoroughly mixed. A blindfolded assistant picked the first piece of paper with the number 13 written on it. We therefore started picking the controls from the 13th record and picked the rest at intervals of 46. This was repeated till the 100 controls were retrieved.

Data capture and analysis

Data entry sheets were used to capture data from the ANC attendance cards and folders of patients.

Where necessary, medical officers involved in management were consulted for clarifications. Quality control checks were performed for completeness, internal consistency and accuracy of data collected. Univariate analysis was done by running frequencies, percentages, and means. Bivariate analysis was performed with the use of odds ratio to compare categorical variables. Student's t-test was used for quantitative variables. Multivariate analysis involved the use of binary logistic regression to show the relationship between binary dependent and independent variables. Data was analyzed with Epi info version 3.5.2 and SPSS version 17.

Results

The number of deliveries complicated by pre-eclampsia for the study period was 115, with total number of deliveries being 4,637. The proportion of pre-eclampsia cases to total deliveries was 2.5%, over the three - year period. The breakdown per year is shown in Table 1.

Table 1: Pre-eclampsia cases from 2008 to 2010.

Year	Number of mothers with pre-eclampsia	Number of deliveries	Proportion of pre-eclampsia/deliveries
2008	29	1488	0.020 (2%)
2009	35	1614	0.021 (2.1%)
2010	51	1535	0.033 (3.3%)
Total	115	4637	0.025 (2.5%)

As shown in Table 2, most of the cases (38%) were in the 25 to 29 age group. Among the controls however, majority were in the 30 to 34 age group (33%).

Table 2: Distribution of cases and controls by age groups

Age group (years)	Frequency		Percent	
	Case N=100	Control N=100	Case N=100	Control N=100
<15	0	2	0	2
15-19	3	4	3	4
20-24	9	21	9	21
25-29	38	26	38	26
30-34	30	33	30	33
35-39	14	9	14	9
40-44	6	5	6	5

The minimum and maximum ages among the cases and controls were 19 and 42, and 13 and 39 respectively. The mean age of the cases were 29.5 ± 5.2, and 29.8 ± 5.3 for the controls respectively. The difference between the mean of the ages was however not statistically significant ($p > 0.05$).

Majority were Christians (85%) with the rest being Muslims, whilst most of the mothers (97%) were married. A total of 186 (93%) records had values for blood group. Majority of the mothers 88 (47.3%) were of blood group O, blood group B were 50 (26.9%), blood group A were 43(23.1%), and blood group AB were 5 (2.7%), as shown in Figure 1.

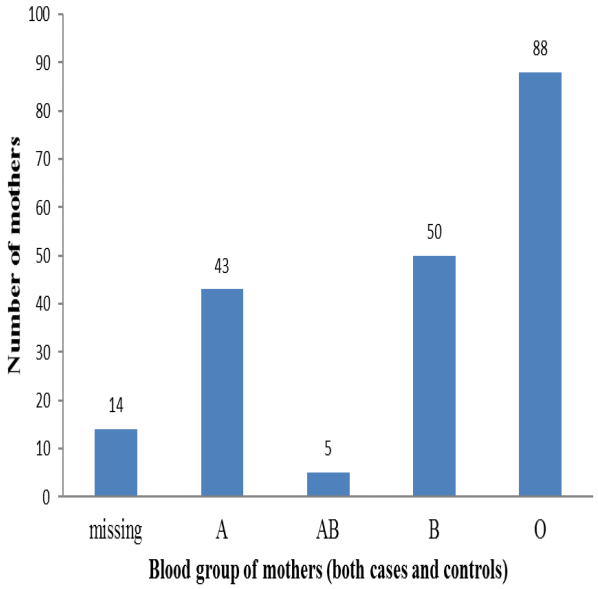

Figure 1: Shows maternal blood groups of mothers for both cases and controls

The minimum and maximum systolic blood pressure (SBP) values among cases were 85 and 190 mmHg. The mean Systolic BP (SBP), of cases and controls were 123.5 ±18.9 and 112.1 ± 10.8 respectively. The mean SBP was significantly higher among the cases ($p < 0.001$). The minimum and maximum diastolic blood pressures (DBP) among cases were 50 and 130, and among controls were 50 and 100 respectively. The mean DBP among cases and controls were 78.8 ± 15.7 and 68.5 ± 8.9. Cases were found to show significantly higher DBP than controls ($p < 0.001$).

Mean number of previous deliveries for the cases and controls were 1.1 ± 1.0 and 1.0 ± 0.9 respectively and showed no statistically significant difference ($p > 0.05$). Mean number of previous pregnancies for cases and controls were 2.5 ± 1.4 and 2.3 ± 1.1 respectively and also showed no statistically significant difference ($p>0.05$). Twenty four percent of cases had a previous history of abortions, as against 11% of controls. Previous history of abortions appeared to be associated with an increased risk of PE. This finding was statistically significant (OR 2.56, 95% CI 1.18-5.55, $p=0.0246$). Eighty-nine percent of cases were 25 years or above as compared to 77% of controls. Maternal age of 25 years and above appeared to increase the risk of

PE. This finding was also statistically significant (OR 2.42, 95% CI 1.11-5.28, p<0.05). Being married was not associated with PE (OR 3.12, 95% CI0.62-15.89, p>0.05). A parity of 1 appeared to be protective against PE (OR 0.5 95% CI 0.27-0.91 p<0.05). Forty-two percent of cases were nulliparous as compared to 28% of controls. Nulliparity appeared to increase the risk of pre-eclampsia, though this finding was not statistically significant (OR 1.86, 95% CI 1.03-3.35 p> 0.05).

Fifty one percent of cases and 55% of controls delivered in the wet season. There were no significant difference between the cases and controls concerning season of delivery (OR 0.85, 95%CI 0.49-1.48, p>0.05).

Table 3: Risk factors of pre-eclampsia

Parameter	**Cases**		**Controls**		**Odds ratio (OR)**	**Confidence interval (CI)**	**P value**
	Number	**%**	**Number**	**%**			
Sickling positive	13	13	19	19	0.64	0.29-1.37	0.2470
Sickling negative	87	87	79	79			
Rhesus positive	85	85	80	80	1.42	0.68-2.96	0.3509
Rhesus negative	15	15	20	20			
Hep B Positive	3	3	6	6	0.5	0.12-2.06	04983
Hep B negative	97	97	94	94			
Syphilis reactive	1	1	0	0	-	-	-
No syphilis	99	99	100	100			
HIV pos	1	1	0	0	-	-	-
HIV neg	99	99	100	100			
Systolic BP≥130	44	44	11	11	**6.38**	**3.03-13.33**	**<0.0001**
Systolic BP<130	56	56	89	89			
Diastolic BP≥90	55	55	27	27	**3.31**	**1.83-5.97**	**<0.0001**
Diastolic BP<90	45	45	73	73			

We found no statistically significant association between maternal blood group and pre-eclampsia.

At the beginning of the study those with previous history of hypertension were excluded. However some records were found with high booking blood pressures but subsequent BP checks proved they were not hypertensive and were not medicated for that. Such records were included in the study.

As seen in Table 3, SBP of 130mm/Hg or more increased the risk of PE (OR 6.38 95% CI 3.03-13.33 p <0.0001), as a DBP of 90mm/Hg or more (OR 3.31, 95% CI 1.83-5.97 p< 0.0001). These findings were statistically significant.

Thirteen percent of cases were sickling positive, as compared with 19% of controls.

Positive sickling status appeared to be protective but this was not statistically significant (OR 0.64, 95% CI 0.29-1.37, p>0.05). Rhesus positive state appeared to be associated with PE, but this was not statistically significant (OR 1.42, 95% CI 0.68-2.96, p>0.05). There was no statistically significant association between PE and maternal infections of hepatitis B, syphilis and HIV.

A multivariate model was constructed for variables that showed a statistically significant association with PE in the univariate analysis.

Table 4: Multivariate analysis of significant variables

Variable	B	S.E	Wald	OR	P value	95% CI
Age	0.895	0.434	4.265	2.448	0.039	1.047 - 5.726
Previous abortions	0.813	0.435	3.496	2.255	0.062	.961- 5.290
Systolic BP	1.264	0.537	5.545	3.540	0.019	1.236 - 10.14
Diastolic BP	0.762	0.604	1.590	2.142	0.207	0.656 - 7.000
Parity	- 0.777	0.347	5.009	0.460	0.025	0.233 - 0.908

These variables were maternal age, previous abortions, parity, SBP and DBP. The results of the multivariate analysis are presented in table 4. Out of the five variables, only three were found to be significant. These were maternal age, parity, and systolic blood pressure.

Discussions

We set out to determine possible predictors of pre-eclampsia before clinical manifestation, which is before the 20th week of pregnancy, with information on the antenatal cards of pregnant women at the first antenatal visit. This first visit must have taken place before the 20th week of pregnancy to be included in the study.

We found the proportion of deliveries complicated by pre-eclampsia for the three year period was 2.5%. This figure falls within the range of 1.5 to 4.2% found elsewhere[15, 16, 17, 18]. Our finding however contrasted with a study done at the Korle - Bu Teaching Hospital[19], which reported prevalence of pre-eclampsia to be 7.03%. This is not surprising, since the Korle-Bu Teaching Hospital is the largest referral center in Ghana with complicated cases referred to it. Though several studies had sought to establish a link between maternal infection and pre-eclampsia with inconsistent results[20, 21] we found no association of pre-eclampsia and maternal infection with HIV, Hepatitis B virus, and syphilis. We found no significant association between pre-eclampsia and season of delivery. This finding is consistent with earlier studies in Iran[22]. Our finding however contrasts with other findings from South Africa[23] which reported that pre-eclampsia occurs more frequently in winter and Nigeria[24], where it peaked in the rainy season.

Again we found no statistically significant association between maternal blood group and pre-eclampsia. This finding is in agreement with a study in the United Kingdom[25] but however contrasts with a population based study in Finland[26] that found that Blood group AB was associated with an increase in the risk for pre-eclampsia. We found that previous history of abortion was 2.6 times more likely to be associated with pre-eclampsia. This was not sustained in the multivariate analysis. Such associations were however found in other studies[27, 8]. Maternal age of 25 and above was associated with increased risk of pre-eclampsia in our study which was confirmed in multivariate analysis. Other studies did not show this association[14, 29]. We found no statistically significant association between PE and nulliparity which is in disagreement with other studies which found nulliparity to be significantly associated with increased risk of PE[14].

In our study, first booking systolic BP of 130 mm/Hg or more significantly increased the risk of pre-eclampsia. This was sustained in multivariate analysis. This finding is in disagreement with a study that reported that a raised diastolic BP at booking increased the risk of pre-eclampsia[14.]

Limitations of the study

Since there was no qualitative arm of this study, mothers were neither examined nor interviewed so we could not study the effect of lifestyle variables on pre-eclampsia. Since this study was done in only one health facility with a relatively small sample size, the findings may not therefore be extrapolated on the general population. Male partner's variables could also not be assessed since these were not available on the records.

Conclusion

We analyzed data from the ANC of the Police hospital from 1st January 2008 to 31st December 2010, with the objective to determine the number of pre-eclampsia cases, the proportion of deliveries complicated by pre-eclampsia, and risk factors of pre-eclampsia.

The total number of deliveries for the period was 4,637 and the number of deliveries complicated by preeclampsia was 115. The proportion of deliveries complicated by PE was 2.5%.

We found in multivariate analysis that, maternal age of 25 years and above, previous parity of one, and systolic blood pressure of 130 mm/Hg or more at booking were statistically significant predictors of pre-eclampsia.

Recommendations

These findings of this study could be used to predict pre-eclampsia among pregnant women at first antenatal clinic attendance. This will enable the selection of these pregnant women for focused surveillance of pre-eclampsia and therefore lead to early detection and management to prevent adverse outcomes.

We recommend further studies should have a qualitative component and involve a larger sample size, preferably from more health facilities.

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