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# Association between antenatal booking visit and occurrence of preeclampsia: A Ghanaian study

F. A. Yeboah, L. A. Fondjo, M. M. Seini, C. A. Turpin, O. Debrah, B.R.D.T. Annan, E. A. Tagoe, A. T. Bawah

## ABSTRACT

**Aims: The first appointment a pregnant woman makes to the antenatal unit of a hospital is often called the Booking Visit (BV). This visit happens towards the end of the first trimester, usually between 8–14 weeks. The medical, obstetric and family history of the woman are taken. This helps to determine the potential for any risks that may occur during the pregnancy and thus allow appropriate medical intervention. Preeclampsia is a multisystem disease of pregnancy of unknown cause. The only effective therapy is to facilitate the delivery. Preeclampsia is also an important cause of maternal and perinatal morbidity and mortality. The aim of this study was to determine whether the timing of the visit has any effect on the occurrence of preeclampsia. Methods: This case - control study was used to recruit a total of 400 primigravida in the second trimester of their pregnancy, comprising two hundred women with preeclampsia (cases) and two hundred age-matched normotensive pregnant women (controls) visiting the Obstetrics and Gynaecology Departments of the KomfoAnokye Teaching Hospital in Kumasi and Ridge Regional Hospital in Accra both in Ghana. The diagnosis of preeclampsia was assessed by a qualified Obstetrician/Gynaecologist at the respective hospitals. The booking visit was abstracted from the medical records of the recruited pregnant women. Urine sample was obtained for the analysis of urine protein and microalbuminuria and blood sample for hemoglobin, calcium and magnesium. Results: The mean gestation of the cases was significantly higher than that of the controls, p < 0.0001. More than 70% of the cases with serum magnesium less than 0.7 mmol/l had BV between 17–24 weeks compared to the control. Also, significant portion (71.5%) of the cases had serum calcium levels below 2.1 mmol/l and were found to have BV between 17–24 weeks compare to 11.1% of the controls with normal calcium levels. Preeclamptic individuals with hemoglobin (Hb) less than 11.0 g/dl reported to the hospital between 17–24 weeks compared to 20% of the controls. Women (9.1 %) diagnosed with anaemia reported to the hospitals after 24 weeks of gestation. More than 50% of the cases were uneducated and only 1% had tertiary education. Conclusion: The current study reports a significantly late booking visit in women with preeclampsia and this as well as luck of education may play a role in the development of preeclampsia.**

**Keywords: Calcium, Hemoglobin, Magnesium, Microalbuminuria, Proteinuria**

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## INTRODUCTION

The first appointment a pregnant woman makes to the maternity unit of any hospital is called the booking visit (BV). This is usually the first introduction to the maternity hospital and the first meeting with the doctors and midwives for pregnancy care. The medical and obstetric history as well as family history are documented to determine potential risks that may occur during the pregnancy [1].

Early booking visit indirectly saves the lives of mothers and babies by promoting and establishing good health during pregnancy. Booking visit often presents the first contact opportunity for a woman to connect with health services, thus offering an entry point for integrated care, promoting healthy home practices, influencing care seeking behaviors, and linking women with pregnancy complications to a referral system. Women are more likely to give birth with a skilled attendant if they have had early BV and maintained their appointment throughout the pregnancy [2].

The first visit is used to distinguish pregnant women who require standard care from those requiring special attention and more visits. Depending on the setting, approximately 25–30 percent of women will have specific risk factors which require more attention. Such women require more visits. Most of the interventions recommended at the BV are supported by scientific evidence, are low cost, and can be implemented in first level facilities in all countries in Africa [2].

Preeclampsia is a medical condition which arises in pregnancy and it is associated with high blood pressure and may be associated with significant amount of protein in the urine of pregnant women. Preeclampsia is a multisystem disease of pregnancy of unknown cause. It is a maternal syndrome, which is characterized by increased blood pressure, edema, proteinuria and abnormal clotting, impaired liver and renal functions all of which may be due to the release of placental toxic factors into the mother's circulation [3]. It affects 7–10% of pregnant Ghanaian women [4, 5]. The only effective therapy to this pregnancy complication is to facilitate the delivery (induction of labour or cesarean section). It appears likely that there are substances from the placenta that can cause endothelial dysfunction in the maternal blood vessel of susceptible women. The epidemiology of this multisystem disorder, varying between little systemic involvements to multi organ failure, is complicated by differences in definition, inaccuracy of diagnosis and the outcomes [3].

Good care during pregnancy is important for the health of the mother and the development of the unborn baby. Pregnancy is a crucial time to promote healthy behaviours and parenting skills. Good ANC links the woman and her family with the formal health system, increases the chance of using a skilled attendant at birth and contributes to good health through the life cycle. Inadequate care during this time breaks a critical link in the continuum of care, and effects both women and their babies [6].

It has been estimated that 25 percent of maternal deaths occur during pregnancy with variability between countries depending on the prevalence of unsafe abortion, violence, and disease in the area. Between a third and a half of maternal deaths are due to causes such as hypertension (pre-eclampsia and eclampsia) and antepartum haemorrhage, which are directly related to inadequate care during pregnancy [6].

Early or appropraite BV is so important that pregnant women in Ghana need to be educated so that late BV is discouraged. This study was therefore aimed at elucidating the relationship between BV and preeclampsia in Ghana.

## MATERIALS AND METHODS

This prospective case-control study comprising two hundred pregnant women with preeclampsia and two hundred normotensive pregnant women visiting the Obstetrics and Gynaecology Departments of the KomfoAnokye Teaching Hospital in Kumasi and Ridge Regional Hospital in Accra all in Ghana, were consecutively selected and recruited from January to December 2016 for this study. Participation was voluntary and informed consent was obtained from each respondent. The diagnosis of preeclampsia was assessed by qualified Obstetrician/Gynaecologist at the respective hospitals based on internationally accepted guidelines. The presence of high blood pressure (systolic blood pressure of 140 mmHg or more and diastolic blood pressure of 90 mmHg or more) on two occasions six hours apart and proteinuria level of 2+ positive result or more on a dipstick, were also considered as presenting with preeclampsia (PE). Each subject had a questionnaire-based interview, which was conducted privately and in person and lasted approximately 30 minutes. Information on booking visit was obtained from the medical records and during the interview. Maternal lifestyle factors such as smoking and alcohol consumption during pregnancy, demographic data, educational level, recent medical history, a complete present and past obstetric history, occupational factors, exercise and information on the parents were all obtained. Ethical clearance was obtained from the joint Committee on Human Research Publication and Ethics of the School of Medical Science, Kwame Nkrumah University of Science and Technology and the KomfoAnokye Teaching Hospital, Kumasi (CHRPE).

## Anthropometric measurements

Anthropometric measurements included height, measured without shoes and weight measured in kilograms with light clothing. Subjects were weighed on a scale (Zhongshan Electronic Co. Ltd, China) and their height measured with a wall-mounted ruler. Maternal weight (MW) was calculated by dividing weight (kg) by height squared ($m^2$). Blood pressure was taken by trained personnel using a mercury sphygmomanometer and stethoscope. Measurements were taken from the left upper arm after subjects had rested for 15 min in accordance with the recommendation of the American Heart Association. Triplicate measurements were taken with a 5 min rest interval between measurements and the mean value was recorded to the nearest 2.0 mmHg.

## Biochemical analysis

About 5 ml of venous blood was drawn and dispensed into EDTA and gel separator vacutainer® tubes respectively. The samples in the gel separator tubes were then taken to the laboratory and centrifuged; the whole blood in the EDTA tubes were used for hemoglobin determination whiles the sera were used for the assay of the serum calcium($Ca^{2+}$) and magnesium($Mg^{2+}$). Urine samples were also collected in sterile containers for the measurement of urine proteins and microalbuminuria. Urine protein was determined using the dip-stick qualitative method (Rapid Lab Ltd, UK). The serum $Mg^{2+}$ and $Ca^{2+}$ were assayed using a commercial test kit obtained from GenWay Biotech, Inc., San Diego, USA and analyzed with Selectra Junior analyzer (Vital Scientific, Ekkerstijt, Netherlands). The hemoglobin was determined by the use of Mindray BC-3600 heamatologyanalyser (Mindray Chiana Ltd). The microalbuminuria was measured by HemoCue Albumin 201 Analyzer (Sweden).

## Statistical analysis

The values were expressed as mean ± standard deviations (mean ± SD). Student t-test was used for comparison of means of variables between case and control subjects. The level of statistical significance was set at $p<0.05$ for all tests and at 95% confidence interval (CI). SPSS version 20 was used to analyze all data.

# RESULTS

The mean age of the controls was not significantly different from the cases (30.83 ± 4.03 and 31.08 ± 4.5), $p = 0.074$ (Table 1). The gestation age at the booking visit of the cases was significantly higher than that of the controls, (20.70 ±3.68 and 9.88 ± 2.59), $p<0.0001$ (Table 1). The mean maternal weight of the Controls was significantly lower compared with the Cases (22.63 ± 2.08 and 26.62± 2.14), $p<0.0001$ (Table 1). The mean systolic and diastolic blood pressure of the cases was significantly higher than that of the controls (121.07±7.5, 160.78±10.38 and 88.03±7.81, 107.44±8.36) respectively $p<0.0001$ (Table 1). The mean $Mg^{2+}$ and $Ca^{2+}$ were both significantly higher in the controls than the cases $p<0.0001$ (Table 1). Hb was also significantly lower in the cases when compared with the controls, $p<0.0001$ (Table 1). The mean microalbuminuria was significantly higher in the cases as compare to the controls (32.40±6.70 and 17.1±2.20) $p<0.0001$ (Table 1). Mean proteinuria was significantly lower in the controls then the cases 0.26±0.45 and 2.95±2.58), $p<0.0001$ (Table 1). A significant number of the controls who had microalbuminuria level less than 20 mg/l had their booking visit between the 8–16 weeks as compared to the cases (94.7% vrs 0%) (Table 2). Higher number of the controls who had microalbuminuria levels between 20–30 mg/l also had their booking visit between 8–16 weeks as compared to the cases (100% vrs 17.5%). About 71.2% of the cases with microalbuminuria levels between 20–30 mg/l visited the hospital for the first time between 17–24 weeks of gestation, whiles 11.2% visited the hospital after 24 weeks. A significant number of the cases with microalbuminuria between 31–40 mg/l reported to the hospital between 17–24 weeks (72.2%) (Table 2). Again 70% of the cases with microalbuminuria more than 40 mg/l had their booking visit between 17–24 weeks whiles 3.3% visited the hospital after 24weeks of gestation (Table 2).

A significantly higher number of the controls with less than +2 proteinuria had their booking visit between 8–16 weeks of gestation (95.5%) (Table 2). About 71.6% of the cases with more than +2 proteinuria had their first antenatal visit between 17–24 weeks and 7.4% of them had their first visit after 24 weeks of gestation (Table 2). More than 70% of the cases group who had serum magnesium levels below 0.7mmol/l had their booking visit between 17–24 weeks. About 4.5% of the controls with serum magnesium levels above 0.7 had their booking visit between 17–24 weeks and only 7.5 % of the cases who had serum magnesium level less than 0.7mmol/l had their booking visit after 24weeks (Table 3). Significantly higher number of the cases who had serum calcium levels below 2.1 mmol/l reported to the hospital between 17–24 weeks (71.5%) as compare to 11.1% of the controls, (Table 3). Significantly higher number of the cases who had Hb less than 11.0 reported to the hospital between 17–24 weeks, (72.1%) whiles 20% of the controls reported at that time (Table 3). 9.1 % of the anemic pregnant women reported after 24 weeks of gestation (Table 3). Higher number of the cases who were illiterates reported to the hospital the first time between 17–24 weeks as compared to the controls, (68.9% vrs 3.8%) (Table 4). Similarly, higher percentage of the cases who had secondary education had their booking visit between 17–24 weeks as compared to the controls, (72.2% vrs 3.0%).

Table 1: Clinical and Socio-demographic parameters of study population

| Parameter | Control (N=200) | Case (N=200) | 95% CI of mean difference | p-value |
|---|---|---|---|---|
| Age (years) | 30.83 ± 4.03 | 31.08 ± 4.5 | 0.31–1.99 | 0.074 |
| BMI (Kg/m²) | 22.63 ± 2.08 | 26.62 ± 2.14 | 3.57–4.40 | 0.0001** |
| SBP (mmHg) | 121.07 ± 7.51 | 160.78 ± 10.38 | 37.93–41.49 | 0.0001** |
| DBP (mmHg) | 88.03 ± 7.81 | 107.44 ± 8.36 | 17.82–21.00 | 0.0001** |
| BV (weeks) | 9.88 ± 2.59 | 20.70 ± 3.68 | 10.19–11.44 | 0.0001** |
| $Mg^{2+}$(mmol/ml) | 0.88 ± 0.08 | 0.56 ± 0.08 | 0.30–0.33 | 0.0001† |
| $Ca^{2+}$(mmol/ml) | 2.36 ± 0.17 | 1.53 ± 0.90 | 0.71–0.96 | 0.0001† |
| Hb (g/dl) | 13.76 ± 0.80 | 10.01 ± 0.73 | 3.56–3.86 | 0.0001† |
| Proteinuria | 0.26 ± 0.45 | 2.95 ± 0.69 | 2.58–2.80 | 0.0001† |
| Microalb (mg/l) | 17.1 ± 2.20 | 32.40 ± 6.70 | 14.30–16.40 | 0.0001† |
| **Education (%)** | | | $\chi^2$ | |
| Uneducated | 53 (26.5) | 103 (51.5) | 26.22 | 0.0001* |
| Primary | 88 (44.0) | 75 (37.5) | 0.83 | 0.3621 |
| Secondary | 33 (16.5) | 18 (9.0) | 5.06 | 0.0350 |
| Vocational | 15 (7.5.0) | 2(1.0) | 336.3 | 0.0001* |
| Tertiary | 11 (5.5) | 2 (1.0) | 6.44 | 0.0111 |

CASE = Women with preeclampsia. Control =Women without preeclampsia. *p < 0.01
MW = Maternal Weight, SBP = Systolic blood pressure, DBP=Diastolic blood pressure
BV = Booking Visit, $Ca^{2+}$ = Calcium ions, $Mg^{2+}$ = Magnesium, Hb = Heamoglobin

Table 2: Comparison of Booking Visit with Proteinuria and Microalbuminuria

| Parameter | BV(weeks) 8- 16 | 17-24 | >24 |
|---|---|---|---|
| **Microalbuminuria** | **N (%)** | **N (%)** | **N (%)** |
| < 20 mg/l | | | |
| **controls** | 161 (94.7) | 9 (5.3) | - |
| **Cases** | | - | - |
| 20–30 mg/l | | | |
| Controls | 29 (100) | - | - |
| Cases | 14 (17.5) | 57 (71.2) | 9 (11.3) |
| 31–40 mg/l | | | |
| Controls | - | - | - |
| Cases | 20 (22.2) | 65 (72.2) | 5 (5.6) |
| >40 mg/l | | | |
| Control | - | - | - |
| Cases | 8 (26.7) | 21 (70.0) | 1 (3.3) |
| **Proteinuria** | | | |
| < +2 | | | |
| Controls | 189 (95.5) | 9(4.5) | - |
| Cases | - | - | - |
| +2 | | | |
| Controls | 1 (100) | - | - |
| Cases | 11 (21.2) | 37(71.2) | 4 (7.7) |
| >+2 | | | |
| Controls | | | |
| Cases | 31 (20.9) | 106 (71.6) | 11 (7.4) |

Case = Women with preeclampsia. Control = Women without preeclampsia. BV= Booking Visit, N= Sample population, % = percentage prevalence.

Table 3: Comparison of Booking Visit with $Mg^{2+}$, $Ca^{2+}$ and Hb of the Study Population

| Parameter | BV(weeks) 8–16 | 17–24 | >24 |
|---|---|---|---|
| **Cases** | N (%) | N (%) | N (%) |
| $Mg^{2+}$ (mmol/l) | | | |
| < 0.7 | 42 (21) | 143 (71.5) | 15 (7.5) |
| **Controls** | | | |
| ≥ 0.7 | 190 (95.5) | 9 (4.5) | - |
| **Cases** | | | |
| $Ca^{2+}$ (mmol/l) | | | |
| < 2.1 | 41 (20.7) | 142 (71.7) | 15 (7.6) |
| ≥ 2.1 | 1 (50) | 1 (50) | - |
| **Controls** | | | |
| $Ca^{2+}$ (mmol/l) | | | |
| < 2.1 | 8 (88.9) | 1 (11.1) | - |
| ≥ 2.1 | 182 (95.8) | 8 (4.2) | - |
| **Cases** | | | |
| Hb (g/dl) | | | |
| < 11.0 | 31 (18.8) | 119 (72.1) | 15 (9.1) |
| ≥ 11.0 | 11(31.4) | 24 (68.6) | - |
| **Controls** | | | |
| Hb (g/dl) | | | - |
| < 11.0 | 4 (80.0) | 1 (20.0) | - |
| ≥ 11.0 | 186 (95.9) | 8 (4.1) | |

Case = Women with preeclampsia. Control = Women without preeclampsia. Mg2+ = Magnesium ions, Ca2+ = Calcium ions, Hb=haemoglobin. BV= Booking Visit

Table 4: Comparison of Booking Visit with Educational Background of the Study Population

| Parameter | BV(weeks) 8–16 | 17–24 | >24 |
|---|---|---|---|
| **Education** | **N (%)** | **N (%)** | **N (%)** |
| **Cases** | | | |
| Illiterates | 26 (25.2) | 71 (68.9) | 6 (5.8) |
| Basic | 13 (17.3) | 56 (74.7) | 6 (8.0) |
| Secondary | 3 (16.7) | 13 (72.2) | 2 (11.1) |
| Vocational | - | 2 (100) | - |
| Tertiary | 1 (50) | 1 (50) | - |
| **Controls** | | | |
| Illiterates | 50 (96.2) | 2 (3.8) | - |
| Basic | 84 (95.5) | 4 (4.5) | - |
| Secondary | 32 (97.0) | 1 (3.0) | - |
| Vocational | 15 (100) | - | - |
| Tertiary | 11 (100) | - | - |

Case = Women with preeclampsia. Control = Women without preeclampsia. BV= Booking Visit

## DISCUSSION

This study reports for the first time the association between booking visit and the occurrence of preeclampsia. Booking visit as a risk factor is not known in Ghnana, this is the first time a research is done with gestational booking visit. The study shows that booking gestation is significantly higher in the preeclamptic women. The lateness in the booking visit among the preeclamptics in the second trimester indicate the possible role of booking visit in the occurrence of preeclampsia. A study in Adis Ababa also showed booking visit to be very late among pregnant women with preeclampsia [7]. A study by the ANC clinic at a University college in Nigeria also showed that early booking of antenatal care is regarded as a cornerstone in improving maternal and neonatal health care. According to the Ethiopian Demographic and Health Survey 2011 report, only 11.2% of women had an ANC visit before their fourth month of pregnancy. According to the National Institute of Clinical Excellence [6] antenatal guidelines, a woman's level of risk for PE in a given pregnancy should be assessed at the first antenatal visit by identifying the presence of one or more predisposing historical risk factors, and they should be

supervised more vigilantly and managed at centers with facilities for specialized neonatal and maternal intensive care. In the guidelines, some of the risk factors for the development of PE are: first pregnancy; previous PE; >10 years since last baby; age >40 years; body mass index (BMI) >35; family history of PE; booking diastolic blood pressure (BP) 80 mmHg; proteinuria at booking of +1 on more than one occasion or 300 mg/24 h; multiple pregnancy; and underlying medical conditions.

Initiation of antenatal care is late due to lack of education and financial constraints. Male dominance influences patients' adequate utilization of antenatal services. Provision for the expectant fathers to attend maternity care activities will improve service uptake, [8]. In Nigeria, pregnant women cannot say they are pregnant, and if they feel unwell, they have to say that they have "swallowed a cockroach" [9]. Booking visit is very important as it is at this visit that the following are done: Blood pressure measurements, weight and height measurement to calculate body mass index, antenatal laboratory investigations to determine Hb, Urine proteins and sugars and other serological investigations. Other studies also identified booking visit as very important [2]. A study in Nigeria had the mean gestational age at booking to be 23.7 weeks, [10]. The sixth month was the peak period for the initiation of antenatal care. The decision to attend antenatal care was taken by the husband alone in 52% of the cases [11]. Late booking is mainly because of ignorance and financial constraints [12]. The study shows that, late booking visit is associated with high BMI and blood Pressure which are all evidence of preeclampsia. A study by Delva, et al, 2010, also showed that, raised BMI before pregnancy or at booking, maternal age > 40, renal disease, hypertension, ≥ 10 years since the last pregnancy, and raised blood pressure at booking all increased the risk of a woman developing pre-eclampsia. Sibai et al 1997 also found that higher systolic and diastolic blood pressures at the first visit were associated with an increased incidence of pre-eclampsia (3.8% in women with diastolic blood pressure of < 55 mm Hg, 7.4% in those with diastolic blood pressure 70–84 mm Hg) [13]. Reiss et al in 1987, matched 30 women with pre-eclampsia for age, race, and parity with normotensive control women and found out that both systolic and diastolic blood pressures were significantly higher in the first tri-mester for women who later developed pre-eclampsia. In a population based nested case-control study [14] also found that a systolic blood pressure ≥ 130 mmHg compared with < 110 mm Hg at the first visit before 18 weeks was significantly associated with the development of pre-eclampsia later in pregnancy.

This study shows that 78.9% of the cases who are traders had their booking visit after the first trimester. A similar study finding in Nairobi, Kenya indicated that 85% of women initiated visits later than the first trimester [2]. Other studies also showed the relationship between stress and preeclampsia. A study by Klonoff et al., 1996 showed that working women had 2.3 times the risk of developing preeclampsia compared with nonworking women [15]. Another study by Kurki in 2000 showed that relative risk for preeclampsia is increased in many stressful situations. Many risk factors for preeclampsia are stress-related [16]. Low-stress situations, on the contrary, are protective. Stress in pregnancy corroborates all physio-pathologic theories for preeclampsia [17].

This study also shows that more than 70% of the preeclamptics who reported to the hospital the first time between 17 and 24 weeks of gestation had very low serum calcium and magnesium levels. Other studies also show the role calcium play in the development of healthy bones and teeth as well as extra-cellular fluid, muscle, and other tissues. It is also involved in vascular contractions and vasodilation, muscle contractions, neural transmission, and glandular secretion. Adequate dietary calcium intake before and during early pregnancy may reduce the risk or severity of pre-eclampsia and therefore adequate dietary intake should be encouraged [18]. A study by FSAI, 2011 also saw the significance of calcium during pregnancy and concluded that pregnant women should be advised to consume 3 portions of dairy or calcium-fortified alternatives daily. This study has shown that 70% of the cases who had late booking visit also had microalbuminuria greater than 40 mg/l [19]. A study by Kissner in 1973 also found out that a study group women had severe disease as 70% had BP 180/120; 68% had urine albumin 3+; 35% had HELLP syndrome; 17% had deranged renal functions and 25% had eclampsia [20].

Traditional believes in Africa also contribute to late booking visits. For instance, in a tribe in Nigeria, pregnant women cannot say they are pregnant, and if they feel unwell, they have to say that they have "swallowed a cockroach" [12]. In some parts of northern Ghana, it is a taboo for pregnant women to go to hospitals for antenatal care, it is believed that children delivered at the hospitals are weak and cannot lead a community [21].

The risk factors for developing preeclampsia which are all high in this study can be used to assess risk at the booking visit, so that a suitable surveillance routine to detect pre-eclampsia can be planned for the rest of the pregnancy, as recommended by the recent NICE guideline on antenatal care.

## CONCLUSION

The current study reports a significantly late booking visit in preeclamptic individuals at the second trimester of pregnancy. The lateness in pregnant women reporting to the hospital may be important in the development of preeclampsia.

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## Author Contributions

F. A. Yeboah – Substantial contributions to conception and design, Acquisition of data, Analysis and interpretation of data, Drafting the article, Revising it critically for important intellectual content, Final approval of the version to be published

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Authors declare no conflict of interest.