Research Article,

Determinants of Preeclampsia in a Tertiary Hospital in South East Nigeria

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Abstract:
Background:
Preeclampsia is a pregnancy-related disorder. Symptoms commonly associated with it include elevated blood pressure, protein in the urine and leg swelling. It is one of the leading causes of maternal and fetal morbidity and mortality especially in limited resource settings. This study was aimed at determining the risk factors for preeclampsia in a tertiary hospital in south east Nigeria.

Methods:
This was a retrospective case-control study carried out at Chukwuemeka Odumegwu Ojukwu University teaching hospital Awka, south east of Nigeria. There were 50 cases with 100 controls. Data was retrieved from hospital case notes of both cases and controls. Tables were used to illustrate the descriptive statistics comparing the cases and controls. Categorical variables were compared using the Chi-square test. To ascertain the determinants of preeclampsia, Univariate and multivariate logistic regression analyses were conducted.

Results:
Maternal age less than 30 years, lower educational status, primigravidity, previous history of pregnancy induced hypertension, polyhydramnios, maternal obesity, chronic hypertension, diabetes, and family history of preeclampsia were predictive of preeclampsia (Adjusted odds ratio (AOR) = 2.50, 9.08, 20.25, 76.47, 5.11, 7.53, 2.73, 10.78, and 3.57 respectively).

Conclusions:
The identified determinants of preeclampsia from this study especially previous history of pregnancy induced hypertension, primigravidity, family history of preeclampsia among others should serve as a basis for the screening of antenatal clinic attendees for preeclampsia. This will serve to identify at risk pregnant women, and enhance early diagnosis and intervention to improve feto-maternal outcomes.

Keywords: Preeclampsia; pregnancy; determinants; Awka; Nigeria

Introduction:
Preeclampsia (PE) is a pregnancy related disorder characterized by development of hypertension and proteinuria, with or without edema beyond 20 weeks of gestation(1–6). Preeclampsia is a major cause of maternal and perinatal morbidity and mortality globally(2,4,6–10). Preeclampsia is a public health problem especially in developing countries where late presentation of cases heightens the felt negative impact of the disease(7,9). The incidence of preeclampsia ranges from 2 – 10%, depending on the population studied(7–9). In Nigeria, the prevalence of preeclampsia ranges from 2 – 16.7%(7). According
The precise etiology of preeclampsia is not known but several factors have been postulated to increase the risk of preeclampsia. These include maternal age, primiparity, chronic hypertension, diabetes mellitus, renal disease, maternal obesity, multiple pregnancy, personal or family history of preeclampsia etc (2,8–12). Early detection, through proper antenatal care and prompt treatment can prevent severity and progression to eclampsia with its attendant complications(5,9,13). Adequate knowledge of predominant risk factors for preeclampsia is essential for clinicians. This will enable them develop a surveillance protocol for rapid risk assessment, at antenatal booking and follow up visits and prompt identification of high risk pregnant women. Therefore, this study was conducted to ascertain the determinants of preeclampsia in the tertiary hospital. Preeclampsia is a serious condition with several complications including maternal and fetal fatalities, accounting for up to 10% of maternal deaths(8). It affects approximately one in 20 pregnancies(8). There was an increase of 40% worldwide in the incidence of preeclampsia between 1990 and 1999(14). In developing countries of the world, characterized by resource limitation, preeclampsia accounts for 20–80% of maternal mortality, this is in spite of a sustained decrease in maternal deaths due to preeclampsia in developed countries(2,8). In the developed countries, on the contrary, preeclampsia results in a more severe outcome for the fetus(2,8). Preeclampsia is a major public health problem by virtue of its contribution to maternal and fetal morbidity and mortality worldwide(7,9). Preeclampsia is not a preventable condition, but early diagnosis and proper intervention will ameliorate severity and obstruct progression to complications(9). Knowledge of determinants of preeclampsia among clinicians will enhance surveillance, identification, and prompt management of pregnant women at risk of developing preeclampsia. Preeclampsia is currently one of the major causes of maternal and perinatal morbidity and mortality. The actual incidence and prevalence of preeclampsia is grossly underestimated especially in developing countries due to underreporting by healthcare workers and poor utilization of healthcare facilities by pregnant women(15). The etiology of preeclampsia is largely unknown(2,4,16,5–10,13,15). Several theories have been proposed linking certain factors to the etiology of preeclampsia including maternal socio-demographic characteristics (age, educational status, occupation etc), obstetric history (Gravidity, previous history of pregnancy induced hypertension, interdelivery interval more than 10 years etc), current pregnancy characteristics (multiple gestations, polyhydramnios etc), medical history (chronic hypertension, diabetes mellitus, autoimmune diseases etc) and family history of preeclampsia. This study was aimed at determining the risk factors of preeclampsia in a tertiary hospital in south east of Nigeria.

Materials and Methods:

Study site
This study was carried out at Chukwuemeka Odumegwu Ojukwu University Teaching hospital (COOUTH) Awka, Anambra State in South East Nigeria. It is a State government owned facility that provides tertiary health care services to residents of Awka and its neighboring cities, including parts of Enugu and Delta States in South East and South South of Nigeria respectively. It is also a training centre for undergraduate medical students of Chukwuemeka Odumegwu Ojukwu University and also postgraduate training for resident doctors in various subspecialties of medicine.

Study design
This was a retrospective case-control study that utilized previous medical records to determine the risk factors for preeclampsia among pregnant women who accessed care at COOUTH Awka from February 2014 to February 2017.

Study population (inclusion and exclusion criteria)
The study population consisted of pregnant women who accessed both antenatal care and delivery services at COOUTH Awka from February 2014 to February 2017.

Inclusion criteria: Pregnant women with gestational age ≥ 20 weeks.

Exclusion criteria: Pregnant women with gestational age < 20 weeks.

Data collection
Hospital case notes of patients who accessed both antenatal care and delivery services at the hospital from February 2014 to February 2017 were retrieved and critically assessed for completeness of history and documentation. Case notes with proper and complete documentation were selected.
for the study. Those with a diagnosis of PE were designated as cases, and comprised those with hypertension beyond twenty (20) weeks of gestation associated with proteinuria. Those without PE were designated as controls.

A total of fifty (50) cases, with fully documented history and write-up, were seen during the period under review. For each case, two controls were selected from the sorted eligible case notes using simple random sampling. Data relating to maternal, obstetric and family factors were retrieved from the hospital records using a pre-designed data retrieval form.

### Data processing and analysis

Data were entered into the Statistical Package for Social Sciences (SPSS) for windows version 20. Categorical variables were summarized as proportions while quantitative variables were summarized as mean and standard deviation. Chi-square test was used to compare categorical variables while unpaired t – test was used to compare quantitative variable. The level of statistical significance was set at p-value of <0.05. Variables with statistically significant association with preeclampsia were entered into Regression model to determine predictors of preeclampsia.

### Ethical issues

Ethical clearance was sought and obtained from COOUTH Health Research Ethical Committee and permission was obtained from the head of the department of Medical records COOUTH.

### Limitations of the study

- This being a retrospective case-control study that utilized hospital records, the researchers were unable to interview the clients for further verification of documented information.
- Some of the hospital case notes were poorly documented with incomplete data. This led to the non-usage of some of the case notes thereby constricting the sample size of the study.

### Results

Majority of the cases were less than 30 years old (66%), while a greater percentage of the controls were greater than 30 years (62%). The proportion of primigravida was high among cases as opposed to controls (80% and 20% respectively). Nine variables were identified to be predictive of preeclampsia in multivariate logistic regression analysis. The predictive variables were age <30 years (AOR = 2.50), lower educational status (AOR = 9.08), primigravida (AOR = 20.25), previous history of pregnancy induced hypertension (AOR = 76.47), presence of polyhydramnios (AOR = 5.11), presence of obesity (AOR = 7.53), history of chronic hypertension (AOR = 2.73), history of diabetes (AOR = 10.78), and family history of preeclampsia (AOR = 3.57).

The observed confidence intervals are wide indicating that the sample size for this study was small.

### Table 1: Socio-demographic characteristics of cases and controls

| Variables                  | Case (n = 50) | Control (n = 100) | X²  | P – value |
|----------------------------|--------------|------------------|-----|----------|
| Age (years)                |              |                  |     |          |
| <30                        | 33 (66.0)    | 38 (38.0)        |     |          |
| ≥30                        | 17 (34.0)    | 62 (62.0)        |     |          |
| Mean ± SD                  | 27.68 ± 6.16 | 30.38 ± 4.80     | t = - 2.72 | 0.008   |
| Educational status         |              |                  |     |          |
| Basic education completed  | 36 (72.0)    | 25 (25.0)        |     |          |
| Secondary education completed | 14 (28.0) | 75 (75.0)        | 30.52 | 0.000   |
| Occupational status        |              |                  |     |          |
| Student                    | 10 (20.0)    | 15 (15.0)        | 5.85 | 0.119    |
| Civil servant              | 15 (30.0)    | 38 (38.0)        |     |          |
| Self employed              | 15 (30.0)    | 39 (39.0)        |     |          |
| House wife                 | 10 (20.0)    | 8 (8.0)          |     |          |
Table 2: Obstetric history and current pregnancy characteristics of cases and controls

| Variables                        | Case (n = 50)       | Control (n = 100)     | X²   | P – value |
|----------------------------------|---------------------|-----------------------|------|-----------|
|                                  | N (%)               | N (%)                 |      |           |
| Gravidity                        |                     |                       |      |           |
| Primigravida                     | 40 (80.0)           | 20 (20.0)             |      |           |
| Multigravida                     | 10 (20.0)           | 80 (80.0)             | 50.00| 0.000     |
| Previous history of PIH          |                     |                       |      |           |
| n = 10                           | n = 80              |                       |      |           |
| Present                          | 6 (60.0)            | 3 (3.8)               |      |           |
| Absent                           | 4 (40.0)            | 77 (96.2)             | 25.31| 0.000*    |
| Pregnancy type                   |                     |                       |      |           |
| Multiple pregnancy               | 16 (32.0)           | 21 (21.0)             |      |           |
| Singleton pregnancy              | 34 (68.0)           | 79 (79.0)             | 2.17 | 0.141     |
| GA at booking                    |                     |                       |      |           |
| <26 weeks                        | 26 (52.0)           | 62 (62.0)             |      |           |
| ≥26 weeks                        | 24 (48.0)           | 38 (38.0)             | 1.378| 0.241     |
| Polyhydramnios                   |                     |                       |      |           |
| Present                          | 16 (32.0)           | 8 (8.0)               |      |           |
| Absent                           | 34 (68.0)           | 92 (92.0)             | 14.29| 0.000     |
| Urinary tract infection          |                     |                       |      |           |
| Present                          | 15 (30.0)           | 21 (21.0)             |      |           |
| Absent                           | 35 (70.0)           | 79 (79.0)             | 1.48 | 0.224     |

PIH = pregnancy induced hypertension; GA = gestational age; * = Continuity correction

Table 3: Clinical Characteristics and Family History of Cases and Controls

| Variables                        | Case (n = 50)       | Control (n = 100)     | X²   | P – value |
|----------------------------------|---------------------|-----------------------|------|-----------|
|                                  | N (%)               | N (%)                 |      |           |
| Obesity                          |                     |                       |      |           |
| Present                          | 11 (22.0)           | 3 (3.0)               |      |           |
| Absent                           | 39 (78.0)           | 97 (97.0)             | 12.07| 0.001*    |
| Chronic hypertension             |                     |                       |      |           |
| Present                          | 12 (24.0)           | 4 (4.0)               |      |           |
| Absent                           | 38 (76.0)           | 96 (96.0)             | 13.99| 0.000     |
| Diabetes mellitus (DM)           |                     |                       |      |           |
| Present                          | 18 (36.0)           | 5 (5.0)               |      |           |
| Absent                           | 32 (64.0)           | 95 (95.0)             | 24.68| 0.000     |
| Family history of PE             |                     |                       |      |           |
| Present                          | 10 (20.0)           | 5 (5.0)               |      |           |
| Absent                           | 40 (80.0)           | 95 (5.0)              | 8.33 | 0.004     |
| Family history of hypertension   |                     |                       |      |           |
| Present                          | 38 (76.0)           | 50 (50.0)             |      |           |
| Absent                           | 12 (24.0)           | 50 (50.0)             | 9.29 | 0.002     |
| Family history of DM             |                     |                       |      |           |
| Present                          | 20 (40.0)           | 29 (29.0)             |      |           |
| Absent                           | 30 (50.0)           | 71 (71.0)             | 1.83 | 0.176     |

* = Continuity correction
### Table 4: Univariate and Multivariate logistic regression analysis of factors associated with pre-eclampsia

| Variables                              | Cases (n = 50) | Controls (n = 100) | COR (95% CI)     | AOR (95% CI)     |
|----------------------------------------|----------------|-------------------|------------------|-----------------|
|                                        | N (%)          | N (%)             |                  |                 |
| Age (years)                            |                |                   |                  |                 |
| <30                                     | 33 (66.0)      | 38 (38.0)         | 3.17 (1.56 – 6.45) | 2.50 (0.64 – 9.86) |
| ≥30                                     | 17 (34.0)      | 62 (62.0)         | 1.15             |                 |
| Educational status                     |                |                   |                  |                 |
| Basic education completed              | 36 (72.0)      | 25 (25.0)         | 7.71 (3.59 – 16.59) | 9.08 (2.72 – 30.32) |
| Secondary education completed          | 14 (28.0)      | 75 (75.0)         | 0.70             |                 |
| Gravidity                              |                |                   |                  |                 |
| Primigravida                           | 40 (80.0)      | 20 (20.0)         | 16.00 (6.85 – 37.39) | 20.25 (5.90 – 69.51) |
| Multigravida                           | 10 (20.0)      | 80 (80.0)         | 0.50             |                 |
| Previous history of PIH                | n = 10         | n = 80            |                  |                 |
| Present                                | 6 (60.0)       | 3 (3.8)           | 38.50 (6.95 – 213.29) | 76.47 (3.24 – 1806.29) |
| Absent                                 | 4 (40.0)       | 77 (96.2)         | 0.50             |                 |
| Polyhydramnios                         |                |                   |                  |                 |
| Present                                | 16 (32.0)      | 8 (8.0)           | 5.41 (2.12 – 13.79) | 5.11 (1.27 – 20.56) |
| Absent                                 | 34 (68.0)      | 92 (92.0)         | 0.50             |                 |
| Obesity                                |                |                   |                  |                 |
| Present                                | 11 (22.0)      | 3 (3.0)           | 9.12 (2.41 – 34.47) | 7.35 (0.79 – 68.76) |
| Absent                                 | 39 (78.0)      | 97 (97.0)         | 0.27             |                 |
| Chronic hypertension                   |                |                   |                  |                 |
| Present                                | 12 (24.0)      | 4 (4.0)           | 7.58 (2.30 – 24.97) | 2.73 (0.45 – 16.59) |
| Absent                                 | 38 (76.0)      | 96 (96.0)         | 0.33             |                 |
| Diabetes mellitus (DM)                 |                |                   |                  |                 |
| Present                                | 18 (36.0)      | 5 (5.0)           | 10.69 (3.67 – 31.12) | 10.78 (1.98 – 58.67) |
| Absent                                 | 32 (64.0)      | 95 (95.0)         | 0.28             |                 |
| Family history of PE                   |                |                   |                  |                 |
| Present                                | 10 (20.0)      | 5 (5.0)           | 4.75 (1.53 – 14.78) | 3.57 (0.48 – 26.62) |
| Absent                                 | 40 (80.0)      | 95 (95.0)         | 0.50             |                 |
| Family history of hypertension         |                |                   |                  |                 |
| Present                                | 38 (76.0)      | 50 (50.0)         | 3.17 (1.48 – 6.76) | 0.48 (0.11 – 2.03) |
| Absent                                 | 12 (24.0)      | 50 (50.0)         | 1.32             |                 |

**COR = crude odds ratio, AOR = adjusted odds ratio, PIH = Pregnancy induced hypertension, CI=Confidence interval**

### Discussion:

This study aimed to determine the factors associated with increased risk of preeclampsia. Nine variables were identified, by the study, to be predictive of preeclampsia in multivariate logistic regression analysis. Maternal age < 30 years was found to be predictive of preeclampsia (AOR = 2.5; CI = 0.64 – 9.86). Some studies have reported younger maternal age to be associated with preeclampsia(2,5,17–20). Others have reported advanced maternal age to be associated with preeclampsia(1,9,21). Others report extremes of age as being associated with preeclampsia(8,15). Further worsening the conflict, others studies report no association between maternal age and preeclampsia(6,11,16,22).

This study revealed that lower educational attainment was predictive of preeclampsia (AOR = 9.08; CI = 2.72 – 30.32), similar to what has been reported in other studies carried out in Nigeria(4), Egypt(2) and Uganda(23). This contrasts with other studies that report no association between educational attainment and preeclampsia(1,5,6,9,16,22). Educational attainment usually impacts on women’s knowledge, financial or purchasing power, decision making, and utilization of healthcare services among other issues. A poorly educated woman is less likely to access pre-natal care in a health facility and thus may not know the danger signs associated with preeclampsia. She is also more likely to experience delay in accessing health care. Similar to other studies(2,4,17–19,21,23,24,5,6,8–10,12,13,15), primigravidity was found to be a significant risk factor for...
Preeclampsia (AOR = 20.25; CI = 5.90 – 69.51). Other studies have reported no association between gravidity and preeclampsia(1,11,16,22). Primigravidity as a risk factor for preeclampsia could be as a result of first contact with fetal chorionic villi. Previous history of pregnancy induced hypertension was found to be predictive of preeclampsia (AOR = 76.47; CI = 3.24 – 1806.29). This is similar to findings in other studies(4–6,8,9,12,15,21,22,24). Previous history of pregnancy induced hypertension could point to the fact of reactivation of the previous disease process in a subsequent pregnancy. It could also be attributed to recall bias. Similar to other studies(2,8,25), polyhydramnios was predictive of preeclampsia (AOR = 5.11; CI = 1.27 – 20.56). Polyhydramnios is associated with gestational hypertension and preeclampsia(25). It was observed in this study that maternal obesity was a significant risk factor for preeclampsia (AOR = 7.35; CI = 0.79 – 68.76) as has been reported in several other studies(2,5,8,9,11,12,15,21,22,24). Another study, however reported no association between maternal obesity and preeclampsia(16). Obesity is linked with several metabolic changes including insulin resistance and oxidative stress leading to endothelial cell dysfunction with increased sympathetic vascular tone, predisposing to elevated blood pressure(23,26). The finding that family history of preeclampsia is predictive of preeclampsia in pregnant women (AOR = 3.57; CI = 0.48 – 26.62) correlates with findings in previous studies(2,5,22). It however contrasts with results from another study(9). This could be as a result of genetic predisposition to diseases. The presence of maternal chronic hypertension was found to be predictive of preeclampsia (AOR =2.73; CI = 0.45 – 16.59). This is similar to previous studies(1,4,5,8,11,12,15,22). Chronic hypertension is associated with insulin resistance and activation of the sympathetic nervous system(23,26). As reported in other studies(2,5,8,11,12,15,16,22), presence of maternal diabetes mellitus was found to be a significant risk factor for preeclampsia (AOR = 10.78; CI = 1.98 – 58.67). Diabetes (type II) is linked with insulin resistance and oxidative stress, with its attendant effect on the vascular tone thereby predisposing to raised blood pressure(26).

**Conclusion/Recommendations:**
Low educational status, maternal age < 30 years, primigravidity, polyhydramnios, previous history of pregnancy induced hypertension, maternal obesity, chronic hypertension, diabetes mellitus and family history of preeclampsia were determined by this study as being predictive of preeclampsia. These risk factors can be utilized to develop a screening protocol to be used during first and subsequent antenatal visits to identify pregnant women at risk of developing preeclampsia. This will enhance close monitoring, early initiation of preventive measures, early diagnosis and management, thereby reducing maternal and perinatal morbidity and mortality as a result of preeclampsia, and increasing the prevalence of favourable outcomes. Further studies can also assess the success indices of the developed screening protocol.

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**Conflict of interest statement:**
The authors declare no conflict of interest

**Authors’ contributions:**
NIA: conception, design, data analysis and interpretation, write up of manuscript, literature search.
NCC: original draft review and literature search.
EGI: data acquisition and manuscript review.
AJ: supervision and manuscript review.
EC: data acquisition and manuscript review.
ICO: supervision and manuscript review.
All authors have read and agreed to the final version of the manuscript.

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