Original Article

# Association between preeclampsia and cancer antigen 125 in women attending antenatal clinic in Usmanu, Danfodiyo University Teaching Hospital, Sokoto

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**ABSTRACT**

**Background:** Preeclampsia is a hypertensive disorder of pregnancy that is characterized by the development of elevated blood pressure and proteinuria after 20 weeks of conception in a previously normotensive and non-proteinuric patient. It is one of the leading and most important causes of maternal and perinatal morbidity and mortality and it occurred in about 6% of human pregnancies. In Usmanu Danfodiyo Teaching Hospital Sokoto, preeclampsia and its complications were the leading causes of death in the year 2016. Preeclampsia has many suggested biomarkers, some of which are not well-defined. It has been assumed that failure in trophoblastic invasion and induction of an inflammatory process within the placenta in patients with preeclampsia may trigger the expression of CA-125 antigen. This study established a definite association between CA-125 and preeclampsia.

**Aims:** This study was conducted to determine the relationship between cancer antigen 125 and preeclampsia and its correlation with severity.

**Settings and Design:** Hospital-based study, comparative cross-sectional study.

**Methods and Materials:** Ninety-seven pregnant women with preeclampsia were recruited as cases while 97 pregnant women without preeclampsia were similarly recruited as controls. In both groups (cases and controls), only women with singleton pregnancies at ≥32 weeks' gestational ages were recruited. Sociodemographic characteristics, obstetric history, family history, and clinical data were obtained using a standard interviewer-administered questionnaire. Anthropometric measurements were taken. Blood samples were taken for measurement of serum cancer antigen 125. Mean arterial pressure (MAP) was used as an indicator of the severity of the disease.

**Statistical Analysis Used:** SPSS computer statistical software version 22, percentages, Chi-square, mean, Pearson correlation test.

**Results:** The age range of the respondents was between 16 and 45 years. The mean age for the control was 28.6 ± 5.9 years, 27.9 ± 7.5 and 28.7 ± 7.2 years, for the control and severe preeclampsia groups, respectively. The mean level of CA-125 in the preeclampsia group was significantly higher than the control (36.13 ± 23.02 vs 24.53 ± 9.42). The mean levels of CA-125 in severe preeclampsia were significantly higher than mild preeclampsia (45.68 ± 23.38 vs 21.94 ± 13.18), $P$ = 0.001. The MAP in mild and severe preeclampsia was 112.82 ± 3.55 mmHg and 130.63 ± 12.87 mmHg respectively. A negligible positive correlation was observed between the MAP and CA-125

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in the mild preeclampsia group (r = 0.01, *P* = 0.48), while a positive correlation, that was statistically significant was observed between the MAP and CA-125 in the severe preeclampsia group (r = 0.62, *P* = 0.001).

**Conclusions:** This study found a significant association between preeclampsia and CA-125. In addition, a positive relationship between the level of CA-125 and the severity of preeclampsia was established.

**Key words:** CA-125; preeclampsia; Sokoto.

## Introduction

Preeclampsia is a leading cause of maternal and perinatal morbidity and mortality worldwide.[1] It is defined as new onset of sustained elevated blood pressure (≥140 mmHg systolic or ≥90 mmHg diastolic on at least two occasions, 6 h apart) and proteinuria (at least 1+ on dipstick or ≥300 mg in a 24-h urine collection) first occurring after 20 weeks of gestation.[1,2] Preeclampsia is severe when systolic blood pressure is ≥160 mmHg systolic or ≥110 mmHg diastolic, urine protein excretion is greater than 5 g in a 24-h collection, and neurologic disturbances.[2] Other criteria include pulmonary edema, hepatic dysfunction, renal compromise, thrombocytopenia, placental abruption, and fetal growth restriction.[1,2]

While its etiology is not completely clear,[3] risk factors include nulliparity, previous history of preeclampsia in multiparas, maternal age, race, familial aggregation, and socioeconomic status.[4-7]

Cancer antigen 125 (CA-125) is an inflammatory mediator which is located on the cell surface.[8,9] It is generally expressed in ovarian cancer,[10] endometriosis, fibroids, pelvic inflammatory disease, and pregnancy.[8] It is theorized that the failure of trophoblastic invasion and the induction of an inflammatory process within the placenta may trigger the expression of CA-125.[8,9,11]

This study examined the association of CA-125 and preeclampsia.

## Subjects and Methods

A comparative cross-sectional study was conducted. Ninety-seven pregnant women with preeclampsia were recruited as cases and 97 pregnant women without preeclampsia were similarly recruited as controls. Sociodemographic characteristics, obstetric history, family history, and clinical data were obtained using a standard interviewer-administered questionnaire. Anthropometric measurements were taken and blood samples were taken for measurement of serum cancer antigen 125. Mean arterial pressure (MAP) was used as an indicator of the severity of preeclampsia. The data obtained were analyzed using mean, *t*-test and Pearson correlation test. Approval from the ethics committee was obtained 27-03-2017.

## Results

The 194 study participants were recruited into three groups: Control ($n$ = 97), mild preeclampsia ($n$ = 39), and severe preeclampsia ($n$ = 58).

Table 1 shows the demographic characteristics of the patients. The age range of the respondents was between 16 and 45 years. The mean age for the control was 28.6 ± 5.9, for the mild preeclampsia group, it was 27.9 ± 7.5 while for the severe preeclampsia group, it was 28.7 ± 7.2. 50.8% of the preeclamptics and 49.2% of the controls made up the married population. Most of the study respondents had either primary 67 (34.5%) or secondary education 87 (44.8%).

Table 2 shows mean systolic and diastolic blood pressure of the control group were lower than the study group (113.92 ± 10.56mmHg vs 162.16 ± 18.44mmHg), and (69.28 ± 8.37 mmHg vs 104.12 ± 12.81mmHg) respectively.

## Discussion

Table 3 shows the highest MAP of 130.63 ± 12.87, with a range of 113–183 mmHg in the severe preeclampsia group.

Tables 4 and 5 show statistically significant differences between the mean concentrations of CA-125 in the control and study groups (24.53 ± 9.42 IU/mL vs 36.13 ± 23.02 IU/mL).

Using Pearson correlation test, Table 5 shows a positive correlation, that was statistically significant between MAP and CA-125 in the preeclamptic group (r =0.70, *P* value = 0.001).

Table 6 shows a negligible positive correlation, was observed between the MAP and CA-125 in the mild preeclampsia group (r =0.01, *P* value = 0.48) but, a positive correlation, that was statistically significant was observed between the MAP and CA-125 in the severe preeclampsia group (r =0.62, *P* value = 0.001).

**Table 1: Sociodemographic characteristics of patients**

| Characteristics | Control *n* (%) | Mild preeclampsia *n* (%) | Severe preeclampsia *n* (%) | $X^2$ | *P* |
|---|---|---|---|---|---|
| Age group (years) | | | | | |
| <20 | 5 (29.4) | 4 (23.5) | 8 (47.1) | | |
| 20-24 | 21 (52.5) | 12 (30.0) | 7 (17.5) | | |
| 25-29 | 33 (62.3) | 5 (9.4) | 15 (28.3) | 14.33 | 0.07 |
| 30-34 | 18 (43.9) | 11 (26.8) | 12 (29.3) | | |
| 35 and above | 20 (46.5) | 7 (16.3) | 16 (37.2) | | |
| Total | 97 (50.0) | 39 (20.1) | 58 (29.9) | | |
| Mean age | 28.63±5.91 | 27.92±7.45 | 28.69±7.15 | | |
| Educational status | | | | | |
| None | 2 (100) | 0 (0.0) | 0 (0.0) | | |
| Primary | 21 (31.3) | 20 (29.9) | 26 (38.8) | | |
| Secondary | 59 (67.8) | 12 (13.8) | 16 (18.4) | 26.54 | 0.001 |
| Tertiary | 8 (47.1) | 2 (11.8) | 7 (41.2) | | |
| Quranic | 7 (33.3) | 5 (23.8) | 9 (42.9) | | |
| Total | 97 (50.0) | 39 (20.1) | 58 (29.9) | | |
| Occupation | | | | | |
| Housewife | 42 (39.3) | 23 (21.5) | 42 (39.3) | | |
| Civil servant | 16 (66.7) | 4 (16.7) | 4 (16.7) | | |
| Trader | 24 (66.7) | 7 (19.4) | 5 (13.9) | 18.86 | 0.001 |
| Student | 8 (61.5) | 4 (30.8) | 1 (7.7) | | |
| Unemployed | 7 (50.0) | 1 (7.1) | 6 (42.9) | | |
| Total | 97 (50.0) | 39 (20.1) | 58 (29.9) | | |

**Table 2: Blood pressure values of study respondents**

| Blood pressure | Control mean (SD) | Preeclamptics mean (SD) |
|---|---|---|
| Systolic blood pressure (mmHg) | 113.92 (10.56) | 162.16 (18.44) |
| Diastolic blood pressure (mmHg) | 69.28 (8.37) | 104.12 (12.81) |

**Table 3: MAP in both the study and the control groups**

| | Control | Mild PE | Severe PE |
|---|---|---|---|
| MAP (mmHg) Mean±SD | 84.16±8.052 | 112.82±3.55 | 130.63±12.87 |

**Table 4: CA-125 levels of study respondents**

| | Control Mean (SD) | Preeclampsia Mean (SD) | *t*-test | *P* |
|---|---|---|---|---|
| CA-125 (IU/mL) | 24.53 (9.42) | 36.13 (23.02) | 4.59 | 0.001 |

**Table 5: CA-125 levels of study respondents and preecclampsia severity**

| | Control mean (SD) | Mild PE mean (SD) | Severe PE mean (SD) | *F* test | *P* |
|---|---|---|---|---|---|
| CA-125 (IU/mL) | 24.53 (9.42) | 21.94 (13.18) | 45.68 (23.38) | 0.001 | 0.001 |

**Table 6: Correlation between CA-125 and map in the control and study groups**

| CA-125 (IU/mL) | Control | Preeclampsia |
|---|---|---|
| MAP (mmHg) | −0.18 | 0.70 |

Control: ($r=-0.18$, $P=0.08$), study ($r=0.70$, $P=0.001$)

This current study showed that the age range was similar to what has been used by other authors.[6,7-9] The mean concentration of maternal serum CA-125 in normal pregnancy was 24.53 ± 9.42 IU/ml in this study. This is similar to 17.2 ± 8.1 IU/mL found by Karaman *et al*. in normal pregnancy.[1] However, a higher level has been reported by Bhattacharya *et al*. who found a mean concentration of 47 ± 3.34 IU/mL in normal pregnancy.[9] Also, Ozat *et al*. in their own study got a mean concentration of 48.25 ± 3.34 IU/mL in normal pregnancies.[8] A much lower level was reported by Miami *et al*. who got a mean level of 13.70 ± 8.44 IU/mL.[7] In addition, Gyawali *et al*. got a mean level of 9.0 IU/mL.[8] The wide variations in these values could be due to the different kits and methods used in the assay of maternal serum CA-125.

The mean level of CA-125 in preeclamptic respondents in this study was 36.13 ± 23.02 IU/mL. A mean level of 21.94 ± 13.18 IU/mL was observed in mild preeclamptics, while a mean level of 45.68 ± 23.38 IU/mL was seen in the severe preeclamptics in this study. This is comparable to a study by Karaman *et al*. who observed a mean concentration of 18.8 ± 8.4 IU/mL in mild preeclamptics, and 38.8 ± 20.9 IU/mL in severe preeclamptics.[1] Bhattacharya *et al*. observed a mean concentration of 53.7 ± 8.52 IU/mL in the mild preeclampsia group, and 58.5 ± 4.02 IU/mL in the severe preeclampsia group.[9]

This current study established a positive relationship between the level of CA-125 and severity of preeclampsia, as shown by the increase in the mean concentrations of CA-125 in the severe preeclampsia group, and also the statistically significant positive correlation between the MAP and CA-125 in the preeclampsia group ($r = 0.07$, $P = 0.001$). This was comparable with the findings of Cereboy *et al*. that reported that CA-125 levels were significantly higher in severe preeclampsia compared to mild preeclampsia.[12] Also, significant correlations were reported between CA-125, and MAP in their study.[12]

Likewise, in the study conducted by Osanyin *et al*., serum levels of CA-125 were higher in severe preeclampsia as compared to mild forms, and CA-125 showed a significant correlation with blood pressure.[13] Similarly, Ozat *et al*. found in their own study that serum CA-125 concentrations were positively correlated with systolic blood pressure and diastolic blood pressure.[8] Furthermore, Karaman *et al*. reported in their study that CA-125 levels were significantly higher in severe preeclampsia than those with mild preeclampsia and normal controls, and CA-125 levels were positively correlated with systolic blood pressure and diastolic blood pressure.[1] Consistently, Miami *et al*. also

concluded in their study that serum CA-125 was significantly higher in the preeclampsia groups in comparison to the control group and the increment was directly correlated with the severity of preeclampsia.[14] In accordance, Bhattacharya *et al*. in their study found out that serum CA-125 concentrations were positively correlated with systolic blood pressure and diastolic blood pressure.[7] They concluded in their study that CA-125 is a biochemical marker that indicates the severity of the inflammatory process in preeclampsia.[7] Bon *et al*. reported in their study that maternal serum levels of CA-125 were higher during the first and third trimester of pregnancy, but that it showed no relation with preeclampsia.[15] However, of the 120 women with pathologic pregnancies involved in their study, only six were preeclamptics, and this number was rather too small to draw conclusions. Also, the method used to detect serum CA-125 was the Enzymun-Test CA-125 11, which used the intensity of the color developed after the addition of substrate as proportional to the concentration of CA-125 in the specimen.[15] This method is observer-dependent and could be biased. A study carried out by Groot *et al*. failed to detect any difference between normal and preeclamptic maternal plasma CA-125 at any time during pregnancy.[16] However, 20 women were studied in all; 10 normal, and 10 preeclamptics. This paucity of patients may have underestimated the association of CA-125 with preeclampsia. Also, the criteria used to diagnose severe preeclampsia in their study was an increase in systolic blood pressure of ≥30 mmHg, and an increase in diastolic blood pressure of ≥15 mmHg, above the booking blood pressure. These criteria are now obsolete, and none of the cases met the recent criteria for the diagnosis of severe preeclampsia.[17-20]

## Conclusion

This study observed the mean concentration of CA-125 in normal pregnancies to be significantly lower than the level in preeclamptics. Also, a positive relationship between the level of CA-125 and the severity of preeclampsia was established. Further research is required to clarify the clinical utility of CA-125 as a predictor of preeclampsia.

### Limitation

There were significant differences in education and occupation of the control and study groups which may have affected the study outcome.

### Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form, the patient (s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

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### Conflicts of interest

There are no conflicts of interest.

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