UTILITY OF SERUM CYSTATIN C AS A PREDICTIVE MARKER FOR PREECLAMPSIA IN PREGNANT NIGERIAN WOMEN

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INTRODUCTION

- Pre-eclampsia is a common syndrome that occurs in the second half of pregnancy, manifesting with hypertension and significant proteinuria.
- It occurs in up to 10% of pregnancies and is the second commonest cause of maternal mortality worldwide, accounting for 17% of maternal deaths in Nigeria.
- Several historical, physical and biochemical methods have been utilized in ensuring an early detection such as risk scoring and midtrimester Doppler ultrasound of the mid-cerebral artery and utero-placental flow.
- However, it was recently suggested that midtrimester serum Cystatin C levels could be a pointer to an earlier detection of patients that will eventually develop pre-eclampsia

STUDY OBJECTIVES

General Objective:

- To determine the usefulness of early midtrimester serum levels of Cystatin C in predicting pre-eclampsia among pregnant women in Ibadan.

Specific Objectives

- To determine the early midtrimester serum levels of Cystatin C in normotensive pregnant women in Ibadan.
- To determine these serum levels of Cystatin C in pregnant women who eventually develop pre-eclampsia.
- To compare these serum levels of normotensive pregnant women to those who eventually develop pre-eclampsia.

METHODOLOGY

STUDY POPULATION

- The study was conducted at the University College Hospital, Ibadan. Ibadan is the capital of Oyo state in the South Western region of Nigeria.
- Most of the inhabitants were civil servants, petty traders, housewives, civil servants, businesspeople and artisans.
- The predominant tribe is Yoruba though it has a significant proportion of other major tribes in Nigeria.

EXCLUSION CRITERIA

- Multiple gestation
- Molar pregnancy
- Women with Chronic Hypertension
- Women with chronic medical illness such as Diabetes Mellitus, Cardiac diseases, Renal pathology and Hepatic dysfunction
- Women with features of urinary tract infection
- Nonconsenting patients.

SAMPLE SIZE

- Minimum sample size required ~107

METHODOLOGY

- Nested case-controlled study
- Consenting, booked pregnant women between the gestational ages of 14 and 19 weeks were recruited after due counseling.
- Prepared proforma was used to obtain their socio-demographic characteristics.
- About 5mls of venous blood was obtained, labelled and kept.
- The women were followed up till delivery and were subsequently divided into 2 groups: those who had pre-eclampsia and those who did not.
- Another 5mls of venous blood sample was collected at delivery or at the point of diagnosis of pre-eclampsia.
- All samples were assayed for serum Cystatin C.
- The samples were run with the aid of Cystatin C (human) ELISA – a sandwich enzyme immunoassay for measurement of human Cystatin C using the Multiskan Ascent photometric microplate reader
- Data analysis was done using SPSS version 23.0.

- **RESULTS**
- 125 participants were recruited but 110 had complete data
  - Primigravidae – 47 (42.7%)

- Mean age of the study participants was 29.71±5.37 years
- All are married and cohabiting
- mean GA at recruitment = 16.75±1.68 weeks
  - mean GA at booking, 15.40±1.26 weeks

- average GA at delivery = 38.9 ± 2.1 weeks
- 7 (6.4%) developed preeclampsia.
  - No eclampsia

- Ave serum Cystatin level
  - At recruitment = 0.715±0.132 mg/dl;
    - range 0.4–1.2mg/dl)
  - At second reading = 0.882±0.246mg/dl

  **(t-test = 8.358; $p<0.05$).

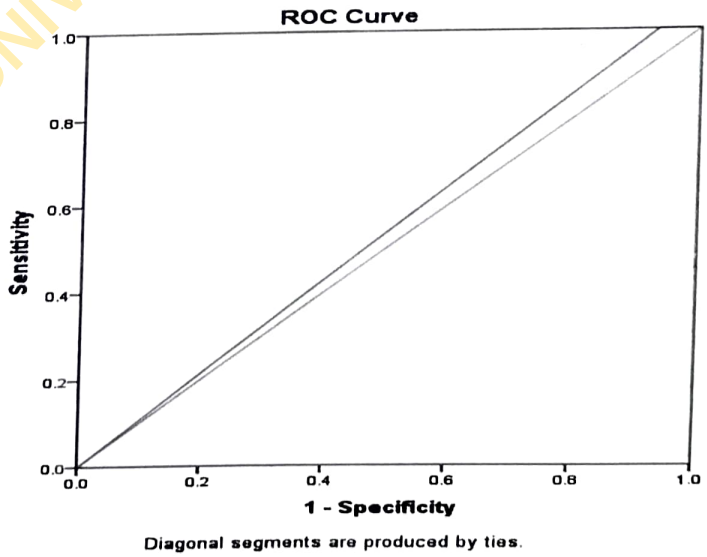
- For non–Pre-eclamptics, mean serum Cystatin C was 0.83±0.16mg/dl

- For Pre-eclamptics, mean serum Cystatin C was 1.6±0.2mg/dl **(t=8.613; p<0.005)
- The best discriminatory value, using ROC, was obtained at 1.0mg/dl.
- No difference in the fetomaternal outcomes vis-à-vis
  - mode of delivery,
  - baby's birth weight,
  - mean APGAR score at 5 minutes, and
  - admission into the special care baby units
- The odds ratio for the mode of delivery:
  - caesarean delivery versus spontaneous vaginal delivery was 3.75, (95% CI 0.789 – 17.861, P = 0.09).
- There was no difference in the serum values of Cystatin C in the HIV-positive and HIV-negative participants.

FETOMATERNAL OUTCOMES

Variable		Preeclampsia	Normotensives
Mean GA at delivery		38.9 ± 2.1 weeks	
Birth weight (kilograms)		3.22 ± 0.54	3.23±0.61
Mean APGAR at 5 mins		8.1±1.12	8.31±1.31
Mode of delivery	Caesarean delivery	4	27
	SVD	3	76
SCBU Admission		2	3

Receiver Operating Characteristics for discriminatory level at 1.0mg/dl



DISCUSSION

- Mean serum Cystatin C level in early gestation is significantly higher among participants who eventually developed preeclampsia.
- This is buttressing the report by previous researchers who have persistently documented elevated values in the disease stage.
- The overall early midtrimester values of serum Cystatin C in pregnant women is similar to values reported in non-pregnant women
- except for the participants who eventually developed preeclampsia.
- This is in tandem with the characteristics of Cystatin C in being unusually influenced by sex, age, body mass or pregnancy state.
- This further buttresses the fact that serum cystatin C is not affected by early pregnancy state vis –a-vis the hormonal changes.
- The higher levels of serum Cystatin C among the women who eventually developed preeclampsia is in tandem with the earliest reports.
- However, when compared with the normotensive women, the early midtrimester levels of serum Cystatin C is significantly higher.
- The higher value noted in the pre-eclamptic population is a pointer that serum Cystatin C may be of value in serving as a biomarker for preeclampsia either in isolation or in combination with other factors
- While the presence of hyperuricaemia with severe pre-eclampsia has been associated with poor fetal prognosis, serum uric acid in itself has been documented to be a poor predictor of pre-eclampsia because its serum concentration only rises significantly about one week before the clinical appearance of the disease.
- In the same vein, the usefulness of serum Creatinine as a marker for glomerular filtration rate (GFR) is limited by the influence of an individual's muscle mass, the tubular secretion and reabsorption, dietary intake and also by analytical difficulties.
- In addition, the vasodilation of the renal vessels in pregnancy causes 50–80% increase in plasma flow and change in GFR, which further complicates the use of serum Creatinine as a marker of GFR in pregnancy.
- This implied that elevation of serum Cystatin C above a critical value is a potential valuable biomarker for early detection of predisposition to development of preeclampsia
- Although the study is underpowered to establish a definitive link between Cystatin C and the severity of the disease, it served the main purpose of predicting its occurrence

CONCLUSION

- Serum Cystatin C is significantly elevated in preeclampsia and its midtrimester assay is a potential, valuable biomarker for the prediction of preeclampsia which should be explored.

FURTHER RESEARCH AREAS

- Potentials for further evaluation of the exact point at which serum Cystatin C will begin to rise in patients that will develop preeclampsia.
- This will require a larger cohort of well-motivated patients as there will be need for serial measurement of their serum Cystatin C levels.
- On the other hand, a point midtrimester assay (btw 18 & 22 weeks) can be explored in isolation or in combination with other parameters such as foetal midcerebral Doppler USS
- in determining the possibility of developing preeclampsia and the potential fetomaternal outcomes.

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