ORIGINAL ARTICLE

Correlation of Serum Cystatin-C and Creatinine as Predictive Prognostic Markers for Renal Impairment in Pre Eclamptic Patients

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ABSTRACT

Background: Renal impairment is becoming more common as adverse effect of preeclampsia in emerging nations. Preeclampsia is a complication of pregnancy that can be prevented by using Cystatin C as a better and earlier renal biomarker than creatinine in order to evaluate the renal function.

Method: The study was done on 150 women in the Obstetrics and Gynecology Department at LUMHS Jamshoro, dividing them into three gestational age groups. The ANNOVA test was used to determine if cystatin-c is a superior marker to serum creatinine. SPSS version 21 was used to analyze the data without any dropout of the patients.

Results: In this study, one hundred fifty (150) pre eclamptic pregnant women in the 20–35-year-old age range were chosen. The cystatin-c level was 1.2 ± 0.7 at 36th weeks of gestation in the forty of the patients of age 20-25, while creatinine was 1 ± 0.7. In sixty-eight (68) patients of age between 25-30 years, cystatin-c levels ranged from 1.6 ± 0.8 ng/mL, while creatinine levels ranged from 1.1 ± 0.9 ng/mL. In patients above > 30 years' age group, the serum cystatin C level was found to be 1.9 ± 0.8, while the creatinine level was found to be 1.2±0.6 at 36th week of gestation.

Conclusion: This research shows that cystatin C levels rise early and proved to be a better predictor of renal problems as compared to serum creatinine, which didn't increase considerably.

Keywords: Cystatin-C, Preeclampsia, kidney impairment

INTRODUCTION

Pregnancy-related hypertension is a leading cause of maternal and fetal mortality and morbidity despite being a non-communicable condition.[1]

Preeclampsia is a hazardous kind of high blood pressure with unknown cause [2] that occurs when a pregnant woman's blood pressure falls above 140/90 mmHg measured on two distinct times, separated by at least six hours, and her proteinuria rises by at least 300 mg in 24 hours. (ACOG) 2002.[3]

According to a study conducted in Pakistan, the prevalence of preclampsia is 15%.[4] More than 16% of maternal fatalities in Western nations are attributed to hypertension complications, but in Africa and Asia, the figure is closer to 20%. [5]

The kidney has a major role in both normal pregnancy physiology and the development of Preeclampsia (PE) [6]. An endothelial defect may lead to glomerular endotheliosis, a condition that affects the integrity of the blood-brain barrier (BBB). [7] There are several risks associated with not evaluating pregnant patients with hypertension for RFTs. Preeclampsia complications include organ malfunction in the mother as well as utero-placental dysfunction.[8]Although serum creatinine and uric acid are reliable indicators of renal function, they fluctuate with diet and blood pressure medications and are nonspecific in some late-pregnancy situations. During pregnancy, widening of renal vessels increases blood flow by 50% to 80%, which significantly alters GFR and results in a miscalculation of creatinine levels which is a common practice to use as an indicator of GFR.[9]

Cystatin-C is indicated as a novel and trustworthy biomarker since existing renal indicators are unable to detect renal impairment and reduce GFR before the development of preeclampsia complications. Serum Cystatin-C [10] with a mean value ranging from 0.52 to 0.98mg/L[11] may be used to assess the GFR status in both healthy and hypertensive pregnant women. Many studies have shown Cystatin-C to be superior to other renal indicators in terms of ease of transit through the glomerular filter and absence of additional renal excretion, making it an excellent GFR monitor. Preeclampsia patients with renal impairment had a 29-39 percent increase in cystatin C serum levels in the third trimester compared to the previous two trimesters.[12]

METHOD

After receiving the permission from the LUMHS Research and Ethical Committee, this cross-sectional research was carried out at the Physiology Department in conjunction with the Gynecology and Obstetrics sections at LUMHS Jamshoro & Diagnostic Laboratory Civil Hospital, Hyderabad. Blood pressures of equal or above than 140/90mmHg and proteinuria +1 among 150 women aged between 20 to 35 with gestational age between 20 and 36 weeks were included. Conditions that might impact GFR (chronic hypertension, endocrine problems and numerous pregnancies) are not included in the study. A 3cc blood sample from each subject's peripheral vein was taken into a Li-heparin tube after all aseptic procedures had been maintained. First, a sample was collected at 20 weeks of gestation; the second sample was taken at 36 weeks gestation. Roche Cobas Modular c501 tested the serum using PETIA (particle enhanced immunoturbidimetric assay).

Statistical Analysis: All variables were being analyzed in Microsoft Excel 2021 and SPSS 26.0. Numbers and percentages were used to describe qualitative data like gestational age, residence status, or educational status (shown in table: 01) Mean and standard deviation were used to represent quantitative data such as blood pressure and BMI. [Table 02] The categorical differences between renal biomarkers were determined by ANOVA (table: 03)

RESULTS

The results of this study was carried out to highlight the significance of Cystatin-C. There were total 150 pre-eclamptic patients.3 gestational age groups were made.. Table 3 shows the distribution of patients according to their gestational age and their blood creatinine and cystatin-c levels. According to this data, the first blood sample of diagnosed preeclampsia patients was collected from gestational group 20-25 weeks to measure serum creatinine and serum Cystatin-C levels. Their second renal biomarker sample was obtained at their 36th week of pregnancy and compared to the first one. Same sampling procedure were applied in other two gestational age groups. When comparing cystatin-c and serum creatinine levels, the ANNOVA test was applied which showed a significant rise in cystatin-c before the onset of preeclampsia complications, but no such rise in creatinine levels. Most of the patients came from the village, based on where

they lived. There were four categories of educational status, as un educated patients having 50%, preeclampsia cases due to lack of antenatal care awareness and graduate patients were making less than 10%. as shown in **Table 1**. Figures for averages of blood pressure and BMI is shown in table2.

Table 1: Demographic Statistics of Preeclapmsia Patients (n=150)

Variables:	Frequency	%
Primigravida	90	60
Multigravida	60	40
Gestational Weeks		
20-25weeks	40	26.6
26-30weeks	68	45.3
>31 weeks	42	28
BMI		
<18.5	10	6.6
18.5-24.9	46	30.6
25-29	69	46
>30	25	16.6
Residential Status		
Urban	60	40
Rural	90	60
Education Status		
Uneducated	75	50
Primary	45	30
Secondary	20	13.3
Graduate	10	6.7

Table 2: Mean arterial Blood pressure and BMI in Preeclampsia patients (n=150)

Parameters	Mean ±SD
Systolic BP mm/Hg	125±23.5
Diastolic BP mm/Hg	85±10
BMI	25±5

Table 3: Distribution of PTS with their serum cystatin and creatinine level

Gestational age (weeks)	No. of patient	Serum creatinine mg/dL			Serum cystain-C mg/l		
		1st sample	36th week	P-value	1st sample	36th week	P-value
20-25	40	0.7±0.6	1±0.7	0.009	1.1±0.2	1.2±0.7	0.007
26-30	68	0.9±0.5	1.1±0.9	0.007	1.5±	1.6±0.8	0.003
>35	42	1±0.5	1.2±0.6	0.003	1.7±	1.9±0.8	0.001

DISCUSSION

This is the first and only research in Pakistan to examine the biomarker cystatin C in pregnant women at risk for preeclampsia. Several pre-eclampsia patient evaluation ideas have shifted as a result of this research, which was limited to the local community.[13] According to numerous prevalence studies, creatinine levels are inaccurately measured in patients with severe renal impairment owing to the fact that creatinine is actively released by proximal renal tubules. According to a Newman et al. research, Cystatin C is a more sensitive indication for GFR alterations, even if they are small. [14]

The presence of Cystatin C in maternal blood was shown to be a quality signal for early identification of preeclampsia in research by Stevens et al.[15]

In Nirmala et al's research, BMI was 28 as well, while in ours, the mean BMI was 25.[16.] Preeclampsia patients in China had higher blood pressure than those in the comparison group, whereas our research found that the mean systolic and diastolic blood pressures were both 125 and 85, respectively. [17]

Cystatin-C levels in preeclampsia were shown to be significantly higher in a control group, according to research by N. Franceschini[18] and K. Kristensen[19].

On the basis of Japanese Society of Nephrology recommendations [20], individuals with mild to moderate renal impairment had almost regular creatinine values, but alarmingly high blood cystatin c levels. [21]

Preeclampsia is a substantial risk factor for women who are first-time mothers, as shown by a research in which most of the participants were first-time mothers, [22] and in our study, where 60% of the patients were first-time mothers.[23]

Many researchers have demonstrated that mediator factors such have no effect on serum Cystatin C [24], which gives it a sensitivity of roughly 96.8%. Since its level is very changeable owing to confounding factors, the sensitivity of serum creatinine was only 61.3%. [25]

A rise in serum Cystatin C is strongly linked to the development of hypertension, which in turn causes renal impairment. In contrast, serum creatinine in the pre-hypertensive and normal blood pressure groups did not provide any early warning of renal damage of any severity. [26] Serum cystatin C is a better indication of renal disease in its early stages than creatinine, according to our research, and our findings are very encouraging. According to our findings, early detection of preeclampsia-induced nephropathy in Pakistan would save many lives if blood Cystatin C tests are widely accessible in every laboratory. [27]

CONCLUSION

Preeclampsia patients who are diagnosed with kidney impairment early are on better able to treat and avoid further future complications. It has been discovered that the levels of cystatin C and serum creatinine increase sooner and more dramatically than serum creatinine when preeclampsia symptoms begin to develop. As a result, in patients with preeclampsia, Cystatin C is the better indicator of renal impairment since it appears sooner.

Recommendation: Studies with greater sample sizes are needed in various sections of the country.

Using the Cystatin-C renal biomarker value, researchers may further evaluate pre-eclampsia related other neurological and cardiovascular risk.

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