Creatinine Concentration in Preeclamptic and Eclamptic Women: a cross sectional study in a tertiary hospital

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Abstract:

  Preeclampsia is a syndrome defined by gestational hypertension and proteinuria. It has substantial adverse effects for pregnant women and their fetuses, and it is a major cause of maternal morbidity and mortality worldwide. The serum level of creatinine in preeclampsia and eclampsia varies in different studies. To compare the creatinine concentration in preeclampsia and eclampsia patients with normal pregnant women was aim of this study. This cross-sectional comparative study was conducted in the Department of Clinical Pathology, in collaboration with the Department of Obstetrics and

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Gynecology, BSMMU, Dhaka and Department of Obstetrics and Gynecology, Dhaka Medical College Hospital (DMCH), Dhaka. Total 96 women with pregnancy of 28 weeks or more were enrolled in the study by purposive sampling. Sample size of each of the three groups; pre-eclampsia (group I), eclampsia (group II) and normal pregnancy (group III); was 32. Random urine sample was collected for measurement of urinary protein. After taking all aseptic precaution, 2 ml of venous blood was collected from each patient to mesure serum creatinine level. The mean±SD age of the patients of group I, II and III were 26.91±4.41, 25.13±4.16 and 25.3±5.15 years respectively with no significant difference (p=0.234) The mean±SD serum creatinine was 0.95±0.19, 0.90±0.22 and 0.68±0.14 mg/dl in group I, II and III respectively. Although the mean Creatinine level of any group did not exceed the normal level, the mean±SD serum creatinine level was significantly higher in preeclamsia and eclampsia group than normal pregnancy (p<0.001).The mean±SD serum creatinine was significantly higher in preeclampsia and eclampsia groups than normal pregnancy.

Key words: Preeclampsia, eclampsia, creatinine

INTRODUCTION

Preeclampsia is a multisystem disorder that has substantial adverse effects for pregnant women and their fetuses, and it is a major cause of maternal morbidity and mortality worldwide.[1] If preeclampsia is associated with convulsion, the condition is called eclampsia.[2]The incidence of preeclampsia in Bangladesh is 7.9%. The causes of this higher incidence are thought to be illiteracy, lack of health awareness, poverty, and superstitious beliefs. As a result most preeclampsia cases remain unrecognized until severe complications such as eclampsia develops.[3] Preeclampsia is one of the most potential complications contributing to preterm labour/delivery, perinatal mortality, maternal mortality, intra-uterine growth

retardation, low birth weight infants and many such related problems.[4] Pre-eclampsia/eclampsia is almost exclusive to humans and delivery of the pregnancy isthe only effective treatment.[5] Abnormal placentation is one of the initial events in the pathogenesis of preeclampsia.[6] Preeclampsia is associated with vasoconstriction and thickening of vascular media which decreases vascular capacity and increases peripheral resistance.[7] It affects almost every organ.[8] The end result is generalized maternal systemic illness manifesting as endothelial injury, hypertension, platelet activation, renal impairment, and other end organ damage.[9,10]

In adult humans, about half of the creatine needed is obtained from diet mostly from meat and dairy products and the other half is synthesized in the kidney and liver. Creatine and its phosphorylated form, phosphocreatine, spontaneously break down to creatinine that is excreted in the urine. Losses of creatinine are restored by new synthesis and dietary intake. [11] Over the years, a lot of interest has been directed at studies on the role of serum creatinine (SCr) in the pathogenesis of pregnancy induced hypertension, such as preeclampsia. A number of important studies are available which confusingly and often conflictingly describe the dependence of serum creatinine levels in pre-eclampsia, eclampsia and normotensive groups. Several studies found that the measured SCr levels were significantly elevated in pre-eclamptics women.[12-13] A cross-sectional, hospital based study found that the levels of serum creatinine was significantly elevated in pre-eclamptics when compared to normotensives.[4] However, Abdulmunem (2005)[14] found that the SCr levels did not show much change in preeclampsia. Another study described that there was insignificant changes in the SCr in both preeclampsia and eclampsia groups.[15] Such confusing results have encouraged us to undertake a study on serum creatinine level with a desire to understand the exact finding. The aim of the study was to

measure and compare the SCr in preeclamptic, eclampsia and normotensive groups.

MATERIAL AND METHODS

This cross-sectional comparative study was conducted in the Department of Clinical Pathology, in collaboration with the Department of Obstetrics and Gynecology, BSMMU, Dhaka and Department of Obstetrics and Gynecology, Dhaka Medical College Hospital (DMCH), Dhaka during the period of March, 2012 to February, 2013. Women with pregnancy of 28 weeks or more who attended at antenatal care unit or admitted into the Department of Obstetrics and Gynaecology, BSMMU or DMCH, Dhaka were enrolled in the study. Sample size of each of the three groups; pre-eclampsia (group I), eclampsia (group II) and normal pregnancy (group III); was 32. Patients were selected by purposive sampling technique. The particulars of the patients and clinical data were recorded in a pre-designed data sheet. Patients with chronic renal disease, chronic liver disease, diabetes mellitus and known bleeding disorder were excluded from the study. The research protocol was approved by the Institutional Review Board (IRB) of BSMMU, Dhaka. Informed written consent was taken from the patient or legal guardian (in case of severely ill patient). Full history regarding age, gestational age, parity, history of any medical or chronic disease were taken from all patients. General physical examination was done to obtain information about height, weight, anaemia, cyanosis, jaundice, edema, pulse, systolic and diastolic blood pressure. Random urine sample was collected for measurement of urinary protein. After taking all aseptic precaution, 2 ml of venous blood was collected from each patient with disposable syringe by venipuncture for measurement of serum creatinine level.

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Sample size and grouping of the patients: The sample size of each of the three groups; pre-eclampsia (group I), eclampsia (group II) and normal pregnancy (group III), was 32 (thirty two). Patients were selected by purposive sampling.

Data collection: Complete obstetrical history and clinical data were recorded on a data collecting sheet designed for the study. Serum Creatinine level was measured for all cases and controls.

Statistical analysis: Data were analyzed by computer based statistical software 'Statistical Package for Social Science (SPSS) program for windows version 16. All quantitative variables were expressed as mean (±SD) for each group and comparison of mean between two groups was done by Student t test and between more than two groups by ANOVA test. Qualitative data were expressed as frequency and percentage and comparison between groups was done by chi-square test. p value ≤0.05 was considered to be significant.

RESULT

Table –I: Age distribution of the study patients (n=96)

Age (in years)	Group I (n=32)	Group II (n=32)	Group III (n=32)	F value	p value
Mean±SD Range (min-max)	26.91±4.41 19-36	25.13±4.16 18-32	25.28±5.15 17-38	1.475	0.234 NS

Group I, preeclampsia; group II, eclampsia; group III normal pregnancy, NS=not significant, p value derived from ANOVA test

The mean±SD age of the patients of group I, II and III were 26.91±4.41, 25.13±4.16 and 25.3±5.15 years respectively with no significant difference (p=0.234) (Table-I).

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Table –II: Distribution of the study patients according to gravid (n=96)

Gravida	Group I (n=32)		Group II (n=32)		Group III (n=32)		Chi-square value	p value
	n	%	n	%	n	%		
Primi	10	31.2	13	40.6	14	43.8		
Multi	22	68.8	19	59.4	18	56.2	1.143	0.565[NS]

Group I, preeclampsia; group II, eclampsia; group III normal pregnancy, [NS] =not significant, p value derived from Chi-square test

Ten (31.2%), 13(40.6%) and 14(43.8%) patients of Group I, II and III were primi gravida respectively and 22(68.8%), 19(59.4%) and 18(56.2%) patients of Group I, II and III were multi gravida respectively with no significant difference among three groups (p=0.565) (Table II).

Table –III: Comparison of mean systolic and diastolic blood pressure of the study patients (n=96)

Blood pressure	Group I (n=32)	Group II (n=32)	Group III (n=32)	F value	p value
	Mean±SD	Mean±SD	Mean±SD		
SBP(mmHg) Range (min-max)	156.56 ±14.05 140-190	163.13 ±25.83 140-240	107.5 ±12.95 80-130	85.912	<0.001 S
DBP(mmHg) Range (min-max)	104.69 ±8.88 90-130	106.72 ±14.51 90-140	69.69 ±7.82 60-80	118.612	<0.001 S

Group I, preeclampsia; group II, eclampsia; group III normal pregnancy, S=significant, p value derived from ANOVA test

Table III shows the mean systolic and diastolic blood pressure of the study patients. The mean systolic blood pressure was 156.56 ±14.05, 163.13 ±25.83 and 107.5 ±12.95 mmHg in group I, group II and group III respectively. The mean systolic blood pressures of the preeclamsia and eclampsia group were higher than normal group. The difference in mean among the groups was found to be significant by ANOVA test (p<0.001).

The mean diastolic blood pressure was 104.69 ±8.88, 106.72
±14.51 and 69.69 ±7.82 mmHg in group I, group II and group
III respectively. The mean diastolic blood pressures of the
preeclampsia and eclampsia group were higher than normal
group. The difference in mean diastolic blood pressures among
the groups was found to be significant by ANOVA test (p<0.001)
(Table III)

**Table–IV: Comparison of mean hemoglobin concentration of the
study patients (n=96)**

Hemoglobin concentration (Gm/dl)	Group I (n=32)	Group II (n=32)	Group III (n=32)	F value	p value
Mean±SD Range (min-max)	11.54±1.95 8.20-15.60	11.98 ±1.49 9.10-15.30	11.12 ±1.63 7.3-15.8	2.084	0.130NS

Group I, preeclampsia; group II, eclampsia; group III normal pregnancy, [NS]
=significant, p value derived from ANOVA test

Table IV shows the mean hemoglobin concentration of the
study patients. The mean hemoglobin concentration was 11.54
±1.95, 11.91 ±1.49 and 11.12 ±1.63 gm/dl in group I, group II
and group III respectively. The mean hemoglobin concentration
of the preeclamsia, eclampsia and normal group were similar
with no significant difference by ANOVA test (p<0.311).

**Table –V: Comparison of total platelet count of the study patients
(n=96)**

Platelet count	Normal pregnancy (n=32)	Preeclampsia (n=32)	Eclampsia (n=32)	F value	p value
	Mean±SD	Mean±SD	Mean±SD		
Platelet (x10⁹/L)	300.94±69.72	219.69 ±63.73	187.50±64.96	24.967	<0.001 s
Range (min-max)	200-450	80-360	90-350		

Group I, preeclampsia; group II, eclampsia; group III normal pregnancy, [S]
=significant, p value derived from ANOVA test

Table V shows Comparison of total platelet count of the study patients. The mean total platelet counts were 219.69 ±63.73 (range 80-360), 187.50±64.96 (range 90-350), and 300.94±69.72 (range 200-450) X10^9/L in group I, group II and group III respectively. The mean total platelet counts of the preeclampsia and eclampsia group were significantly lower than normal group (Figure-6) as calculated by ANOVA test (p<0.001).

Table–VII: Distribution of the study patients according to spot urinary protein estimation (n=96)

Spot urinary protein	Group I (n=32)		Group II (n=32)		Group III (n=32)		Chi-square value	p value
	f	%	f	%	f	%		
Nil	0	0	0	0	31	96.9	101.7	<0.001^S
1+	0	0	0	0	1	3.1		
2+	11	34.4	7	21.9	0	0		
3+	15	46.9	12	37.5	0	0		
4+	6	18.8	13	40.6	0	0		

Group I, preeclampsia; group II, eclampsia; group III normal pregnancy, [NS] =not significant, p value derived from Chi-square test

Among the normal pregnant women 31 (96.9%) had no proteinuria and 1(3.1%) had '1+' proteinuria. Eleven (34.4%), 15 (46.9%) and 6(18.8%) preeclamptic patients had '2+', '3+' and '4+' proteinuria respectively. Seven (21.9%), 12 (37.5%) and 13(40.6%) eclamptic patients had '2+', '3+' and '4+' proteinuria respectively. Proteinuria was significantly more pronounced in patients with eclampsia (p<0.001). (table–VII).

Table –VI: Comparison of serum Creatinine level among the study groups (n=96)

Biochemical variable	Group I (n=32)	Group II (n=32)	Group III (n=32)	F value	p value
	Mean±SD	Mean±SD	Mean±SD		
Serum creatinine (mg/dl)	0.95±0.19	0.90±0.22	0.68±0.14	19.001	<0.001*^{S}

Group I, preeclampsia; group II, eclampsia; group III normal pregnancy, ^{S} =significant, *=p value derived from ANOVA test

Table VI shows comparison of serum Creatinine level among the study groups. The mean±SD serum creatinine was 0.95±0.19, 0.90±0.22 and 0.68±0.14 mg/dl in group I, II and III respectively. Although the mean Creatinine level of any group did not exceed the normal level, the mean±SD serum creatinine level was significantly higher in preeclamsia and eclampsia group than normal pregnancy (p<0.001).

Table –VIII: Comparison of serum creatinine level between pre-eclamsia, eclampsia and normal pregnancy groups (n=96)

Comparison groups	Serum creatinine level (mg/dl)	
	p value	95% CI
Group I vs Group II	0.339[NS]	-.05331 to 0.15369
Group I vs Group III	<0.001[S]	0.18641 to 0.35734
Group II vs Group III	<0.001[S]	0.12982 to 0.31483

Group I, preeclampsia; group II, eclampsia; group III normal pregnancy, [NS] =significant, * [S] =significant, P value derived from student t test, CI, confidence interval

Table VIII shows comparison of serum creatinine level between the study groups. No significant difference was observed in serum creatinine level between group I vs II (p=0.339, 95% CI; -.05331 to 0.15369). Highly significant difference were observed in serum Creatinine level between group I vs III (p<0.001, 95% CI; 0.18641 to 0.35734) and between group II vs III, (p<0.001, 95% CI; 0.12982 to 0.31483).

DISCUSSION

Pre-eclampsia and eclampsia remains the important cause of maternal death and perinatal mortality in most developing countries. The etiology of pre-eclampsia is still unknown. Many theories suggested that abnormal placentation is one of the initial events in the pathogenesis of preeclampsia. Abnormal placentation produces placental hypoxia and ischaemia, causes an increase release of vasoactive substances like endothelin-1,

nitric oxide, tumour necrosis factor-α (TNF-α), interleukin (IL)-6, IL-1α, IL-1ß, and thromboxane A_2 which contribute to systemic endothelial dysfunction.[10]

In order to compare the concentration of creatinine between normal pregnancy, preeclampsia and eclampsia we enrolled 96 patients, 32 patients in each three groups in the study. In our study we found that the mean age of the patients with preeclampsia, eclampsia and normal pregnant women was 26.91±4.41, 25.13±4.16 and 25.3±5.15 years. The difference of mean age was not statistically significant among three study groups (p=0.234). These findings are consistent with the findings of Abubakar et al., (2011)[16] and Ustun et al., (2007)[17]. Ustun and co-investigators[17] found that the median age of mild, moderate, severe preeclampsia group and control group were 29, 29.5, 27 and 28 years respectively with no significant difference between groups (p= 0.243).

In our study we found that 31.2%, 40.6% and 43.8% patients were primi gravida in group I, group II and group III respectively. The difference was not statistically significant among the three groups. Our study results are consistent with the observations of Ustun et al., (2007).[17]

In the present study the mean total platelet counts were 300.94±69.72, 219.69 ±63.73 and 187.50±64.96 in normal pregnancy, patients with preeclampsia and eclampsia respectively. The mean total platelet counts of the preeclampsia and eclampsia group were significantly lower than normal group (p<0.001) which was supported by several studies.[17,18-22]

Among the normal pregnant women 31 (96.9%) had no proteinuria and 1(3.1%) had '+' proteinuria. Eleven (34.4%), 15 (46.9%) and 6(18.8%) preeclamptic patients had '2+', '3+' and '4+' proteinuria respectively. Seven (21.9%), 12 (37.5%) and 13(40.6%) eclamptic patients had '2+', '3+' and '4+' proteinuria respectively. Proteinuria was significantly more pronounced in

patients with eclampsia (p<0.001). This finding was explained by Hladunewich, Karumanchi, and Lafayette (2007).[9]

Hladunewich, Karumanchi, and Lafayette (2007)[9] stated that healthy pregnant women exhibit marked glomerular hyperfiltration, peaking above normal, nongravid levels by 40 to 60%. This hyperfiltration seems to result primarily from depression of the plasma oncotic pressure in the glomerular capillaries. In preeclampsia, variable degrees of renal insufficiency are associated with a characteristic glomerular lesion, "glomerular endotheliosis." The GFR was significantly depressed to 91 ml/min per 1.73 m2 in women with preeclampsia compared with a value of 149 ml/min per 1.73 m2 in the control subjects. Subendothelial fibrinoid deposits and mesangial cell interposition were found only in women with preeclampsia.[9] We found that the serum creatinine level was significantly higher in preeclampsia (p<0.001) and eclampsia (p<0.001) than normal pregnant women, the serum creatinine level did not exceed the highest normal range. Our findings were consistent with the finding of Egwuatu (1986)[12] and Weerasekera and Peiris (2003)[13] Manjareeka and Nanda (2013)[4] and Magee et al (2014).[23]

Egwuatu (1986) [12] and Weerasekera and Peiris (2003) [13] found that the measured SCr levels were significantly elevated in pre-eclamptics women. Manjareeka and Nanda (2013)[8] found in a hospital based cross-sectional study that the levels of serum creatinine, was significantly elevated in pre-eclamptics when compared to normotensives.[4] Magee et al (2014)[23] stated in the "Clinical Practice Guideline for the diagnosis, evaluation, and management of the hypertensive disorders of pregnancy" that elevated serum creatinine was associated with the risk of development of adverse conditions in the patients with hypertensive disorders of pregnancy.

Another study by Salako et al (2003) also found that there was insignificant changes in the SCr in both preeclampsia

and eclampsia groups.[15] Such confusing results have
encouraged us to undertake a study on serum creatinine level
with a desire to understand the exact finding. The aim of the
study was to measure and compare the SCr in preeclamptic,
eclampsia and normotensive groups.

However, the findings of our study was not consistent
with the findings of Abdulmunem (2005) and Salako et al
(2003). Abdulmunem (2005) found that the SCr levels did not
show much change in preeclampsia. Similarly Salako et al
(2003) observed insignificant changes in the SCr in both
preeclampsia and eclampsia groups.

CONCLUSION

The serum creatinine level was significantly higher in
preeclampsia and eclampsia patients than normal pregnancies
but their levels did not cross the upper limit of normal range in
any group.

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