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Original Article

Serum Iron Parameters, Adenosine Deaminase, and Zinc – As Diagnostic Significant Markers of Preeclampsia

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Abstract

Introduction: Preeclampsia is characterized by persistently elevated blood pressure of >140/90 mmHg, proteinuria, and edema after 20 weeks of gestation (ACOG, 2002). It is described as a transient but potentially dangerous complication of pregnancy. Those affected need rest and close monitoring or, in severe cases, admission in the hospital.

Materials and Methods: In the present study, 90 pregnant women were studied. 30 women who had normal uncomplicated pregnancies were matched for maternal age and gestational age with patients and were selected as a control group. Another 60 women presented with clinical features of preeclampsia were selected as cases.

Results: A total of 90 women in third trimester from Government Maternity Hospital participated in the present study, of which 30 pregnant women with uncomplicated pregnancies included 60 pregnant women with preeclampsia.

Conclusion: Preeclampsia a multisystemic syndrome characterized by hypertension, proteinuria, and edema that occurs after 20 weeks of gestation and usually resolves soon after delivery. It is one of the most important complications of pregnancy that is associated with increased maternal and fetal mortality.

Key words: Preeclampsia, Pregnancy, Serum Zinc

INTRODUCTION

Preeclampsia is characterized by persistently elevated blood pressure (BP) of >140/90 mmHg, proteinuria, and edema after 20 weeks of gestation (ACOG, 2002). It is described as a transient but potentially dangerous complication of pregnancy those affected need rest and close monitoring or, in severe cases, admission in the hospital. This usually resolves soon after delivery, but early delivery increases the risk of complications to the baby. This has to be balanced against delay, which increases the risk that eclampsia will develop, with seizures and organ damage threatening the lives of both mother and baby (Williams *et al*., 2007).

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Preeclampsia occurs in 3%–5% of pregnancies and is the major cause of maternal mortality which accounts to 15%–20% in developed countries and is a leading cause of preterm and intrauterine growth retardation.[1,2]

In the presence of catalyticamounts of transition metal ions, particularly iron,which may arise in the ischemic placenta by destructionof red blood cells from thrombotic, necrotic, and hemorrhagic areas ,the reactive oxygen species produced by ischemic tissues can generate the highly reactive hydroxyl radical by Fenton chemistry . This radical can initiate the process of lipid peroxidation, which, if uncontrolled, may result in endothelial cell damage[3-5] Hubel *et al*.,).

Ferritin is a acute phase reactant and is a major iron storage protein found not only in spleen, liver, and bone marrow but also in found in mucosal cells of small intestine, in placenta, kidney, testes, skeletal muscle, and in plasma (Circhton, 1973). The serum ferritin was the best sensitive marker of iron status parameters reflecting the preeclampsia and the result may support the role of iron

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as a catalyzer of oxidative stress and lipid peroxidation in pathophysiology of preeclampsia (Kwon *et al*., 2007).[6-8]

Zinc, an antioxidant, is a catalyst for the endogenous antioxidant enzyme superoxide dismutase (SOD) which has been demonstrated to be reduced in red blood cell (RBCs) in preeclampsia. Zinc deficiency results in increased sensitivity to oxidative stress.[9-11]

Adenosine deaminase (ADA) is an enzyme which catalyzes conversion of adenosine and 2`-deoxyadenosine to inosine and 2`-deoxyinosine, respectively. ADA is essential for differentiation of lymphoid cells and the possible role of cell-mediated immunity in preeclampsia has been evaluated by assessing the ADA activity. ADA is increased where cell-mediated immunity is enhanced.[12,13]

Hyperuricemia occurs in approximately 75% of preeclamptic pregnancies and is clearly associated with severity and adverse pregnancy outcomes in preeclampsia including increased preterm delivery, fetal growth restriction, and fetal death. Increased uric acid in preeclampsia is not entirely due to decreased glomerular filtration and changes in tubular urate handling and/increased uric acid production.[14,15]

MATERIAL AND METHODS

The study was conducted at the Department of Obstetrics and Gynecology at Government Maternity Hospital, Nayapool and the Department of Biochemistry Osmania General Hospital, Hyderabad.

In the present study, 90 pregnant women were studied. 30 women who had normal uncomplicated pregnancies were matched for maternal age and gestational age with patients and were selected as a control group. Another 60 women presented with clinical features of preeclampsia were selected as cases. They were subclassified into mild and severe preeclampsia depending on the classification given by ACOG.

- Group I – controls (normal pregnant women)
- Group II – a) Mild preeclampsia
  b) Severe preeclampsia

Inclusion Criteria: Cases

The following criteria were included in the study:

1. Preeclamptic women whose BP was normal during the first 20 weeks of gestation.
2. No previous history of hypertension.
3. Age between 20 and 35 years
4. All the cases were in the third trimester of pregnancy.
5. Mild preeclampsia – BP <160/110 mm Hg. on two or more occasions at least 6 h and proteinuria >300 mg/day.
6. Severe preeclamptic – BP >160/110 mm Hg. on two or more occasions at least 6 h and proteinuria >500 mg/day.
7. 30 cases of mild preeclampsia and 30 cases of severe preeclampsia were selected for the study.

Inclusion Criteria: Controls

The following criteria were excluded from the study:

1. 30 normal pregnant women were selected as controls.
2. Age between 20 and 35 years.
3. There was no previous history of hypertension.

Exclusion Criteria

1. Patients with history of liver disease, diabetes, renal failure, anemia, stroke, coronary artery disease, chronic lung diseases, abruption placenta, disseminated intravascular coagulation (DIC), seizures, and eclampsia were excluded from the study.
2. Patients with a history of smoking and alcoholism were excluded.
3. Women on any medication known to be toxic to liver and kidney were excluded.
4. Patients on blood transfusions were excluded.

History was taken regarding parity, age, socioeconomic status, obstetric history, history, family history, and personal history. History of headache, visual disturbances, upper abdominal pain, oliguria, convulsions, and breathlessness was also enquired. General examination was done specially done for BP, edema, and weight gain. BP was recorded in the right arm in sitting position and V Korotkoff sound was taken as the diastolic BP.

RESULTS

The present study was undertaken in the Department of Biochemistry, Osmania Medical College and Osmania General Hospital, Hyderabad.

A total of 90 women in third trimester from Government Maternity Hospital participated in the present study of which

Group I: Included 30 pregnant women with uncomplicated pregnancies (control group)

Group II: Included 60 pregnant women with preeclampsia; and further subdivided into:

- Group (a): Included 30 patients with mild preeclampsia.
- Group (b): Included 30 patients with severe preeclampsia.

The clinical diagnosis of preeclampsia was based on the presence of the clinical triad of hypertension, proteinuria,

and edema. Subjects were categorized into a mild and severe group depending on the BP taken 6 h apart on more than two occasions and degree of proteinuria.

The following parameters were analyzed.

1. Serum iron.
2. Serum total iron-binding capacity (TIBC).
3. Percentage of transferrin saturation.
4. Serum transferrin.
5. Unsaturated iron binding capacity (UIBC).
6. Serum ferritin.
7. Serum zinc.
8. Serum ADA.
9. Serum uric acid.

The results were expressed in μg/dl for serum iron, serum TIBC, serum zinc, UIBC; ng/ml for serum ferritin; units/liter for ADA; mg/dl for serum uric acid; gm/l for serum transferrin; and percentage for percent transferrin saturation and are represented in the master sheet.

The data were analyzed using SPSS (statistical package for the social sciences) software version 17.0, descriptive results are expressed as mean and standard deviation of various parameters in different groups.

Multiple comparisons ANOVA was used to assess the significance of the difference of mean values of different parameters in between the groups, controls, mild, and severe preeclampsia. The significance of the difference of mean values of different groups and within groups is represented by *P*-values and $P < 0.05$ is considered as significant.

The mean values of serum iron, percentage transferrin serum ferritin, ADA, and serum uric acid are significantly higher in mild and severe preeclampsia when compared to controls.

The mean values of serum TIBC, serum transferrin, UIBC, and serum zinc are decreased in mild and severe preeclampsia when compared to controls.

As shown in the table, *P* value is statistically significant for the above-studied parameters, *post hoc* test was done.

P-values of serum iron, percentage transferrin, UIBC, serum ferritin, and serum uric acid are very much significant in between controls and mild preeclampsia, controls and severe preeclampsia, and in between mild and severe preeclampsia.

P-values of serum TIBC and serum transferrin are significant in between controls and mild preeclampsia and not significant in between controls and severe preeclampsia, and between mild and severe preeclampsia.

P-values of serum zinc and ADA are significant in between controls and mild and control and severe preeclampsia, and not significant in between mild and severe preeclampsia.

To assess the correlation between various studied parameters in controls and different groups of patients the data are subjected to Pearson's correlation and the coefficient of correlation (r) values and *p* values are calculated and presented in Tables 1-4.

To assess the maximum sensitivity and specificity of various parameters in identifying abnormality, the best cutoff

Table 1: Reference ranges of various parameters in controls

Parameter	Reference range
Serum iron	49.95–90.75 μg/dl
Serum TIBC	289.75–432.91 μg/dl
% transferrin	13.05–26.13%
Serum transferrin	2.02–3.02 g/L
Serum UIBC	211.83–363.47 μg/dl
Serum ferritin	8.3–29.06 μg/dl
Serum zinc	60.3–92.58 μg/dl
Serum ADA	14.67–26.51 U/L
Serum uric acid	2.04–4.32 mg/dl

ADA: Adenosine deaminase, UIBC: Unsaturated iron binding capacity, TIBC: Total iron-binding capacity

Table 2: Sensitivity and specificity at best cutoff value in discriminating controls and mild preeclampsia

Parameter	Best cutoff value	Sensitivity (%)	Specificity (%)
Serum iron	103.00 μg/dl	100	100
Serum TIBC	299.00 μg/dl	100	0
% transferrin	30.00%	100	100
Serum transferrin	1.10 g/L	100	0
Serum UIBC	89.00 μg/dl	100	0
Serum ferritin	32.5 μg/ml	83.3	100
Serum zinc	53.00 μg/dl	100	0
Serum ADA	24.4 U/L	73.3	90
Serum uric acid	4.15 mg/dl	86.7%	100

ADA: Adenosine deaminase, UIBC: Unsaturated iron binding capacity, TIBC: Total iron-binding capacity

Table 3: Mild preeclampsia versus controls area under curve

parameter	AUC	95% CI	*P* value
Serum iron	1.00	0.00–1.00	<0.001
Serum TIBC	0.326	0.189–0.463	0.021
%Transferrin	1.00	0.00–1.00	<0.001
Serum transferrin	0.326	0.189–0.463	0.021
Serum UIBC	0.021	0.00–1.00	<0.001
Serum ferritin	0.963	0.00–1.00	<0.001
Serum zinc	0.132	0.041–0.223	<0.001
Serum ADA	0.840	0.732–0.948	<0.001
Serum uric acid	0.958	0.905–1.00	<0.001

ADA: Adenosine deaminase, UIBC: Unsaturated iron binding capacity, TIBC: Total iron-binding capacity

values are calculated using ROC analysis. Best cutoff values are established by selecting a point closer to the top left-hand curve that provides greatest sum of sensitivity and specificity as shown in Table 5.

Best cutoff values for different parameters along with sensitivity, specificity for total cases and severe preeclampsia compared to controls and mild preeclampsia are presented in Tables 5.

Area under curve provides unbiased estimates of sensitivity and specificity; it is a comprehensive representation of pure accuracy, i.e., discriminating ability over the entire range of the test. It does not require selection of a particular decision threshold because the whole spectrum of possible decision threshold is included.

Serum iron and percentage transferrin showed the highest sensitivity and specificity followed by serum ferritin, serum ADA, and serum uric acid.

All parameters are statistically significant.

Serum iron, percentage transferrin, and serum ferritin are best discriminatory markers followed by serum uric acid and ADA in discriminating mild preeclampsia from controls.

Serum iron, percentage transferrin, serum ferritin, and serum uric acid showed the highest sensitivity and specificity followed by serum ADA in discriminating controls and severe preeclampsia.

All parameters are statistically significant except for serum TIBC and serum transferrin.

Serum ferritin, serum uric acid followed by serum iron and percentage transferrin showed the highest sensitivity and specificity in discriminating mild and severe preeclampsia. Other parameters showed less sensitivity and specificity.

Table 4: Sensitivity and specificity at best cutoff values in discriminating control and severe preeclampsia

Parameter	Best cutoff value	Sensitivity	Specificity
Serum Iron	133.5 µg/dl	100	100
Serum TIBC	319 µg/dl	86.7	16.7
% transferrin	40.54%	100	100
Serum transferrin	2.233 g/L	86.7	16.7
Serum UIBC	9.00 µg/dl	100	00
Serum ferritin	175.00 ng/ml	100	100
Serum zinc	46.5 µg/dl	100	00
Serum ADA	25.35 U/L	66.7	100
Serum uric acid	4.8 mg/dl	100	100

ADA: Adenosine deaminase, UIBC: Unsaturated iron binding capacity, TIBC: Total iron-binding capacity

Table 5: Controls versus severe preeclampsia area under curve

Parameter	AUC	95% CI	*P* value
Serum Iron	1.00	0.00–1.00	<0.001
Serum TIBC	0.356	0.213–0.498	0.055
% transferrin	1.00	0.00–1.00	<0.001
Serum transferrin	0.357	0.214–0.499	0.056
Serum UIBC	0.00	0.00–0.00	<0.001
Serum ferritin	1.00	0.00–1.00	<0.001
Serum zinc	0.165	0.00–0.061	<0.001
Serum ADA	0.859	0.764–0.954	<0.001
Serum uric acid	1.00	0.00–1.00	<0.001

ADA: Adenosine deaminase, UIBC: Unsaturated iron binding capacity, TIBC: Total iron-binding capacity

Mild Versus Severe Preeclampsia Area Under Curve

Serum iron, percentage transferrin, UIBC, serum ferritin, and seum uric acid are statistically significant and are best discriminatory markers in discriminating mild and severe preeclampsia.

Sensitivity and Specificity at Best Cutoff Value in Discriminating Controls and Total Cases (Mild+Severe Preeclampsia)

Serum iron, percentage transferrin, serum ferritin, and serum uric acid followed by ADA showed the highest sensitivity and specificity in discriminating total cases (mild and severe preeclampsia) from controls.

Table 6: Means and SD of different parameters in controls, mild, and severe preeclampsia

Parameter	Controls (*n*=30)	Mild preeclampsia (*n*=30)	Severe preeclampsia (*n*=30)
	Mean±SD	Mean±SD	Mean±SD
Serum iron (µg/dl)	70.35 (10.20)	162.55 (33.46)	240.85 (50.39)
Serum TIBC (µg/dl)	361.33 (35.79)	337.95 (28.61)	343.04 (28.38)
% transferrin (%)	19.59 (3.26)	48.44 (11.05)	70.42 (14.28)
Serum transferrin (gm/L)	2.52 (0.24)	2.36 (0.20)	2.40 (0.19)
Serum UIBC (µg/dl)	287.64 (37.90)	175.40 (44.39)	99.51 (50.65)
Serum ferritin (ng/ml)	18.67 (5.18)	133.13 (138.40)	579.75 (210.79)
Serum zinc (µg/dl)	76.43 (8.07)	64.54 (7.08)	65.64 (8.13)
Serum ADA (U/L)	20.58 (2.96)	27.02 (5.55)	27.04 (5.08)
Serum uric acid (mg/dl)	3.18 (0.57)	5.17 (0.96)	6.93 (1.05)

SD: Standard deviation, ADA: Adenosine deaminase, UIBC: Unsaturated iron binding capacity, TIBC: Total iron-binding capacity

Controls versus Total Cases (Mild and Severe Preeclampsia) Area Under Curve

All parameters are statistically significant in discriminating total cases (mild and severe preeclampsia) from controls (Tables 1-9).

DISCUSSION

The development of hypertension and proteinuria and/or edema induced by pregnancy after the 20th week of gestation is described as preeclampsia, and if convulsion or coma is added, it is named as eclampsia. It is one of the components of the deadly triad along with hemorrhage and thromboembolism during pregnancy and found in 3–7% of pregnancies. It is associated with increased maternal and fetal mortality and 18% of maternal deaths are attributed to preeclampsia. Preeclampsia occurs in about 6% of the general population and the incidence varies with geographic location. Other major complications of preeclampsia are premature delivery resulting in the need of intensive care admissions for neonates, intracranial hemorrhage, acute tubular or cortical necrosis, heart failure, pulmonary edema, rupture of the liver, DIC, hemolysis, increased liver enzymes, and about 10% of preeclampsia and eclampsia develop HELLP syndrome.

Predisposing factors are nulliparity, black race, and maternal age below 20 or over 35 years, low socioeconomic status, multiple gestations, hydatidiform mole, polyhydramnios, twins, obesity, and underlying renal disease.

To prevent the disease, it is necessary for early diagnosis and treatment. The clinical triad of hypertension, edema, and proteinuria is not specific nor sensitive enough; therefore, the search is on for a reliable biomarker which can get inside to pathogenesis. In the present study, we have evaluated different parameters for the purpose of selecting markers with high sensitivity and specificity.

The present study was undertaken to study serum iron, TIBC, percentage saturation of transferrin, transferrin, UIBC, ferritin, zinc, ADA, and uric acid levels in preeclampsia and compared with age-matched normal pregnant women. A total of 90 patients were analyzed including 30 controls and 60 preeclampsia, out of which 30 are mild and remaining 30 are severe, preeclampsia cases were analyzed after obtaining consent.

The pathophysiology of preeclampsia involves a complex mechanism leading to multiorgan dysfunction. Despite decades of intensive research, preeclampsia remains among the most important unsolved problems in obstetrics but evidence points to the placenta as a key source of factors that lead to the maternal endothelial cell dysfunction in preeclampsia because the clinical signs and lesions of preeclampsia remit after delivery, implicating the placenta as a main culprit in the disease. Endothelial cell activation has become the central piece in understanding the pathogenesis of preeclampsia. Vascular endothelium plays an important role in controlling the smooth muscle tone through the release of vasoconstrictor and vasodilatory substances and regulation of anticoagulation, antiplatelet, and fibrinolysis functions through the release of different soluble factors-fibronectin, thrombomodulin, von Willebrand factor, PCAM-1, VCAM-1, ICAM-1, E-Selectin, thromboxane, cytokines, lipid peroxides and reactive oxygen intermediates, endothelins, and antiangiogenic factors. In response to the placental factors released by ischemic changes or any other inciting cause, a cascade of events is set into motion.

Table 7: ANOVA multiple comparisons of F value and significance between three groups

Parameter	F value	Significance between groups
Serum iron (µg/dl)	174.17	<0.001
Serum TIBC (µg/dl)	4.68	0.012
% transferrin (%)	173.51	<0.001
Serum transferrin (g/L)	4.49	0.014
Serum UIBC (µg/dl)	134.96	<0.001
Serum ferritin (ng/ml)	124.34	<0.001
Serum zinc (µg/dl)	21.39	<0.001
Serum ADA (U/L)	19.04	<0.001
Serum uric acid (mg/dl)	134.15	<0.001

TIBC: Total iron-binding capacity, ADA: Adenosine deaminase, UIBC: Unsaturated iron binding capacity

Table 8: Comparison of significance in between groups

Parameter	Controls		Mild preeclampsia
	Mild preeclampsia	Severe preeclampsia	Severe preeclampsia
Serum Iron (µg/dl)	<0.001	<0.001	<0.001
TIBC (µg/dl)	0.018	0.081	0.819
% transferring (%)	<0.001	<0.001	<0.001
Serum transferrin (g/L)	0.020	0.093	0.811
UIBC (µg/dl)	<0.001	<0.001	<0.001
Serum ferritin (ng/ml)	0.012	<0.001	<0.001
Serum zinc (µg/dl)	<0.001	<0.001	0.859
ADA (U/L)	<0.001	<0.001	1.0
Serum uric acid (mg/dl)	<0.001	<0.001	<0.001

UIBC: Unsaturated iron binding capacity, TIBC: Total iron-binding capacity, ADA: Adenosine deaminase, TIBC: Total iron-binding capacity

Table 9: Sensitivity and specificity at best cutoff value in discriminating mild and severe preeclampsia

Parameter	Best cut off value	Sensitivity	Specificity
Serum Iron	185.5 µg/dl	96.7	70
Serum TIBC	346.5 µg/dl	50	70
% transferrin	53.25%	100	66.7
Serum transferrin	2.4255gm/L	50	70
Serum UIBC	264.5 µg/dl	0	100
Serum ferritin	312.5 ng/ml	100	83.3
Serum zinc	63.8 µg/dl	66.7	46.7
Serum ADA	25.35 U/L	66.7	40
Serum uric acid	6.55 mg/dl	73.3	96.7

TIBC: Total iron-binding capacity, UIBC: Unsaturated iron binding capacity, ADA: Adenosine deaminase

Vascular constriction causes increased resistance and subsequent hypertension causing endothelial cell damage causing interstitial leakage. With diminished blood flow due to abnormal trophoblastic invasion, ischemia of the surrounding tissue leads to necrosis, hemorrhage, and other end-organ disturbances characteristic of the syndrome. The pathophysiological deterioration can be life threatening for both mother and fetus.

In our study, we observed a statistically significant increase in concentrations of serum iron, percentage saturation of transferrin, serum ferritin, ADA, and serum uric acid and a statistically significant decrease in serum TIBC, serum transferrin, UIBC, and serum zinc. Significant correlations were observed between various studied parameters in preeclampsia. Hence, the study supports the view that preeclampsia is a disease evolving multiorgan systems.

In the present study, mean of serum iron showed statistically significant higher levels in mild and severe preeclampsia compared to the control group in accordance with other studies. Source of iron is from injured RBCs from necrotic and hemorrhagic areas of infarcted or ischemic placental tissue which is potentially toxic. These iron species are capable of initiating and propagating lipid peroxidation, both in the placenta and in the vasculature and are the significant etiologic factor in the endothelial cell damage of preeclampsia.

In our study, serum TIBC and transferrin showed statistically significant lower levels in preeclampsia compared to the control group in accordance with other studies. Transferrins are specialized proteins for the transport of iron and efficient distribution of iron. Decrease transferrin levels may be due to the increased iron levels which have negative feedback mechanism.

In our study, percent transferrin showed that statistically significant higher levels and serum UIBC showed statistically significant lower levels in mild and severe preeclampsia compared to the control group in accordance with the other studies. Because UIBC and percent transferrin saturation are inversely related. UIBC reflects the concentration of both apotransferrin and monoferric transferrin species.

In our study, serum ferritin showed statistically significant higher levels in mild and severe preeclampsia compared to the control group in accordance with other studies. Ferritin is an acute phase reactant. Hyperferritinemia is due to hemoconcentration and altered hemodynamics in preeclampsia. When iron is increased in the cell, the iron regulatory protein (IRP) dissociates from iron-responsive element (IRE), which enables the initiation of translation of ferritin mRNA and rapid degradation of transferrin receptor mRNA, resulting in increased synthesis of ferritin and reduced transferrin synthesis.

In the present study, serum zinc showed a statistically significant decrease in preeclampsia compared to controls. This study is in agreement with previous studies. However, significant decrease was not observed in severe preeclampsia compared to mild preeclampsia. Zinc is an antioxidant and acts as peroxynitrite scavenger. In the present study, zinc showed a statistical decrease due to oxidative stress in preeclampsia. Normally decreased in pregnancy and more decrease is seen in preeclampsia dueto decrease in plasma volume, decreased estrogen levels, decreased zinc-binding albumin, and increased glucocorticoid levels in preeclampsia. Hence, zinc supplementation during pregnancy could offer more benefit than preventing preeclampsia alone as zinc has a role in preventing neural tube defects and low birth weight babies also.

In the present study, serum ADA showed a statistically significant increase in preeclampsia compared to control group. However, a significant increase was not observed in severe preeclampsia compared to mild preeclampsia. This study is in agreement with previous studies.

Elevation of adenosine is seen in preeclampsia which counteracts the enhanced platelet activation. However, increased adenosine levels elicit cytotoxic effects, so increase in ADA activity enhance deamination of adenosine to inosine, which would be the protective mechanisms against excess adenosine. Another explanation for the elevation of ADA in preeclampsia is the modulation of immune responses in preeclampsia. In preeclampsia, there is shift in Th1/Th2 balance to Th1 predominance. Hence, preeclampsia is characterized by enhanced cell immunity and serum ADA is altered.

In the present study, serum uric acid showed a statistically significant increase in preeclampsia compared to control

group and is correlating with the severity of the disease. This study is in agreement with previous studies.

There are several potential origins for uric acid in preeclampsia; abnormal renal handling, increased tissue break down, acidosis and increased activity of the enzyme xanthine oxidase/dehydrogenase. Kang *et al.* hypothesized that uric acid is not a simple marker of disease severity but rather contributes to the pathogenesis of the disorder. Uric acid is plasma antioxidant capable of scavenging by superoxide, hydroxyl radical, and singlet oxygen. It also reduces nitrosylation of tyrosine residues on proteins by peroxynitrite and is capable of maintaining SOD activity. Conversely, uric acid can itself become a pro-oxidant (urate radical) in a setting of compromised antioxidant availability, particularly reduces ascorbate availability. Uric acid is also a mediator of inflammation, stimulating the production of monocyte chemoattractant protein-1, IL-1β, IL-6, and TNF-α. Uric acid thus has a "jekyll and hyde" in that, although it is an antioxidant, it can also contribute to endothelial damage and has a central role in the pathogenesis. Estimation of serum uric acid is as important as proteinuria and should become routine investigation in preeclampsia.

Limitations of the study are due to the small size of study population and absence of information on other parameters of body iron status such as apotransferrin, hemopexin, RBC count, hematocrit, RBC indices, and platelet count.[7-15]

CONCLUSION

Preeclampsia a multisystemic syndrome is characterized by hypertension, proteinuria, and edema that occurs after 20 weeks of gestation and usually resolves soon after delivery. It is one of the most important complications of pregnancy that is associated with increased maternal and fetal mortality. Although inflammation and extensive endothelial dysfunction of vessels are the main possible mechanisms of preeclampsia, the pathogenesis of this syndrome has not been well-understood.

Therefore, the hallmark of the present study is to identify parameters with high sensitivity and specificity, and their possible role in the etiopathogenesis of preeclampsia.

Free iron radicals from RBCs due to the ischemic placenta in preeclampsia resulting in increased serum iron are capable of initiating and propagation of lipid peroxidation both in placenta and vasculature and may be the significant etiologic factor in endothelial damage of preeclampsia. When iron is increased in the cell, the IRP dissociates from IRE, which enables the initiation of translation of ferritin mRNA and rapid degradation of transferrin receptor mRNA, resulting in increased synthesis of ferritin and reduced transferrin synthesis.

The decrease in serum zinc may be implicated as one of the nutritional deficiencies or antioxidant deficiency in the etiology of preeclampsia. The present observations may indicate maintenance of adequate dietary zinc nutrition during pregnancy, particularly in preeclampsia is important.

The increase in serum ADA is observed since preeclampsia is characterized by enhanced cell immunity. The role ADA may implicate as an indirect modulation of immune responses as an etiological role in preeclampsia that is by controlling increased adenosine levels by increased deamination of adenosine to inosine by enhanced activity of ADA which is a protective mechanism against cytotoxic effects of adenosine.

The increase in serum uric acid with an increase in severity is observed indicating its role as pro-oxidant in the environment of antioxidant deficiency in preeclampsia contributing to endothelial damage, or it may be due to glomerular endotheliosis causing altered renal handling of uric acid.

ROC curve analysis in our study showed that serum iron, percentage saturation of transferrin, serum ferritin, and serum uric acid are markers with highest sensitivity and specificity in mild and severe preeclampsia compared to normal pregnant women.

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