

The involvement of non heme iron, heme enzymes and oxygen in ETC suggests that the increased production of partially reduced oxygen atoms leads to overproduction of free radicals, causing oxidative stress in pre eclampsia, where free iron levels are very much increased.

The present study was conducted to evaluate iron status and MDA levels in preeclampsia and their involvement in the pathophysiology of preeclampsia

MATERIALS AND METHODS

A case control study was conducted in the department of biochemistry, Vinayaka Missions Medical College, Karaikal. Samples were collected from the department of obstetrics and gynecology, Rajiv Gandhi hospital, Pondy and investigations were done in Vinayaka Missions Medical College, Karaikal. Study was performed on 100 pregnant women having gestational age between 28 to 34 weeks. Fifty obstetrics patients were identified as having pre eclampsia according to specific criteria. Fifty healthy pregnant subjects were taken as controls and were normotensive throughout gestation.

Serum iron and iron binding capacity was estimated using ferrozine method.^(12, 13 and 14) Transferrin Saturation was calculated by the following formula:

$$\text{Transferrin Saturation} = 100 \times \text{Serum Iron} / \text{TIBC}$$

UIBC is the amount of transferrin unsaturated (unbound to) by Iron. It is about two third of TIBC, as normally about one third is saturated. The UIBC is calculated by the following formula:

$$\text{UIBC (mg \%)} = \text{TIBC} - \text{Serum Iron Concentration.}$$

Serum Ferritin was estimated by enzyme immuno assay (ELISA) kit⁽¹⁵⁾ Plasma lipid peroxide product, MDA was estimated by Esterbauer and Steinberg method (1989)⁽¹⁶⁾

Statistical analysis was done using MS Excel. Data are presented as percentages for the variables of serum iron status. Chi square value was calculated. P value less than 0.05 was taken as the level of significance. Also Odds ratio was determined.

For blood pressure variables and 24 hour urinary protein, t- value was calculated. P value less than 0.05 was taken as the level of significance.

RESULTS

In pre eclampsia cases there are increased levels of serum iron, Ferritin, % saturation of transferrin, and MDA. Whereas there is decreased levels of TIBC and UIBC, when compared to normal pregnant women. Systolic and diastolic pressure in preeclamptic women is in the range of 140 -180mm Hg and 90 – 130 mmHg, respectively. In controls, it is 100 – 120mmHg and 60 – 80 mmHg respectively.

As shown in **table – 1**, there is massive proteinuria in pre eclampsia of 3.79 ± 0.85 g/d, whereas in controls, it is only 0.135 ± 0.09 g/d. Protein Creatinine ratio is very high in pre eclampsia, about 4321.6 ± 1166 mg / g and that in control is 145 ± 48 mg / g. There is not much difference in urinary creatinine of cases and controls, showing that proteinuria is not of renal origin.

In pre eclampsia, elevated serum iron, % transferrin saturation, and ferritin are observed. There is a decrease in TIBC and UIBC. As shown in **table – 2**, 92% of the controls have serum iron in the lower range of 20 – 80 µg/dl, whereas only 42% of the pre eclamptic women are in this range. 58% of the cases have iron in the higher range between >80µg/dl. This level of iron has 14.2 times the risk of having pre eclampsia (OR = 14.2). 96% of the control has lower Ferritin level of 13 – 50 ng/ml. 76% of cases have a higher ferritin level of 51 – 170 ng/ml. Ferritin in this range, has high risk of having preeclampsia (OR = 76). 92% of cases have %transferrin saturation of 12 – 45%. But only 64% of the controls have this range. 60% of the controls have higher TIBC (450 – 520 µg/dl), when compared to 64% of the cases having TIBC of 300 – 400 µg/dl. 82% of cases have UIBC 160 - 360 µg/dl, whereas, 86% of the controls have a range of 360 - 500 µg/dl, significantly increasing the risk of having pre eclampsia at a lower range of UIBC. 92% of cases have %transferrin saturation of 12 – 45%. But only 62% of the controls have this range.

TABLE – 1:- Comparison of 24 Hours Urinary Protein, Protein Creatinine Ratio and Urinary Creatinine in preeclamptic women and normal pregnant women

PARAMETERS	Cases (n = 50)	Controls (n= 50)	T - value	P - value
24 Hour Urinary protein (g/d)	3.79 ±0.85	0.135 ± 0.09 (N < 0.15 g/d)	9.15	0.0001
Protein Creatinine Ratio (mg/g)	4321 ± 1166	145 ±48	8.11	0.0001
Urinary Creatinine (g/d)	0.88 ± 0.03	0.94 ± 0.21 (N = 0.8–2 g/d)	0.043	NS

Table – 2: Distribution of variables related to Iron Homeostasis

Variable	Cases		Controls		P – value *
	No.	%	No.	%	
Iron (µg / dl)					
20-80	21	42	46	92	<0.001
>80	29	58	4	8	
Mean±SD	89.7 ± 30.62		58.7 ± 22.3		
TIBC (µg / dl)					
300-400	32	64	5	10	<0.001
>400	18	36	45	60	
Mean±SD	385.6 ± 47.34		452.6 ± 37.6		
Ferritin(ng/ml)					
13-50	12	24	48	96	<0.001
51-170	38	76	2	4	
Mean±SD	115.5 ± 57.62		30.66 ± 7.2		
UIBC (µg / dl)					
160-360	41	82	10	20	<0.001
360-500	9	18	40	80	
Mean±SD	295.9 ± 60.32		393.94 ± 43.12		
% Transferrin Saturation					
12-45	46	92	32	64	0.001
<12	4	8	18	36	
Mean±SD	23.7 ± 8.83		13.05 ± 5.09		

* --- P value based on Chi square value.

DISCUSSION

The underlying pathophysiology of pre eclampsia is that the excessive formation of free radicals brings about lipid peroxidation, which increases oxidative stress, and thereby bring about endothelial dysfunction⁽⁸⁾ leading to multisystem disorders. This is supported by the current study, in which TIBC is decreased causing elevated serum iron status, having a contributory role in oxidative stress in pre eclampsia. There is evidence that increased serum iron level plays a pathogenic role in the development of pre eclampsia.^(17, 18) Iron status markers such as, serum iron and ferritin act as an acute phase reactant^(19, 20, 21) Similarly, UIBC, measure of iron binding reserve of serum is also significantly lower in women with pre eclampsia relative to normal pregnancy.⁽⁸⁾ It seems that serum free iron is more in pre eclampsia due to destruction of RBCs⁽²²⁾ and this increased level brings about partial reduction of oxygen molecules involved in ETC, leading to increased formation of free radicals and exacerbate lipid peroxidation and endothelial cell damage. The close association of non heme iron proteins and heme containing enzymes with ETC should be borne in mind. Serum ferritin is found elevated in pre eclamptic group, which is in agreement with studies previously conducted⁽¹¹⁾

CONCLUSION

It is concluded that decreased TIBC and therefore increased serum iron, ferritin, % transferrin saturation, and MDA is observed in pre eclampsia. Excess iron is postulated as the causal factor in oxidative stress. Iron status of pregnant women should be assessed before giving iron supplements as these may cause more harm than benefit. Free iron might be involved in the production of free radicals in ETC. Whether pre eclampsia is an OXPHOS disease is yet to be established.

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