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Original Research Paper

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STUDY OF SERUM ISCHEMIA MODIFIED ALBUMIN IN PREGNANT WOMEN WITH PREECLAMPSIA AND CHRONIC HYPERTENSION

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ABSTRACT **Objective:** Hypertensive disorders of pregnancy remain a major health issue for women and their infants. Preeclampsia, either alone or superimposed on preexisting (chronic) hypertension, presents the major risk on female's health. Immunological, nutritional and genetic factors as well as vascular and inflammatory changes are contributing for the development of hypertensive disorders of pregnancy. The purpose of this study is to compare serum ischemia modified albumin(IMA) levels in pregnant women with preeclampsia, chronic hypertension and healthy controls. **Materials and Methods:** The study included 66 pregnant women with preeclampsia, 66 pregnant women with chronic hypertension and 66 healthy pregnant women. We measured their serum IMA levels. Additionally, we performed pearson's correlation analysis of IMA with albumin and uric acid. **Results:** There was no difference with respect to maternal age and gestational age between the groups. Ischemia modified albumin levels were higher in preeclampsia and chronic hypertension group as compared to control group (0.60±0.18 ABSU ,0.53±0.14 ABSU & 0.47±0.04 ABSU respectively; p value<0.001). IMA correlated positively with uric acid in preeclampsia and chronic hypertension group and IMA correlated negatively with albumin in preeclampsia group. **Conclusion:** Altered levels of serum ischemia modified albumin may play a role in the development, progression and severity of preeclampsia and chronic hypertension.

KEYWORDS : ischemia modified albumin, preeclampsia , chronic hypertension, pregnant women

INTRODUCTION:

Hypertension in pregnancy is considered to be one of the common problem occurring in 10%-15% in expectant mothers along with infection and post-partum hemorrhage collectively called as hypertensive disorders of pregnancy (HDP) (1).Approximately 1% of pregnancies are complicated by pre-existing(chronic) hypertension, 5-6% by gestational hypertension and 1-2% by preeclampsia(2).Preeclampsia is characterized by hypertension of the extent of 140/90 mmHg or more with proteinuria (300mg of protein or more in a 24h urine sample) after 20 weeks of gestation in a previously normotensive and non-proteinuric woman(3).In the absence of proteinuria, preeclampsia is diagnosed as hypertension in association with thrombocytopenia, impaired liver function, new development of renal insufficiency, pulmonary edema, or a new-onset cerebral or visual disturbances. Chronic hypertension characterized by systolic blood pressure≥140 mmHg or diastolic blood pressure≥90 mmHg present pre-pregnancy or <20 weeks of gestational age(4). The fetuses of hypertensive mothers are also at risks of inappropriate placental oxygen transfer, intrauterine growth restriction (IUGR), premature delivery, still birth and neonatal death(5).The etiology of preeclampsia is unknown. It is believed that the defect starts from the failure of vascular remodelling in placenta, which results in reduction of uteroplacental perfusion and placental hypoxia. Placental ischemia releases various noxious substances such as cytokines and interleukins contributing to the oxidative stress ultimately leading to injury of endothelial cells. Which results in endothelial cell dysfunction including decreased prostacyclin, nitric oxide production and release of procoagulant proteins(6).

Albumin is a significant component of most extracellular fluids, including lymph, interstitial and cerebrospinal fluid. Albumin plays a role as an antioxidant scavenging carbon centered free radicals. Albumin undergoes certain modification under ischemic attacks associated with oxidative stress, production of reactive oxygen species(ROS) and development of acidosis. The N-terminal sequence of albumin is highly susceptible to biochemical modifications and degradations induced by oxidative stress. Consequently, the affinity of N-terminal sequence to transition metals, especially to cobalt, is reduced. This variant of albumin is called ischemia modified albumin.

Preeclampsia and chronic hypertension remains an important obstetric complication, there have been ongoing studies on the biochemical markers for the early detection of these diseases. The investigation of serum markers related to oxidative stress involved in etiology of preeclampsia and chronic hypertension can be useful in this matter. Based on this observation, the purpose of this study is to assess serum level of ischemia modified albumin in preeclampsia and chronic hypertension and to correlate with other biochemical and clinical parameters.

MATERIALS AND METHODS

We conducted this study between June 2021 and October 2022 in the Department of Biochemistry, SMS Medical College, Jaipur in collaboration with the Zanana Hospital, SMS Medical College, Jaipur. We have taken necessary permission from ethics committee, Research Review Board and department of Obstetrics and Gynecology. Importantly, we obtained written informed consent from all the pregnant women who agreed to participate in the study. A total of 198 pregnant women recruited from the Antenatal clinic of Zanana Hospital participated in this study. The study group A consisted of 66 pregnant women who were diagnosed with preeclampsia according to the recommendations of New American College of Obtetricians and Gynecologists(7).The study group B consisted of 66 pregnant women diagnosed

with chronic hypertension according to the recommendations of ACOG(8).The control group consisted of 66 normotensive(BP<140/90) and non proteinuric healthy pregnant women.

The blood pressure of participants in the outpatient clinic was measured with an adult-type digital sphygmomanometer. Proteinuria was measured by dipstick method. We did not included pregnant women with a history of Diabetes Mellitus, renal disease, heart disease, liver disease, severe anemia and any other chronic medical illness affecting ischemia modified albumin level and with age below 18 yrs or above 35 yrs in this study. After overnight fasting(12 hours) 5 ml venous blood sample was taken from all the participants.

The serum ischemia modified albumin level was evaluated by using the method proposed by Bar-Or-et al. (9).A 200μl patient sample was taken and 50μl cobalt chloride(CoCl2.6H2O, 1g/L) was added to it. This procedure was followed by vigorous mixing. The mixture was incubated for 10 minutes to ensure the binding of cobalt albumin. A 50μl(1.5mg/ml) amount of dithiothreitol was added as a coloring agent and later mixed. After a two-minute incubation period, 1 ml sodium chloride(0.9%) was added.

The absorbance of assay mixtures was read at a wavelength of 470nm by using colorimeter. A blank was similarly prepared with the exclusion of dithiothreitol. The results were reported as absorbance units(ABSU).

Statistical Analysis

We performed statistical analysis by using the Statistics Package for Social Sciences Software (ver.20.0;SPSS). Descriptive analyses were presented as Mean±SD. Statistical significance was set by using p value less than 0.05.The association between continuous and categorical variables were assessed by comparisons by means using one-way ANOVA test . The correlation coefficient was calculated by the Pearson test according to the normal distribution of data.

RESULTS

We divided 198 pregnant women ,who agreed to participate in this study into three groups. Group A consisted of 66 pregnant women with preeclampsia, Group B consisted of 66 pregnant women with chronic hypertension and Group C consisted of 66 healthy pregnant women.

Table 1. General Characteristics of Study Population

S. No.	General Characteristics	Group A	Group B	Group C	P Value
		(Mean±SD)	(Mean±SD)	(Mean±SD)	
1.	BMI(kg/m2)	30.66±4.60	32.78±3.38	29.28±3.97	<0.001S
2.	Systolic BP(mmHg)	159.75±5.58	146.67±5.73	115.03±6.95	<0.001S
3.	Diastolic BP(mmHg)	97.07±5.26	87.06±5.38	74.15±4.67	<0.001S
4.	Gravida	1.91±0.72	2.20±0.83	2.21±0.97	<0.001S
5.	Parity	1.00±.88	1.21±0.81	1.18±0.91	<0.001S
6.	Age(years)	27.22±4.54	28.49±3.53	27.35±4.23	0.125NS
7.	Gestational Age(Weeks)	29.33±2.53	29.27±2.96	29.23±3.49	0.09NS

P<0.05 is Significant

Table1 shows the comparison of demographic and clinical data of study population. There was no significant difference with respect to maternal age and gestational age between the groups(p>0.05).We compared BMI, gravida, parity, systolic and diastolic blood pressure and found a significant difference(p<0.05) between the groups as we expected (Table 1).

Table 2. Biochemical Parameters among the groups

S. No.	Parameter	Group A Mean ±SD	Group B Mean ±SD	Group C Mean ±SD	P Value
1	IMA (ABSU)	0.60±0.18	0.53±0.14	0.47±0.04	<0.001S
2	Urea(mg/dl)	35.12±9.85	24.38±7.98	22.62±7.08	<0.001S
3	Creatinine(mg/dl)	0.86±0.21	0.82±0.20	0.72±0.21	<0.001S
4	Uric Acid(mg/dl)	5.96±1.03	4.97±0.81	4.34±0.69	<0.001S

P Value <0.05 is Significant.

Table 2, shows the comparison of biochemical parameters in between the study groups. Urea and creatinine levels were found mildly higher in preeclampsia group in comparison to chronic hypertension and controls group.

Mean uric level is moderately higher in preeclampsia and chronic hypertension as compared to control group(5.96±1.03mg/dl,4.97±0.81mg/dl&4.34±0.69mg/dl respectively ;p value<0.001). Mean albumin levels are observed moderately lower in preeclampsia group as compared to chronic hypertension as compared to control group (3.11±0.70 g/dl,3.94±0.46 g/dl & 4.1±0.67 g/dl respectively ;p<0.001. Ischemia modified albumin levels were higher in preeclampsia and chronic hypertension group as compared to control group(0.60±0.18 ABSU ,0.53±0.14 ABSU & 0.47±0.04 ABSU respectively;p value<0.001).

Table 3. Liver Function Test among the groups

S. No.	Parameter	Group A (Mean± SD)	Group B (Mean± SD)	Group C (Mean± SD)	P Value
1.	Bil-T(mg/dl)	0.69±0.15	0.68±0.17	0.69±0.16	0.06NS
2.	Bil-D(mg/dl)	0.28±0.08	0.28±0.06	0.28±0.07	0.09NS
3.	AST(U/L)	51.91±17.59	25.91±6.97	27.80±7.69	<0.001S
4.	ALT(U/L)	44.27±14.21	23.58±5.67	25.38±6.96	<0.001S
5.	ALP(IU/L)	252.59±45.41	210.35±32.21	212.12±22.34	<0.001S
6.	LDH(U/L)	442.94±76.94	311.77±49.76	315.91±39.21	<0.001S
7.	GGT(U/L)	29.96±10.1	25.41±6.26	23.58±5.44	<0.001S
8.	Protein(g/dl)	7.17±0.75	7.33±0.58	7.42±0.53	<0.001S
9.	Albumin(g/dl)	3.11±0.70	3.94±0.46	4.10±0.67	<0.001S
10	Globulin(g/dl)	4.05±1.03	3.38±0.67	3.35±0.77	<0.001S

P Value <0.05 is Significant ,AST=Aspartate Amin otransferase ,ALT=Alanine Aminotransferase, ALP=Alkaline Phosphatase ,LDH=Lactate Dehydrogenase, GGT=Gamma Glutamyl Transferase

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Mean levels of AST,ALT,ALP,LDH,GGT were moderately raised in preeclampsia group in comparison to chronic hypertension and controls group(Table 3). Total protein levels were mildly lower in preeclampsia group when compared to chronic hypertension and controls group.

Table 4. Correlation of Various Parameters with IMA

S.No.	Parameter	Preeclampsia		Chronic Hypertension	
		Correlation Coefficient(r)	P value	Correlation Coefficient(r)	P Value
1.	Uric Acid(mg/dl)	0.212	0.038S	0.178	0.027S
2.	Albumin(g/dl)	-0.655**	<0.001S	0.085	0.196NS

P Value <0.05 is Significant

Furthermore, a significant positive correlation between IMA and uric acid was found in preeclampsia and chronic hypertension group(r=0.212, 0.178 respectively). IMA correlated negatively with albumin(r=-0.655) in preeclampsia group(Table 4).

DISCUSSION

Hypertensive pregnancy is associated with oxidative stress when there is imbalance of reactive oxygen species in

vascular walls which causes constriction of blood vessels thus leading to the development of hypertension. Oxidative stress is an imbalance in the production and elimination of reactive oxygen species(ROS) and reactive nitrogen species(RNS) as well as their clearance by defensive antioxidants(10).

In the present study, decreased total protein and albumin levels were seen in preeclampsia group. Which indicates antioxidant role of albumin and its consumption in inflammatory conditions. Preeclampsia is associated with increased capillary permeability leading to proteinuria and reduced hepatic blood flow. The ongoing oxidative stress in preeclampsia cause protein damage particularly serum serum albumin leading to hypoalbuminemia. Significantly increased levels of serum ischemia modified albumin were seen in preeclampsia and chronic hypertension as compared to controls. Inadequate supply of oxygen to trophoblastic cells results in preeclampsia and oxidative stress is increased in chronic hypertension and preeclampsia. The hypoxia and established oxidative stress alters serum albumin with N-terminal modification into ischemia modified albumin. Increased ischemia modified albumin concentrations have been shown to be associated with inflammation, oxidative stress and endothelial dysfunction(11).Sapna Vyakarnam demonstrated ischemia modified albumin as oxidative stress marker and its level helps in differentiating preeclampsia from normal pregnancy(12).A similar study by Ustun Y in 2011 showed correlation of IMA with severity of preeclampsia (13).Osmanagaoglu MA et al. in 2011 observed significant increase in total carnitine and ischemia modified albumin preeclampsia in comparison to normotensive pregnancy. In 2020,Suleyman Serkan Karasin conducted a study and found higher levels of IMA in patients of preeclampsia than healthy pregnancies(14).Ischemia modified albumin is also an early marker of ischemic disorders like stroke, Alzheimers disease, neurodegenerative diseases, psychiatric disorders and traumatic brain injuries and various gynecological disorders that cause oxidative stress. There are a wide range of studies implicating oxidative stress in the pathophysiology of preeclampsia because it damages the maternal vascular endothelium, therefore compromising its important function(15).

CONCLUSION:

Oxidative stress plays an important role in pathogenesis of preeclampsia. This study evaluated serum ischemia modified albumin level and found that IMA level was raised in preeclampsia and chronic hypertension group. According to our hypothesis, IMA may play a role in the development, progression and severity of preeclampsia and chronic hypertension.

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