Ischemia Modified Albumin in Maternal Serum and Cord Blood in Relation to Preeclampsia Severity and Neonatal Outcome

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ABSTRACT:

BACKGROUND:

Preeclampsia is associated with ischemia and increased oxidative stress in the placenta. Ischemia-modified albumin has been widely accepted as a serological biomarker in preeclampsia.

OBJECTIVE:

To evaluate the relationship between maternal serum and cord blood ischemia modified albumin levels with preeclampsia severity and neonatal outcome.

PATIENTS AND METHODS:

This study includes 90 pregnant women who were divided into three groups: **Group 1** includes 30 pregnant women with severe preeclampsia. **Group 2** includes 30 pregnant women with mild preeclampsia. **Group 3** includes 30 normotensive pregnant women with uncomplicated pregnancy considered as control group. The three groups were matched for age and gestational age. Maternal blood sample and neonatal cord blood were collected from all groups and level of ischemia Modified Albumin concentration was measured by kit uses enzyme – linked immune sorbent assay.

RESULTS:

The mean of maternal serum and cord blood Ischemia modified albumin of group A and Group B were significantly higher than that of group C (P- value =0.001), The study shows significant inverse correlation with neonatal birth weight and level of ischemia modified albumin within the study groups.

CONCLUSION:

Maternal serum and cord blood Ischemia Modified Albumin levels were significantly higher in severe preeclampsia than in mild and uncomplicated normotensive pregnant women, also their levels were inversely correlated with neonatal birth weight.

KEY WORDS: Severe preeclampsia, Mild preeclampsia, Ischemia modified albumin.

INTRODUCTION:

Pre-eclampsia (PE) is a hypertensive pregnancy specific syndrome characterized by new onset of hypertension with either significant proteinuria or end organ dysfunction presented after 20 weeks of gestation in a previously normotensive women and resolving completely by the 6th postpartum week. [1] one of the most important advances or amendments is the American College of Obstetricians and Gynecologists definition of preeclampsia: it no longer requires the presence of proteinuria as long as there is evidence of other end organ damage. [2]

Globally, Pre-eclampsia has been estimated to cause between 10 and 25% of perinatal loss. Preeclampsia remains a significant cause of direct maternal death. Up to 5% of women will develop Pre-eclampsia in their first pregnancy. [1]

The incidence is markedly influenced by race and ethnicity and thus by genetic predisposition. The incidence of pre- eclampsia in nulliparous populations ranged from 3 to 10 %. While in multiparous varies and ranges from 1.4 to 4 %. [3]

The pathogenesis of pre-eclampsia originates in the placenta and manifestations of the disease will only resolve following its delivery. Pre-eclampsia is determined at the outset of pregnancy when placental trophoblast invades the maternal uterine spiral arteries at the time of implantation. [1]

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Pre-eclampsia progresses in 2 stages: [4]

(1) Abnormal placentation early in the first trimester followed by:

(2) A maternal syndrome in the later second and third trimesters characterized by an excess of antiangiogenic factors.

pre-eclampsia can be classified based on :

1- Severity of symptoms into:[3] A-mild (non severe) : include DBP < 110 mmHg ,SBP < 160 mm Hg, positive proteinuria, absence of (headache, visual disturbances, upper abdominal pain, oliguria, eclampsia, thrombocytopenia, fetal growth restriction and pulmonary edema), with normal serum creatinine, minimal serum transaminase elevation and usually present at a late gestational age .

B-Severe : include DBP ≥ 110 mmHg , SBP ≥ 160 mmHg , positive proteinuria, and/or presence of renal insufficiency, liver involvement, neurological symptoms and/or biochemical and/or hematological impairment, uteroplacental dysfunction and fetal growth restriction and usually present at early gestational age.[3]

2-Time of onset: [5]

A-Early-onset PE**:** the signs and symptoms usually appear before 34 weeks of gestation.

B-Late-onset PE**:** the clinical features are usually recognized at or after 34 weeks of gestation.

Maternal and fetal complications of Pre-eclampsia:

Maternal Complications: [6] Abruptio placentae, Disseminated coagulopathy/HELLP syndrome, Pulmonary edema/aspiration, Acute renal failure, Eclampsia, Liver failure or hemorrhage, Stroke (rare), Death (rare), Long-term cardiovascular morbidity.

Neonatal Complications: [6] Preterm delivery, Fetal growth restriction, Hypoxia-neurologic injury, Perinatal death, Long-term cardiovascular morbidity associated with low birth weight (fetal origin of adult disease).

Ischemia modified albumin (IMA): is a modified form of albumin, it is a marker of cardiac ischemia is also increased in normal pregnancy. So continuous monitoring of serum IMA can give us an idea regarding progress of pregnancy. Any deviation or increase can suggest complications in pregnancy. This can help us to intervene earlier in complications and prevent the mortality and morbidity related to it.[7] In particular, some recent reports and other literature showed IMA as a simple and novel measure of oxidative stress in several human pathologies and pregnancies. [8] IMA is solely characterized by its reduced cobalt-binding affinity, which can be measured indirectly by the Food and Drug Administration-approved albumin cobalt-binding (ACB) assay. [9]

AIM OF THE STUDY:

To evaluate the relationship between maternal serum and cord blood ischemia modified albumin levels with preeclampsia severity and neonatal outcome.

PATIENTS AND METHODS:

This is a case control study that was conducted in the Department of Obstetrics and Gynecology of Al-Yarmouk Teaching Hospital / Baghdad in cooperation with the laboratories department of hospital from 1st of March through November 2019. The study was approved by Iraqi Board for Medical Specializations.

The study included 90 pregnant women with singleton pregnancy and gestational age (32-38) weeks, (gestational age was assessed depending on accurate last menstrual period and / or by early ultrasonography), presented either with labor pain and were admitted to the labor room or admitted and prepared for emergency or elective cesarean section. They were informed about the nature of the study and verbal consent was obtained from them. The data were collected on questionnaire which was designed for the study. The women included in the study were divided into three groups:

Group A: Included 30 pregnant women diagnosed with severe preeclampsia.

Group B: Includes 30 pregnant women diagnosed with mild preeclampsia, Both **A** and **B** considered as the study groups.

Group C: Includes 30 pregnant women with uncomplicated pregnancy considered as the control group matched with the study groups for age and gestational age.

Pre-eclampsia was diagnosed when systolic blood pressure ≥ 140 mmHg or diastolic

BP ≥ 90 mmHg on two occasions at least four hours apart, and proteinuria of ≥ 0.3 g per 24 hours or ≥ 1+ proteinuria, detected by urine dipstick after 20 weeks of pregnancy, or in the absence of proteinuria as long as there is evidence of other end organ damage.

Inclusion criteria:

1. Single viable pregnancy,
2. Gestational age between (32-38) weeks,
3. Any maternal age and parity status.

Exclusion criteria:

1. Multiple pregnancy;
2. Pregnancy with fetal anomalies;
3. Women with medical illness like diabetes; chronic hypertension, metabolic disease, preexisting renal disease, neurological disorders and those with nutritional or hemorrhagic complication;
4. Women with history of recurrent miscarriage;
5. Premature rupture of membranes and chorioamnionitis;
6. History of smoking;
7. History of preeclampsia in previous pregnancies.

Clinical assessment:

Detailed history was obtained including age, parity, gravidity, history of abortion, gestational age, obstetrical history, gynecological history, past medical, surgical and social history. General, systemic examination including vital signs and BMI (weight before pregnancy or in early pregnancy) were done. Obstetrical examination for assessment of symphysis fundal height and fetal heart rate for each participant.

The patient subjected to measurement of blood pressure by mercurial sphygmomanometer after sitting awhile for a rest. When the measured blood pressure was ≥ 140/90 but < 160/110 then reassessed the BP after four hours, if still the same reading or more then sent the patient for urine for albumin and if the result was +ve then the patient was being diagnosed with preeclampsia and then directly taking blood sample from the patient which was divided into two parts, the first one was sent to laboratories in our hospital for urea, creatinine, AST, ALT, uric acid, coagulation profile and platelet. The other part, after was been centrifuged and freezed, took it to private lab for Ischemia Modified Albumin assay.

The studied groups investigated for the following:

- Maternal blood sample collected at the time of admission and sent to the laboratory for blood group and Rh, full blood count, random blood sugar, liver function test, renal function test, coagulation profile.
- General urine examination.
- U/S was done for gestational age and fetal wellbeing.

After delivery either by vaginal or C/S, sample of neonatal cord blood was taken for measurement of IMA level and neonates were examined and assessed by pediatrician for Apgar score, weight and if they need admission to neonatal intensive care unit (NICU).

Statistical analysis:

Each patient was assigned a serial identification number. The collected data were admitted into Microsoft Excel sheet 2016 and data loaded into Statistical Package for Social Sciences (SPSS) version 26 statistical program. Descriptive statistics presented through tables and graphs, Qui square test was used to find out significance of association between related categorical variables, Two independent sample t- test and one way ANOVA were used to find out significance of differences between means of numerical variables, P value less than 0.05 was considered as discrimination point of significantly.

RESULTS:

The total number of pregnant women included in this study was 90. Group A included 30 pregnant women who had diagnosed with severe preeclampsia, group B included 30 pregnant women who had diagnosed with mild preeclampsia, and group C included 30 normotensive non protein uric pregnant women. The distribution of pregnant women between study groups by general characteristics is shown in table (1).

Qui square test shows no significant association noticed between any independent study variable and type of study, P value more than (0.05) as shown in table (1).

Table 1: Distribution of study participants by general characteristics.

Variable	Group A (%) n= 30	Group B (%) n= 30	Group C (%) n= 30	P value
Age (Years)				
< 25	13 (43.3)	16 (53.3)	13 (43.3)	0.837
25 – 35	9 (30.0)	9 (30.0)	11 (36.7)	
> 35	8 (26.7)	5 (16.7)	6 (20.0)	
Gravida				
Prim gravida	11 (36.7)	8 (26.7)	10 (33.3)	0.700
Multigravida	19 (63.3)	22 (73.3)	20 (66.7)	
Gestational Age (Weeks)				
< 37	15 (50.0)	11 (36.7)	10 (33.3)	0.378
≥ 37	15 (50.0)	19 (63.3)	20 (66.7)	
BMI Level (Kg/ m^2)				
Normal (18.5-24.5)	3 (10.0)	4 (13.4)	6 (20.0)	0.751
Overweight (25-29.5)	15 (50.0)	16 (53.3)	16 (53.3)	
Obese ≥ 30	12 (40.0)	10 (33.3)	8 (26.7)	

Table (2) shows the mean maternal serum and cord blood IMA levels were significantly higher in group A than group B and C (241.6 versus 160.5 and 63.1 ng/ml, p= 0.001) and (102.8 versus 70.56 and 24.53 ng/ml, p= 0.001) respectively.

Table 2: Maternal serum and cord blood IMA levels in the study groups.

IMA Level (ng/ml)	Study group			P – Value
	A Mean ± SD	B Mean ± SD	C Mean ± SD	
Maternal	241.6 ± 46	160.5 ± 36.6	63.1± 22	0.001
Cord	102.8 ± 41.71	70.56 ± 21.46	24.53 ± 4.90	0.001

Table (3) shows, (63.3%)of delivered neonates got body weight less than 2.5 kg in group A, while is significantly higher than low birth weight neonates in group B (16.7%) and 10% in group C P value (0.001), Apgar score of neonate scored after 1 minute of delivery was found to be significantly better in neonates with uncomplicated pregnancy in comparison with group A and group B neonates (P- value 0.001), While no significant difference in NICU and Apgar score after 5 minute between different studied groups.

Table 3: Neonatal outcome in the study groups.

Variable	Group A(%)	Group (B%)	Group(C%)	P value
	n=30	n=30	n=30	
Birthweight (Kg) < 2.5 ≥ 2.5	19 (63.3) 11 (36.6)	5 (16.7) 25 (83.3)	3 (10.0) 27 (90.0)	0.001
APGAR Score 1 minute < 7 ≥ 7	22(73.3%) 8(26.7%)	22(73.3%) 8(26.7%)	2(6.7%) 28(93.3%)	0.001
APGAR Score 5 min (mean ± SD)	8.33± 0.7	8.6 ± 0.5	8.2 ± 0.4	0.059
NICU admission Yes No	8 (26.7) 22 (73.3)	4 (16.7) 26 (83.3)	7 (23.3) 23 (76.7)	0.638

Table 4 show that IMA level in mothers with low birthweight and normal birthweight neonate of group A were significantly higher than IMA level of mother of group B and C, P value less than 0.05. The IMA level of mothers with neonates admitted to NICU in group A was significantly higher than mothers in group B and C, P value (0.001).

The IMA level of mothers with neonates not admitted to NICU was also significantly higher in group A mothers than that of group B and C, P value (0.001).

Table 4: Maternal serum IMA level by certain neonatal outcome.

	Variable		IMA level in the Study groups					P – Value
			A		B		C	
		N	Mean ± SD	N	Mean ± SD	N		Mean ± SD
Birth weight	<2.5 Kg	19	261.9±57.29	5	206.6 ± 39.39	3	64 ± 36.29	0. 004
	≥2.5 Kg	11	206.2±47.85	25	151.3± 28.7	27	63±20.93	0.001
	P - Value		0.001		0.001		0.942	
Apgar score in 1 minute	low	22	260±53.71	22	161.5±37.78	2	78.5±19.09	0. 001
	Normal	8	197.77±51.66	8	157.9±35.44	28	62±22.08	0.001
	P - Value		0.006		0.056		0.314	
NICU admission	Yes	8	297.8±47.86	4	172 ±23.62	7	71.4±27.33	0.001
	NO	22	220.9±49.51	26	158.8±35.50	23	60.6±4.2	0.001
	P - Value		0.001		0.510		0.260	

DISCUSSION:

In the current study, no significant difference was noticed between study groups regarding maternal age, maternal BMI, gravidity, gestational age with (P-value = 0.837), (P-value =0.751), (P-value =0.700), and (P-value =0.378) respectively. These observations were in accordance with a case – control study done by **Reza Ahmadi MSc** et al **2012**; This study showed that there were no significant differences regarding maternal age and gestational age between study groups (P- value 0.94), (P- value 0.21) respectively.[10] Another study done by **Tanja Roien Jakobsen** et al **2013;** which revealed that there is no significant association between study groups regarding maternal age and gravidity (P- value 0.532) and (P- value 0.096) respectively which was in agreement with current study. [11]

Table (2) shows the mean maternal serum and cord blood IMA of group A and Group B were significantly higher than that of group C (maternal 241.6, 160.5, 63.1), (cord 102.8, 70.56, 24.53) respectively, these results are in consistent with a cross sectional study done by **YUSUF USTUN** et al **2011;** The study revealed that maternal serum IMA levels were elevated in women with preeclampsia compared to women with normal pregnancy, maternal serum IMA levels were significantly higher in the mild and severe pre-eclamptic groups than in the control group (P- value =0.000) [12]. Another study done by **Jyotirmayee Bahinipati et al 2014;** showed that mean of maternal serum IMA was elevated in preeclampsia as compared to normal pregnant women (P- value < 0.001). [13]The study conducted by **McKenzie KA** et al **2018;** which revealed that mean birth weight and gestational age of neonates born to women with preeclampsia were significantly less than that of neonates born to women with un complicated pregnancy (P value> 0.001) this was in agreement with current study. [14]

Another study done by **Weiner E** et al **2018;** which revealed that Neonates in the severe PE group had a lower birth weight and a higher rate of SGA as compared to the mild PE group. Furthermore, neonates in the severe PE group had higher rates of NICU admission (p = 0.019), as compared to the mild PE group, there was no significant differences in 5-minute Apgar score between study groups, (P- value 0.594) which was in agreement with current study as shown in table 3. [15]

Table 4 shows IMA level in mothers with low birthweight and normal birthweight neonates of group A were significantly higher than IMA level of mother of group B and C, (P value less than 0.05).

The IMA level of mothers with neonates admitted to NICU in group A was significantly higher than mothers in group B and C, (P value 0.001).

The IMA level of mothers with neonates not admitted to NICU was also significantly higher in group A mothers than that of group B and C, (P value 0.001). This result was in agree with study conducted by **JMP D'souza** et al **2014;** They found significantly adverse correlation between maternal serum IMA level and neonatal birth weight in PE (p value 0.001), which was in agree with current study according to neonatal birthweight between study groups. [16]

CONCLUSION:

Maternal serum and cord blood Ischemia Modified Albumin levels were significantly higher in severe preeclampsia than in mild and uncomplicated normotensive pregnant women, also their levels were inversely correlated with neonatal birth weight.

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