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Study of the clinical significance of serum albumin level in Preeclampsia and in the detection of its severity

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Abstract

Pre-eclampsia is a form of severe disorder of pregnancy, leading to maternal and perinatal morbidity and mortality. Many biochemical markers of preeclampsia have been recognized in maternal serum one of them is serum albumin. The objective of this study is to determine whether plasma albumin level (ALB) is associated with preeclampsia (PE) complications and to evaluate the usefulness of its level as a marker of preeclampsia severity. The studied group were collected in the labor word. First group were normotensive as a control group, the second group with a gestational hypertension, the third group were mild preeclampsia and fourth group had sever preeclampsia. A comparison of the characteristic of each group and the correlation between serum albumin levels and gestational age at time of delivery, pregnancy complications and outcome were statistically analyzed. The results are showed that serum albumin level had statistically significant decline at ($P \leq 0.01$) in severe preeclampsia with mean level (2.618-0.328) than in mild preeclampsia (3.155-0.293) in comparison to hypertensive and control group (3.500-0.386), (4.076-1.448) respectively so there is positive correlation between serum albumin levels and severity of disease. We are concluded that serum albumin level in pre-eclampsia can be used as a significant determinant of disease severity and may be used as a useful marker for predicting time of delivery or termination of pregnancy and pregnancy outcomes.

Keywords: Pregnancy; Preeclampsia; Severe preeclampsia; Serum albumin

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Introduction

The general prevalence of pre-eclampsia in pregnancy is between 3-8% of pregnancies and is considered a significant management problem for every obstetrician [1, 2]. It is a pregnancy specific disease characterized by development of concurrent hypertension and proteinuria, sometimes progressing into a multiorgan cluster of varying clinical features. There are 2 categories of preeclampsia, mild and severe, where severe preeclampsia is diagnosed when the blood pressure greater than 160 mm Hg systolic or 110 mm Hg diastolic, proteinuria exceeding 2g in a 24-hour period or 2-4+ on dipstick testing, increased serum creatinine (> 1.2 mg/dL unless known to be elevated previously), oliguria ≤500 mL/24 h, cerebral or visual disturbances, epigastric pain, elevated liver enzymes, thrombocytopenia (platelet count < 100,000/mm3), retinal hemorrhages, exudates, or papilledema; and pulmonary edema [3].

Pre-eclampsia is a disease of theories" where the exact etiology is still unknown [3]. Albumin is a water soluble protein is moderately soluble in concentrated salt solutions. It is produced in the liver in abundant amount and form a large proportion (60%) of all plasma protein. Serum albumin is important in regulating blood volume by maintaining the oncotic pressure (colloid osmotic pressure) of the blood compartment, it also serve as carrier for molecules of low water solubility this way isolating their hydrophobic nature, including lipid soluble hormones, bile salts, unconjugated bilirubin, free fatty acids (Apoprotein), calcium, ions (transferrin) and some drugs like warfarin, phenobutazone and phenytoin. For this reason it is sometimes referred as a molecular “taxi” [4].

Albuminuria in which albumin is excreted in the urine is considered an abnormal state because the cells of the kidney called podocytes act like a seal that allow only very simple molecules to pass and prevent red blood cells and bigger molecules like albumin, therefore if albuminuria occurs, it is a sign of kidney impairment however this is not absolute and in some situation albuminuria occur even without overt indications of kidney disease.

So hypoalbuminemia can be identified as an early sign in developing preeclampsia [5], and many clinicians consider serum albumin level as one of the important laboratory findings in treatment of hypertensive disorders in pregnancy [6]. Our study was done to determine whether plasma albumin level (ALB) is associated with preeclampsia (PE) complications and to define its role in the detection of the severity of PE.

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Method

This study was done in Al-Zahra'a Hospital Teaching Hospital between April 2011 and September 2011, total 100 pregnant women who were admitted at the time of delivery or termination of pregnancy due to complications of hypertension. These women who participated in the study were divided into 4 groups:

- Control group consist of 21 pregnant women having no hypertension;
- The second Hypertensive group consist of 26 pregnant ladies with hypertension and no protein in urine;
- Mild pre-eclamptic group was the third group consist of 20 pregnant ladies;
- Severe pre-eclamptic group 33 pregnant having sever preeclampsia.

The study was approved the medical ethics committee of the college of medicine/ university of Kufa. We exclude DM, chronic renal disease and chronic hypertension in the selected ladies.

At time of admission a complete clinical history was taken from each subject with emphasis on her age, date of last menstrual cycle, family history, this is followed by a complete physical examination and an assessment of the lower extremity for edema. The weight of the patients were measured and the blood pressure taken twice on the right arm in the sitting position with the patient at rest using a mercury sphygmomanometer with an appropriate cuff placed at heart level. korkoff sound 5 was taken of diastolic BP only on rare occasion when the disappearance phase continue to zero mmhg korkoff sound 4 was taken.

Investigations and procedures

Urine sample was taken for estimation of albumin in urine. A dipstick urine measurement for albumin was performed on a random urine specimen collected by the patient, testing was performed with multistick reagent strips. Blood sample was taken for biochemical and hematological investigations, Serum albumin level, Renal function test, liver function test, and complete blood picture.

A sample of blood had been aspirated from each patient send for above investigation, the sample used for estimation of serum albumin level was centrifuged at 200 round/minute for 10 minutes after one hour from aspiration in room temperature estimated by bromocresol green method [BCG] and read spectrophotometry for single measurement. Serum albumin level measured by bromocresol green [BCG] method, this method is linear

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up to 1000 nmol/l [69gm/l]. The principle depend on that albumin, in a buffered solution, reacts with the green of bromocresol [BCG] to form a red-color complex [7].

- We prepared 3 test tubes for sample, standard and blank.
- Putting 2 ml of bromocresol green in each test tube.
- Pipate into test tubes, we add 10 micro ml for standard and sample tubes, mix and read after 5 minutes the OD of sample and standard against blank the color is stable for 30 minutes.
- At wavelength 628 mm, temperature 20-25 centigrade and cuvette 1 cm light path, read against blank reagent, standard and sample. The BCG reagent must be brought at 15-25 °C before use.
- The calculation is done according to the following:

(OD Sample)/(OD Standard)×n (OD=optical density)

- The reference values is 3.8-5.4 gm/d [8].

Data collected to each subject with laboratory finding was recorded and statistically analyzed.

Data handling

All analyses were performed using commercially available software (SPSS version 18). Significant differences of continuous variables were assessed by ONE WAY ANOVA. Analysis (F-tests ($P \leq 0.01$). Category data were assessed by Chi squared ($\chi 2$) test. A *P*-value ≤0.05 and ≤0.01 was considered as statistically significant and highly significant at 1% and 5% respectively.

Result

In our study the lower serum albumin level below 3.00 gm/dl was found in pregnant women with immenent eclampsia, eclampsia, pulmonary edeme, HELLP syndrome and IUD but not in IUGR, placental abruption, severe oligohydraminios and uncontrolled hypertension.

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Characteristics	*Normal*	*Hypertensive*	*Mild Preeclampsia*	*Sever Preeclampsia*	*P-value*
Number	21	26	20	33	
Age	27.28±6.14	27.93±6.387	26.20±6.67	24.64±5.968	0.211 NS
Gestational Age	37.93±1.18	37.09±1.94	35.45±2.71	33.42±3.01	0.000**
Weight	86.24±9.37	90.58±11.73	88.80±8.76	85.48±10.07	0.236 NS
Parity	1.43±1.28	1.462±1.61	1.15±1.69	1.24±1.44	0.878 NS
Systolic BPmmhg	117.4±9.95	155.0±15.56	150.2±11.71	179.7±16.29	0.000**
Diastolic BPmmhg	76.7±9.13	96.9±9.70	103.5±6.71	114.5±7.65	0.000**
Birth weight kg	3.19±0.38	2.950±0.30	2.58±0.38	2.12±0.53	0.000**
Cesarean (%)	3(14.28)	9(34.61)	13(65)	28(84.84)	0.000**

Table 1.

Clinical baseline patient characteristics of the studied groups.

**significant at $P \leq 0.01$ values of all characteristics are presented as mean ±SD

[NS= not significant]

- No significant differences were observed in the age, weight and parity of hypertensive and pre-eclamptic groups in comparison with normal.
- Lower gestational age ($P \leq 0.01$) was recorded in the severe preeclamptic patients.
- Systolic and diastolic blood related significantly ($P \leq 0.01$) with severity of preeclampsia, higher blood pressure were recorded in the three studied groups in comparison with normal.
- Comparison of birth weight between patients groups showed that lowering of birth weight related to severity, mean that lower birth weight ($P<0.01$)was recorded in the women with sever preeclampsia .
- 84% of sever pre-eclamptic women delivered by C/S in comparison with 65% of mild pre-eclampsia and 34.6% of hypertensive and 14.28% of normal women.

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*Significant at $P \leq 0.05$, **Significant at $P \leq 0.01$, using ANOVA values are presented as mean ±SD [NS=not significant].

Characteristics	*Normal*	*Hypertensive*	*Mild Preeclampsia*	*Sever preeclampsia*	*P-value*
Blood urea mg/dl	27.619±3.248	31.077±3.908	31.050±4.979	39.364±7.822	0.000**
S. Creatinine Mg/dl	0.633±0.153	0.838±0.240	0.845±0.296	1.094±0.452	0.000**
S. Uric acid Mg/dl	4.848±0.786	4.496±1.231	5.625±1.947	6.345±1.447	0.000**
PCV %	34.048±2.418	34.000±2.683	33.545±2.818	36.050±4.148	0.032*
GPT u/l	5.762±1.972	7.346±3.249	9.200±3.764	9.945±3.152	0.000**
GOT u/l	14.333±9.947	15.462±8.363	23.400±11.325	33.009±13.610	0.014*
S.A.P. Mg/dl	175.143±23.277	186.192±15.998	187.200±23.896	205.091±92.503	0.000**
Platelate ($x10^9$)	232±15.0	227±18.1	192±15.1	125±30.2	0.000**

Table 2.
Demonstrate laboratory results of each group.

- Sever pre-eclamptic women showed higher ($P \leq 0.01$) blood urea, S. creatinine, and S. uric acid than other groups.
- PCV increased in relation with severity of pre-eclampsia, significant differences at ($P \leq 0.05$) were recorded for studied groups due to haemoconcentration.
- Liver function tests showed clear relationship with severity of preeclampsia, all enzymes titration elevated in sever pre-eclamptic women. A decreasing of platelate count were observed in sever pre-eclamptic women that mean significant differences were recoded between groups.

Characteristics	*Control*	*Hypertensive*	*Mild Preeclampsia*	*Sever preeclampsia*	*P-value*
S. Albumin gm/dl	4.076±1.448	3.500±0.386	3.155±0.293	2.618±0.328	0.000**

Table 3.
Show a comparison of serum albumin level in four studied groups, there is statistical significant decrease in serum albumin level at ($P \leq 0.01$) in sever preeclampsia then mild preeclampsia in comparison to hypertensive and control group.

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Groups	<37 weeks				≥37 weeks			
	No	GA (wks)		S. Albumin		No	GA (wks)		S. Albumin	
		Mean	±SD	Mean	±SD		Mean	±SD	Mean	±SD
Normal	3	36.16	0.288	3.767	0.379	18	38.22	1.003	4.128	1.559
Hypertensive	9	35.11	1.516	3.533	0.374	17	38.156	1.169	3.482	0.402
Mild	13	34.31	2.673	3.162	0.304	7	37.57	0.932	3.143	0.294
Sever	27	32.48	2.433	2.581	0.269	6	37.666	0.817	2.7	0.482
P-value		0.004**		0.000**			0.413 NS		0.018**	

Table 4.
Demonstrated S. albumin level of studied groups according to G.A.
**significant at $P \leq 0.01$ using ANOVA, values are presented as mean ±SD [NS=not significant]

- We compared the serum albumin levels at different weeks of pregnancy in four studied group sever pre-eclamptic women showed a decreasing in the S. albumin level in comparison to other groups of patient , and it is lower in those who GA less than 37 WKs.

Complication	S. albumin		P value
	≤3.0gm/dl n=45	>3.0gm/dl n=55	
Immenent eclampsia	12(26.67)	4(7.27)	0.000**
Eclampsia	6(13.33)	2(3.64))	0.000**
IUGR	7(15.55)	5(7.27)	NS
HELLP syndrome	3(6.66)	0(0)	0.003**
Pulmonary edema	2(4.44)	0(0)	0.000*
Uncontrolled BP	1(2.22)	3(5.45)	NS
placental abruption	0(0)	4(7.27)	NS
Sever oligohydramnios	2(4.44)	3(5.45)	NS
fetal distress	0(0)	2(3.63)	NS
IUD	4(8.89)	0(0)	0.003**

*significant at $P \leq 0.05$, **significant at $P \leq 0.01$ [NS, not significant] using Chi squared (χ^2) test, data represents as no (%).

Table 5. Demonstrate serum albumin level according to specific pregnancy complications

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Preeclampsia remain a leading cause of maternal and prenatal morbidity and mortality. Because our hospital is a referral center, the rates of sever preeclampsia and eclampsia were higher than generally expected for overall pregnant population. In the present study there is significant relation between severity of PE and low gestational age due to the risk of preterm labor and iatrogenic termination of pregnancy to prevent and decrease maternal and fetal complications. This agreed by Cruz, et al [9], who found that risk of preterm labor and pre maturity increase with severity of preeclampsia.

In the same time there is significant low birth weight in mild and sever PE group which is more significant in sever group and which may be attributed to placental insufficiency and intra uterine growth retardation as a complication of PE and iatrogenic prematurity as the delivery is the only cure for PE, prematurity account 15% of all premature birth and one in five very low birth weight infant (less than 1500 gm) [10].

Also statistically in our study 84% of patients in sever PE group and 65% of mild group was delivered by C/S due to increase maternal and fetal complications that need immediate delivery to decrease maternal and perinatal morbidity and mortality, a study done by Seong, et al on 454 patients with pregnancy related hypertension found that 71% of pre-eclamptic patients were delivered by C/S [11].

In our study we demonstrate laboratory results of each group, and we found that there is significant deterioration in renal function test represented by increase B. urea, S. creatinine and S. uric acid, that may be due to ischemic changes, arterial constriction, endothelial swelling and intravasation fibrin deposition all that explain the deterioration of renal function which increase with severity of PE in comparison with control group which is within normal level. also there is increase in PCV in sever PE group due to associated haemoconcentration, about platelet count there is markedly decrease in sever group due to platlate depletion as a complication of PE specially with HEELP syndrome. Our results showed that marked elevation in the liver enzymes (GPT, GOT, S.A.P.) in sever pre-eclamptic group, this results were confirmed with TAYLAR et al [12].

The present study found that serum albumin level significantly decrease in severe PE group and correlated with severity of PE, which was agree with the study done by Gojnic, et al [6] on 60 patients admitted with a diagnosis of PE in 3rd trimester of pregnancy and they found that serum albumin levels were correlated with severity of preeclampsia and nearly all patients with severe preeclampsia had values less than 3.0 gm/dl. W.E. Olooto, et al. also found that sever preeclampsia were significantly associated with low serum albumin levels where timing delivery should be considered [13].

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Our result in table [4] demonstrates s. albumin level according to GA, there is marked decrease in s. albumin in severe group and this decrease is more in those who GA less than 37 wks, this is contrary to the fact that serum albumin will decrease as the pregnancy progresses due to the dilution effect of increase maternal plasma volume over increase total serum albumin during pregnancy. It is thought that early stage hypertension has a low serum albumin level and ,our result goes with Seong, et al [11] study on 454 patient with pregnancy related hypertension, who found that s. albumin level between 27-34 wks GA was significantly lower than those with GA more than 37 wks GA at (P=0.001).

According to complications in table [5] imminent eclampsia, eclampsia, pulmonary odema, HELLP syndrome IUGR and IUD were higher in women with low serum albumin level (below 3.00 gm/dl), but the risk of placental abruption, sever oligohydraminios and uncontrolled HPT was not greatly affected by serum albumin level. This is clinically important to choose proper time for delivery and termination of pregnancy complicated by hypertension. Witlin et al .suggested that serum albumin (less than 3 gm/dl) could be considered as a predictor of eclampsia in their study on 445 consecutively managed women with sever preeclampsia and ecclampsia [14] while Seong, et al [11] found that low serum albumin level was associated with increase maternal complications except for IUGR which was not greatly affected in low serum albumin group.

Conclusion and recommendations

The results of our study showed that the level of serum albumin in both form of pre eclampsia (sever and mild) is lower compared to that of normal and hypertensive cases and this was lower in sever form than in mild form, so serum albumin level in preeclampsia can be used as a determinant of disease severity and may be used as a useful marker for termination of pregnancy and pregnancy outcomes.

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Disclosure of interests

None to declare.

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Contribution to authorship

The authors were directly involved in the care and collection of cases and also collaborated on the content of the paper and approved with the final outcome.

Details of ethics approval

Details of ethics approval was obtained from the medical ethics committee of the college of medicine / university of kufa

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