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CASE SERIES

Association of Hypoproteinemia in Preeclampsia With Maternal and Perinatal Outcomes

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Abstract

Background: **Preeclampsia (PE) is a condition that develops after 20 weeks of pregnancy and may manifest as late as 4−6 weeks after delivery. It is characterized by extensive vascular endothelial dysfunction and vasospasm.**

Aim and objective: **This study's primary objective was to analyze the maternal and perinatal outcomes in PE in relation to serum albumin levels.**

Patients and methods: **This prospective observational cohort research was carried out at Hussein Hospital, Al-Azhar University's Department of Obstetrics and Gynecology. Between September 2021 and March 2022, cases were recruited from the emergency unit. A total of 100 severe preeclamptic women were included in the trial, and they were divided into two groups according to their blood albumin levels: group I PE with an albumin level of greater than 25 g/l [mild hypoproteinemia (MHP)) and group II PE with an albumin level of less than or equal to 25 g/l [severe hypoproteinemia (SHP)].**

Results: **Preterm birth, fetal growth restriction, and NICU admission were significantly more common in the SHP group compared with the MHP group. Poor maternal and neonatal outcomes were significantly more common in the SHP group compared with the MHP group.**

Conclusion: **Estimation of albumin levels in pregnancy is of value in the early prediction of PE. SHP PE warrants careful monitoring throughout pregnancy owing to its increased risk of unfavorable maternal and newborn outcomes compared with MHP PE.**

Keywords: Albumin, Fetal growth restriction, Hypoproteinemia, Preeclampsia, Pregnancy

1. Introduction

One of the main causes of maternal and newborn death and morbidity is preeclampsia (PE).[1]

PE is thought to complicate two to eight percent of pregnancies worldwide. Nearly 26% of maternal fatalities in Latin America and the Caribbean are caused by hypertensive diseases, compared with 9% of deaths in Africa and Asia.[2]

On a global scale, PE is responsible for ~50 000 deaths annually.[3]

Overweight, past high blood pressure, advanced age, and diabetes mellitus are risk factors for PE.[4] Additionally, if a woman is expecting twins and if it is her first gestation, it is more typical.

PE manifests after 20 weeks of pregnancy and is marked by proteinuria and hypertension. Hypoalbuminemia and severe PE often coexist; it was proposed that hypoalbuminemia may be used as a gauge for the severity of PE. Hypoalbuminemia is primarily caused by systemic small vessel spasm, increased angiotensin secretion, and enhanced vascular endothelial cell permeability. As a result, many proteins and liquids leak out of tissues, and many plasma proteins − especially serum albumin − are lost, resulting in intravascular dehydration.[5]

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The purpose of the research was to ascertain if there was a relationship between maternal and perinatal outcomes and PE-related hypoproteinemia, and how to measure the effects of PE on the mother and the fetus based on the blood albumin level.

2. Patients and methods

A prospective observational cohort research was carried out in the Department of Obstetrics and Gynecology, Al-Hussein Hospital, Al-Azhar University. Cases were recruiting from the emergency unit during the period from September 2021 to March 2022.

The research included 100 severe preeclamptic women who were divided into two groups based on the blood albumin level: mild hypoproteinemia (MHP) in Group I PE with an albumin value greater than 25 g/l, and PE in group II with an albumin value less than or equal to 25 g/L. (severe hypoproteinemia (SHP)]. The study's definition of SHP was based on a serum albumin content of less than or equal to 25 g/l.

2.1. Patient selection

The sample size was calculated using the MedCalc version 12.3.0.0 program (Ostend, Belgium); statistical software depending on a 95% confidence interval (95% CI) and an 80% research power with a 5% error rate.

Inclusion criteria were women who were pregnant and had a gestational age (GA) of greater than or equal to 28 weeks with severe PE. The following criteria were used for identification of severe PE: sustained systolic blood pressure of greater than or equal to 160 mm Hg or sustained diastolic blood pressure of greater than or equal to 110 mm Hg, proteinuria as assessed by the presence of at least one dipstick or a 24-h urine collection with proteinuria of greater than or equal to 0.3 g, oliguria, or creatinine of greater than 1.1 mg%, HELLP (Hemolysis Elevated Liver enzymes Low Platelet) syndrome-specific laboratory abnormalities, and symptoms of severe PE, such as a strong headache, blurred vision, and epigastric discomfort.

Exclusion criteria were multifetal pregnancy, epilepsy history, diabetes, renal illness, fetal congenital abnormalities, and pregnancy while using anticoagulants like heparin (unfractionated or low molecular weight).

Maternal results were assessed based on the delivery method [spontaneous vaginal delivery, instrumental vaginal delivery, or cesarean section (CS)], eclampsia, HELLP disorder, high blood pressure, impaired liver function, irregular renal function, ascites, oligohydramnios, thrombocytopenia, and placenta abruption.

Fetal growth restriction, preterm delivery (37 and 28 weeks of gestation), and perinatal mortality were used to examine the outcomes of newborns Fetal growth restriction (FGR), defined as actual birth weight below than 10% of gestation age). Additionally, birth weight was evaluated in the interim.

2.2. Methodology

All participants were counseled, and informed consent was obtained. The following procedures were applied to all patients: detailed history taking, including information on the patient's personal, menstrual, and obstetric histories as well as their current and former lives. A thorough physical examination was done. Examinations of the chest, abdomen (obstetric), and pelvis were performed. Analysis of the urine as well as laboratory evaluations of the blood hemoglobin, platelets, serum creatinine, serum uric acid, liver activity tests, and serum albumin levels were all part of the investigations.

Blood pressure was measured according to the following methodology: the patient was placed in the sitting or semisitting position, and then a cuff was used of appropriate size. The cuff was placed at the value of the heart, and Korotkoff phase V was used to determine the diastolic blood pressure.

2.2.1. Ethical considerations

The Al-Azhar University Faculty of Medicine's Obstetrics and Gynecology Department's Ethical Committee received the study protocol for clearance. Each participant in the research was informed of its objectives and procedures before giving their informed verbal and written permission. At all stages of the research, confidentiality and personal privacy were maintained.

2.3. Statistical analysis

SPSS 22.0 for Windows was used for statistically examining all the data that were gathered and tabulated (SPSS Inc., Chicago, Illinois, USA). Employing the Shapiro–Wilk test, the distribution of the data was examined for normality. Frequencies and relative proportions were used to depict qualitative data. The variance between the qualitative variables was evaluated using χ^2-test and Fisher's exact test, as shown. For parametric and

nonparametric data, respectively, the mean and SD were used to describe quantitative data. Every statistical comparison used a two-tailed significance test. Level of *P* value less than or equal to 0.05 denotes a significant difference, *P* less than 0.001 denotes a very significant difference, and *P* greater than 0.05 denotes nonsignificant difference.

3. Results

There was no significant difference between the two study groups regarding age, BMI, and parity (Table 1).

There was a significant difference between the two study groups regarding albumin and 24-h proteinuria (Table 2).

This table shows that most of patients underwent elective CS (45.7 and 56.7%), with statistically significant difference between the two groups (Table 3).

There was a significant difference between the two study groups regarding GA and birth weight (Table 4).

Tables 5–7 shows that poor maternal and perinatal outcomes is more frequent in SHP group than MHP group.

4. Discussion

This prospective observational cohort research was carried out at Hussein Hospital, Al-Azhar University's Department of Obstetrics and Gynecology. Between 2021 September and March 2022, cases were recruited from the emergency unit. A total of 100 severe preeclamptic women were included in the trial, and they were divided into two groups according to their blood albumin levels: mMHP in group I PE with an albumin value greater than 25 g/l, and PE in group II with an albumin value less than or equal to 25 g/l (SHP). The study's definition of SHP was based on a serum albumin content of less than or equal to 25 g/l.

Table 1. Demographic data of the two researched groups.

	MHP ($N = 70$) [n (%)]	SHP ($N = 30$) [n (%)]	t	P
Age (years)	28.45 ± 3.24	29.17 ± 3.66	0.979	0.330
Mean ± SD (years)				
<35	58 (82.9)	23 (76.7)	0.523	0.469
>35	12 (17.1)	7 (23.3)		
BMI (kg/m^2)				
Mean ± SD	26.82 ± 1.69	27.32 ± 1.43	1.42	0.160
<25	5 (7.1)	2 (6.7)		
25–30	34 (48.6)	12 (40)	0.708	0.702
>30	31 (44.3)	16 (53.3)		
Parity				
Mean ± SD	1.22 ± 0.95	1.48 ± 0.89	1.28	0.204

MHP, mild hypoproteinemia; SHP, severe hypoproteinemia.

Table 2. Proteinuria characteristics between the two study groups.

	MHP ($N = 70$)	SHP ($N = 30$)	t	P
Albumin (g/dl)			MW	
Mean ± SD	2.91 ± 1.23	2.26 ± 1.04	279	0.009
Proteinuria (mg/dl/24 h)				
Mean ± SD	3515.23 ± 412.46	4681.9 ± 531.4	12	0.000

MHP, mild hypoproteinemia; MW, Mann–Whitney test; SHP, severe hypoproteinemia.

Table 3. Mode of delivery distribution between the two study groups.

	MHP ($N = 70$) [N (%)]	SHP ($N = 30$) [N (%)]	χ^2	P
Vaginal delivery	17 (24.3)	1 (3.3)		
Emergency CS	21 (30)	12 (40)	6.27	.043
Elective CS	32 (45.7)	17 (56.7)		

CS, cesarean section; MHP, mild hypoproteinemia; SHP, severe hypoproteinemia.

Table 4. Neonatal characteristics between the two study groups.

	MHP ($N = 70$)	SHP ($N = 30$)	t	P
GA (weeks)				
Mean ± SD	37.85 ± 2.68	36.42 ± 2.74	2.43	0.017
Birth weight (kg)				
Mean ± SD	2.92 ± 0.314	2.74 ± 0.435	2.33	0.022
Apgar at 1 min				
Mean ± SD	6.73 ± 1.65	7.11 ± 0.964	1.18	0.242
Apgar at 5 min				
Mean ± SD	9.67 ± 0.499	9.85 ± 1.21	1.06	0.293

GA, gestational age; MHP, mild hypoproteinemia; SHP, severe hypoproteinemia.

Our findings on the demographic information of the two analyzed groups revealed that there is no significant difference between them with respect to age, BMI, and parity.

The current study was supported by the study by Chen *et al.*[6] which included 299 preeclamptic women who were retrospectively categorized into moderate hypoproteinemia (MHP, $n = 220$) and SHP ($n = 79$) PE according to the value of albumin to assess maternal and perinatal results in PE. Age, BMI, and parity did not significantly vary between the two study groups.

Our findings indicated that there is no significant difference between the two study groups with reference to routine laboratory measures.

However, the study by Chen *et al.*[6] reported that compared with women with MHP, women with SHP were more likely to presenting with ascites, abruption placenta, impaired hepatic or renal functions, and other symptoms ($P < 0.05$). HELLP syndrome, platelets, and oligohydramnios were comparable in both groups. This disagreement may be owing to the difference in the sample size and comorbidities.

Table 5. Maternal outcome distribution between the two studied groups.

	MHP ($N = 70$) [N (%)]	SHP ($N = 30$) [N (%)]	χ^2	P
Eclampsia	2 (2.9)	3 (10)	2.26	0.133
HELLP syndrome	6 (8.6)	2 (6.7)	0.104	0.748
Oligohydramnios	5 (7.1)	6 (20)	3.55	0.060
Abnormal liver function	9 (12.9)	11 (36.7)	7.4	0.007
Abnormal renal function	6 (8.6)	9 (30)	7.56	0.006
Ascites	10 (14.3)	10 (33.3)	4.76	0.029
Thrombocytopenia	5 (7.1)	5 (16.7)	2.12	0.146
Abruption placenta	3 (4.3)	7 (23.3)	8.47	0.004

This table shows that ascites, abruption of the placenta, impaired renal activity, and impaired liver activity were significantly more frequent in the SHP group compared with the MHP group.
MHP, mild hypoproteinemia; SHP, severe hypoproteinemia.

Table 6. Neonatal outcome distribution between the two studied groups.

	MHP ($N = 70$) [N (%)]	SHP ($N = 30$) [N (%)]	χ^2	P
Preterm birth	21 (30)	17 (56.7)	6.34	0.012
Fetal growth restriction	9 (12.9)	15 (50)	15.8	0.000
NICU admission	14 (20)	18 (60)	15.4	0.000
Neonatal asphyxia	3 (4.3)	3 (10)	1.22	0.271
Fetal death	2 (2.9)	3 (10)	2.26	0.133

This table shows that preterm birth, fetal growth restriction, and NICU admission were significantly more frequent in the SHP group compared with the MHP group.
MHP, mild hypoproteinemia; SHP, severe hypoproteinemia.

Table 7. Overall poor outcome distribution between the two studied groups.

	MHP ($N = 70$) [N (%)]	SHP ($N = 30$) [N (%)]	χ^2	P
Poor maternal outcome	13 (18.6)	16 (53.3)	12.3	.000
Poor neonatal outcome	18 (25.7)	17 (56.7)	8.84	.003

MHP, mild hypoproteinemia; SHP, severe hypoproteinemia.

Moreover, the study by Kamel *et al.*[7] reported that there were statistically significant decreases in impaired hepatic or renal activity, ascites, and abruption placenta in mild group when compared with severe group. In addition, there was insignificant decrease in eclampsia, HELLP disorder, oligohydramnios, and thrombocytopenia in mild cases versus severe group. Compared with the MHP group, women with SHP were more likely to present with impaired liver or/and renal activity, ascites, and abruption placenta.

The study by Seong *et al.*[8] revealed that albumin was significantly correlated with platelets.

Regarding proteinuria characteristics between the two studied groups, our results revealed that albumin and 24-h proteinuria showed significant difference between the two groups.

In accordance with our findings, Seong *et al.*[8] revealed that albumin was significantly correlated with urine protein.

Regarding neonatal characteristics between the two studied groups, our results revealed that there was a significant difference between the two examined groups regarding GA and birth weight, whereas the Apgar scores at 1 and at 5 min were comparable in both groups. Our results also showed that preterm birth, fetal growth restriction, and NICU admission were significantly more common in the SHP group compared with the MHP group.

This was in line with the research by Chen *et al.*[6] as they revealed that in comparison with the MHP group (2940.1 ± 768.0 g), the SHP group's median birth weight was substantially lower (2498.1 ± 866.5 g). Preterm births, hospitalization to the neonatal ICU, and FGR were all more prevalent among the neonates of the SHP group of mothers ($P < 0.01$).

Moreover, the study by Kamel *et al.*[7] reported that there was a statistically significant increase in preterm birth in the severe group when compared with the mild cases. There was a highly statistically significant increase in fetal growth restriction in severe cases. Given that there was a very significant difference in FGR ($P < 0.001$) and a significant difference in preterm birth ($P = 0.035$) between the SHP group and the MHP, neonatal results were poorer in the SHP group.

Moreover, regarding the maternal outcome distribution between the two studied groups, our results showed that ascites, abruption placenta,

impaired renal activity, and impaired liver activity were significantly more frequent in the SHP group compared with the MHP group.

This was supported by Chen *et al.*[6] who revealed that in the SHP group compared with the MHP group, severe hypertension was more common ($P = 0.01$ and < 0.01, respectively). In comparison with women in the MHP group, women with SHP were more likely to present with ascites, placental abruption, decreased renal activity, and impaired liver activity ($P = 0.05$).

Moreover, the study by Kamel *et al.*[7] reported that there were statistically significant decreases in ascites, abruption placenta, impaired renal activity, and impaired liver activity in mild group when compared with severe group. In addition, insignificant decreases of eclampsia, HELLP disorder, oligohydramnios, and thrombocytopenia were seen in mild cases versus the severe group. Compared with the MHP group, women with SHP were more likely to present with ascites, abruption placenta, and impaired liver or/and renal performance.

Finally, regarding the overall poor outcome distribution between the two studied groups, our results reported that the poor maternal and neonatal outcomes were significantly more common in the SHP group compared with the MHP group.

This was in line with the study by Chen *et al.*[6] who used univariate logistic regression and found that SHP was a substantial risk variable for CS, poor maternal results, and poor newborn findings in PE women [odds ratio (OR): 2.99, 95% CI: 1.13–7.91; OR: 5.83, 95% CI: 3.32–10.24; and OR: 4.43, 95% CI: 2.57–7.62, respectively).

Moreover, the study by Kamel *et al.*[7] revealed that there was a substantial reduction in poor maternal outcomes and poor neonatal outcomes in mild cases versus severe cases, with statistically significant differences. SHP was found to be a highly major risk variable for poor maternal outcomes ($P = 0.005$) and significant risk factor for neonatal outcomes ($P = 0.040$).

In addition, the study by Benoit and Rey[9] concluded that because all of the women with low plasma albumin levels also had other undesirable conditions, it was determined that the plasma albumin level below 20 g/l was not a reliable indicator of severe PE.

Furthermore, according to the literature, hypoalbuminemia is thought to contribute to poor maternal and newborn outcomes.[10]

4.1. Conclusion

Identification of women who are at increased risk for PE could potentially enhance the effectiveness of the gestation care because intensive maternal and fetus monitoring in these patients would enable an early identification of the disease's clinical manifestations and the resulting fetal growth restriction. This would allow for the avoidance of the progress of serious complications through interventions such as the administering of antihypertensive medicines and early delivery. Estimation of albumin levels in pregnancy is of value in the early prediction of PE. SHP PE warrants careful monitoring throughout pregnancy owing to its increased risk of unfavorable maternal and newborn outcomes compared with MHP PE.

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Conflict of interest

There are no conflicts of interest.

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