https://doi.org/10.48047/AFJBS.6.6.2024.6749-6757

African Journal of Biological Sciences

Research Paper Open Access

A comparative study on serum antithrombin III levels in pregnant women with preeclampsia and chronic hypertension and healthy pregnant individuals

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Article History

Volume 6, Issue 6, 2024
Received: 03 Feb 2024
Accepted: 06 Apr 2024
doi:10.48047/AFJBS.6.6.2024.6749-6757

Abstract

Background and Objective: Reduced plasma levels of antithrombin III have been observed in pregnant mothers with preeclampsia. However, there is very limited information about the relationship between antithrombin, preeclampsia, and chronic hypertension during pregnancy.

Methods: This case-control study included 120 pregnant mothers who were divided into three groups including preeclampsia, chronic hypertension, and control (40 in each group). Women with twin or multiple pregnancies or fetuses with hydatidiform mole and hydrops fetalis were excluded from the study. All people with diabetes, liver disease, kidney disease, etc., and infectious diseases were excluded from the study. Testing and sampling were simultaneous with the termination of pregnancy in three groups. One cc was sampled from the subjects. After completion, the data were entered into SPSS 17 software and analyzed using an independent t-test and chi-square test with a significance level of less than 0.05.

Results: The mean and standard deviation of serum antithrombin III levels were 18.80 ± 5.30 mg/dL in women of the chronic hypertension group, 20.11 ± 7.52 mg/dL in women of the preeclampsia group, and 19.44 ± 6.07 mg/dL in women of the control group (P>0.05). A pairwise comparison of the mean serum antithrombin III levels of patients using the Tukey HSD post hoc test revealed that this difference was not statistically significant between any of the two study groups (P>0.05). In the chronic hypertension group, 22 cases (55%) had abnormal antithrombin III levels, in the preeclampsia group, 21 cases (52.5%) had abnormal antithrombin III levels, and 19 cases in the control women (47.5%) had abnormal antithrombin III levels (less than 20 mg/dL) (P>0.05).

Conclusion: The results revealed that despite the differences in the etiologies of preeclampsia and chronic hypertension and the known role of antithrombin III in these diseases and pregnancy, there was no statistically significant difference between the plasma levels of antithrombin III in the three study groups including pregnant women with preeclampsia, pregnant women with chronic hypertension, and healthy pregnant mothers.

Keywords: Antithrombin III, Preeclampsia, Chronic hypertension

Introduction

Hypertensive disorders occur in 5-10% of pregnancies and account for 16% of maternal deaths (1). These disorders are divided into different types. One of the most important types is preeclampsia. Preeclampsia complicates 5-10% of pregnancies and is considered one of the three major causes of maternal mortality and morbidity along with hemorrhage and infection (2). It accounts for 25% of perinatal deaths even in developed societies. In developed countries, its incidence rate is one in every 2000 deliveries. Its rate has been reported as one in 2000 deliveries in England, one in 2500 deliveries in Southern Ireland, one in 2000 deliveries in Scandinavia, and one in 1600 deliveries in the Netherlands.

Its rate has been estimated to be up to 10% in other countries and up to 7% in Iran (4, 3). Preeclampsia is a pregnancy-specific syndrome characterized by hypertension with edema, proteinuria, or both. It mostly occurs after the 20th week of gestation and often near term (5). Hypertension is the most important criterion for the diagnosis of preeclampsia. It is defined as a blood pressure higher than 140/90 mm Hg or an increase of 30 mm Hg in systolic blood pressure or 15 mm Hg in diastolic blood pressure. Subcutaneous edema is a normal finding in pregnancy. However, non-subcutaneous edema in the hands and face upon arising from sleep is considered a disease, or a weight gain of 2 pounds per week or a sudden weight gain over 1 to 2 days raises suspicion of preeclampsia. Proteinuria is the last symptom to develop and is defined as the presence of more than 300 mg of protein in the 24-hour urine. Predisposing factors include previous nulliparity, maternal age under 20 or over 35 years, low socioeconomic status, multiple pregnancies, hydatidiform mole, polyhydramnios, non-immune hydrops fetalis, diabetes, chronic hypertension and underlying renal disease, positive family history, and previous history of preeclampsia (7 and 6).

Complications of preeclampsia were also examined in two categories maternal and fetal complications. Maternal complications included brain complications such as eclampsia, hypertensive encephalopathy, cerebral hemorrhage, coma, blindness and retinal detachment, HELLP syndrome, pulmonary edema, glomeruloendotheliosis, kidney failure, and placental abruption. Fetal complications included IUFD-IUGR, preterm, stillbirth, fetal distress, and meconium excretion. Preeclampsia, especially severe forms and those occurring below 35 weeks of gestation is associated with a significant increase in maternal and fetal morbidity and mortality (8).

Preeclampsia was defined as systolic blood pressure higher than 140 mmHg and diastolic blood pressure higher than 90 mmHg, or an increase of 30 mmHg to the initial systolic blood pressure and 15 mmHg to the initial diastolic blood pressure, or proteinuria higher than 300 mg/dL in 24 hours, or urination more than 100 mg/dL or more in two urine samples collected 6 hours after the 20th week of pregnancy. Severe preeclampsia is defined as systolic blood pressure higher than 160 mmHg and diastolic blood pressure higher than 110 mmHg with proteinuria higher than 2 g/dL in 24 hours occurs along with clinical symptoms such as headache, blurred vision, epigastric pain, and oliguria. Finally, eclampsia is when severe preeclampsia is accompanied by generalized seizures in the absence of other causes (9). Preeclampsia mainly occurs between the 20th week of pregnancy and 48 hours

after termination of pregnancy. However, a few cases of the disease occur within 48 hours of termination of pregnancy up to 4 weeks after termination of pregnancy, which is called preeclampsia or late eclampsia (19). Simultaneous late eclampsia and PRES are rare (9).

Friedman and Neff examined 38,000 pregnant women 30 years ago. They reported that a diastolic blood pressure of 95 mm Hg or more was associated with a threefold increase in the risk of fetal death. Severe hypertension, especially if accompanied by proteinuria, was a more ominous sign. Proteinuria without hypertension was much more benign (10). However, Newman et al. (2003) reported that severe proteinuria increased the risk of preterm delivery but did not significantly change the survival rate of infants (11). After analyzing more than 9000 nulliparous women from the Perinatal Cooperative Project (a large cohort study conducted between 1959 and 1965), Zhang et al. (2001) concluded that neither blood pressure nor proteinuria were sensitive predictors of adverse outcomes (12).

Some researchers concluded that women with higher socioeconomic status have a lower incidence of preeclampsia, but Lawlor et al. did not find this result in a cohort study on 3485 women. (13) The incidence of hypertension in healthy nulliparous women was examined in a trial of calcium supplementation. Out of the 4302 nulliparous women who delivered at or after 20 weeks of gestation, one-quarter had pregnancy-related hypertension. When all nulliparous women were included, preeclampsia was present in 7.6% of cases and severe preeclampsia in 3.3% (14). Vatten and Skjaerven reported a rate of 2.6% in more than 1.6 million Norwegian nulliparous women (15).

Chavarria et al. began sampling every four weeks from 16 weeks of gestation in 378 nulliparous women belonging to the low-risk group. In women who later developed preeclampsia, its level was significantly higher at 12 weeks. The positive predictive value of the test was only 29%, but its negative predictive value was 98% (16). Preeclampsia treatment is complicated due to the presence of the fetus. Although termination of pregnancy is the definitive treatment of the disease and is beneficial to the mother, it can be dangerous for the fetus since preterm birth is one of the major causes of neonatal mortality and disability. Thus, preeclampsia treatment must be based on a careful and systematic plan. Step-by-step treatment of gestational hypertension (17), screening of pregnant women regarding the signs of hypertension and the presence of risk factors, regular monitoring of blood pressure, referral of high-risk patients to the antenatal care unit, regular measurement of blood pressure, measurement of urine protein, platelet count, serum uric acid concentration, and liver function tests are essential in the treatment of hypertension if blood pressure is higher than 170.110 mm Hg (18).

Severe preeclampsia is the primary cause of maternal death in severe preeclampsia and eclampsia. Many scientists and the National Hypertension Education Group in the United States argue that pharmacotherapy in acute hypertension should be started when the diastolic pressure (phase five) exceeds 105 mm Hg to reduce it to 90-100 mm Hg. Cerebral hemorrhage is negligible in this range of blood pressure. When all patients suffer from severe and persistent preeclampsia and in women with eclampsia, treatment includes the following items: 1- seizure prevention or control, 2- Correction of hypoxia and acidosis, 3- blood

pressure control, 4- Delivery after seizures are controlled with blood pressure-lowering drugs. Hypertension is a serious risk factor for the mother. In the United Kingdom, the use of low-dose medications has increased the risk of death over the past 20 years. The rate of maternal brain lesions leading to maternal death has also decreased during this period (21, 20, and 19).

Qqawa et al. (2014) examined the association between antithrombin, albumin, and total protein levels in patients with gestational hypertension and preeclampsia. Their results revealed that plasma antithrombin III levels in patients with gestational hypertension and preeclampsia were associated with albumin and total protein levels, indicating a decrease in antithrombin III activity during gestational hypertension and preeclampsia (22). James et al. (2014) also studied the characteristics of antithrombin levels during pregnancy. They concluded that overall antithrombin levels during pregnancy were 20% lower than baseline and that their levels were negatively correlated with gestational age and decreased by 13% in the last trimester (23).

Despite several decades of extensive studies in this area, the mechanism of initiation or exacerbation of hypertension during pregnancy remains unresolved, and hypertensive disorders are still the most important unsolved problem in obstetrics. Regarding pathogenesis, the disease is characterized by segmental vascular constriction and persistent reduction in placental blood flow, leading to the release of several factors and finally, vascular dysfunction. Considering the mentioned maternal and fetal complications, including intrauterine growth restriction (IUGR), prematurity, and placental abruption, and the prevention of this pregnancy-specific syndrome is one of the goals of obstetricians and gynecologists. Due to the high importance of pregnancy and the physiological and hormonal changes that occur during this period, which in some cases lead to pathologies for the mother and fetus, including gestational hypertension, preeclampsia, and the high importance of hypertensive disorders, the present comparative study investigated the antithrombin III levels in patients with preeclampsia and chronic hypertension compared to healthy pregnant mothers, considering various findings about diagnostic markers in the prevention and treatment of these disorders, including antithrombin III levels and the lack of such studies in Iran, especially in the of Sistan and Baluchestan province.

Materials and Methods

The statistical population of this case-control study included all pregnant women with preeclampsia and chronic hypertension in the case group and healthy pregnant women in the control group referring to Ali bin Abitaleb Hospital in Zahedan. The inclusion criteria of the study included preeclampsia (based on defined clinical and laboratory criteria including blood pressure equal to or higher than 140/90 mmHg from the twentieth week of pregnancy and proteinuria of 300 mg or more in 24 hours or +1 or more in a urine dipstick test in a random urine sample.

The exclusion criteria of the study included multiple pregnancies, hydatidiform moles, and underlying diseases such as diabetes, lupus, and infectious diseases. Based on the Altman Nomogram formula with an alpha error of 0.05, and a power of 80%, the required sample size

was determined 40 people in each group. Pregnant women were studied in three groups. Pregnant women with chronic hypertension were included in the first case group (n = 40), pregnant women with preeclampsia were included in the second case group (n = 40), and all women with normal pregnancies (n = 40) were included in the control group. The preeclampsia diagnosis was based on blood pressure equal to or higher than 140/90 mmHg after 20 weeks of gestation and proteinuria of 300 mg or more in 24 hours or +1 or more (on dipstick) in a random urine sample.

Chronic hypertension was defined as blood pressure equal to or higher than 140/90 mmHg before pregnancy or diagnosed before 20 weeks of gestation not attributable to gestational trophoblastic disease or hypertension first diagnosed after 20 weeks of gestation and persisting after 12 weeks of delivery. Subjects with twin or multiple pregnancies or fetuses with hydatidiform mole and hydrops fetalis were excluded from the study. All subjects with diabetes, liver disease, kidney disease, etc., and infectious diseases were excluded from the study. The study subjects were matched in two groups in terms of age and body mass index. Moreover, other variables such as parity, history of preeclampsia, and literacy were also recorded. After explaining the study to the patients and obtaining their informed consent, the relevant information was first recorded in the information form.

The test time was simultaneous with the termination of pregnancy in the three groups. To perform serological tests, 1 cc of blood was taken from the case and control groups and immediately sent to the laboratory using the relevant form. Then, a sample of 1 cc of plasma was taken from the patients based on the referral letter and sent to the laboratory with a specific form, and the sample was examined for antithrombin III levels, and tests were performed. After completion, the data were entered into SPSS-17 software and all were analyzed using independent t-test and chi-square test with a significance level of less than 0.05. In this study, codes 1, 2, 3, 4, 5, 7, 8, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 24, 25, 26, 27, 28, 29, 30, and 31 approved by the ethics committee of the university were observed. All study patients were informed of the inclusion criteria of this study, and if they gave informed consent, they were included in the study.

Results

The results revealed that the mean and standard deviation of age was 32.87 ± 6.23 years in women of the chronic hypertension group, 29.27 ± 6.92 years in women of the preeclampsia group, and 26.10 ± 6.55 years in women of the control group. The mean and standard deviation of body mass index (BMI) were 27.12 ± 4.52 kg/m2 in women of the chronic hypertension group, 24.4 ± 95 kg/m2 in women of the preeclampsia group, and 21.52 ± 3.89 kg/m2 in women of the control group. The mean and standard deviation of gestational age was 27.35 ± 8.52 weeks in women of the chronic hypertension group, 34.65 ± 5.26 weeks in women of the preeclampsia group, and 35.22 ± 4.45 weeks in women of the control group. The mean and standard deviation of the number of pregnancies was 5.72 ± 3.32 in women of the chronic hypertension group, 3.65 ± 2.42 in women of the preeclampsia group, and 2.65 ± 1.73 in women of the control group.

In women of the chronic hypertension group, 16 cases (40%), in women of the preeclampsia group, 6 cases (15%), and in women of the control group, 4 cases (10%) had a history of miscarriage. In women of the chronic hypertension group, 9 cases (22.5%), in women of the preeclampsia group, 5 cases (12.5%), in women of the control group, 3 cases (7.5%) had a history of stillbirth. In women of the chronic hypertension group, 3 cases (7.5%), in women of the preeclampsia group, 3 cases (7.5%), and in the women of the control group, 1 case (2.5%) had used assisted reproductive methods.

Table 1: Comparison of mean serum antithrombin III levels separately based on the study groups using the ANOVA test

Group	N	Mean	SD	Min	Max	P value
Chronic hypertension	40	18.80	5.30	8	36	0.65
Preeclampsia	40	20.11	7.52	5	42	
Control	40	19.44	6.07	6	28	

Based on Table (1), the mean and standard deviation of serum antithrombin III levels were 18.80 ± 5.30 mg/dL in women of the preeclampsia group, 20.11 ± 7.52 mg/dL in women of the chronic hypertension group, and 19.44 ± 6.07 mg/dL in women of the control group. The ANOVA test showed that this difference was not statistically significant (P>0.05).

Table 2: Comparison of mean serum antithrombin III levels in the two study groups using the Tukey HSD test

Group		Mean difference	Standard error	P Value
Chronic hypertension	Preeclampsia	-1.31	1.42	0.62
	Control	-0.63	1.42	0.89
Preeclampsia	Chronic hypertension	1.31	1.42	0.62
	Control	0.67	1.42	0.88
Control	Chronic hypertension	0.63	1.42	0.89
	Preeclampsia	-0.67	1.42	0.88

Based on Table (2), a pairwise comparison of the mean difference in serum antithrombin III levels of patients using the Tukey HSD post hoc test showed that this difference was not statistically significant between any of the two study groups (P>0.05.(

Table 3: Comparison of the frequency distribution of abnormal antithrombin III levels (less than 20 mg/dL) based on study groups using the chi-square test

Group	abnormal antithrombin III levels (less than 20 mg/dL)				P Value
	yes		no		
	n	%	n	%	
Chronic hypertension	22	55	18	45	0.79
Preeclampsia	21	52.5	19	47.5	
Control	19	47.5	21	52.5	

Based on Table (3), 22 cases (55%) in women with chronic hypertension, 21 cases (52.5%) in women with preeclampsia, and 19 cases (47.5%) in control women had abnormal antithrombin III levels (less than 20 mg/dL). The chi-square test showed that this difference was not statistically significant (P>0.05).

Discussion

The present study included three groups including patients with chronic hypertension, preeclampsia, and healthy pregnant women. The mean age of these patients ranged from 17 years in the normal pregnancy group to 46 years in the chronic hypertension group. This age range is similar to other studies including Leiberman et al. (1988), Aghai and Qqawa (1990), and Qaqawa (2014). The proven factors of preeclampsia are young or old maternal age and chronic hypertension, so the mean age of the patients was considered in this study (25, 24). Another predisposing factor for preeclampsia is high body mass index, which was seen between pregnant mothers with preeclampsia and pregnant mothers with hypertension compared to the control group. Its mean values were 20 to 27 with a minimum value of 17 and a maximum value of 35. Gestational age was one of the other factors examined in this study. Its results revealed that the age at onset of preeclampsia and chronic hypertension in pregnant mothers can be involved in preterm labor. This study also revealed that the mean gestational age was 27 weeks in pregnant mothers with chronic hypertension, 34 weeks in pregnant patients with preeclampsia, and 35 weeks in the control group women.

The number of pregnancies was another factor affecting the pregnancy process as it affects the two spectrums of nulliparous and multiparous preeclampsia. In the present study, the number of pregnancies reported in the patients studied varied from 1 to 14 cases. We also investigated the number of miscarriages and stillbirths in these groups, and the descriptive statistics showed that 16 (40%) women in the chronic hypertension group, 6 cases (15%) in the preeclampsia group, and 4 cases (10%) of the control women had a history of miscarriage. Moreover, 9 cases (22.5%) in the preeclampsia group, 5 cases (12.5%) in the preeclampsia group, and 3 cases (7.5%) in the control group had a history of stillbirth.

The mean serum antithrombin III level in the three studied groups showed that it was 80.18 ± 30.5 mg/dL in women of the chronic hypertension group, 52.7 ± 20.11 mg/dL in

women of the preeclampsia group, and 19.44 ± 6.07 mg/dL in the women of the control group. This difference was not statistically significant. This result is consistent with the results reported by Aghai et al. (1990) and Leiberman et al. (1988) as they reported that antithrombin III activity has a weak association with platelet count and blood pressure of the patient. However, it is inconsistent with the results of the studies by Weiner et al. (1985), Qqawa et al. (2014), and James et al. (2014). This difference can be attributed to common laboratory errors, differences in the kits used, differences in the methodology of the studies in terms of sample size, and the selection of patients compared to the present study (22, 23, 24, 25, 9).

In the present study, the laboratory cut-off for abnormal plasma antithrombin III levels was considered to be below 20 mg/dL. The results revealed that 22 cases (55%) in women of the chronic hypertension group, 21 cases (52.5%) in women of the preeclampsia group, and 19 cases (47.5%) in control women had abnormal antithrombin III levels (less than 20 mg/dL). These results could be due to several reasons. For example, the diagnosis of preeclampsia is based on clinical criteria and some of these patients are not sometimes preeclamptic and are included in this category, as the sensitivity and specificity measured for plasma antithrombin III in this group of patients, as investigated in other studies, have also reported to be 70%, which confirms this issue. Additionally, the study center consisted of a population of patients who had many overlaps in many symptoms and characteristics due to demographic, genetic, and most importantly, the cultural context in most cases, making the distortion of the results expected. Another reason could be the techniques used in antithrombin measurement and differences in devices and kits. Sampling time could be also another reason. In many studies, antithrombin plasma levels of patients were measured in three trimesters and then the results were analyzed. However, the possibility of examining patients in three trimesters, comparing the results, and expressing a quantitative number was limited in the present study due to the high testing cost. Thus, these factors could justify this difference in the results.

Conclusion

The results revealed that despite the differences in the etiologies of preeclampsia and chronic hypertension and the known role of antithrombin III in these diseases and pregnancy, there was no statistically significant difference between the plasma levels of antithrombin III in the three study groups, including pregnant women with preeclampsia, pregnant women with chronic hypertension, and healthy pregnant mothers. Considering a more accurate patient selection system in addition to clinical criteria in combination with renal biopsy in combination with measurement of plasma antithrombin levels in three trimesters of pregnancy and comparison of these values among the groups, a prospective study design is recommended to achieve more accurate results.

References

1. Scott JR, Gibbs RS, Karlan BY, Haney AF. Danforth KLJ. Obstetrics & Gynecology. 9th Ed. Lippincott Williams & Wilkins. 2003;:309-327.

2. Cunningham FG, Leveno KJ, Bloom SL, Hauth JC, Gilstrap LC, Wenstrom KD. Williams Obstetrics. 22th Ed. McGraw-Hill Companies. 2005;761-808.
3. Burrow GN, Duffy TP. Medical complication during pregnancy. 5th Ed. WB.Saunders Company. 1999; 25-53.
4. Creasy RK, Renisk R, Iames JD, Maternal-fetal medicine. 5th Ed. Saunders Company. 2004; 859-901.
5. James DK, Steer PG, Weiner CP, Gonik B. High Risk Pregnancy. 2th Ed. WB.Saunders Company. 1999; 639-660.
6. Mutlu-Turkoglu U, Ademoglu E, Ibrahimoglu L, Aykac-Toker G, Uysal M. Imbalance between lipid peroxidation and antioxidant status in preeclampsia. Gynecol Obstet Invest. 1998;46(1):37-40.
7. Schiff E, Friedman SA, Stampfer M, Kao L, Barrett PH, Sibai BM. Dietary consumption and plasma concentrations of vitamin E in pregnancies complicated by preeclampsia. Am J Obstet Gynecol. 1996;175(4):1024-1028.
8. Sibai BM. Diagnosis and management of gestational hypertension and preeclampsia. Obstet Gynecol. 2003;102(1):181-92.
9. Malek A. The Impact of metabolic disease associated with metabolic syndrome on human pregnancy. Curr Pharm Biotechnol 2014;10(3):15-21.
10. Friedman EA, Neff RK. Pregnancy, outcome as related to hypertension, edema, and proteinuria. Perspect Nephrol Hypertens 1976;5:13-22.
11. Newman MG,Robicahaun AG,Stedman CM.Prinatal proteinuria.Am J Obstet Gynecol 2003:118-264
12. Zhang J,Klebanoff MA,Roberts JM.Predictiion of adverse outcomes by common definitions of hypertention in pregnancy.Obstet Gynecol 2001:97-98.
13. Lawlor DA, Morton SM, Nitsch D, Leon DA. Association between childhood and adulthood socioeconomic position and pregnancy induced hypertension: results from the Aberdeen children of the 1950s cohort study. J Epidemiol Community Health 2005;59(1):49-55.
14. Hauth JC, Ewell MG, Levine RJ, Esterlitz JR, Sibai B, Curet LB, Catalano PM, Morris CD. Pregnancy outcomes in healthy nulliparas who developed hypertension. Calcium for Preeclampsia Prevention Study Group. Obstet Gynecol 2000;95(1):24-8
15. Vatten LJ, Skjaerven R. Is pre-eclampsia more than one disease? BJOG 2004;111(4):298-302.
16. Bainbridge SA, Smith GN. HO in pregnancy. Free Radic Biol Med 2005 15;38(8):979-88.
17. Chararria ME,Lara-Gonzalez L,Gonzalez-Gleuson A.Maternal plasma cellular fibronectin concentration in normal and preeclamptic pregnancies : Alongitudinal study for early predictio of preeclampsia.Am J Obstet Gynecol 2003:189-192.
18. Sibai BM, Barton JR, O'brien JM, Bergauer NK, Jacques DL. Mild gestational hypertension remote from term: progression and outcome. Am J Obstet Gynecol 2001;184(5):979-83.

19. Olsen SF, Secher NJ, Tabor A, Weber T, Walker JJ, Gluud C. Randomised clinical trials of fish oil supplementation in high risk pregnancies. Fish Oil Trials In Pregnancy (FOTIP) Team. BJOG 2000;107(3):382-95.
20. Steegers EA, von Dadelszen P, Duvekot JJ, Pijnenborg R. Pre-eclampsia. Lancet. 2010;376(9741):631-44.
21. Deak TM, et al. Hypertension and pregnancy. Emergency Medicine Clinics of North America. 2012;30:903.
22. James AH, Rhee E, Thames B, Philipp CS. Characterization of antithrombin levels in pregnancy. Thromb Res. 2014;134(3):648-51.
23. Halligan A., Bonnar J., Sheppard B., Darling M. & Walshe J. (1994) Haemostatic, fibrinolytic and endothelial variables in normal pregnancies and pre-eclampsia. British Journal of Obstetrics and Gynaecology 101, 488–492.
24. Aghai E, Brunstein J, Quitt M, Abramovici H, Froom P. Antithrombin III levels in preeclampsia. Isr J Med Sci. 1990;26(3):142-3.
25. Ogawa M, Matsuda Y, Kobayashi A, Mitani M, Makino Y, Matsui H. Plasma antithrombin levels correlate with albumin and total protein in gestational hypertension and preeclampsia. Pregnancy Hypertens. 2014;4(2):174-7.