The Effects of Preeclampsia Severity and Thrombocytopenia on the Prognosis of Hypertensive Pregnant Women

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OBJECTIVE: The present study was aimed to determine the effects of preeclampsia severity and thrombocytopenia on maternal and fetal prognosis in hypertensive pregnant women, and to discuss the clinical and biochemical findings in light of the literature.

STUDY DESIGN: Three hundred and one pregnant patients, who had been admitted to the Department of Obstetrics and Gynecology of our clinic, with the diagnosis of preeclampsia between October 2006 and October 2008, were retrospectively evaluated.

The patients were divided into two groups as patients with mild and severe preeclampsia. Additionally, the patients were analyzed in two subgroups according to their platelet counts, as the groups with low and normal platelet counts.

RESULTS: When the patients with mild and severe preeclampsia were compared with regard to maternal complications, no significant difference was determined between the two groups ($p>0.05$). However, a significant difference was noted between the groups with respect to the development of eclampsia and HELLP syndrome ($p<0.05$). Eclampsia (n=17; 12%) and HELLP syndrome (n=30; 21.1%) were more common in the patients with severe preeclampsia. On the other hand, no significant difference was noted between the two groups in terms of fetal outcomes ($p>0.05$).

When the patients with low and the normal platelet counts were compared with respect to maternal complications, it was noted that HELLP syndrome (n=39; 51%) and eclampsia (n=11; 14.5%) were more common in patients with low platelet counts, when compared to the patients with normal platelet counts, and difference between the two groups was significant ($p<0.05$). Birth weight was significantly lower in patients with low platelet counts ($p<0.05$).

CONCLUSIONS: There is a significant relationship between the severity of preeclampsia and potential complications. The risk for the development of HELLP syndrome and eclampsia increases in patients with severe preeclampsia. Furthermore, the risk for the development of complications increases with a decreased platelet count.

Key Words: Prognosis, Preeclampsia, Thrombocytopenia

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Introduction

Preeclampsia, which continues to be one of the most important causes of maternal and fetal complications, has become the most commonly researched subject in obstetrics nowadays.[1] Preeclampsia and eclampsia may be responsible for 30% of all maternal mortalities in developing countries. The effects of preeclampsia on the mother and the fetus show differences with regard to the underlying cause.[2] It is known that thrombocytes play an important role in the pathophysiology and clinical follow-up of preeclampsia.[3] Preeclampsia is a multisystem disease characterized with generalized vasoconstriction, increased blood pressure, thrombocyte activation and increased capillary permeability.[4]

The increase in the levels of vasoconstrictor substances in the circulation is an important indicator of thrombocyte activation in preeclampsia.[5] It is thought that endothelial activation or intrinsic changes in the thrombocytes lead to this activation.[6] On average, a 10% decrease in the thrombocyte count is observed during the course of pregnancies in all pregnant women, and this most often manifests in the third trimester. Despite the progressive thrombocyte damage, thrombocytopenia is thought to be a late finding in preeclampsia.[5]

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In this study, 301 patients presenting to the Obstetrics and Gynecology Department of our clinic with the diagnosis of hypertension between October 2006 and October 2008, were retrospectively evaluated. It was aimed to determine the maternal and fetal prognostic effects of preeclampsia severity and thrombocytopenia on patients that were hospitalized and followed up with the diagnosis of preeclampsia in light of the literature.

Material and Method

The data of 301 patients who were hospitalized and followed-up with the diagnosis of preeclampsia in the Obstetrics and Gynecology Department of our clinic between October 2006 and October 2008, were retrospectively evaluated from the patient files.

Demographic characteristics (age, gravidity parity, number of abortions, gestational week), detailed anamnesis (stillbirth, intrauterine death, number of living children, history of preeclampsia in previous pregnancies), physical examination findings at admission, level of consciousness, perinatal ultrasound (US) measurements, blood pressure, results of routine hematological tests (hemoglobin, thrombocyte count, white blood cell count), liver function tests (AST, ALT), renal function tests (BUN, creatinine), and levels of blood glucose, sodium, potassium and calcium, and spot urine protein measurements of the patients were recorded. The data related to the delivery of the mother and health of the newborn (mode of delivery, birth weight and 1 minute Apgar score of the newborn), perinatal complications such as intrauterine death and intrauterine growth retardation (IUGR), and maternal complications such as maternal mortality, placental abruption and acute renal failure (ARF), were also recorded. Preeclampsia was defined as a blood pressure140/90 mmHg, on two successive measurements, 6 hours apart, and spot urine protein concentrations≥ 30 mg/dl on at least two consequent measurements.

The diagnosis of mild preeclampsia was made upon determination of a blood pressure between 140/90 and 160/110 mmHg on two successive measurements, 6 hours apart and a proteinuria of 300 mg/dl in spot urine analysis.

The diagnosis of severe preeclampsia was made upon determination of a blood pressure ≥160/110 mmHg on two successive measurements, 6 hours apart, and proteinuria≥5 g in 24-hour urine analysis or proteinuria ≥500 mg/dl in spot urine analysis.

The diagnosis of eclampsia was made upon concomitant presence of tonic (contraction) and clonic (shaking) convulsions of non-neurological origin along with the clinical picture of preeclampsia.[7]

Meanwhile, HELLP syndrome was diagnosed upon presence of an abnormal peripheral blood smear (with schistocytes), increased bilirubin levels (>1.2 mg/dl), high LDH levels (>600 IU/L), increased liver enzymes (AST>70 IU/L) and a thrombocyte count of <100000/mm^3 [8]

The patients were divided into two groups as mild and severe preeclampsia. These two groups were compared in terms of demographic features, laboratory parameters, and maternal and fetal complications.

The patients were also analyzed in two groups according to thrombocyte counts. Patients with a thrombocyte count >150000/mm^3 were considered in the "normal platelet count group", and those with a thrombocyte count <150000/mm^3 were considered in the "low platelet count group". The two groups were evaluated in terms of maternal and fetal complications. Patients with maternal complications such as HELLP syndrome, eclampsia, placental detachment and ARF, and those with fetal complications such as intrauterine death, oligohydramnios, anhydramnios and IUGR were assessed one by one in terms of preeclampsia severity according to thrombocyte counts.

Following the coding, the data were entered into the computer using the SPSS package program and analyzed. In the evaluation of the data, continuous variables were expressed as mean ± standard deviation, and frequency data were expressed as percentages (%). In the statistical analyses, the normality of the distribution of all measured variables was tested using the Kolmogorov-Smirnov test. The non-parametric 'Mann-Whitney U Test' was used for paired comparisons, and the Pearson Test was utilized for determination of the correlation of the measured data.

Countable data were compared using the Chi Square Test and the Fisher's Exact Test. The level of statistical significance was set at $p < 0.05$ for all tests.

Results

The mean age of the 301 cases was 29.1±6.3 years (range, 17-45 years). The distribution of the patients according to the number of pregnancies and parity was evaluated. Distribution of the patients according to the demographic features is presented in Table 1.

Table 1: Distribution of the cases according to demographic characteristics

Demographic Features	Minimum	Maximum	Mean±SD
Age (years)	17	45	29.1±6.3
Gravidity (n)	1	13	2.49±2.0
Parity (n)	0	10	1.18±1.65
Number of abortions (n)	0	7	0.32±0.77
Gestational week (n)	21	42	34.3±3.9

The mean gestational week was 34.3±3.9 weeks (range, 21-42 weeks). According to gestational age, 172 cases (57.1%) were preterm, 121 cases (40.2%) was term, and 8 cases (2.7%) were postterm.

Fifty-nine of the cases had a medical history of preeclampsia in their previous pregnancies (35.8%). The medical histories of the remaining 106 cases (64.2%) were unremarkable.

Statistical correlations regarding the demographic characteristics are demonstrated in Table 2. In intergroup comparisons, gravidity was higher in patients with severe preeclampsia. However, no significant difference was found between the groups in terms of age, number of abortions and gestational week.

The statistical relationship between the groups regarding the laboratory results and the clinical findings is displayed in Table 3.

The complications developed in both groups are presented in Table 4**.** A significant difference between the groups was found in terms of eclampsia and HELLP syndrome development. Eclampsia and HELLP syndrome were seen more frequently in the severe preeclamptic group.

No significant difference was determined between the groups in terms of fetal outcomes.

In the evaluations performed on two subgroups divided according to thrombocyte counts.

Table 2: The demographic features of patients with mild and severe preeclampsia

Demographic Features	Mild Preeclampsia Mean±SD	Severe Preeclampsia Mean±SD	P value
Age (years)	29.0±6.2	29.2±6.3	>0.05
Gravidity (n)	2.23±1.74	2.78±2.23	<0.05
Parity (n)	0.93±1.32	1.47±1.93	<0.05
Number of abortions (n)	0.32±0.88	0.32±0.63	>0.05
Gestational week (n)	34.5±3.7	34.1±4.1	>0.05

Table 3: Laboratory and clinical findings of patients with mild and severe preeclampsia

Laboratory and clinical findings	Mild Preeclampsia Mean±SD	SeverePreeclampsia Mean±SD	p value
Hemoglobin (mg/dl)	12.2±1.4	12.3±1.6	>0.05
Thrombocyte (1000/mm³)	213±75	195±80	<0.05
WBC (/ mm³)	11148±3200	12180±4000	<0.05
AST (IU/L)	37±57	72±139	<0.05
ALT (IU/L)	28±42	60±146	<0.05
BUN (mg/dl)	12.0±5.1	12.3±5.1	>0.05
Creatinine (mg/dl)	0.6±0.2	0.7±0.2	>0.05
Glucose (mg/dl)	88±23	90±20	>0.05
Na (mEq/L)	134±3	134±3	>0.05
K (mEq/L)	4.3±0.4	4.2±0.5	>0.05
Ca (mg/dl)	8.6±0.6	8.4±0.6	<0.05
Protein in spot urine (mg/dl)	193±117	257±84	<0.05
Systolic blood pressure (mmHg)	146±10.4	172.5±17.5	<0.05
Diastolic blood pressure (mmHg)	92.5±7.4	113.2±10.7	<0.05

Table 4: Comparison of Maternal Mortality Rates in patients with mild and severe preeclampsia

Maternal Complications	Mild Preeclampsia n=159	Severe Preeclampsia n=142	Total	p value
Placental Detachment	6 (3.8%)	6 (4.2%)	12	>0.05
HELLP	15(9.4%)	30 (21.1%)	45	<0.05
ARF	10 (6.3%)	11 (7.7%)	21	>0.05
Maternal Mortality	0	3 (2.1%)	3	>0.05
Eclampsia	6 (3.8%)	17 (12%)	23	<0.05

Statistical relationships between the groups in terms of demographic characteristics are demonstrated in Table 5. No significant difference was found between the groups in terms of age, gravidity, parity, number of abortions, and gestational week.

A statistically significant difference was determined between the groups in terms of maternal complications such as HELLP syndrome, eclampsia and ARF. These complications were observed more frequently in the thrombocytopenic group (Table 6).

No significant difference was determined between the two groups in terms of fetal complications. However, a statistically significant difference was found between the groups with regard to birthweight. Birthweight was significantly lower in the group with low thrombocyte counts (Table 7).

Thrombocyte counts were low in 17.6% and normal in 82.4% of the patients with mild preeclampsia. In patients with severe preeclampsia, 33.8% had a low thrombocyte count while 66.2% of the cases had normal thrombocyte counts (Table 8).

According to the correlation analyses:

Blood AST, ALT, BUN and creatinine levels, and blood pressure values increased ($p<0.05$), and blood calcium levels decreased ($p<0.05$) with a decrease in blood platelet counts.

Discussion

Hypertensive disorders, which are the most common medical complications of pregnancy, lead to a substantial increase in maternal and perinatal mortality.[9]

Table 5: The demographic features of preeclamptic patients according to thrombocyte counts

Demographic Features	Low Thrombocyte count	Normal Thrombocyte count	p Value
Age (years)	29.1±6.3	29.1±6.3	>0.05
Gravidity (n)	2.4±1.9	2.4±2.0	>0.05
Parity (n)	1.2±1.6	1.1±1.6	>0.05
Number of Abortions (n)	0.3±0.9	0.3±0.7	>0.05
Gestational week (n)	33.5±4.2	34,6±3.8	>0.05

Table 6: Maternal complications in patients with low and normal thrombocyte counts

Maternal complications	Low Thrombocyte Count	Normal Thrombocyte count	p value
Placental Detachment	5 (6.6%)	7 (3.1%)	>0.05
HELLP sydrome	39 (5%1)	6 (2.7%)	<0.05
ARF	12 (15.8%)	9 (4%)	<0.05
Maternal Mortality	3 (3.9%)	0	
Eclampsia	11 (14.5%)	12 (5.3%)	<0.05

Table 7: Fetal complications in patients with low and normal thrombocyte counts

Fetal complications	Low Thrombocyte levels	Normal Thrombocyte counts	p Value
Intrauterine death	9 (11.8%)	11 (4.9%)	>0.05
1 minute APGAR score	6.0±2.8	7.0±2.1	>0.05
IUGR	8 (10.5%)	42 (18.7%)	>0.05
Oligohydramnios	15 (19.7%)	28 (12.5%)	>0.05
Anhydramnios	6 (7.9%)	15 (6.7%)	>0.05
Low birthweight	2076.8±988.3	2290.3±990.3	<0.05

Table 8: The severity of preeclampsia according to thrombocyte counts

	Low Thrombocyte Count	Normal Thrombocyte Count	Total
Mild Preeclampsia	28 (17.6%)	131 (82.4%)	159
Severe Preeclampsia	48 (33.8%)	94 (66.2%)	142
Total	76 (25.2%)	225 (74.8%)	301

In our country, deaths due to pregnancy-related hypertension comprise 25% of all causes of maternal death.[10] The Turkey National Maternal Death study has shown that preeclampsia/eclampsia with a percentage of 18.4%, ranks second among the causes of maternal death, following peripartum bleeding.[11] In general, preeclampsia and HELLP syndrome result in poor maternal outcomes, and maternal mortality rates can increase as high as 24%.[12]

In our clinic, the frequency of preeclampsia among women delivering within a period of two years was found to be 13.7%. The rates of mild preeclampsia and severe preeclampsia were 52.8% and 47.2%, respectively while the rate of those with HELLP syndrome was 15.0%. Overall, 7.6%.of the women developed eclampsia.

In a study performed in the province of Erzurum, maternal mortality rate due to eclampsia was 7.4%,[13] while this rate was found to be 9.4% in another study in Diyarbakır.[14] In our study, eclampsia-related maternal mortality was 8.7%, consistent with the results of the other studies performed in our country.

Maternal mortality and morbidity rates increase with an increase in the severity of preeclampsia.[9] In the study performed by Yayla et al. on 287 preeclamptic patients, the maternal mortality rate in severe preeclamptic cases was found as 3.94%.[15] In their study on 73 preeclamptic pregnant cases, Murphy et al. reported HELLP syndrome in 15 (21%), ARF in 9 (13%), abruptio placentae in 11 (15%), and intrauterine fetal mortality in 12 (16.4%) of the cases.[16]

In our study, maternal complication rate in patients with severe preeclampsia was 47.9%, while the rate in mild preeclamptic cases was 23.3%. Placental detachment and ARF was seen in 12 (4%) and 21 (7%) patients in our study, respectively. The maternal mortality rate was 1% in (n=3). Eclampsia and HELPP syndrome were more frequent in severe preeclamptic patients.

It has been determined that hemoglobin level decreases throughout pregnancy, while thrombocyte counts decrease in the third trimester. The increased consumption of thrombocytes causes a mild and temporary thrombocytopenia in the mother during pregnancy, which is the mother's first immune response to pregnancy.

The rate of thrombocytopenia in pregnant women ranges between 6.6% and 11.6%. The most frequent cause is gestational thrombocytopenia; and the second most frequent cause is preeclampsia and eclampsia.[17] Similarly, in our study, the frequency of thrombocytopenia in all preeclamptic patients was 25.2%.

It has been determined that the presence of concomitant thrombocytopenia increases the severity of the primary disease, as well as the rates of perinatal complications such as, premature placental detachment, preterm birth, low Apgar scores, and stillbirth.[17]

In preeclamptic patients, the thrombocyte counts determined 3-6 weeks prior to delivery have been found to be lower than that in normal pregnant women. Thrombocyte counts at the time of delivery have also been found to be significantly lower. In the second half of pregnancy, subclinical thrombocytopenia (thrombocyte counts at the lower limit of the normal range) occurs before the development of preeclampsia.[18] In their study on 67 preeclamptic patients with normal liver function tests and thrombocyte counts, Nieger et al. found the thrombocyte levels to be lower than that of the control group comprising 71 normal pregnant women.[19] Isolated thrombocytopenia in preeclamptic patients has been reported to be a risk factor in terms of HELLP Syndrome.[20] In spite of the fact that thrombocyte counts may remain within normal ranges in preeclamptic patients, it is emphasized that decreases in platelet counts must be taken into consideration.[21]

Although the relation of thrombocytopenia with hypertension and IUGR in preeclamptic patients is known, there is insufficient information regarding the morbidity in patients with a thrombocyte count at the lower limit of normal range.[22] Leduc et al. determined the risk of thrombocytopenia development as 50% in those with platelet counts lower than 200000/mm3 on admission, and stated that platelet counts on admission is of predictive value in the development of thrombocytopenia.[4]

It has been observed that platelet counts between 150.000/mm^3 and 200.000/mm^3 increase the risk of development of HELLP syndrome.[21] Platelet counts, which are within normal limits but show a decreasing tendency, are thought to be important in the development of thrombocytopenia and HELLP syndrome. Similarly, in our study, together with the fact that HELLP Syndrome was seen significantly more frequently in patients with a low thrombocyte count, cases with HELLP Syndrome were encountered in patients with a normal thrombocyte count in the follow-up period. These findings show that even if the thrombocyte count is within normal limits, thrombocytopenia and HELLP syndrome may develop in the follow-up of preeclamptic patients. It is of utmost importance to monitor the thrombocyte levels closely.

In our study, eclampsia was observed significantly more frequently in patients with a low thrombocyte count; nevertheless, eclamptic cases were also seen in patients with a normal thrombocyte count. Previous studies reported a relationship between eclampsia development and thrombocytopenia on admission.[4] Since there is a risk of development of eclamp-

sia and HELLP Syndrome even in preeclamptic patients with thrombocyte counts >150.000/mm^3 it may be important to closely monitor these patients for symptoms like headache, nausea, vomiting and abdominal pain, in addition to thrombocyte counts. It must be emphasized that attention must be paid to the decreases in thrombocyte counts in preeclamptic patients even if they remain within normal limits.[21]

In their study, Sibai et al. determined thrombocytopenia at a rate of 17% in cases with severe preeclampsia.[23] Jaremo et al. demonstrated that platelet counts were significantly lower in preeclamptic cases.[24]

In a study performed by Üstün et al., while no differences in the hemoglobin level was found between mild and severe preeclamptic groups, thrombocyte counts were observed to be significantly lower in patients with severe preeclampsia.[25] In their study on 56 preeclamptic pregnant patients, Ceylan et al. could not detect a significant difference in hemoglobin levels and thrombocyte counts between the patients with mild and severe preeclampsia.[26] In our study, there was no significant difference in the hemoglobin values of the mild and the severe eclamptic patients. As is known, although improper, the use of iron preparations during the course of pregnancy is widespread, and this can have an effect on the level of hemoglobin. Preeclampsia patients included in our study were not followed up, and we do not have sufficient data regarding the use of iron preparations. However, in our study, we found that platelet counts were significantly lower in patients with severe preeclampsia. This result puts forth the relationship between platelet levels and the severity of preeclampsia. Furthermore, independent from preeclampsia severity, we observed that thrombocytopenia pose a risk for the development of ARF, low birthweight, and eclampsia.

More randomized controlled studies with higher patient numbers are needed to evaluate the relation, as the total number of patients in studies that failed to determine a significant difference between the preeclampsia severity and thrombocytopenia was lower than our sample size. In this way, the relation between the severity of preeclampsia and thrombocytopenia can be squarely put forth.

Hipertansif Gebelerde Preeklampsi Şiddeti ve Trombositopenin Prognoz Üzerine Etkileri

AMAÇ: Hipertansif gebelerde preeklampsi şiddeti ve trombositopeni varlığının maternal ve fetal prognoz üzerine olan etkilerinin değerlendirilmesi, klinik ve biyokimyasal sonuçların incelenerek literatür eşliğinde tartışılması amaçlandı.

GEREÇ VE YÖNTEM: Ekim 2006 - Ekim 2008 tarihleri arasında Ondokuz Mayıs Üniversitesi Tıp Fakültesi Kadın Hastalıkları ve Doğum Kliniği'ne preeklampsi tanısıyla başvuran 301 olgu retrospektif olarak incelendi.

Hastalar hafif ve ağır preeklamptik olgular olmak üzere iki gruba; trombosit sayılarına göre de, düşük ve normal trombosit grupları olmak üzere iki alt gruba ayrıldı.

BULGULAR: Hafif ve ağır preeklamptik hastalar maternal komplikasyonlar açısından karşılaştırıldığında; gruplar arasında istatistiksel olarak anlamlı fark saptanmadı (p>0,05). Eklampsi ve HELLP sendromu gelişimi açısından ise anlamlı fark saptandı (p<0,05). Ağır preeklamptik grupta, eklampsi 17(%12) ve HELLP sendromu 30(%21,1) daha sık izlendi. İki grup, fetal sonuçlar açısından karşılaştırıldığında ise; gruplar arasında anlamlı fark saptanmadı (p>0,05).

Trombosit sayılarına göre ayrılan gruplar, maternal komplikasyonlar açısından karşılaştırıldığında; düşük trombosit grubunda HELLP sendromu 39 (%51), eklampsi 11 (%14,5), normal trombosit grubundan daha sık izlendi ve gruplar arası fark istatistiksel olarak anlamlı tespit edildi (p<0.05). Bebek doğum ağırlığı, düşük trombosit grubunda istatiksel anlamlı olarak daha düşük izlendi (p<0,05).

SONUÇ: Preeklampsinin şiddeti ile gelişebilecek komplikasyonlar arasında anlamlı ilişki bulunmaktadır. Ağır preeklamptik grupta HELLP sendromu ve eklampsi gelişme olasılığı artmaktadır. Yine trombosit sayısı düştükçe, komplikasyon gelişme olasılığı artmaktadır.

Anahtar Kelimeler: Prognoz, Preeklampsi, Trombositopeni

References

1. Worley RJ. Pregnancy-induced hypertension in: Danforth Obstetrics and Gynecology Ch 23, 6th ed, JB Lippincott Company, Philadelphia, 1990, pp: 489-515
2. Miller DA. Hypertension in Pregnancy. In: Mishell DR,Goodwin M, Brenner PF, eds. Management of common problems in obstetric and gynecology. Fourth edition. Blackwell Publishing, Los Angeles 2002:112-9.
3. Kenny L, Baker PN. Maternal pathophysiology in preeclampsia. Bailliere's Clinical Obstetrics and Gynaecology 1999;13:59-75.
4. Leduc L, Wheeler JM, Kirshon B, Mitchell P, Cotton DB. Coagulation profile in severe preeclampsia. Obstet Gynecol 1992;79:14-8.
5. Ballegeer VC, Spitz B, De Baene LA, Van Assche AF, Hidajat M, Criel AM. Platelet activation in vascular damage in gestational hypertension. Am J Obstet Gynecol 1992;166:629-33.
6. Socol ML, Weiner CP, Louis G, Rehnberg K, Rossi EC. Platelet activation in preeclampsia. Am J Obstet Gynecol 1985;151:4947.
7. Steegers EAP. Textbook of perinatal medicine London 1998;1889.

8. Sibai BM, Taşlımı MM, EL-Nazer A. Maternal-perinatal outcome associated with the syndrome of hemolysis, elevated liver enzymes, and low platelets in severe preeclampsia-eclampsia. Am J Obstet Gynecol 1986;155: 501-509.
9. Kesim M, Erdemir M, Kaya İ, Karlık İ, Aydemir A. Gebeliğin indüklediği hipertansiyon olgularında maternal-perinatal morbidite ve mortalite. Perinatoloji Dergisi 2001;9:116-20.
10. Erden AC, Yayla M. Preeklampsi-eklampside maternal fetal morbidite-mortalite. Perinatoloji Dergisi. 1993;1:23-30.
11. Hacettepe Üniversitesi Nüfus Etütleri Enstitüsü, ICON-INSTITUT Public SectorGmBH ve BNB Danışmanlık (2006) Ulusal Anne Ölümleri Çalışması, 2005.
12. Saudan P, Brown MA, Buddle ML, Jones M. Does gestational hypertension become preeclampsia? Br J Obstet Gynaecol 1998;105:1177-84.
13. İngeç M, Kumtepe Y, Börekçi B, Bebek Z, Kadanalı S. 2001-2003 yıllarındaki 81 eklampsi olgusunun maternal ve perinatal sonuçları. Jinekoloji ve Obstetrik Dergisi 2005;19:135-41.
14. Taner CE, Hakverdi AU, Aban M, Erden AC, Ozelbaykal U. Prevalence, management and outcome in eclampsia. Int J Gynaecol Obstet 1996;53:11-5.
15. Yayla M , Bayhan G, Elbey M, Uysal E, Erden AC. On yıllık dönemde 287 hafİf ve ağır preeklampsi olgusunun retrospektif analizi. Jinekoloji ve Obstetrik Dergisi 1999; 13:57-61.
16. Murphy DJ, Stirrat GM. Mortality and morbidity associated with early-onset preeclampsia. Hypertens Pregnancy 2000;19:221-31.
17. Parnas M, Sheiner E, Shoham-Vardi I, Burstein E, Yermiahu T, Levi I, Holcberg G, Yerushalmi R. Moderate to severe thrombocytopenia during pregnancy. Eur J Obstet Gynecol Reprod Biol 2006;128:163-8.
18. Fallahian M, Nabaie F. Subclinical thrombocytopenia and preeclampsia. Int J Gynaecol Obstet 2005;89:47-8.
19. Neiger R, Contag SA, Coustan DR. Preeclampsia effect on platelet count. Am J Perinatol 1992;9:378-80.
20. Jaleel A, Baseer A. Thrombocytopenia in preeclampsia: an earlier detector of HELLP syndrome. J Pak Med Assoc 1997;47:230-2.
21. Sezik M, Toyran H. Preeklampside normal trombosit değerleri ve morbidite. T Klin J Gynecol Obst 2002; 12:112-15.
22. Brown MA Buddie ML. Hypertension in pregnancy: maternal and fetal outcomes according to laboratory and clinical features. MJA 1996;165:360-5.
23. Sibai BM, Taslimi M, Abdella TN, Brooks TF, Spinnato JA, Anderson GD. Maternal ve perinatal outcome of conservative management of severe preeclampsia in midtrimester. Am J Obstet Gynecol 1985;152:32-7.
24. Jaremo P, Lindahl TL, Lennmarken C, Forsgren H. The use of platelet density and volume measurements to estimate the severity of pre-eclampsia. Eur J Clin Invest 2000; 30:1113-8.
25. Üstün YE, Kezban Doğan K, Türkçüoğlu İ, Üstün Y. Hafif, orta ve şiddetli preeklampsi olgularında hemoglobin ve trombosit düzeylerinin karşılaştırılması. Perinatoloji Dergisi 2007;15:93-8.
26. Ceyhan T, Beyan C, Başer İ, Kaptan K, Güngör S, İrfan A. The effect of pre-eclampsia on complete blood count, platelet count and mean platelet volume. Ann Hematol 2006;85:320-2