Influence of AB0 Blood Groups on Major Maternal Complications in HELLP Syndrome

HELLP Sendromundaki Majör Maternal Komplikasyonlara AB0 Kan Gruplarının Etkisi

İclal ÖZDEMİR KOL, MD,[a]
Gonca İMİR, MD,[b]
Cem YENİCESU, MD,[c]
Kenan KAYGUSUZ, MD,[a]
Meral ÇETİN, MD[b]

Departments of
[a]Anesthesiology and Reanimation,
[b]Obstetrics and Gynecology
Cumhuriyet University School of Medicine, SİVAS
[c]Department of Family Medicine,
Çayıralan State Hospital,
YOZGAT, TURKEY

Geliş Tarihi/*Received:* 29.01.2008
Kabul Tarihi/*Accepted:* 22.09.2008

Yazışma Adresi/*Correspondence:*
İclal ÖZDEMİR KOL, MD
Department of Anesthesiology and Reanimation, Cumhuriyet University School of Medicine, SİVAS, TURKEY
driclal@gmail.com

ABSTRACT Objectives: The aim of this retrospective study was to determine the effect of the maternal blood groups on major maternal complications in women with Hemolysis, Elevated Liver Enzymes, and Low Platelet Count HELLP syndrome. **Material and Methods:** Maternal medical records of pregnancies complicated by HELLP syndrome between January 1996 and August 2006 were reviewed. Eighty-nine women with HELLP syndrome were included in the study and the patients were divided into 8 groups according to their blood groups: A Rh-positive (n=40), B Rh-positive (n=14), AB Rh-positive (n=9), 0 Rh-positive (n=20), A Rh-negative (n=2), B Rh-negative (n=0), and AB Rh-negative (n=2), 0 Rh-negative (n=2). The last 4 groups were removed from the study because of the small sample size. **Results:** There were no significantly respect to maternal age, parity, gestational age, initial and highest systolic blood pressure, hospital stay, hemoglobin, leukocyte count, platelet counts, prothrombin time, partial thromboplastin time, blood urea nitrogen, creatinine, alanine aminotransferase, aspartate aminotransferase, and lactic dehydrogenase in all groups. In the overall study population, the incidence of major maternal complications was 57.8%. The incidence of major maternal complications in HELLP syndrome was increased (71.4%) in B Rh-positive blood group in our study population. **Conclusions:** Our results may provide preliminary information that could be used to design future prospective studies to determine the influence of AB0 blood groups on major maternal complications in HELLP syndrome.

Key Words: HELLP syndrome; pregnancy complications; risk factors; AB0 blood-group system; pregnancy

ÖZET Amaç: Bu retrospektif çalışmada amaç Hemolysis, Elevated Liver Enzymes, and Low Platelet Count HELLP sendromundaki majör maternal komplikasyonlara AB0 kan gruplarının etkisini araştırmaktır. **Gereç ve Yöntemler:** Ocak 1996 ile Ağustos 2006 tarihleri arasında HELLP sendromu ile komplike olmuş gebeliklerin kayıtları değerlendirildi. Çalışmaya 89 HELLP sendromlu hasta alındı. Hastalar kan gruplarına göre 8 gruba ayrıldı: A Rh-pozitif (n=40), B Rh-pozitif (n=14), AB Rh-pozitif (n=9), 0 Rh-pozitif (n=20), A Rh-negatif (n=2), B Rh-negatif (n=0), AB Rh-negatif (n=2), ile O Rh-negatif (n=2). Son 4 grup hasta sayısı azlığı nedeni ile değerlendirmeden çıkarıldı. **Bulgular:** Kan gruplarına göre ayrılan hasta gruplarının hiçbirinde anne yaşı, parite, gestasyonel yaş, başvurudaki ve en yüksek sistolik kan basıncı, hastanede kalış süresi, hemoglobin, lökosit sayımı, trombosit sayımı, protrombin zamanı, parsiyel tromboplastin zamanı, kan üre nitrojeni, kreatinin, alanin aminotransferaz ve laktat dehidrogenaz bakımından bir fark saptanmadı. Çalışma hastalarımızda genel maternal komplikasyon oranı %57.8 idi. Çalışma grubumuzda HELLP sendromunda majör maternal komplikasyonlar en sık (%71.4) B Rh-pozitif kan grubu olan hasta grubunda görüldü. **Sonuç:** Bizim sonuçlarımız daha önce yeterli çalışılmamış olan bu konuda daha kapsamlı planlanmış çalışmalar için önemli bilgiler sağlayan bir ön çalışmadır.

Anahtar Kelimeler: HELLP sendromu; gebelik komplikasyonları; risk faktörleri; AB0 kan grupları; gebelik

Turkiye Klinikleri J Gynecol Obst 2008;18(5):289-93

The HELLP syndrome, originally described by Weinstein as an acronym in 1982, includes signs of hemolysis (H), elevated liver enzymes (EL), and low platelet count (LP), and is a variant of presentation of severe preeclampsia.[1] The incidence of HELLP syndrome in women with severe preeclampsia and eclampsia ranges from 2 to 30% depending on the population studied and the criteria used to establish the diagnosis.[2] HELLP syndrome has been shown to increase maternal and perinatal morbidity and mortality rates.[3] The etiology of this condition has not been clarified. In addition to genetic predisposition, abnormal placentation and maternal vascular endothelial dysfunction as well as immunological disturbances may be important events in the pathogenesis of this disorder.[4-6]

Certain pathological disorders have been found to be associated with the AB0 or rhesus blood groups.[7,8] Data on the relationship between major maternal complications in women with HELLP syndrome and the maternal blood groups was not found, although the relationship between the maternal blood groups and preeclampsia or HELLP syndrome has been reported.[9-11] This retrospective study was designed to evaluate the relationship between maternal blood groups and major maternal complications in women with HELLP syndrome.

MATERIALS AND METHODS

We reviewed the charts of patients with HELLP syndrome admitted to obstetric service in Cumhuriyet University Hospital between January 1996 and August 2006 retrospectively. The diagnosis of HELLP syndrome required the presence of thrombocytopenia (perinatal platelet nadir ≤150.000 /μL), evidence of hepatic dysfunction (increased aspartate aminotransferase (AST) level of ≥ 40 IU/L, increased alanine aminotransferase (ALT) level of ≥ 40 IU/L, or both, with increased lactate dehydrogenase (LDH) level of ≥ 600 IU/L), and evidence of hemolysis (increased LDH level, progressive anemia), usually in association with hypertension or proteinuria considered to represent preeclampsia or eclampsia.[12] The exclusion criteria were hypertension and proteinuria before the 20th gestational week and other significant medical conditions, including renal, hepatic, hematologic, or cardiovascular diseases and diabetes mellitus that could cause proteinuria and hypertension.

Eighty-nine women with HELLP syndrome were included in the study. We collected the demographic data and clinical findings including maternal age, parity, prenatal care, pregnancy induced hypertension (PIH) history, gestational age at admission, and systolic blood pressures at admission and highest during the management, the ratio of postpartum HELLP syndrome, and total hospital stay. Laboratory evaluation included liver function tests, complete blood cell count, coagulation profile, and renal function tests. Major maternal complications recorded including eclampsia, ablatio placenta, disseminated intravascular coagulopathy (DIC), acute renal failure (ARF), pulmonary edema and acute respiratory distress syndrome (ARDS), intracranial infarct or hemorrhage, and maternal death. Eclampsia was defined as tonic- clonic seizures occurring in a hypertensive pregnancy, with or without proteinuria. Pulmonary edema and ARDS were diagnosed based on clinical findings and chest radiograph. DIC was defined as the presence of three or more of the following criteria: low platelets (<100.000 /μL), low fibrinogen (<300 mg/dL), positive D-dimers (≥50 mg/dL), or prolonged prothrombin (≥14 seconds) and partial thromboplastin (≥40 seconds) times. ARF was diagnosed in the presence of oliguria or anuria in association with a creatinine clearance of ≤20 mL/min or an elevated serum creatinine level of ≥2 mg/dL. Intracranial infarct or hemorrhage was diagnosed based on computerized tomography.

The patients were divided into 8 groups according to their AB0 and Rh blood group-types: A Rh-positive (n=40), B Rh-positive (n=14), AB Rh-positive (n=9), 0 Rh-positive (n=20), A Rh-negative (n=2), B Rh-negative (n=0), AB Rh-negative (n=2), and 0 Rh-negative (n=2). The last 4 groups (A Rh-negative, B Rh-negative, AB Rh-ne-

gative, and 0 Rh-negative) were removed from the study because of the small sample size. Major maternal complications were recorded in all study groups.

STATISTICAL ANALYSIS

Statistical analyses were performed with the software program SPSS (version13, Chicago, IL, USA). Distribution of data was evaluated by the Kolmogorov-Smirnov test. Statistical analysis of the data was undertaken by parametric or non-parametric methods, as required. Data were presented as mean ± SD or the median (min-max) and percentage. Continuous variables compared with the Kruskal-Wallis or ANOVA tests, as appropriate. Categorical data were compared with the $\chi 2$ test. Odds ratios with 95% confidence intervals (CI) for developing major maternal complications in HELLP syndrome were calculated for each blood group. A value of $p < 0.05$ was considered as statistically significant.

RESULTS

During the study period, 89 medical charts with a diagnosis HELLP syndrome were identified and reviewed. Total 83 patient records were evaluated in 4 groups. Table 1 summarizes the demographic data and the presenting symptoms of women with HELLP syndrome. Table 2 lists the laboratory findings in these patients with HELLP syndrome. There were no differences among the groups with respect to maternal age (p=0.3), parity (p=0.8), gestational age (p=0.2), initial systolic blood pressure (p=0.2), highest systolic blood pressure (p=0.6), hospital stay (p=0.6), hemoglobin (p=0.6), leukocyte count (p=0.1), platelet counts (p=0.8), prothrombin time (p=0.9), partial thromboplastin time (p=0.06), blood urea nitrogen (p=0.6), creatinine (p=0.4), ALT (p=0.1), and AST (p=0.2), and LDH (p=0.1).

TABLE 1: Demographic data and clinical findings.

Data and findings	Value	No.
Maternal age (y, mean ± SD)	29.5 ± 6.8	-
Gestational age (wk, mean ± SD)	31.9 ± 4.2	-
Nulliparous (%)	37.3	31
Ratio of postpartum HELLP (%)	14.5	12
Antenatal care (%)	33.7	28
PIH history (%)	19.3	16
Hospital stay (day) (median, min-max)	8 (2-72)	-
Initial systolic blood pressure (mm Hg) (median, min-max)	160 (90-265)	-
Highest systolic blood pressure (mm Hg) (mean±SD)	181±41.4	-

PIH, Pregnancy induced hypertension.

TABLE 2: Laboratory findings.

Findings	Value
Aspartate aminotransferase (IU/L) (median, min-max)	279 (50-9856)
Alanine aminotransferase (IU/L) (median, min-max)	178 (50-5904)
Lactic dehydrogenase (IU/L) (median, min-max)	1150 (600-19200)
Blood urea nitrogen (mg/dL) (median, min-max)	16 (3-155)
Creatinine (mg/dL) (median, min-max)	1.1 (0.2-7)
Hemoglobin (g/dL) (mean ± SD)	10.5 ± 2.5
Leukocyte count (10^3/μL) (mean ± SD)	16.8 ± 6.8
Platelet count (10^3/μL) (mean ± SD)	62.3 ± 25.7
Prothrombin time (s) (mean ± SD)	13.2 ± 2.5
Partial thromboplastin time (s) (mean ± SD)	29.6 ± 6.9

Major maternal complications were documented in 48 women having HELLP syndrome, constituting 57.8% of the study group. Table 3 shows the distribution of patients with major maternal complication in HELLP syndrome according to blood groups and odds ratios. Although the most of patients (48.2%) have blood group of A Rh-positive, the ratio of major maternal complications in HELLP syndrome was higher (71.4%) in B Rh-positive blood group with a risk factor of 3.5 compared to others.

DISCUSSION

The results of the present study demonstrated an increased risk of major complications with HELLP syndrome for mothers with blood type B Rh-positive compared to other blood groups.

To our knowledge, this is the first report investigating the relationship between maternal blood groups and maternal complications in HELLP syndrome. Sezik et al.[9] investigated the relationship between the incidence of HELLP syndrome and maternal blood groups, retrospectively. They found that the blood group 0 Rh-ne-

TABLE 3: Odds ratios for developing major maternal complications in HELLP syndrome.

Blood group	Frequency of maternal complications (%)	Odds ratio	95% CI	p-value
A Rh-positive	42.5	0.8	0.3-1.8	0.5
B Rh-positive	71.4	3.5	1.01-12.4	0.03
AB Rh-positive	33.3	0.6	0.1-2.4	0.4
O Rh-positive	45	0.9	0.3-2.6	0.9

gative had HELLP syndrome associated with an increased risk by a factor of 3.1. Spinillo et al.[10] also evaluated the relation of maternal blood group to preeclampsia with a case-control study in primigravidae. They reported an increased risk of preeclampsia for mothers with blood group AB by a factor 3.07.

Lawoyin and Ani[11] studied on the etiologic factors in mothers complicated with preeclampsia. They found an increased risk in mothers with 0 Rh-positive blood group is more than twice as likely as others to develop preeclampsia. In all these previous studies, the underlying mechanism of the relationship between preeclampsia or HELLP syndrome and blood groups is uncertain.

In our study, the overall incidence of major maternal complications was 57.8%. The high incidence of maternal complications in HELLP syndrome in our study population is because of our perinatal center, which serves as the main referral center for the population of 1.000.000 inhabitants. Many patients were referred because of significant complications before or after delivery. Most of the patients were not received antenatal care (66.3%), which might be the reason of high incidence of complications.

The distribution of the blood group in Turkish population is as follows: A blood group 44.6%, B blood group 15.5%, AB blood group 7.7%, and 0 blood group 32.2%.[13] In our study, the most common blood group of the patients was A Rh-positive (48.2%) while the ratio of B Rh-positive blood group was (16.9%). The incidence of major maternal complications in HELLP syndrome was 71.4% in B Rh-positive blood group with a risk factor of 3.5 compared to other blood groups.

In conclusion, the increased incidence of major maternal complications in HELLP syndrome was detected in B Rh-positive blood group in our study population. In various populations, however, the incidence of HELLP syndrome and its complications were higher in various blood groups. In addition to maternal blood groups, other certain variables may affect the proportion of major maternal complications in women with HELLP syndrome. Although these results should be considered with caution, they support the hypothesis of a linkage mechanism-involving blood group in the inheritance of tenderness to develop major maternal complications in HELLP syndrome. Our results may provide preliminary information that could be used to design future prospective studies to determine the influence of AB0 blood groups on major maternal complications in HELLP syndrome.

REFERENCES

1. Weinstein L. Preeclampsia/eclampsia with hemolysis, elevated liver enzymes, and thrombocytopenia. Obstet Gynecol 1985; 66:657-60.
2. Cetin A. Hypertension, elevated liver enzymes, and low platelets (HELLP). In: Mohler III ER, Townsend RR, eds. Advanced Therapy In Hypertension and Vascular Disease. 1st ed. Hamilton: BC Decker; 2006. p.416-20.
3. Özdemir Kİ, İmir G, Kaygusuz K, Gürsoy S, Çetin A, Mimaroğlu C. [The management of patients with hellp syndrome and intracranial complications in intensive caree unit: 3 case reports] Turkiye Klinikleri J Gynecol Obst 2008;18:153-6.
4. Bussen S, Sütterlin M, Steck T. Plasma endothelin and big endothelin levels in women with severe preeclampsia or HELLP-syndrome. Arch Gynecol Obstet 1999;262:113-9.
5. Steinborn A, Sohn C, Rebmann V, Grosse-Wilde H. Haemolysis, elevated liver enzymes, low platelet count (HELLP) syndrome associated with increased maternal serum levels of soluble HLA-DR antigens. Aust N Z J Med 2000;30:511-2.
6. Cetin M, Pinarbasi E, Percin FE, Akgün E, Percin S, Pinarbasi H, et al. No association of polymorphisms in the glutathione S-transferase genes with pre-eclampsia, eclampsia and HELLP syndrome in a Turkish population. J Obstet Gynaecol Res 2005;31:236-41.

7. Moeller A, Weippert-Kretschmer M, Prinz H, Kretschmer V. Influence of ABO blood groups on primary hemostasis. Transfusion 2001;41: 56-60.
8. van Wayjen RG, Linschoten H. Distribution of ABO and rhesus blood groups in patients with gastric carcinoma, with reference to its site of origin. Gastroenterology 1973;65:877-83.
9. Sezik M, Toyran H, Yapar EG. Distribution of ABO and Rh blood groups in patients with HELLP syndrome. Arch Gynecol Obstet 2002;267:33-6.
10. Spinillo A, Capuzzo E, Baltaro F, Piazzi G, Iasci A. Case-control study of maternal blood group and severe pre-eclampsia. J Hum Hypertens 1995;9:623-5.
11. Lawoyin TO, Ani F. Epidemiologic aspects of pre-eclampsia in Saudi Arabia. East Afr Med J 1996;73:404-6.
12. Martin JN Jr, Rinehart BK, May WL, Magann EF, Terrone DA, Blake PG. The spectrum of severe preeclampsia: comparative analysis by HELLP (hemolysis, elevated liver enzyme levels, and low platelet count) syndrome classification. Am J Obstet Gynecol 1999;180(6 Pt 1):1373-84.
13. Ergun A, Yardımcı S. Türkiye Genelinde ABO Kan Grupları ve Rh Faktörünün Dağılımı. Ankara Üniv Tıp Fak Mec 1993;46:527-33.