

# Are ABO Blood Groups and Rh Factor Risk Factors for Hypertensive Diseases of Pregnancy?

## ABO Kan Grupları ve Rh Faktörü Gebeliğin Hipertansif Hastalıkları için Risk Faktörü mü?

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### ABSTRACT

**Introduction:** The primary aim of our study was to investigate the relationship between hypertensive diseases of pregnancy (HDP) and blood groups. Our secondary aim is to determine the risk factors that play a role in the development of HDP.

**Methods:** Pregnant women aged 15-49 years were included in this cross-sectional, observational, and prospective study. Pregnant women were divided into two groups. Group 1 (n=266) included patients admitted to the intensive care unit due to HDP. Group 2 (n=402) included normotensive patients without any complications during pregnancy. The groups were compared in terms of age, blood groups, Rh factor, gravida, parity, gestational week, and primiparity-multiparity.

**Results:** There was no statistically significant difference between the groups in terms of ABO blood group and Rh factor. The mean age, gravida, and parity were significantly higher in Group 1 than in Group 2 (p=0.028; 0.001; 0.004, respectively), while mean gestational age was lower than Group 2 (p<0.001). We also found that high gravida, low gestational age, presence of comorbidity, and primiparity were risk factors for HDP.

**Conclusion:** We did not find any relationship between HDP and blood groups. We found that high gravida, low gestational age, presence of comorbidity, and primiparity are risk factors for HDP.

**Keywords:** ABO blood group, Rh factor, hypertensive diseases of pregnancy, risk factors

### ÖZ

**Amaç:** Çalışmamızın öncelikli amacı gebeliğin hipertansif hastalıkları (GHH) ile kan grupları arasındaki ilişkiyi incelemektir. İkincil amacımız ise GHH'lerin gelişiminde rol oynayan risk faktörlerini belirlemektir.

**Yöntemler:** Kesitsel, gözlemsel ve prospektif olarak planlanan çalışmamıza 15-49 yaş arası gebeler dahil edildi. Gebeler iki gruba ayrıldı. Grup 1 (n=266), GHH nedeniyle yoğun bakım ünitesine kabul ettiğimiz hastalar; grup 2 (n=402), gebelik süresince herhangi bir komplikasyon gelişmeyen ve normotansif olan hastalardan oluştu. Gruplar yaş, kan grupları, Rh faktörü, gravida, parite, gebelik haftası ve primiparite-multiparite açısından karşılaştırıldı.

**Bulgular:** Gruplar arasında ABO kan grubu ve Rh faktörü açısından istatistiksel olarak anlamlı bir fark saptanmadı. Grup 1'in yaş, gravida ve parite ortalaması grup 2'ye göre istatistiksel olarak anlamlı bir şekilde daha yüksek saptanırken (sırasıyla, p=0,028; 0,001; 0,004), gebelik haftası ortalaması grup 2'ye göre daha düşük idi (p<0,001). Ayrıca yüksek gravida, düşük gebelik haftası, komorbidite varlığı ve primiparitenin GHH için risk faktörleri olduğunu saptadık.

**Sonuç:** Çalışmamızda GHH ile kan grupları arasında herhangi bir ilişki saptamadık. Yüksek gravida, düşük gebelik haftası, komorbidite varlığı ve primiparitenin GHH için risk faktörleri olduğunu gösterdik.

**Anahtar Kelimeler:** ABO kan grubu, Rh faktörü, gebeliğin hipertansif hastalıkları, risk faktörleri

### Introduction

Many risk factors such as age, parity, history of preeclampsia, multiple pregnancy, comorbidities [Diabetes Mellitus (DM), chronic hypertension, etc.], history of thrombophilia and obesity have been defined related to hypertensive diseases of pregnancy (HDP), which is the cause of approximately 18% of maternal deaths in the world (Table 1) (1,2). Despite this, the pathogenesis of preeclampsia and other HDP is not

fully understood (3). Although it is not known, oxidative stress in the spiral arterioles in the placenta and endothelial dysfunction developed by various mediators may be responsible for the pathogenesis of preeclampsia (3). One of the risk factors identified for preeclampsia is the history of thrombophilia (4). Due to being a risk factor for preeclampsia, thrombophilia increased the interest in ABO blood groups that play an essential role in coagulation by interacting with factor VIII and von



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Willebrand factor (5). Studies have shown that bleeding is more common in people with blood group O and that thromboembolic events and ischemic heart diseases are more common in people with other blood types (6-8).

Different results have been found in studies investigating the relationship between preeclampsia and ABO in different parts of the world. While no relationship has been reported between preeclampsia and blood groups in some studies (9-12), other studies have reported an association between preeclampsia and blood groups A, AB, or O (13-17). These conflicting results also were observed in our country (11,17). We aimed to investigate the relationship between HDP and ABO blood group-Rh factor and contribute to the literature by examining the factors that play a role in the development of HDP in Diyarbakır Obstetrics and Gynecology Hospital, where the patient density is much higher than most hospitals in our country.

### Methods

After the approval of the University of Health Sciences, Gazi Yaşargil Training and Research Hospital Ethics Committee (decision no: 27, date: February 16, 2018), our study was carried out between February 20, 2018, and February 01, 2019, in Diyarbakır Obstetrics and Gynecology Hospital, where there are approximately 24.000 births annually. Our study was planned as a cross-sectional, prospective, and observational study. Pregnant women aged 15-49 years were included in the study. Pregnant women were divided into two groups. Group 1 (n=266) included the patients who were hospitalized and followed up in the intensive care unit (ICU) due to HDP. Group 2 (n=402) was randomly selected among normotensive and follow-up patients who did not develop any complications during pregnancy. Patients under the age of 15, patients older than 49 years, patients who were pregnant and hospitalized in the ICU for non-HDP reasons, and those hospitalized in the ICU after gynecological surgeries were not included in the study. This study was conducted in accordance with the Helsinki Declaration 2008 criteria.

Age, blood group, Rh factor, gravida, parity, gestational week, comorbidities, and primiparity-multiparity status of the patients were recorded. Also, the length of ICU stay of group 1 patients was recorded. The groups were firstly compared in terms of blood groups and Rh

factor, and then in terms of other factors. Then, statistically significant values were considered as independent risk factors, and estimated relative risk and 95% confidence interval (CI) were calculated by logistic regression analysis.

### Statistical Analysis

SPSS 16.0 for Windows program was used for statistical analysis. Statistical data were expressed as mean and standard deviation (SD), and categorical data were expressed as number and percentage. The comparison of the categorical data was made with a chi-square test, and the results were given as n (%). The Kolmogorov-Smirnov test was used to determine whether the non-categorical data showed normal distribution. Mann-Whitney U test was used because the data did not show normal distribution. Results regarding numerical data were given as mean ± SD. Age, gravida, parity, gestational age, comorbidity, and primiparity-multiparity status were accepted as independent risk factors for HDP and evaluated by logistic regression. P<0.05 was accepted as statistically significant.

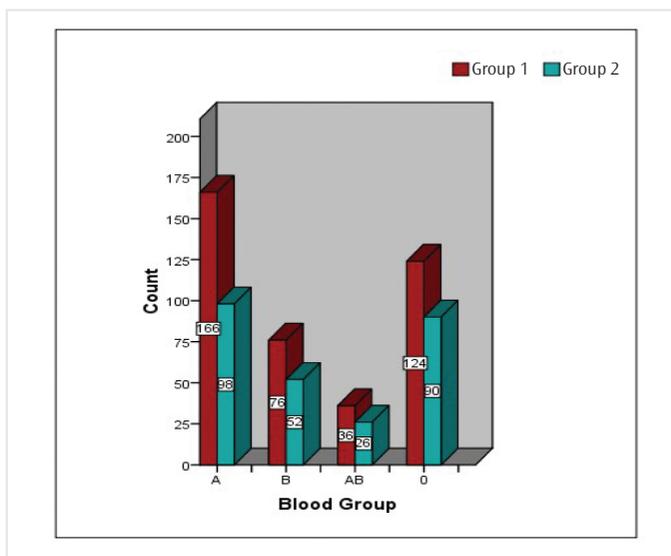
### Results

A total of 668 patients were included in the study. The mean age of the patients included in the study was 30.30±6.73 years, gravida was 3.22±2.1, parity was 2.81±1.75, and the gestational week was 36.73±2.98. One hundred and twenty-nine patients (19.3%) were primiparous, and 539 patients (81.7%) were multiparous. Thirty-one patients (4.6%) had comorbidity. The most frequent comorbidities were hypertension, anemia, and DM. The most frequently observed blood group was A blood group (264 patients, 39.5%), and 591 patients (88.5%) were Rh (+). Blood group and Rh types according to groups are shown in Graphs 1, 2.

Of all patients admitted to the ICU due to HDP (group 1), 23 (8.64%) had pregnancy-related hypertension, 229 had (86.09%) preeclampsia, 10 (3.75%) had eclampsia, and four (1.5%) had HELLP syndrome. The mean length of ICU stay was 2.25±0.79 days.

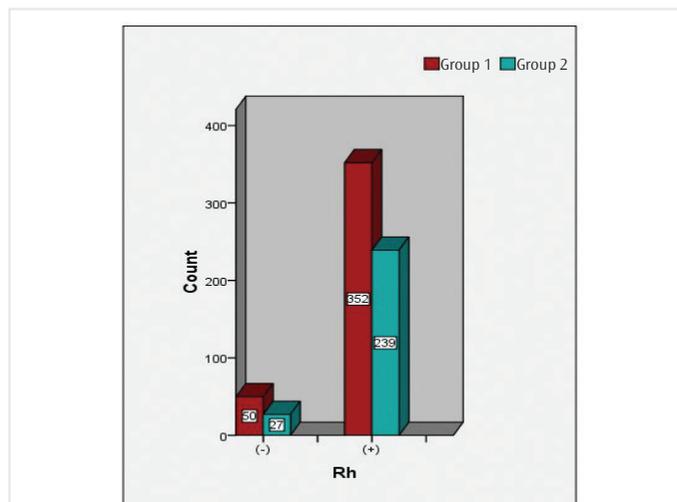
Primiparity
History of preeclamptic pregnancy
Chronic hypertension, chronic kidney disease or both
History of thrombophilia
Multiple pregnancies
<i>In vitro</i> fertilization
Family history for preeclampsia
Type 1 or type 2 Diabetes Mellitus
Obesity
Systemic lupus erythematosus
Advanced maternal age (>40)

\*: Hypertension in pregnancy. American College of Obstetricians and Gynecologists, 2013



**Graphic 1.** Blood group frequency in groups

When group 1 and group 2 were compared in terms of age, gravida, parity, and gestational week, the following results were observed: The mean age of group 1 was higher than group 2, and this difference was statistically significant ( $p=0.028$ ). The mean gravida and parity of group 1 were also significantly higher than group 2 ( $p=0.001$  and  $0.004$ , respectively). The mean gestational age of the patients in group 1 was found to be significantly lower than group 2 ( $p<0.001$ ) (Table 2).



Graphic 2. Distribution of groups according to Rh factor

When group 1 and group 2 were evaluated in terms of primiparity-multiparity, it was found that HDP developed more than expected in the primiparous, and this difference was statistically significant ( $p=0.001$ ). When group 1 and group 2 were evaluated in terms of comorbidity, it was found that HDP developed more than expected in patients with comorbidity, and this difference was statistically significant ( $p<0.001$ ). When group 1 and group 2 were compared in terms of blood groups and Rh factor, no statistically significant difference was found between the groups ( $p=0.706$  and  $0.365$ , respectively) (Table 3).

The logistic regression analysis performed by accepting age, gravida, parity, gestational week, comorbidity and primiparity-multiparity status as independent risk factors for HDP revealed that high gravida [odds ratio (OR): 1.43, 95% CI: 1.142-1.811,  $p=0.02$ ], low gestational week (OR: 0.59, 95% CI: 0.527-0.666,  $p<0.001$ ), the presence of comorbidity (OR: 4.64, 95% CI: 1.817-11.662,  $p=0.001$ ) and primiparity (OR: 0.152, 95% CI: 0.084-0.274,  $p<0.001$ ) were found to be independent risk factors for HDP (Table 4).

## Discussion

In studies examining the relationship between preeclampsia and ABO blood groups in HDP, it has been reported that AB blood group is mostly associated with preeclampsia, and blood group A was also reported in some studies (14-18). Compared to other blood groups, Placental protein 13 was reported to bind more strongly to AB blood group (15). Also, high

Table 2. Comparison of groups in terms of age, gravida, parity and gestational age

	Group 1 (Mean $\pm$ SD) <sup>1</sup>	Group 2 (Mean $\pm$ SD)	p*
Age	31.04 $\pm$ 7.37	29.81 $\pm$ 6.21	0.028
Gravida	3.86 $\pm$ 2.64	2.81 $\pm$ 1.52	0.001
Parity	3.26 $\pm$ 2.28	2.51 $\pm$ 1.20	0.004
Gestational age	35.09 $\pm$ 3.92	37.80 $\pm$ 1.27	<0.001

<sup>1</sup>: standard deviation, \*Mann-Whitney U test result p-value

Table 3. Comparison of groups in terms of blood group, Rh factor, primiparity-multiparity and comorbidity

Blood group	Group 1 (n) (%)	Group 2 (n) (%)	p <sup>#</sup>
A	98 (37.12)	166 (62.88)	0.706
B	52 (40.62)	76 (59.38)	
AB	26 (41.93)	36 (58.07)	
O	90 (42.05)	124 (57.95)	
<b>Rh</b>			
(+)	239 (40.45)	352 (59.55)	0.365
(-)	27 (35.06)	50 (64.94)	
<b>Primiparity-multiparity</b>			
Primiparous	68 (52.72)	61 (47.28)	0.001
Multiparous	198 (36.73)	341 (63.27)	
Total	266	402	-
<b>Comorbidity</b>			
(+)	22 (8.3)	9 (2.2)	<0.001
(-)	244 (91.7)	393 (97.8)	
Total	266 (100%)	402 (100%)	-

<sup>#</sup>: Chi-square test result p-value

**Table 4. Risk factors for the development of hypertensive diseases of pregnancy**

Risk Factor	RR (95% CI)*	p**
Age	0.99 (0.965-1.034)	0.94
Gravida	1.43 (1.142-1.811)	0.02
Parity	1.204 (0.917-1.581)	0.182
Gestational age	0.59 (0.527-0.661)	<0.001
Comorbidity	4.64 (1.817-11.662)	0.001
Primiparity-multiparity	0.152 (0.084-0.274)	<0.001

\*RR: estimated relative risk and 95% confidence interval indicated by odds ratio, \*\*: p value after logistic regression analysis, CI: confidence interval

levels of coagulation factors (including factor VIII and von Willebrand factor) leading to preeclampsia and triggering pathophysiological events were reported in women with AB blood group (11). The fact that thromboembolic events are more common in other blood groups compared to the O blood group is another evidence supporting the association between the AB blood group and preeclampsia (15,18). However, there are studies in the literature indicating that there is no relationship between preeclampsia and the ABO blood group (9-12). In these studies, other factors (such as obesity, cardiovascular disease, and hypertensive diseases) were suggested to play a role in the development of preeclampsia except for the ABO blood group (9). In our study, no relationship was found between preeclampsia and ABO blood groups. However, in accordance with some publications in the literature, we found that the presence of comorbidity in pregnant patients (hypertension, DM) is a risk factor for the development of HDP.

There are some studies in the literature examining the relationship between the Rh factor and preeclampsia. Sharami et al. (12) stated that Rh (-) is a significant risk factor for moderate and severe preeclampsia and that the reason for this may be an immunological incompatibility between mother and fetus. Lee et al. (15) reported that women with Rh (+) had a slightly increased risk for HDP and preeclampsia. Avci et al. (17) also reported that Rh (+) was a risk factor in the development of preeclampsia and postpartum hypertension. The ratio of people with Rh (+) factor in our country is between 83.7-90.83%, and the ratio of Rh (-) is between 9.17-16.30% (19). In our study, 88.5% of the patients were Rh (+), and 11.5% were Rh (-), reflecting the general population. However, we could not find any relationship between the Rh factor and HDP in our study.

In the literature, various risk factors for HDP have been described in various publications. One of these publications is the guideline for hypertension in pregnancy, published in 2013 by The American College of Obstetricians and Gynecologists (4). In addition to the risk factors described in this guideline, in 2016, Rezk et al. (20) stated that having a history of miscarriage might be a risk factor for the development of preeclampsia. In our study, in accordance with the literature, we detected the presence of comorbidity and primiparity as risk factors for HDP development. Another result of our study, which was consistent with the literature, was that the mean age of patients with HDP was statistically higher than the control group. We think that increased frequency of preeclampsia with increasing age may be related to the increase in the incidence of chronic hypertension and other comorbid

diseases with advanced age. Oxidative stress and endothelial dysfunction due to hypertension, DM, and many other chronic diseases may increase the risk of developing preeclampsia. In addition to these risk factors, we found that high gravida and low gestational age were also risk factors for preeclampsia. We could not find any literature examining the relationship between gravida and preeclampsia. In most of the studies in the literature, parity and primiparity-multiparity status were examined for preeclampsia (1,10,13,21,22). The fact that patients with high gravida are older, and the possibility of comorbidity increases with older age may cause preeclampsia to be seen more frequently in this patient group.

In their study, Khader et al. (22) reported that the incidence of preeclampsia was high in pregnant women with a gestational age of  $\leq 31$  weeks. In our study, we found that the gestational week was lower in the HDP group than the control group and that the low gestational week was a risk factor for preeclampsia. We believe that this result was due to the control group, including full-term pregnancies without any problems (mean gestational age:  $37.8 \pm 1.27$ ) and HDP group, including mostly preterm pregnant women (mean gestational age:  $35.09 \pm 3.92$ ). Pregnancy was terminated by cesarean section in most cases in order to maintain the well being of mother and fetus in HDP group.

## Conclusion

No significant relationship was found between HDP and ABO blood groups and Rh factor. We found that high gravida, low gestational age, presence of comorbidity, and primiparity were risk factors for HDP. We think that more comprehensive studies on HDP, which is one of the most important diseases of the pregnancy that has many unclarified issues related to its pathophysiology, will contribute to understanding the pathophysiology of the disease and reducing maternal morbidity and mortality.

**Ethics Committee Approval:** After the approval of the University of Health Sciences, Gazi Yaşargil Training and Research Hospital Ethics Committee (decision no: 27, date: 16/02/2018).

**Informed Consent:** Informed consent was obtained from the parents of the children.

**Peer-review:** Externally peer-reviewed.

**Author Contributions:** Concept - O.U., A.Y.; Design - O.U., C.K.K., C.A., A.Y.; Data Collection and/or Processing - O.U., C.K.K., C.A.; Analysis and/or Interpretation - O.U., A.Y.; Literature Search - O.U., C.K.K., C.A., A.Y.; Writing Manuscript - O.U.

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