Ann Med Res 2021;28(10):1845-52

Annals of Medical Research

DOI: 10.5455/annalsmedres.2020.11.1098

Original Article

Investigation of fetomaternal consequences of placental chorangiosis in women with preeclampsia

Mesut Alci[1], Oguzhan Gunenc[2], Ethem Omeroglu[3]

[1]Department of Gynecology, Aydin Gynecology and Pediatric Hospital, Aydın, Turkey
[2]Department of Gynecology, Konya Education and Research Hospital, Konya, Turkey
[3]Department of Patology, Konya Education and Research Hospital, Konya, Turkey

Abstract

Aim: This study aimed to investigate of fetomaternal consequences of placental chorangiosis in preeclamptic and normal pregnant women.

Materials and Methods: The study population for this retrospective case-control study was consist of 183 pregnant women (91 pregnant women with preeclampsia and 92 healthy pregnant women). The data on the pregnant women and their infants were obtained from their records; additionally, the placental data were obtained by the histopathological examination of placental samples. Chorangiosis is a vascular hyperplastic process in terminal chorionic villi; that >10 capillary vessels in at least 10 villi of the placenta is called chorangiosis.

Results: The case and control groups were similar in terms of their age, gravida, parity, and living and abortion characteristics. The prevalence of chorangiosis, necrosis, and fibrotic villus was high in the placenta of preeclamptic pregnant women; also, their blood values were impaired, and the hospitalization period was longer. Furthermore, the weights and APGAR scores of the infants were low, and the mortality and hospitalization rates were significantly higher. Hence, the presence of preeclampsia and chorangiosis is an important risk factor for the health of both infants and mothers.

Conclusion: Although chorangiosis was directly related to negative maternal and fetal outcomes in pregnant women with preeclampsia, more clinical studies with different perspectives are required because chorangiosis was observed in healthy pregnant women as well.

Keywords: Chorangiosis; fetal and maternal outcomes; preeclampsia

INTRODUCTION

Preeclampsia is a pregnancy-specific, multisystemic, and complex syndrome that affects 5%–8% of all pregnancies worldwide. It is characterized by high blood pressure and associated with significant mortality and morbidity (1). Although high blood pressure occurs after 20 weeks of pregnancy as the main criterion, many systemic symptoms may also accompany preeclampsia (2). Among the obstetric causes of maternal mortality in the world and our country, preeclampsia-eclampsia ranks second with postpartum hemorrhage after cardiovascular diseases (3,4). Additionally, in the United States, approximately 9% of maternal deaths are directly associated with preeclampsia and eclampsia, and more than one-third of severe obstetric outcomes are associated with preeclampsia (5). According to the Republic of Turkey Ministry of Health, the maternal mortality rate was 14.6 per 100.000 live births in 2017. This statistic for Central Anatolia was 13.7 per 100.000 live births below the national average in Turkey (3). In a notification published by the Republic of Turkey Ministry of Health, it was reported that 14% of maternal deaths in 2014 were due to pregnancy-related hypertensive disorders (6).

Preeclampsia is a condition that a previously normotensive pregnant woman's blood pressure rises to more than 140 mmHg systolic and 90 mmHg diastolic. It is usually diagnosed and confirmed by two separate measurements at an interval of four hours after 20 weeks of pregnancy. It can occur alone or be accompanied by proteinuria, thrombocytopenia, increased liver function test (AST-ALT), impaired renal function, visual symptoms, pulmonary edema, severe headache, and pain in the epigastric region (7).

Although the etiopathogenesis of preeclampsia is not clearly understood, various studies state that it is multifactorial and can be related to placental, genetic,

Received: 03.11.2020 **Accepted:** 15.02.2021 **Available online:** 18.10.2021
Corresponding Author: Mesut Alci, Department of Gynecology, Aydin Gynecology and Pediatric Hospital, Aydın, Turkey
E-mail: mesdral@gmail.com

immunity-related, maternal, and fetal origin (8). Regarding its physiopathology, in most studies, it is believed that decreased uteroplacental blood flow can increase oxidative stress and causes systemic manifestations via maternal inflammatory mediators (9,10). Defects in spiral artery remodeling and trophoblast invasion are interrelated, causing hypertensive disorders and fetal growth restriction during pregnancy (11). Hypoperfusion, hypoxia, and ischemia are critical components in the pathogenesis of preeclampsia because placental hypoperfusion and ischemia prepare various factors for maternal blood circulation that alter maternal endothelial cell function and result in the characteristic systemic signs and symptoms of preeclampsia (12,13) Among the late placental changes consistent with ischemia are atherosclerosis (lipid deposition in the arterial wall), fibrinoid necrosis, thrombosis, sclerotic narrowing of arterioles, and placental infarction (14).

Chorangiosis is another change associated with chronic hypoxia in the placenta (15). Chorangiosis is commonly associated with fetal, maternal, and placental disorders. Chorangiosis is correlated with increased fetal morbidity and mortality (15). Chorangiosis is a vascular hyperplastic process in terminal chorionic villi arising from prolonged, low-grade hypoxia in placental tissues (15). Chronic hypoperfusion and tissue hypoxemia can cause excessive villous neoangiogenesis and high proliferative activity of connective tissue, possibly mediated by growth factors (Vascular Epidermal Growth Factor-VEGF, Fibroblast Growth Factor b-bFGF, and Platet Derive Growth Factor-PDGF) (16). The etiology of chorangiosis includes hypertensive diseases of pregnancy, diabetes, and drugs; additionally, the incidence of maternal anemia increases with smoking and living at high altitudes (17).

This study was conducted to examine the frequency of chorangiosis in the placenta of pregnant women with preeclampsia and healthy pregnant women and investigate its fetal, maternal, and clinical outcomes.

MATERIALS and METHODS

Design and Sampling

This was a retrospective case-control study conducted at Konya Education and Research Hospital in Turkey between January 2015 and November 2018, 400 pregnant women, whose placenta was sent for pathological testing, were diagnosed with preeclampsia in this hospital. The pregnant women with preeclampsia constituted the case group, and the healthy pregnant women who gave birth in the hospital during the same period constituted the control group. A power analysis was performed to determine the sample size, which was calculated with an effect size of 0.5, an alpha error margin of 5%, and a power rate of 95%. Accordingly, it was determined that at least 176 (88 cases and 88 controls) pregnant women should be included in the study. Hence, a total of 183 pregnant women, 91 cases, and 92 controls, who met the inclusion and exclusion criteria were included in the study (N = 183). The inclusion and exclusion criteria of pregnant women with preeclampsia are described in Figure 1.

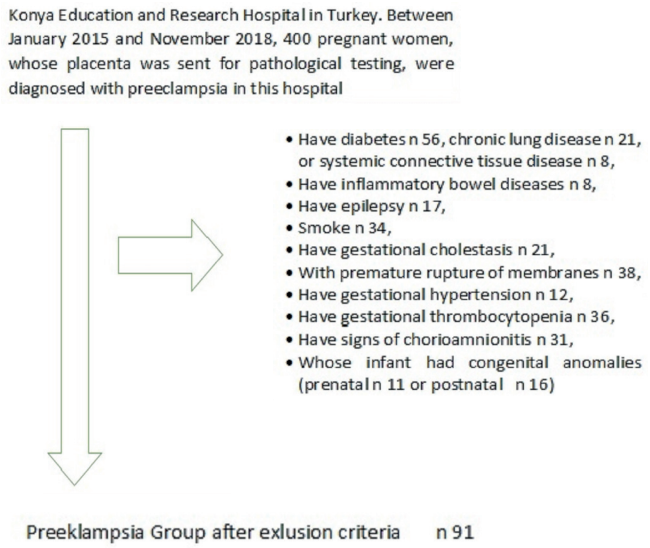

Figure 1. The inclusion and exclusion criteria of pregnant women with preeclampsia

Inclusion Criteria

•Case group: Having a diagnosis of preeclampsia according to the guideline of the American College of Obstetricians and Gynecologists (ACOG) in 2013 (7),

•Control group: Not having a diagnosis of preeclampsia.

Exclusion Criteria (for case and control groups): Pregnant women who have

Diabetes, chronic lung disease, systemic connective tissue disease, inflammatory bowel diseases, epilepsy, gestational cholestasis, premature rupture of membranes, gestational hypertension, gestational thrombocytopenia, signs of chorioamnionitis, an infant with congenital anomalies (prenatal or postnatal), and smoking habits.

For patient's admission to the intensive care unit and neonatal intensive care unit, the World Health Organization (WHO) Maternal Near Miss Criteria (The WHO Near Miss criteria) (18) and the Neonatal Near Miss criteria (19) were used, respectively.

Data Collection

The data were collected by the Pregnant Woman and Newborn Information Form and pathological examination of the placentas.

Pregnant Woman and Newborn Information Form: This form, designed by the researchers according to the literature (7,18-20), included information about the pregnant women's age, gravida, parity, abortion, previous birth characteristics, gestational week, blood pressure, pre and postnatal blood values, ultrasonography results, drugs used, duration of hospitalization, and status of receiving intensive care. Also, this form contained APGAR scores, hospitalization details, and the survival status of the newborns. This data was obtained from patient files and hospital laboratory records.

Histopathological examination of the placentas: The placentas were previously sent to the pathology laboratory because of the clinical requirements. The placental specimens were routinely stained using the hematoxylin-eosin staining method for clinical evaluation of umbilical cord, membrane, and placental pathologies. The archived hematoxylin-eosin stained slides were reexamined by a pathologist using an Olympus brand BX53F model microscope after blinding the information in the case or control group. In the placental samples, the terminal villi were analyzed for chorangiosis, necrosis, and fibrosis. The Altshuler Criteria were used for diagnosing chorangiosis (15,18-22).

Histologic description

•Having more than 10 capillaries in more than terminal chorionic villi in at least 10 different noninfarcted areas in 3 low power fields of the placenta

•Capillaries have distinct basement membranes but not surrounded by a continuous layer of pericytes or associated with stromal fibrosis

•May be associated with other features of villous dysmaturity, chorangioma, amnion nodosum, chronic villitis

•Must distinguish from congestion and tissue ischemia

Cases with >10 capillary vessels in at least 10 villi from non-necrotic areas of the placenta were diagnosed with chorangiosis. Normally, a villus rarely exceeds 5 vessels (18-22).

Data Analysis

The data were analyzed using IBM-Statistical Package for Social Sciences (IBM-SPSS) 22.0 and PASTE programs. The compliance of the data to normal distribution was analyzed using Kolmogorov–Smirnov test and Shapiro–Wilk test. A parametric test (independent sample t-test) was used for analyzing the variables that were normally distributed whereas a non-parametric test (Kruskal–Wallis test) was used for analyzing the variables that were not normally distributed. The descriptive parameters for normally distributed variables were expressed as mean and standard deviation (mean ± SD). Additionally, the median [min–max] values were used for expressing the variables that were not normally distributed. The categorical data were analyzed using Pearson's chi-square test and were expressed as number (n) and percentages (%). Pearson's correlation and Spearman's rho tests were used to examining the correlation between the variables. Single and multi-category logistic regression analysis was used to determine the risk factors associated with adverse maternal outcomes, perinatal outcomes, and intrauterine fetal death (IUFD) in preeclamptic pregnant women. Multivariate regression analysis includes age, systolic and diastolic blood pressure, Hemoglobin, Platelet, Urea, Creatinine, AST, ALT, LDH, Chorangiosis, necrosis, and fibrotic villi. The data were analyzed at a 95% confidence interval (CI) and $p < .05$ was considered statistically significant.

Ethical Considerations

The principles of the Helsinki Declaration were followed in the study. Additionally, approval was obtained from the University of Health Sciences, Konya Education and Research Hospital, TUEK (07.06.2018/774).

RESULTS

In this section, results of this study conducted to investigate the fetomaternal consequences of placental chorangiosis in preeclamptic and normal pregnant women are given.

As shown in Table 1, 183 pregnant women (91 preeclamptic and 92 controls) were included in the study. There was no significant difference between the ages of the women in preeclamptic and control groups ($p = .931$). The primipara ratio and systolic blood pressure (SBP), diastolic blood pressure (DBP), Urea, Creatinine, AST, ALT, and LDH levels were significantly higher in the preeclamptic group than in the control group ($p < .05$). However, the platelet levels of the preeclamptic group were found to be lower than those of the control group ($p < .05$) (Table 1).

Table 1. Comparison of demographic and clinical characteristics in both groups

Characteristics	Preeclamtic n=91	Control n=92	p value
Age*	29.64 ±6.08	29.72±6.34	.931
Parity***			
Primipara	28 (%30.8)	14 (%15.2)	.010
Multipara	63 (%69.2)	78 (%84.8)	
Systolic blood pressure-SBP(mm-Hg)*	171.26± 15.87	115.76± 11.50	<.001
Diastolic blood pressure-DBP(mm-Hg)*	108.96±8.18	66.41±7.78	<.001
Hemoglobin-Hbg (g/dl)*	10.23±1.86	10.67±1.56	.086
Platelets-Plt (10^3/mm^3)*	176.55±70.94	198.37±60.86	.027
Urea (mg/dl)**	24.41 (7-63)	16.65 (7-40)	<.001
Creatinine (mg/dl)**	0.74 (0.43-1.70)	0.61 (0.45-0.85)	<.001
Aspartat aminotransferaz-AST (U/L)**	105.56 (12-3375)	21.75 (12-39)	.034
Alanin aminotransferaz-ALT (U/L)**	66.41 (5-1783)	12.55 (4-37)	.014
Laktat dehidrogenaz_LDH (U/L)*	415.17±139.33	251.70±144.08	.004

*Independent Sample t-test (Mean ± Standard Deviation), **Kruskal Wallis Test, Nonparametric Post-hoc Test (Median [min-max]), ***Pearson chi-square test (%)

As table 2 shows the presence of chorangiosis, necrosis, and fibrotic villus in the placenta of preeclamptic pregnant women was significantly higher than in the control group (p < .05) (Table 2).

In preeclamptic pregnancies, a negative and significant correlation was found between placental chorangiosis and SBP (r = −.453, p < .001), DBP (r = −.468, p < .001), and serum urea (r = −.166, p = .024) and creatinine (r = −.157, p = .034) levels. A positive and significant correlation was found between placental necrosis and SBP (r = .395, p < .001), DBP (r = .395, p < .001) and serum urea (r = .224, p = .002) and creatinine (r = .213, p = .004) levels. Additionally, a negative and significant correlation was found between placental fibrotic villus and SBP (r = −.321, p < .001) and DBP (r = −.299, p < .001) (Table 3).

Table 2. Comparison of placental histopathological findings in both groups

Histopathological findings	Preeclamtic n=91	Control n=92	p value
Chorangiosis			
Positive	57 (%62.6).	14 (%15.2)	<.001
Negative	34 (%37.4)	78 (%84.8)	
Necrosis			
Positive	29 (%31.9)	2 (%2.2)	<.001
Negative	62 (%68.1)	90 (%97.8)	
Fibrotic villi			
Positive	50 (%54.9)	19 (%20.7)	<.001
Negative	41 (%45.1)	73 (%79.3)	

* Pearson chi-square test (%)

Table 3. Correlation analysis of risk factors associated with adverse postnatal outcomes in preeclamptic pregnant women

Factors Associated	Adverse Postnatal Outcomes					
	Chorangiosis		Necrosis		Fibrotic villi	
	r	p	r	p	r	p
Age	.036	ns*	.033	ns	.144	ns
SBP (mm-Hg)	-.453	<.001	.395	<.001	-.321	<.001
DBP (mm-Hg)	-.468	<.001	.395	<.001	-.299	<.001
Hgb (g/dl)	-.004	ns	.0141	ns	-.041	ns
Plt (10^3/mm^3)	.016	ns	-.017	ns	.005	ns
Urea (mg/dl)	-.166	.024	.224	.002	-.062	ns
Creatinine (mg/dl)	-.157	.034	.213	.004	-.118	ns
AST (U/L)	-.013	ns	-.026	ns	-.073	ns
ALT (U/L)	-.013	ns	-.023	ns	-.084	ns
LDH (U/L)	.040	ns	-.053	ns	-.097	ns

*Non significant

Table 4. Intergroup comparison of ultrasonography and perinatal features

		Preeclamtic n=91	Control n=92	p value*
Fetal Biometry **		31.47 (20-40)	37.64 (34-41)	<.001
Amniotic fluid index ***	Oligohydroamnios	47 (%51.6)	2 (%2.2)	<.001
	Normal	44 (%48.4)	90 (%97.8)	
Umbilical artery Doppler ***	Anormal	46 (%50.5)	0	<.001
	Normal	45 (%49.5)	92 (%100)	
Retroplacental pathology (c)**	Detachment	9 (%9.9)	1 (%1.1)	.009
	Normal	82 (%90.1)	91 (%98.9)	
Form of delivery ***	Normal vaginal delivery	5 (%5.5)	16 (%17.4)	.010
	Cesarean section	86 (%94.5)	76 (%82.6)	
Total fetal weight **		1708.00 (350-4330)	3137.50 (2200-4350)	<.001
Intrauterine fetal death ***		19 (%20.9)	0	<.001
APGAR 1/5. Munite ***	≤ 3	27 (%29.7)	0	<.001
	4-6	36 (%39.6)	1 (%1.1)	
	≥ 7	28 (%30.8)	91 (%98.9)	
NICU Hospitalization ***	Yes	52 (%57.1)	4 (%4.3)	<.001
	No	39 (%42.9)	88 (%95.7)	
NICU Hospitalization mean day (Min-max)		17 (1-135)	9 (2-13)	
Infant survives ***	Survive	63 (%69.2)	92 (%100)	<.001
	Death	28 (%30.8)	0	

* p <.05 significantly ; ** Kruskal Wallis Test, Nonparametric Post-hoc Test (Median [min-max]) ; ***Pearson chi-square test (percent of %)

As Table 4 manifests, the fetal ultrasonographic biometric measurements in the preeclamptic pregnant women were lagging significantly compared to those in the control group (p < .001). The incidences of placental detachment after delivery were 9 (9.9%) in the preeclamptic group and 1 (1.1%) in the control group. Hence, the rate of placental detachment in the preeclamptic group was significantly higher than in the control group (p = .009). Furthermore, the intrauterine fetal mortality rate was 19 (20.9 %) in the preeclampsia group, but there were no IUFDs in the control group. The preeclampsia group had 27 (29.7%) newborns with an APGAR score of ≤3, 36 (39.6%) newborns with an APGAR score between 4 and 6, and 28 (30.8%) newborns with an APGAR score of ≥7. On the contrary, the control group had 1 (1.1%) newborn with an APGAR score between 4 and 6 and 91 (98.9%) newborns with an APGAR score of ≥7. In the preeclamptic women, the proportion of newborns with an APGAR score of <7 at 1/5 minutes after birth was found to be significantly higher than in the control group (p < .001). Additionally, 52 (57.1%) newborns born from the women in the preeclamptic group were admitted to the intensive care unit, and their average length of stay in the intensive care unit was 17 [1–135] days. Conversely, only 4 (4.3%) newborns from the women in the control group were admitted to the intensive care unit, and their average length of stay in the intensive care unit was 9 [2–13] days. The rate of admission and the length of stay in the intensive care unit was found to be significantly higher for the preeclamptic newborns than the controls (p < .001). The infant death in the postpartum neonatal period was 28 (30.8%) in the preeclamptic group, whereas there was no death in the control group (Table 4).

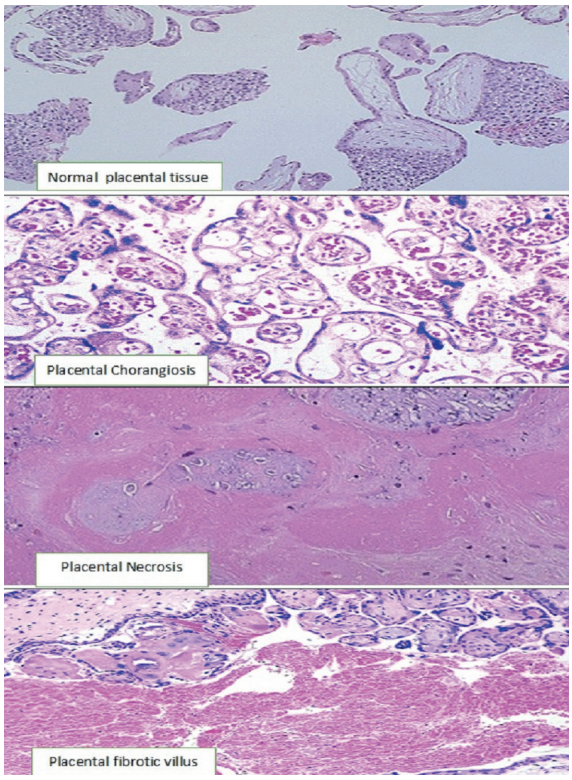

Figure 2. Some microscopic figures representing chorangiosis, necrosis, fibrosis, and normal placentas

Table 5. Regression analysis of risk factors associated with adverse postnatal outcomes, intrauterine fetal death, and early-onset preeclampsia

	Adverse Postnatal Outcomes		Intrauterine Fetal Death (IUFD)		Early Onset Preeclampsia (EOPE)	
	OR* (CI**%95	p value	OR (CI%95)	p value	OR (CI%95)	p value
Age	0.960 (0.909-1.014)	.141	0.963 (0.891-1.042)	.351	0.976 (0.926-1.028)	.358
SBP (mm-Hg)	0.981 (0.934-1.031)	.453	1.065 (1.064-1.096)	<.001	1.062 (1.043-1.082)	<.001
DBP (mm-Hg)	1.097 (1.037-1.160)	.008	1.129 (1.055-1.208)	<.001	1.108 (1.072-1.145)	<.001
Hgb (g/dl)	1.227 (0.996-1.512)	.055	0.962 (0.724-1.278)	.787	1.109 (0.912-1.349)	.300
Plt (10^3/mm^3)	0.996 (0.991-1.001)	.112	1.001 (0.995-1.008)	.639	0.997 (0.992-1.002)	.193
Urea (mg/dl)	1.071 (1.031-1.111)	<.001	1.043 (1.002-1.086)	.039	1.054 (1.018-1.092)	.003
Creatinine (mg/dl)	4.494 (1.051-9.904)	.001	9.410 (7.610-11.637)	<.001	2.193 (0.287-16.769)	.003
AST (U/L)	1.003 (1.000-1.007)	.054	1.000 (0.998-1.002)	.892	1.004 (1.000-1.007)	.053
ALT (U/L)	1.004 (1.000-1.007)	.079	0.999 (0.995-1.004)	.810	1.003 (1.000-1.007)	.085
LDH (U/L)	1.001 (1.000-1.002)	.168	1.000 (0.998-1.001)	.681	1.001 (1.000-1.002)	.171
Chorangiosis	4.331 (2.156-8.699)	<.001	3.960 (1.429-10.969)	.008	5.077 (2.557-10.083)	<.001
Necrosis	0.296 (0.133-0.660)	.003	0.224 (0.082-0.617)	.004	0.216 (0.096-0.484)	<.001
Fibrotic villi	2.248 (1.149-4.397)	.018	1.977 (0.761-5.140)	.162	3.013(1.573-5.889)	.001

* OR: odds ratio ; ** Confidence Interval

The risk factors that may be associated with adverse postnatal outcomes, Intra Uterine Fetal Death (IUFD), and early-onset preeclampsia (EOPE) in the preeclamptic pregnant women were evaluated by logistic regression analysis (Table 5). In the preeclamptic group, the risk factors associated with adverse postnatal outcomes were high, serum urea, and creatinine levels (p<.01). Besides, placental chorangiosis, necrosis, and fibrotic villi were found to be associated with adverse postnatal outcomes (p<.01). Also, SBP, DBP, urea, creatinine, placental chorangiosis, and necrosis were found to be the risk factors for IUFD and EOPE in preeclamptic pregnant women, respectively (p<.01).

Figure 2 plots some microscopic figures representing chorangiosis, necrosis, fibrosis, and normal placentas.

DISCUSSION

The purpose of this study was to investigate the chorangiosis in the placenta of pregnant women with preeclampsia and to examine the effects of hypoxia on the placenta and maternal and fetal outcomes.

There was no statistically significant difference between the case and control groups in terms of age, gravida, living children, and abortion characteristics (p > .05).

In this study, placental chorangiosis, necrosis, and fibrotic villus rates were significantly higher in the placentas of preeclamptic pregnant women compared to those of the control group. It is an expectable result that chorangiosis develops in a hypoxic environment and is detected significantly more in the preeclamptic group due to a decrease in uteroplacental blood flow. Placental necrosis and fibrotic villi together with chorangiosis are a response to hypoxia in the placenta of pregnant women with preeclampsia due to insufficient uteroplacental blood flow (23-27). However, it is understood that chorangiosis is not a preeclampsia-specific condition, as it was also seen in the control group, which is consistent with other publications (27,28).

In this study, increased placental chorangiosis and necrosis rates, increased DBP, increased prenatal AST level, decreased postpartum thrombocyte levels were determined as the risk factors associated with adverse maternal outcomes in preeclamptic pregnant women. The diagnostic criteria for severe preeclampsia include increased DBP and AST and decreased platelets, which are detected as adverse maternal outcomes in pregnant women with preeclampsia (9). In some studies, it was reported that the effect of chorangiosis and placental necrosis on adverse maternal outcomes may be due to mediators released through tissue hypoxia (23,25,27). But, it can also be seen in placentas that are considered to be normal and healthy (28). However, in some studies, it was stated that chorangiosis may be a consequence rather than a cause (28).

In this study, adverse perinatal outcomes were found to be associated with increased DBP. Among the histopathological findings of the placenta, only the increased placental chorangiosis rate was determined to be a risk factor associated with adverse perinatal outcomes in preeclamptic pregnant women. Impaired fetal circulation is directly related to both intrauterine deaths and negative consequences during the neonatal period (22,29). In terms of its etiopathogenesis, the negative effect of chorangiosis on negative perinatal outcomes, which also contains hypoxia after hypoperfusion, is related to placental insufficiency (23-25,30). On the contrary, the fact that it can also be seen in normal, healthy pregnant women suggests that its development is not limited to hypoxic conditions and is related to hypoperfusion (23,25). In conclusion, chorangiosis and necrosis, which are among the histopathological findings in the placentas of preeclamptic pregnant women, were found to be the risk factors associated with adverse maternal outcomes and intrauterine and fetal death. Although placental necrosis was not directly related to adverse perinatal outcomes, it had an indirect effect because it was positively correlated with placental chorangiosis. Also, placental fibrotic villi were not considered as a risk factor associated with adverse maternal outcomes, perinatal outcomes, or IUFD in preeclamptic pregnant women. Additionally, chorangiosis causes adverse maternal and fetal consequences (15,16,23,25,26,30). Since placental necrosis is associated with chorangiosis, it adversely affects the perinatal consequences.

In this study, Preeclampsia, and chorangiosis, which may occur in impaired uteroplacental blood flow, had a strong correlation, but necrosis was found to have indirect effects. Although it was determined that chorangiosis causes negative maternal and fetal outcomes, it was also observed in the control group, suggesting that chorangiosis may not only be a response to hypoxia. It was reported that chorangiosis can occur in women with diabetes, gestational hypertensive diseases, and fetal growth restriction, in addition to those who smoke and live at high altitudes (15,16,23-26,28,30,31). The fact that chorangiosis also occurs in healthy pregnancies may suggest a relation with hypoperfusion. A relationship between uteroplacental flow disorder and chorangiosis has been reported (15,16,23,30). Hence, chorangiosis may be an adaptation of the placenta to impaired uteroplacental flow or may cause further deterioration of the existing flow.

Some limitations should be taken into account when evaluating the results of this study. The first of these is the termination of pregnancy in the preeclampsia group for treatment purposes regardless of the gestational week. In other words, the gestational week of a fetus whose mother has preeclampsia is shorter. However, normal healthy pregnant women delivered between 39-41 weeks. Also, intrauterine fetal growth retardation (IUFR) is higher in fetuses of pregnant women whose preeclampsia begins before the 34th week of pregnancy (Early Onset Preeclampsia-EOPE). Therefore, differences were observed in the biometric measurements of the

fetuses of pregnant women whose preeclampsia started before and after the 34th week. Furthermore, although some of the patients gave information about the date of their last menstrual period, biometric measurements were used for determining gestational week because some of them did not know it. The average gestational week in the pregnant group with preeclampsia was calculated as 32. The difference in gestational weeks of pregnant women with preeclampsia and healthy pregnant women may have caused some differences in fetal outcomes. Therefore, it should be kept in mind that the differences determined between the fetal outcomes of pregnant women with preeclampsia and healthy pregnant women cannot be related only to chorangiosis.

Another limitation of this study is related to obesity. The body weight of all women at delivery is known. However, since most of the patients were not followed up in our hospital during pregnancy, the weight information obtained during pregnancy or the body weight before pregnancy could not be obtained. Therefore, obesity could not be excluded in both groups.

The detection of corangiosis may have a clinical significance in determining the causes of fetal morbidity and mortality. Especially in the case of fetal morbidity and mortality, the detection of placental corangiosis may be of clinical importance. In these cases, the physician may be blamed for not determining the appropriate time of delivery, delaying delivery, or using the wrong methods at birth.

In this study, the incidence of chorangiosis was significantly higher in the preeclamptic group and was found to be directly associated with negative maternal and fetal outcomes. Since chorangiosis was also observed in the control group, further studies are recommended.

CONCLUSION

Preeclampsia is one of the leading causes of maternal and fetal morbidity and mortality worldwide. As a decrease in uteroplacental blood flow is a common etiopathogenesis of preeclampsia and chorangiosis, we evaluated chorangiosis in placentas of preeclamptic and normal pregnant women whose clinical data were available.

In general, this study showed that in the preeclamptic group, chorangiosis frequently coexisted with adverse maternal and fetal outcomes. The fetal and neonatal mortality rate reached 30%, which is quite high. Also, the incidence of placental detachment was found to be 9 times higher in the preeclamptic group compared to the control group. Among the other histopathological data, necrosis and fibrotic villi affected chorangiosis, which eventually contributed to the negative outcomes due to the resultant chorangiosis.

Chorangiosis was observed not only in pregnant women with preeclampsia but also in healthy pregnant women without any known diseases. Since there were no neonatal and fetal losses in the control group, it would be inappropriate to suggest that chorangiosis was solely responsible for the adverse outcomes. If chorangiosis is defined as an increase in veins in terminal villi based on hypoxia, it may be suggested that chorangiosis may be an adaptation mechanism of the placenta in hypoxic conditions.

Although it was found that chorangiosis is directly associated with adverse maternal and fetal outcomes in pregnant women with preeclampsia, further studies on this topic with different clinical perspectives are needed as it was also observed in healthy pregnant women.

Competing Interests: The authors declare that they have no competing interest.

Financial Disclosure: There are no financial supports.

Ethical Approval: S.B. University Konya Training and Research Hospital TUEK approval. Decision dated 07.06.2018 and numbered 8929119/774.

REFERENCES

1. Henderson JT, Thompson JH, Burda BU, et al. Screening for Preeclampsia: A systematic evidence review for the US preventive services task force. Rockville, MD: Agency for Healthcare Research and Quality (US) 2017; Apr. Report No.: 14-05211-EF-1. PMID: 28813128.
2. Ananth CV, Keyes KM, Wapner RJ. Pre-eclampsia rates in the United States, 1980-2010: age-period-cohort analysis. BMJ 2013;347:6564.
3. TR. Ministry of Health Health Statistics Yearbook. https://dosyamerkez.saglik.gov.tr/Eklenti/27344,saglik-istatistikleri-yilligi-2017-haber-bultenipdf.pdf?0 Access date: 02.11.2020
4. Ronsmans C, Graham WJ. Maternal mortality; who, when, where and why. Lancet 2006;368:1189-200.
5. Creanga AA, Berg CJ, Ko JY, et al. Maternal mortality and morbidity in the United States: where are we now? J Womens Health (Larchmt) 2014;23:3-9.
6. TR. Ministry of Health, Public Hospitals Institution of Turkey. Intervention steps for emergency hypertension in pregnant and postpartum women. https://www.tmftp.org/files/bildiriler/tc-saglik-bakanligi-gebelik-ve-hipertansiyon-25042016.pdf Access date 02.11.2020
7. American College of Obstetricians and Gynecologists; Task Force on Hypertension in Pregnancy. Hypertension in pregnancy. Report of the American College of Obstetricians and Gynecologists' Task Force on Hypertension in Pregnancy. Obstet Gynecol 2013;122:1122-31.
8. Huppertz B. Placental origins of preeclampsia: challenging the current hypothesis. Hypertension 2008;51:970-5.
9. Myatt L, Roberts JM. Preeclampsia: syndrome or disease? Curr Hypertens Rep 2015;17:83.
10. Redman C. Pre-eclampsia: a complex and variable disease. Pregnancy Hypertens 2014;4:241-2.
11. Pijnenborg R, Vercruysse L, Hanssens M. The uterine spiral arteries in human pregnancy: facts and controversies. Placenta 2006;27:939-58.

12. Makris A, Thornton C, Thompson J, et al. Uteroplacental ischemia results in proteinuric hypertension and elevated sFLT-1. Kidney Int 2007;71:977-84.
13. Maynard S, Epstein FH, Karumanchi SA. Preeclampsia and angiogenic imbalance. Annu Rev Med 2008;59:61-78.
14. Zhou Y, Damsky CH, Fisher SJ. Preeclampsia is associated with failure of human cytotrophoblasts to mimic a vascular adhesion phenotype. One cause of defective endovascular invasion in this syndrome? J Clin Invest 1997;99:2152-64.
15. Suzuki K, Itoh H, Kimura S, et.al. Chorangiosis and placental oxygenation. Congenit Anom (Kyoto) 2009;49:71-6.
16. Barut A, Barut F, Kandemir NO, et al. Placental chorangiosis: the association with oxidative stress and angiogenesis. Gynecologic and Obstetric Investigation. 2012;73:141-51.
17. Srinivasan AP, Parijatham BO, Lavanya KA. Prospective study of villous capillary lesions in complicated pregnancies. J Pregnancy 2014;1-5.
18. Say L, Souza JP, Pattinson RC. WHO working group on maternal mortality and morbidity classifications. maternal near miss--towards a standard tool for monitoring quality of maternal health care. Best Pract Res Clin Obstet Gynaecol 2009;23:287-96.
19. Santos J.P. Cecatti J.G. Serruva S.J. et al. Neonatal near miss: the need for a standard definition and appropriate criteria and the rationale for a prospective surveillance system Clinic (Sao Paulo). 2015;70:820-6.
20. Williams B, Mancia G, Spiering W, et al. ESC Scientific Document Group, 2018 ESC/ESH Guidelines for the management of arterial hypertension: The task force for the management of arterial hypertension of the European Society of Cardiology (ESC) and the European Society of Hypertension (ESH). European Heart J 2018;39: 3021-104.
21. Hall JE, Granger J P, do Carmo JM, et al. Hypertension: physiology and pathophysiology. Comprehensive Physiology 2012;2:2393-442.
22. Sharma D, Shastri S, Sharma P. Intrauterine Growth Restriction: Antenatal and Postnatal Aspects. Clin Med Insights Pediatr 2016;10:67-83.
23. Altshuler G, Chorangiosis: an important placental sign of neonatal morbidity and mortality. Arch Pathol Lab Med 1984;108:71-4.
24. Benirschke K, Kaufmann P. Pathology of the Human Placenta. Third edition. Springer, New York, 1995;715-6.
25. Schwartz D.A. Chorangiosis and its precursors: underdiagnosed placental indicators of chronic fetal hypoxia, Obstet Gynecol Surv 2001;56:523-5.
26. Akbulut M, Sorkun HC, Bir F, et al. Chorangiosis: The potential role of smoking and air pollution. Pathology – Research and Practice 2009;205:75-81.
27. Baergen RN, Gersell DJ, Kraus FT. Diseases of the Placenta. In: Kurman R., Hedrick Ellenson L., Ronnett B. (eds) Blaustein's Pathology of the Female Genital Tract. 7th edition. Springer, Cham; 2019.p.1223-305.
28. Asmussen I. Ultrastructure of the villi and fetal capillaries of the placentas delivered by non-smoking diabetic women (white grup D). Acta Pathol Microbiol Immunol Scand A 1982;90:95-101.
29. Madazlı R, Somunkiran A, Calay Z, et al. Histomorphology of the placenta and the placental bed of growth restricted foetuses and correlation with the doppler velocimetries of the uterine and umbilical arteries. Placenta 2003;24:510-6.
30. Burton GJ, Reshetnikova OS, Milovanov AP, et al. Stereological evaluation of vascular adaptations in human placental villi to differing forms of hypoxic stress. Placenta 1996;17:49-55.
31. Rabinovich A, Holtzman K, Shoham-Vardi I, et al. Oligohydramnios is an independent risk factor for perinatal morbidity among women with pre-eclampsia who delivered preterm. J Matern Fetal Neonatal Med. 2019;32:1776-82.