

Histolojik Koroamniyonitin Erken Doğum Üzerindeki Etkisi

Oya Demirci, Özlem Bozoklu, Elif Demirci, Semih Tuğrul, Ayşe Gürbüz, Sadiye Eren, Handan Çetiner

Adres: Zeynep Kamil Kadın ve Çocuk Hastalıkları Eğitim ve Araştırma Hastanesi Perinatoloji Kliniği,
Üsküdar/İstanbul 34668. Cep: 05058241417

ÖZET:

Amaç: Histolojik koroamniyonitin erken doğum üzerindeki etkisini ve erken doğumu etkileyen diğer faktörleri araştırmak amaçlanmıştır. **Yöntem:** Çalışmada aktif eylemde olan , erken membrane rupture olmayan ve tekil gebelikleri içeren 65 preterm ve 71 term gebelerden alınan plasentalar histopatolojik olarak incelenmiştir. Bunun yanında tüm hastalardan obstetric anamnez, kan, idrar ve vajinal kültür örnekleri alınarak olası etiyolojik faktörler araştırılmıştır.

Bulgular: Plasentaların histopatolojik olarak incelenmesi sonrası preterm doğumlar içerisinde 2 (3.1%), term doğumlar içerisinde 1 (%1.4) oranında histolojik koroamnionit saptanmıştır. Geçirilmiş sezaryen doğum öyküsü, bu gebeliğinde saptanan gestasyonel diyabet ve idrar yolu enfeksiyonu hikayesi preterm doğum yapan gebelerde istatistiksel anlamlı olarak daha yüksek bulunmuştur.

Sonuç: Bu çalışmanın sonucunda histolojik koroamnionit ve preterm doğum ilişkisi koroamnionit vakalarının sayıca yetersiz olmasından dolayı söylenemez. Bu nedenle bu konuda daha fazla sayıda ve uzun süreli çalışmalara ihtiyaç vardır.

Anahtar Kelimeler: Koroamnionit, Histopatoloji, Preterm doğum

ABSTRACT:

Histologic Chorioamnionitis and Preterm Delivery

Objective: To determine the effects of histological chorioamnionitis in preterm delivery and to investigate the other causes.

Material and Methods: The study group consisted of 65 preterm and 71 term pregnancies who are singleton, in active labor and without rupture of membranes. The patients were questioned about their obstetric history, and blood, urine sample for laboratory analysis and vaginal culture were obtained. All placentas were evaluated histopathologically and searched for histological chorioamnionitis.

Results: In 2 (3.1%) of 65 preterm labors and 1 (%1.4) of 71 term labors, histological chorioamnionitis was detected. In terms of histological chorioamnionitis, there was no statistical difference between the groups ($p>0.05$). Also, in terms of history of previous cesarean section, gestational diabetes mellitus and history of urinary tract infection, statistically significant difference were present between preterm and term groups ($p=0.007, 0.043, 0.04$).

Conclusion: The result of our study does not show the relationship between histological chorioamnionitis and preterm delivery. It might be due to the small size of our sample group. Therefore, a better understanding of the presence of histological chorioamnionitis on preterm delivery, there is requirement of longdated several studies.

Keywords: Chorioamnionitis; Histopathology; Preterm delivery

INTRODUCTION

6-10% of all births are preterm that account for 70% of the perinatal mortality and nearly half of the long term neurologic morbidity (1, 2). In approximately half of the cases the cause of the preterm labor is not known (3). In case

of preterm delivery with unknown etiology a subclinical intrauterine infection might be responsible (4, 5). Recent studies suggested a positive relationship between preterm delivery, chorioamnion infection, and histological

chorioamnionitis (polymorphonuclear leukocytic infiltration of the amnion and chorion) (6). Unlike clinically apparent chorioamnionitis, specific signs and symptoms may not be seen in case of histological chorioamnionitis and preterm labor may be the only sign (7). Histological chorioamnionitis is reported to be observed more commonly in association with preterm delivery than with delivery at term (8).

In this prospective study, our objective was to evaluate histological chorioamnionitis as an etiologic factor of preterm delivery.

MATERIAL AND METHODS

All patients who are singleton, in active labor, without membrane rupture were enrolled between April 2008 and June 2008 from the labor and delivery unit of Zeynep Kamil Gynecologic and Pediatric Training and Research Hospital which is a tertiary center for high risk pregnancies. The institution's ethics committee approved the study and informed consent was obtained from the participants. Women were excluded from enrollment if they had multiple gestations, preeclampsia, anhydramnios, uterine or fetal anomalies, cervical incompetence, fetal demise and clinically apparent chorioamnionitis. Women who needed cesarean section because of fetal distress were not included in the study. Preterm delivery was accepted as a delivery occurring before the completion of 37 weeks of gestation. The case group consisted of 65 women who were admitted to the hospital with preterm labor and with intact membranes at a gestational age of 20 to 36+6 weeks and who were delivered before 37 weeks. Preterm labor was defined as regular painful contractions occurring at least 3 times in every 10 minutes accompanied by progressive cervical dilatation or by a Bishop score >4 that included $\geq 50\%$ cervical effacement and ≥ 1 cm dilatation (9). The control group consisted of 71 women without preterm labor who were delivered at ≥ 37 weeks' gestation. Gestational age was estimated by the date of the mother's last menstrual period and ultrasonography (10). Following admittance of the patients to the clinic, they were questioned about their obstetric

history, and blood, urine sample for laboratory analysis and vaginal culture were obtained. Following delivery all placentas were weighed and fixed with 10% buffered formalin. All placentas were investigated macroscopically and microscopically. Thereafter, tissue samples were obtained from each placenta including two sections from the umbilical cord, two 1-cm wide slices from the chorionic plate, two decidual sections from the placental disc, and a roll of membranes extending from the rupture point to the placental margin. All samples were embedded in paraffin and tissue blocks were stained with hematoxylin and eosin. Histologic examination was performed by a pathologist who was blinded to the clinical information.

The histopathologic diagnosis of chorioamnionitis was made when one focus of at least five polymorphonuclear leukocytes was present at the amnion and chorion-decidua (11). The chi-square test was used to compare the statistical difference between patient groups and p 0.05 values were accepted as statistically significant

RESULTS

The study group consisted of 136 patients, of these 65 (47.8%) had preterm delivery and 71 (52.2%) were delivered at term. 7 (10.8%) of 65 preterm deliveries were < 34 gestational age and the remaining 58 (89.2%) were ≥ 34 gestational age. The mean age of preterm group was significantly lower than the term group. In the preterm group, the mean of gravidity and parity was significantly lower than the term group. In terms of BMI (body mass index), number of abortion, occupation of the patients, educational background of the patients and husbands, economical condition, history of smoking, history of preterm delivery, and anemia, vaginitis and proliferation bacteria in vaginal culture, nephrolithiasis at diagnosis, there was no statistically significant difference between the preterm and term groups. (**Table 1**). In 2 (3.1%) of 65 preterm labors and 1 (1.4%) of 71 term labors, histological chorioamnionitis was detected. In terms of histological chorioamnionitis, there was no statistical difference between the groups (**Table 2**).

Table 1: Comparison of preterm and term groups according to the demographic and clinical characteristics

	Preterm group (n: 65)	Term group (n: 71)	p
Maternal age	24,75±5,43	27,42±6,07	0,008
BMI	26,43±3,41	27,19±3,17	NS
Gravidity	1,95±1,23	2,52±1,52	0,019
Parity	1,78±1,01	2,24±1,25	0,022
Abortion	0,11±0,4	0,15±0,53	NS
Working	- 95,40%	97,20%	NS
	+ 4,60%	2,80%	
Educational background of patient			NS
Elementary school	75,40%	78,90%	
Highschool	16,90%	11,30%	
University	1,50%	2,80%	
Illiterate	6,20%	7,00%	NS
Educational background of husband			
Elementary school	76,90%	70,40%	
Highschool	15,40%	23,90%	
University	6,20%	4,20%	
Illiterate	1,50%	1,40%	NS
Economic condition			
Low	12,30%	9,90%	
Medium	73,80%	70,40%	NS
High	13,80%	19,70%	
Smoking	- 92,30%	91,50%	NS
	+ 7,70%	8,50%	
History of PTD	- 95,20%	97,10%	NS
	+ 4,80%	2,90%	
Anemia	- 53,80%	38,00%	NS
	+ 46,20%	62,00%	
Vaginitis	- 33,80%	43,70%	NS
	+ 66,20%	56,30%	
Nephrolithiasis	- 96,90%	98,60%	NS
	+ 3,10%	1,40%	
Proliferation of bacteria in vaginal culture	- 83,70%	72,90%	NS
	+ 16,30%	27,10%	

BMI; body mass index, PTD, preterm delivery

Table 2: Comparison of preterm and term groups in terms of histologic chorioamnionitis, history of previous Cesarean section, gestational diabetes mellitus and history of urinary tract infection.

		Preterm group (n:65)	Term group (n:71)	p
Histologic Chorioamnionitis	-	96,90%	98,60%	NS
	+	3,10%	1,40%	
History of Previous Cesarean Section	-	87,67%	100,00%	0,007
	+	12,33%	0,00%	
Gestational Diabetes Mellitus	-	92,70%	100,00%	0,043
	+	7,30%	0,00%	
History of Urinary Tract Infection	-	46,20%	64,80%	0,04
	+	53,80%	35,20%	
Urinary Tract Infection	-	60,70%	59,70%	NS
	+	39,30%	40,30%	

In the study, 8 (12.33%) of 65 preterm patients, had a history of previous cesarean section. The mean history of previous cesarean section in the preterm group was significantly higher than the term group. Also, there was a statistically significant difference between preterm and term groups in terms of presence of gestational diabetes mellitus ($p=0.043$). 35 (53.8%) of 65 women in the preterm group and 25 (35.2%) of 71 women in the term group had a history of urinary tract infection during antenatal visits. While in terms of history of urinary tract infection, there was a statistically significant difference between the groups, there was no significant difference

between groups in terms of presence of urinary tract infection during admission to the hospital for labor (Table 2).

DISCUSSION

Chorioamnionitis is thought to be an important ethiological factor in premature labor and delivery (12). Intrauterine infections caused by bacteria are considered to be the leading cause of infection-associated preterm birth. Moreover, preterm parturition (with intact or ruptured membranes) is associated with a maternal systemic inflammatory response characterized by phenotypic and metabolic changes (13). Most cases of histopathological inflammation and histological chorioamnionitis, both in preterm and term labor, are subclinical in nature (14).

In a study by Duff et al, the incidence of subclinical intra-amniotic infection in asymptomatic patients who had intact membranes was investigated. They concluded that subclinical infection was an uncommon cause of refractory preterm labor (15). However, in the study by Hillier, Guzick and Winn, histological chorioamnionitis was found more frequent in preterm deliveries (6, 16). On the contrary to these studies (6, 16), in our study; we found no difference in terms of histological chorioamnionitis between the groups. These difference may be related the samples size. On the other hand, some study that consistent with our results reported that this might be in consideration of a result of implicating the patient who has intact membranes other than patients with rupture of membranes (16, 17). Previous studies have indicated that up to 50% of patient presenting with painless cervical dilatation before 24 weeks of gestation have a positive amniotic fluid culture for microorganism(18,19). In these cases, infection can be a cause of cervical insufficiency, or may be secondary to prolonged exposure of chorioamnionic membranes to the microbial flora present in the lower genital tract(19). In addition, Gray et al. reported that all women with a positive amniotic fluid culture for *Ureaplasma urealyticum* at the time of genetic amniocentesis delivered a preterm neonate with histologic evidence of chorioamnionitis(20).

Abu Hamad et al. carried out a study with 200 women with preterm births and had 200 controls with term births(21). In this study, previous history of cesarean section was found to be a significant risk factor for preterm birth. Similarly, we found that the mean history of previous cesarean section in the preterm group was significantly higher than the term group. Covarrubias et al, evaluated 3018 preterm births between 2000 and 2004. In this study, urinary tract infection and gestational diabetes mellitus were found out as risk factors for preterm birth (22). Similarly, in our study, history of urinary tract infection and presence of gestational diabetes mellitus in the preterm group was significantly higher than the term group. But, there was no significant difference between groups in terms of presence of urinary tract infection during admission to the hospital for labor. Also; in a review by McDonald et al, they concluded that antibiotic treatment before 20 weeks' gestation reduced the risk of preterm birth (23). In a meta-analysis, treating women at a risk of preterm delivery with antibiotics reported that it did not reduce the risk of subsequent preterm birth (24).

The result of our study does not show the relationship between histological chorioamnionitis and preterm delivery. It might be due to the small size of our sample group. Therefore, a better understanding of the presence of histological chorioamnionitis on preterm delivery, there is requirement of longdated several studies

REFERENCES

1. Lettieri L, Vintzileos AM, Rodis JF, Albin SM, Salafia CM. Does idiopathic preterm labor resulting in preterm birth exist? *Am J Obstet Gynecol* 1993; 168:1480-5.
2. Hack M, Fanaroff AA. Outcomes of extremely immature infants-a perinatal dilemma. *N Engl J Med* 1985; 312:82-90.
3. Rush RW, Keirse MJNC, Howat P, Baum JD, Andersen ABM, Turnbull AC. Contribution of preterm delivery to perinatal mortality. *Br Med J* 1976; 2 : 965-8.
4. Gibbs RS, Romeo R, Hillier SL, Eschenbach DA, Sweet RL. A review of premature birth and subclinical infection. *Am J Obstet Gynecol* 1992; 166:1515-28.
5. Minkoff H. Prematurity: infection as an etiologic factor. *Obstet Gynecol* 1983; 62: 137-44.
6. Hillier SL, Martius J, Krohn MA, Kiviat NB, Holmes KK, Eschenbach DA. A case-control study of chorioamnionic infection and histologic chorioamnionitis in prematurity. *N Engl J Med* 1988; 319:972-8.
7. Aquino TI, Zhang J, Kraus FT, Knefel R, Taff T. Subchorionic fibrin cultures for bacteriologic study of the placenta. *Am J Clin Pathol* 1984; 81:482-6.
8. Svensson L, Ingermarsson I, Mardh PA. Chorioamnionitis and the isolation of microorganisms from the placenta. *Obstet Gynecol* 1986; 67: 403-9.
9. Larson JF, Eldon K, Lange AP, et al. Ritodrine in the treatment of preterm labor: second Danish multicenter study. *Obstet Gynecol* 1986; 67: 607-13.
10. Ballard J, Novak KK, Driver M. A simplified score for assessment of fetal maturation of newly born infants. *J Pediatr* 1979; 95: 769-74.
11. Salafia CM, Weigl C, Silberman L. The prevalence and distribution of acute placental inflammation in uncomplicated term pregnancies. *Obstet Gynecol* 1989; 73:383-98.
12. Romero R, Sirtori M, Oyarzun E, et al. Infection and labor. V. Prevalence, microbiology, and clinical significance of intraamniotic infection in women with preterm labor and intact membranes. *Am J Obstet Gynecol* 1989; 161:817-24.
13. Romero R, Espinoza J, Goncalves LF, Kusanovic JP, Friel L, Hassan S. The role of inflammation and infection in preterm birth. *Semin Reprod Med* 2007; 25:21-39.
14. Romero R, Espinoza J, Goncalves LF, Kusanovic JP, Friel LA, Nien JK. Inflammation in preterm and term labour and delivery. *Seminars in Fetal and Neonatal Medicine* 2006; 11: 317-26.
15. Duff P, Kopelman JN. Subclinical intra-amniotic infection in asymptomatic patients with refractory preterm labor. *Obstet Gynecol* 1987; 69: 756-9.

16. Guzik DS, Winn K. *The association of chorioamnionitis with preterm delivery. Obstet Gynecol* 1985; 65:11-6.
17. Hillier SL, Krohn MA, Kiviat NB, Watts DH, Eschenbach DA. *Microbiologic causes and neonatal outcomes associated with chorioamnion infection. Am J Obstet Gynecol.* 1991; 165:955-61.
18. Mays JK, Figueroa R, Shah J, Khakoo H, Kaminsky S, Tejani N. *Amniocentesis for selection before rescue cerclage. Obstet Gynecol* 2000; 95:652.
19. Romero R, Gonzalez R, Sepulveda W, Brandt F, Ramirez M, Sorokin Y, Mazor M, Treadwell MC, Cotton DB. *Infection and labor. VIII. Microbial invasion of the amniotic cavity in patients with suspected cervical incompetence: prevalence and clinical significance. Am J Obstet Gynecol.* 1992 ;167:1086-91.
20. Gray DJ, Robinson HB, Malone J, Thomson RB Jr. *Adverse outcome in pregnancy following amniotic fluid isolation of Ureoplasma urealyticum.*
21. Abu Hamad Kh, Abed Y, Abu Hamad B. *Risk factors associated with preterm birth in the Gaza Strip: hospital-based case-control study. East Mediterr Health J* 2007; 13:1132-41.
22. Covarrubias LO, Aguirre GE, Chapuz JR, May AI, Velázquez JD, Eguiluz ME *Maternal factors associated to prematurity Ginecol Obstet Mex.* 2008; 76:526-36.
23. McDonald HM, Brocklehurst P, Gordon A. *Antibiotics for treating bacterial vaginosis in pregnancy. Cochrane Database Syst Rev.* 2007; 24:CD000262.
24. Simcox R, Sin WT, Seed PT, Briley A, Shennan AH. *Prophylactic antibiotics for the prevention of preterm birth in women at risk: a meta-analysis. Aust N Z J Obstet Gynaecol* 2007; 47:368-77.