Abstract. – Objective: The underlying inflammation of endometrium may impede normal implantation of placenta during pregnancy. Our objective is to show cervical colonization of ureaplasm and/or mycoplasma and/or mycoplasma as a marker of endometritis in pregnancies complicated with placenta previa that can be a risk factor for placenta accreta and peripartum hemorrhage.

Patients and Methods: Cervical cultures for ureaplasm urealyticum and mycoplasma genitalium have been taken from the endocervical region of the cervix of the patients. Subsequent uterine lower segment bleeding suggesting placenta implantation defects have been evaluated during cesarean section.

Results: Of 25 patients; ten (40%) had negative cervical cultures for cervical mycoplasma and/or ureaplasm, 9 (36%) were found to be culture positive for cervical ureaplasm, 1 (4%) was found to be culture positive for cervical mycoplasma. Half of the 10 patients with positive cervical cultures for ureaplasm or mycoplasma and 6 of (40%) 15 patients with negative results had experienced lower uterine segment bleeding during cesarean section.

Conclusions: Bacterial colonization of cervix in particular with ureaplasm and/or mycoplasma is found to be strongly associated with placenta previa. Before a planned pregnancy, treatment of this infection with appropriate antibiotics is necessary to prevent underlying uterine endometritis that increases the risk for abnormal implantation of placenta.

Keywords: Antepartum bleeding, Obstetric infections-bacterial, Cesarean section, Postpartum hemorrhage, Placental pathology.

Introduction

Placenta previa is a condition which placenta implanted in the lower segment of the uterus, completely or partially obstructing the internal os of the cervix presenting ahead of the leading pole of the fetus. The prevalence of placenta previa is about 0.2 and 0.3% of third trimester pregnancies. The clinical outcomes of pregnancies complicated with placenta previa varies. The risks of preterm delivery, antepartum hemorrhage, several blood transfusions and peripartum hysterectomy is higher than normal pregnancies. Perinatal mortality rates are three to four times higher than normal pregnancies. Newborns which born from a pregnancy complicated with placenta previa has lower weight than normal pregnancies because of emergency preterm deliveries or intrauterine growth restriction due to abnormal implantation of the placenta. Risk factors for placenta previa are: advanced maternal age, parity, closely spaced pregnancies, maternal smoking, infertility treatments, previous cesarean deliveries or uterine surgeries and recurrent spontaneous or elective abortions. In last decades placenta previa incidence is increased parallel with the increased utilization of fertility treatments, advanced maternal age, and elective cesarean deliveries. Uterine scars related previous uterine surgeries cause abnormal implantation of placenta. Some trials showed that, in pregnancies complicated with placenta previa, the presence of ult-
rasound findings such as placental edge thickness, shortening of the cervix, presence of a sponge-like appearance of the cervix, anterior wall location of placenta and presence of placental lacunae are related with massive peripartum or antenatal hemorrhage. Presence of one or more of these findings may lead to a severe antepartum bleeding, peripartum hysterectomy and perinatal or maternal mortality. Normal vaginal flora members of sexually active women include *Enterococcus faecalis*, *Escherichia coli*, *Klebsiella pneumoniae*, *Proteus mirabilis*, *Streptococcus* spp., *Staphylococcus* spp., *Ureaplasma urealyticum* and *mycoplasmas* which could cause ascending infections through the upper genital tract. The ascending infections of uterus are responsible for the complications of pregnancy such as preterm delivery, premature rupture of membranes and chorioamnionitis. These prophlogistic microorganisms can cause intraterine infections and inflammation which lead to immune response, inducing an inflammatory mediators such as cytokines, chemokines, prostaglandins, and other effector molecules that result with uterine contractions and rupture of fetal membranes and preterm labour. Also ascending infections of uterus in nonpregnant woman can cause asymptomatic endometritis. Our hypothesis in this study is that the endometritis of uterus and inflammation of endometrium may impede normal implantation of placenta to the decidua. Our objective is to show cervical colonization of these bacteria as a marker of endometritis in pregnancies complicated with placenta previa that can be a risk factor for placenta accreta and peripartum hemorrhage.

### Patients and Methods

This cross-sectional study was conducted in our Hospital’s High Risk Pregnancy Unit between May and October in 2011. Totally 35 patients with a diagnosis of placenta previa and greater than 24 weeks of gestation who were hospitalized for painless vaginal bleeding have been included. The exact location of placenta to establish a diagnosis of placenta previa totalis, partialis and marginalis have been evaluated by one author ultrasonographically and the presence or absence of placental lacuna (swiss cheese view) and/or venous lakes on doppler ultrasonography have been determined (Aloka Prosound SSD-5500 SV, Tokyo, Japan). Cervical cultures for *mycoplasma genitalium* and *ureaplasma urealyticum* have been taken from the endocervical region of the cervix of the patients upon admission by taking into account that these pathogens are obligatory intracellular microorganisms so we especially cared to get endocervical cells during the application of sterile dacron swab of the culture media to the cervix. The culture specimens have been applied to the MycoView (Zeakon Diagnostics S.A.R.L, Besancon, France) system for detection of *mycoplasma hominis* and/or *ureaplasma urealyticum*. The test strips have been evaluated following incubation of 24 hours for *ureaplasma urealyticum* and of 48 hours for *mycoplasma hominis* upon application to the test system according to the identification and sensitivity test results. Patients who were detected to have genital mycoplasma and/or ureaplasma infection have been treated with 1 g of aztreomycine orally. Of those, 10 patients were dropped out of the study after discharge from the hospital who have not presented back for follow up and/or delivery. Remaining 25 patients were followed until delivery by cesarean section. Uterine bleeding suggesting placenta accreta, increta or percreta that necessitates the utilization of focal suture application, uterine balloon tamponade system and/or hysterectomy utilization have been evaluated during cesarean section.

### Statistical Analysis

Statistical analysis was performed by using IBM SPSS Statistics Software 19.0 (SPSS Inc., Chicago, IL, USA). The results were presented as mean± standard deviation values and compared by using the independent samples t test. The comparison of nonparametric values was accomplished by using Fisher’s exact test or chi-square test. p values < 0.05 were considered statistically significant.

### Results

The mean age of the patients was 30.2±5.6 (19-42), the mean body mass index (BMI) of the patients was 26.8±4.9 and the mean birthweight of the neonates was 2816±548 g respectively. Five patients (20%) were primigravid, 9 patients (36%) were multipara. 8 patients (32%) have previously been delivered by cesarean section in their first pregnancy and 3 patients (12%) have been delivered by cesarean section twice before their current pregnancy. Ten patients (40%) had negative cultures for cervical
mycoplasma and/or ureaplasma, 9 women (36%) were found to be culture positive for cervical ureaplasma, 1 patient (4%) was found to be culture positive for cervical mycoplasma. 3 patients (12%) were found to be culture positive for cervical eschericia coli and 2 patients (8%) were found to be culture positive for cervical candida colonization. Three patients (12%) were diagnosed with placenta previa marginalis, 6 women (24%) were diagnosed with placenta previa partialis and 16 patients (64%) were diagnosed with placenta previa totalis. Five women (20%) had increased number of placental lacunas and the remaining 20 patients (80%) did not have placental lacunas on sonography. Three patients (12%) had increased venous lakes and the remaining 22 women (88%) did not have venous lakes on doppler ultrasonography.

When we compared cervical culture results according to the uterine lower segment bleeding and/or need for utilization of uterine balloon tamponade system, there was not a significant relationship respectively (p = 0.46; p = 0.47). When we compared the gestational age at cesarean section according to the uterine bleeding from the lower uterine segment during the cesarean section, bleeding patients mean gestational age was 36 ± 2 and nonbleeding patients mean gestational age was 37 ± 1 weeks of gestation respectively (independent samples t test p = 0.19). All of the 5 women with increased number of placental lacunas and 13 (65%) of the 20 patients without increased number of placental lacunas have experienced uterine lower segment bleeding during cesarean section (p = 0.11; OR: 1.53 95% CI: 1.11-2.12). Two (66%) of the 3 patients with increased number of venous lakes on doppler ultrasonography and 16 (72%) of the 22 women without increased number of venous lakes on doppler ultrasonography have experienced uterine lower segment bleeding during cesarean section (p = 0.82; OR: 0.91 95% CI: 0.39-2.12). Eight of (73%) of 11 women who were operated in elective conditions and 10 of (71) 14 patients who were operated in emergent conditions like vaginal bleeding preoperatively have experienced uterine lower segment bleeding during cesarean section (p = 0.94; OR:1.01 95% CI: 0.62-1.66).

Four of (40%) 10 patients with positive cervical culture results for ureaplasma or mycoplasma and 1 of (7%) 15 women with negative culture results for ureaplasma or mycoplasma showed placental lacunas on preoperative ultrasonography (p = 0.04; OR: 6.00 95% CI: 0.78-46.14). A positive correlation was determined between cervical ureaplasma or mycoplasma colonization and the existence of placental lacunas on ultrasonography (Correlation coefficient r = 0.408). However, 1 of (10%) 10 women with positive cervical culture results for ureaplasma or mycoplasma and 2 of (13%) 15 patients with negative culture results for ureaplasma or mycoplasma had increased venous lakes on doppler ultrasonography (p = 0.80; OR: 0.75; 95% CI: 0.07-7.21). A positive correlation was determined between cervical ureaplasma or mycoplasma colonization and uterine lower segment bleeding during cesarean section (Correlation coefficient r = 0.145; p = 0.48; OR: 1.20; 95% CI: 0.74-1.92). Five of (50%) 10 patients with positive cervical culture results for ureaplasma or mycoplasma and 6 of (40%) 15 patients with negative culture results for ureaplasma or mycoplasma needed uterine balloon tamponade system utilization during cesarean section to alleviate uterine lower segment bleeding (p = 0.62; OR: 1.25 95% CI: 0.52-3.00).

Of 10 patients with positive cervical cultures for ureaplasma or mycoplasma; 4 of (80%) 5 women with one or two previous cesarean sections and 4 of (80%) 5 women without previous cesarean sections had experienced lower uterine segment bleeding during cesarean section (p > 0.05). Of 15 women without positive cervical cultures for ureaplasma or mycoplasma; 6 of (100%) 6 patients with one or two previous cesarean sections and 4 of (44%) 9 patients without previous cesarean sections had experienced lower uterine segment bleeding during cesarean section (p = 0.02). Overall, whether cervical cultures for ureaplasma/mycoplasma were positive or not, 10 of (91%) 11 patients with one or two previous cesarean sections and 8 of (57%) 14 patients without previous cesarean sections had experienced lower uterine segment bleeding during cesarean section (p = 0.06). Previous one or two cesarean sections were found to increase the lower uterine segment bleeding during the current pregnancy’s cesarean section substantially (p > 0.05; OR: 4.71; 95% CI: 0.66-33.60). Nine of (56%) 16 patients who were diagnosed as placenta previa totalis and 1 of (11%) 9 patients who were diagnosed as placenta previa partialis and/or marginalis had positive cervical culture results for ureaplasma or mycoplasma colonisation that revealed a positive correlation between placen-
ta previa totalis and cervical ureaplasma or mycoplasma colonisation ($p = 0.02$; Correlation coefficient $r = 0.442$; OR: 5.06; 95% CI: 0.75-33.77). When analyzed with ROC curve, patients with lower gestational age were related to an increased risk for lower uterine segment bleeding during cesarean section ($p = 0.21$; AUC: 0.337). Women with lower gestational age have been found to be related to an increased risk for uterine balloon tamponade utilization during cesarean section ($p = 0.01$). Nine of (56%) 16 patients with a placenta previa totalis diagnosis and 2 of (22%) 9 with a diagnosis of placenta previa partialis and/or marginalis necessitated uterine balloon tamponade system utilization during cesarean section ($p = 0.10$; OR: 2.53; 95% CI: 0.69-9.25).

**Discussion**

Ureaplasma spp. and Mycoplasma spp. are the most detected microorganisms in cervical cultures of sexually active women who attend Gynaecology Departments of hospitals. In many studies the cervical colonisation of these bacteriae are found to be related with complicated pregnancies such as preterm delivery, premature rupture of membranes, idiopathic vaginal bleeding during pregnancy, intrauterine growth retardation and postpartum endometritis. Madan I et al. found that patients having placenta previa concomitant with intraamniotic infection or inflammation and vaginal bleeding have an increased risk for preterm delivery in 48 hours. Our study is the first that determines the relationship between placenta previa and cervical colonisation of these prophlogistic microorganisms. In this report cervical cultures are found to be more prevalent in pregnancies complicated with placenta previa totalis. In our work 80% of placenta previa patients with increased number of lacunae had positive cervical cultures. Thus, antenatal ultrasound finding of placental lacunae in pregnancies complicated with placenta previa can be a marker for intrauterine infection and inflammation. All of the women with placental lacunae had lower segment bleeding during cesarean section revealing that the ultrasonographic detection of placental lacunae and venous lakes can be used to predict lower uterine segment bleeding in cesarean section. Seventy three percent of patients with placenta previa who were operated electively and 71% who were operated in emergent conditions had lower uterine segment bleeding so scheduled cesarean section do not reduce the risk of intraoperative bleeding. We needed to utilize an uterine balloon tamponade system in patients with positive mycoplasma/ureaplasma cultures more frequently than patients with negative cultures. The positiveness of cervical cultures in patients with placenta previa should be a warning for intraoperative bleeding and additional preparations such as blood products and uterine balloon tamponade system devices should be available for preferably experienced surgeons before cesarean section. Patients and their relatives should be informed about the possible necessity of blood transfusions, peripartum hysterectomy and perinatal morbidity and mortality. In this study, we demonstrated that the earlier gestational week the cesarean section is performed, the more the intrauterine balloon tamponade system utilization for uterine lower segment bleeding is needed. Also we found that the women with placenta previa totalis have a higher risk for lower segment uterine bleeding than other placenta previa localizations such as partialis, marginalis and low-lying placenta. Like many other studies, in our study we found that previous uterine surgeries as a risk factor for placenta previa and lower uterine segment bleeding.

**Conclusions**

Bacterial colonisation of cervix, in particular with ureaplasma and/or mycoplasma, is found to be strongly associated with placenta previa. Every women who are planning to get pregnant should be tested for cervical cultures before pregnancy. If the cervical cultures are found to be positive they should be treated with appropriate antibiotics before pregnancy for prevention of probable endometritis that increases the risk for abnormal implantation of placenta. The clinicians should also reduce the frequency of unnecessary uterine surgeries and elective cesarean sections that increase the peripartum complication incidence during the subsequent pregnancies by facilitating the abnormal placental implantation.
Conflict of Interest

The Authors declare that they have no conflict of interests.

References

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