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The impact of *Ureaplasma* infections on pregnancy complications

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ABSTRACT

The aim of this study was to assess if ureaplasmas are associated with pregnancy complications and diseases in newborns. Pregnant women with complaints and threatening signs of preterm delivery were included. A sample, taken from the endocervical canal and from the surface of the cervical portion, was sent to the local microbiology laboratory for DNA detection of seven pathogens: *Chlamydia trachomatis, Mycoplasma hominis, Mycoplasma genitalium, Ureaplasma parvum, Ureaplasma urealyticum, Neisseria gonorrhoeae,* and *Trichomonas vaginalis*. The Pearson Chi-Square test was used to determine the difference in unpaired categorical data. A two-sided p value <0.05 was considered to be statistically significant. In all, 50 pregnant women with complaints and threatening signs of preterm delivery were included. Premature rupture of uterine membranes was found in 23 (46%) of the patients and 38 women (76%) had preterm delivery. *Ureaplasma* infections were associated with a premature rupture of membranes ($p < 0.004$), the placental inflammation ($p < 0.025$), a newborn respiratory distress syndrome ($p < 0.019$). Ureaplasmas could have affected the preterm leakage of fetal amniotic fluid and are associated with the placental inflammation and a newborn respiratory distress syndrome.

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Ureaplasmas; preterm delivery; pregnancy complications

1. Introduction

Ureaplasma parvum and *Ureaplasma urealyticum* are very frequent and can be found in 40–80% of sexually active women [1,2].

Ureaplasmas are related to *Mycoplasma* species; they lack a cell wall, and thus they bind to the host cell surface [3–5]. Urea is the sole source of energy for ureaplasmas which they hydrolyse to produce their ATP requirements [4–6]. As a result, ureaplasmas can be found in the female and male urogenital systems – the mucosal surface of the vagina, the cervix, the urethra, the endometrium, the seminal fluid, attached to the surface of the spermatozoa and also in the amniotic fluid, the placenta during pregnancy [7,8]. The transmission of ureaplasmic infections from the mother to the fetus occurs in the uterus or during labour. The frequency of *Ureaplasma* transmission presented by studies varies from 18% to 88% [9,10]. The infection can cause a preterm delivery due to activations of the immune system, leading to the increase of the production of cytokines, prostaglandins, uterine contractions, dilatation of the cervix and a preterm prelabour rupture of the fetal membranes [11]. There are studies that ureaplasmas can cause symptomatic vaginitis, urinary tract infections, preterm delivery, chorioamnionitis, funisitis, neonatal morbidity, postpartum endometritis [12–16]. However, there are also other scholarly publications that consider ureaplasmas to be commensal microorganisms, not correlated with preterm delivery or other complications of pregnancy [17,18].

The aim of this study was to assess if ureaplasmas are associated with pregnancy complications and newborn diseases.

2. Material and methods

This prospective cross-sectional study and was performed at the Department of Pregnancy Pathology of our Clinic from January to September of 2013. In all, 50 pregnant women with complaints and threatening signs of preterm delivery were included. All the patients gave informed consent after the procedure had been fully explained. The ethical approval was obtained from The Vilnius Regional Biomedical Research Ethics Committee (Ref. No, 158200–13-574-169 of 11 January 2013).

All the patients underwent a gynaecological speculum examination. During this examination, a sample of vaginal secretion taken from the posterior vaginal fornix with a cotton-tipped swab was placed on two glass slides, dried and sent to a local microbiology laboratory for Gram stain analysis. The Gram stain analysis evaluated the count of polymorphonuclear

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leukocytes per high power field, epithelial cells, clue cells, *Trichomonas*, budding yeast, or hyphae. Taking into account that the vaginal smear evaluation could have been affected by the leakage of amniotic fluid found in almost half of the subjects (23%), only large leukocytes (covering the field of vision) from vaginal smears were used in statistical analysis.

A sample taken from the endocervical canal and the surface of the cervical portion was sent to the local microbiology laboratory for the DNA detection of seven pathogens: *Chlamydia trachomatis, Mycoplasma hominis, Mycoplasma genitalium, Ureaplasma parvum, Ureaplasma urealyticum, Neisseria gonorrhoeae,* and *Trichomonas vaginalis*. These seven pathogens were detected by multiplex real-time PCR using *Anyplex™ II STI-7 Detection (V1.1) kit* (Seegene Inc.) and CFX96^{TM} (Bio-Rad) real-time PCR system. Women's childbirth histories and the case histories of their newborns were analysed. The evaluation involved the gestation week, the week of birth, the number of childbirths in the anamnesis, the number of fetuses, premature amniotic fluid leakage, the patohistological examination of the umbilical cord and the placenta. The newborn case histories were evaluated in terms of gestational age, newborn congenital infections, and a respiratory distress syndrome.

Statistical calculations were performed by using the SPSS, version 16.0 (SPSS Inc., Chicago, IL).

The Pearson Chi-Square test was used to determine the differences in the unpaired categorical data. A two-sided p value <0.05 was considered to be statistically significant.

3. Results

The characteristics of 50 pregnant women including the threatening signs of preterm delivery and the characteristics of their newborns are summarized Table 1.

The mean age of women was 30 years. The majority of women (26 (52%)) were primiparous with a single fetus (94%). The gestational week on hospitalisation was from 19 to 36 weeks, premature rupture of uterine membranes was found in 23 (46%) of the patients and 38 women (76%) had preterm delivery. Preterm delivery was not associated with *Ureaplasma* infection (Table 2).

The Gram stain analysis showed thick leukocytosis in 15 (30%) of all the cases, there were only 2 cases of bacterial vaginosis. *Ureaplasma* infection was found in 26 (52%) of all the cases, there were no cases of *Mycoplasma hominis*, vaginal trichomonosis, and *Neisseria gonorrhoea*. The inflammation of placenta (chorioamnionitis, deciduitis) was found in 22 (44%) cases.

The mean gestational age of newborns was 31 weeks, 64% of them had congenital infection, and 47% of them had a respiratory distress syndrome.

Table 1. Characteristics of the women and the newborns.

Characteristics	
Number of women	50
Age, mean, (95% CI) (range)	30 (28–32, 18–44)
Gestational week, mean, (95% CI) (range)	29 (28–30, 19–36)
Premature rupture of uterine membranes, n (%)	23 (46)
Inflammation of placenta	22 (44)
Thick leukocytosis in Gram stain, n (%)	15 (30)
Ureaplasma infection (total), n (%)	26 (52)*
Ureaplasma parvum infection, n (%)	24 (48)
Ureaplasma urealyticum infection, n (%)	6 (12)
Mycoplasma genitalium infection, n (%)	4 (8)
Chlamydia trachomatis infection, n (%)	2 (4)
Number of newborns	53
Gestational age of the newborns, mean, (95% CI) (range)	31 (30–33, 19–40)
Newborn congenital infection, n (%)	34 (64)
Newborn respiratory distress syndrome, n (%)	25 (47)

*The total number of cases with *Ureaplasma* infection is less than the sum of all cases with *Ureaplasma parvum* and *Ureaplasma urealyticum* infections because there were cases with both infections.

Ureaplasma infections were associated with premature rupture of membranes ($p < 0.004$), the placental inflammation ($p < 0.025$), a newborn respiratory distress syndrome ($p < 0.019$), while thick leukocytosis in the Gram stain analysis was not associated with rupture of membranes, placental inflammation, a newborn respiratory distress syndrome (Table 2).

One pregnancy ended in miscarriage in 19th week of pregnancy. There was no association between the miscarriage (19th week of gestation) or between one stillborn (22 gestational weeks) and the maternal genital tract infection.

4. Discussion

The most important findings of our study are as follows: *Ureaplasma* could have affected the preterm leakage of fetal amniotic fluid and are associated with placental inflammation and a newborn respiratory distress syndrome. An interesting and unexpected finding of the study is that the abundant leukocytes in the vaginal discharge Gram stain analysis did not correlate to the premature leakage of fetal

Table 2. The relations of *Ureaplasma* infection, leukocytosis in Gram stain and pregnancy complications.

	Ureaplasma infection, n (% of total)		p*	Thick leukocytosis in Gram stain, n (% of total)		p*
Complications	Yes	No		Yes	No	
Premature rupture of uterine membranes	17 (34)	6 (12)	0.004	4 (8)	19 (38)	0.073
Inflammation of placenta	15 (33)	7 (16)	0.025	6 (13)	16 (36)	0.815
Newborn congenital infection	13 (25)	6 (11)	0.057	5 (9)	14 (26)	0.810
Newborn respiratory distress syndrome	17 (32)	8 (15)	0.019	8 (15)	17 (32)	0.572

*Pearson Chi-Square test.

amniotic fluid, placental inflammation, or a newborn respiratory distress syndrome.

As *Ureaplasma* is commonly found in pregnant women, it was also observed in more than half of the women in our study, which is in line with the results obtained by other studies [1,19]. Since 2000, *Ureaplasma parvum* has been distinguished as an autonomous species and is found more frequently than *Ureaplasma urealyticum* and is thought to be more threatening during pregnancy than *Ureaplasma urealyticum* [19]. *Ureaplasma parvum* (48%) was also most frequently observed in our study.

Preterm delivery, according to our study, was not affected by *Ureaplasma* because *Ureaplasma* was found in 20 women who had given preterm childbirth, was absent in 18 subjects, as well as half of the 12 women with timely childbirth had *Ureaplasma*, half of them did not. Our findings are also consistent with the publications of other scholars who claim that this micro-organism can be detected even in cases of timely deliveries [6].

However, our study showed that *Ureaplasma* was statistically reliably related to the preterm amniotic fluid leakage ($p < 0.004$), inflammation of the placenta ($p < 0.025$), and a newborn respiratory distress syndrome ($p < 0.019$). The reason may be other influential factors. *Ureaplasma parvum* has been found to have different subtypes (serovars) that may be more virulent [2,10,11,20]. Also, a woman's condition, her immune system is likely to be responsible for the occurrence of pregnancy complications triggered by ureaplasmic infection. An interesting result obtained in this study is that the abundant leukocytes in the vaginal discharge Gram stain analysis did not associate with preterm amniotic fluid leakage, inflammation of the placenta or a newborn respiratory distress syndrome, while the ureaplasmic infection was related. Although these results did not achieve statistical reliability, most likely due to a small sample, Table 2 shows a clear tendency that a few times [2–4] lower number of complications of pregnancy (preterm labour, rupture of premature amniotic fluid membranes, placenta infections, newborn congenital infection, a newborn respiratory distress syndrome) were found in the cases where leukocytes covered the field of vision in the vaginal discharge Gram stain analysis. Abundant leukocytes in the vaginal smear were likely to have been caused by a strong immune response and the defence against ureaplasmic infection.

Ureaplasma is associated with bacterial vaginosis, while bacterial vaginosis is also associated with the complications of pregnancy and childbirth. However, our study identified only two cases of bacterial vaginosis in the vaginal Gram stain analysis. The preterm amniotic fluid leakage could have affected the results of the vaginal smear, and bacterial vaginosis was found only in a few cases. The limitation of our study was a small sample of patients; however, the results obtained were significant and clinically relevant.

In summary, it should be stated that ureaplasmic infection, irrespective of the abundance of white blood cell count in the vaginal smear, triggered pregnancy complications, newborn morbidity. However, other factors are also important for the virulence of *Ureaplasma* – the female immune system, which is a subtype of ureaplasms (serovar). More research should be carried out in the future that could help to determine the causes for the conversion of *Ureaplasma* into pathogenic microorganisms.

Disclosure statement

No potential conflict of interest was reported by the authors.

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