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*Wellness of pregnant women with colonization
of *Ureaplasma urealyticum**

**Dobrostan ciężarnych z wykrytym nosicielstwem
*Ureaplasma urealyticum***

Key words: *Ureaplasma urealyticum*, PROM, premature rupture of membranes, preterm labour, premature baby, perinatal complications

INTRODUCTION

Ureaplasma urealyticum is a gram negative bacterium belonging to the order Mycoplasmatales. It is transmitted sexually and vertically [9]. It presents significant affinity to epithelium-covered areas and a great resistance to dryness and temperature changes [20]. *U. urealyticum* is present in the lower genital tract mucosa of about 40-80% of sexually active women. Higher levels of colonization are present in women with low socioeconomic status, having multiple sex partners and tobacco smokers [20].

Due to the vast prevalence of this bacterium in the genital tract its role as a part of normal flora is often emphasized [9]. However, despite its low virulence, it can cause serious infections. Especially exposed are people immunologically compromised, including pregnant women and neonates, premature ones in particular [1].

U. urealyticum is isolated from the lower genital tract of about 60-80% of pregnant women [16]. There are postulates of a link between *U. urealyticum* colonization and pregnancy complications such as amniotic fluid infection, chorioamnionitis, premature rupture of membranes and, consequently, a preterm labour [18]. The risk of preterm contractions is more than ten times higher in women with *U. urealyticum* amniotic fluid colonization by *U. urealyticum* and the risk of a preterm labour is seven times higher [20]. It has been shown that *U. urealyticum* is present in the amniotic fluid of 30% of women with premature rupture of membranes [10]. According to research, the higher the level of colonization, the greater the colonization of the placenta and therefore greater the risk of chorioamnionitis, whereas at low levels of colonization these bacteria don't exert an effect on the prevalence of mentioned pregnancy complications [2]. Despite these data, the correlation between vaginal or cervical colonization by *U. urealyticum* and a preterm labour remains controversial [17]. It is unclear whether *U. urealyticum* alone causes mentioned pregnancy complications or is it a net result of an *Ureaplasma* infection and an additional influence of other microorganisms [7]. The risk of a preterm labour seems higher when infection with *U. urealyticum* is accompanied by infection by other bacteria [8]. Nevertheless, when using standard microbiological culture methods, *U. urealyticum* is often the only microorganism identified in the amniotic fluid of women who had a preterm labour [7].

In humans 2 strains and 14 serotypes of *U. urealyticum* have been isolated. According to research, strain 2 and serotypes 4 and 8 are of exceptional importance in non-gonococcal urethritis, impaired fertility, habitual abortion, pregnancy complications and incidence of the neonates [20]. However, results of other analysis suggest that a diversity of *U. urealyticum* strains grown from amniotic fluid correlate neither with the intensity of the inflammatory reaction nor with the pregnancy outcome [1].

Pathophysiology of the *U. urealyticum* infection is also interesting. Once it has colonized vagina it produces urease, an [enzyme](#) that [catalyzes](#) the [hydrolysis](#) of [urea](#) into [carbon dioxide](#) and [ammonia](#). This causes the pH of the vagina to rise, facilitating infection with other bacteria [8]. Invasiveness of *U. urealyticum* is probably increased by its ability to break down IgA antibodies with special proteases. Examined women with pathological flora present lower levels of IgA antibodies in the mucosa of the cervix in comparison with women with physiological flora [20]. Furthermore, this bacterium is also connected with higher levels of inflammatory cytokines in the amniotic fluid [7]. The direct mechanism of preterm labour induction by *U. urealyticum* is probably due to its transmission to the amniotic fluid through the intact amniotic sac. Low virulence of the pathogen often causes lack of symptoms which explains the chronicity of the infection. *U. urealyticum* can survive in the upper genital tract up to weeks before rupture of membranes and a preterm labour occur [13].

Such course of pregnancy has undoubtedly a negative influence on the neonate. The neonate may have low birth mass and is subject to different complications, including cerebral palsy, intraventricular haemorrhage or respiratory disorders such

as pneumonia, bronchopulmonary dysplasia and other chronic lung diseases. [16, 18]. It has been shown, that in 18-55% of infected mothers the infection is transmitted to the neonate. *U. urealyticum* is a single microorganism most often isolated from the nervous system and lower respiratory tract of premature babies [1].

The aim of this study is to determine the connection between *U. urealyticum* infection with premature rupture of membranes. Furthermore we will draw attention to the link between the level of colonization and course of pregnancy and neonate's condition.

The analysis is conducted based on the microbiological cultures of material taken from the patients of the Obstetrics Clinic of the Medical University of Gdańsk in the year 2013.

METHODS AND RESEARCH MATERIAL

Analysed data comes from patients' histories of patients admitted to the Obstetrics Ward of the Medical University of Gdańsk between January 2013 and December 2013 in order to undergo labour. The analyzed group consisted of 2406 women admitted to the Ward during that period. Microbiological cultures of the swab from the lower genital tract, taken routinely at the admission, have been used as a research material. Inclusion criterium of this study was testing positive in the microbiological culture for the presence of *Ureaplasma urealyticum*. This criterium was fulfilled by 254 patients of studied 2406. The patients, whose swab culture descriptions said "single colonies" in regard to *Ureaplasma urealyticum*, were excluded from further analysis. Within the analyzed group were eight twin pregnancies. The patients' histories of neonates whose mothers tested positive for *Ureaplasma urealyticum* were used as well. Sixteen neonates from the twin pregnancies were excluded because of frequent complications occurring in twins. Eight other neonates were excluded from the analysis due to lack of documentation.

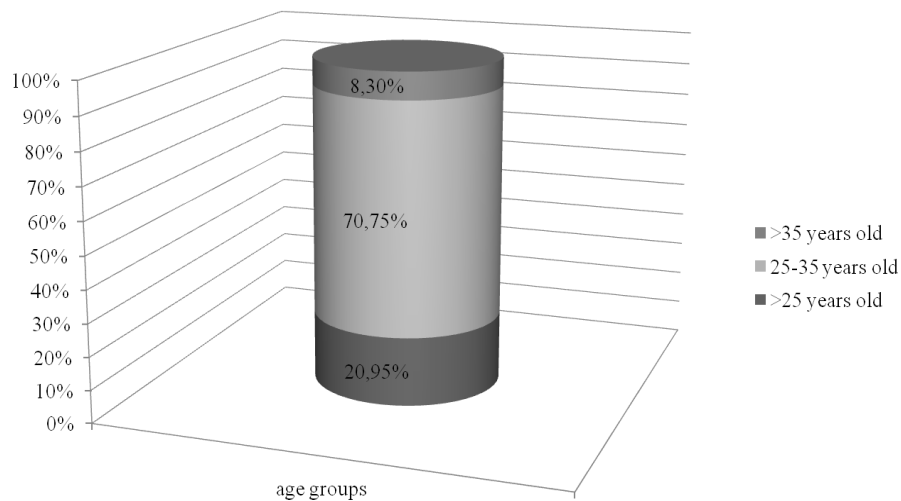
Main issues studied:

1. Prevalence of *Ureaplasma urealyticum* infection in the Obstetrics Ward of the Medical University of Gdańsk
2. Prevalence of obstetrical complications in the group of patients infected by *Ureaplasma urealyticum*.
3. Prevalence of complications in the neonates of mothers who tested positive for *Ureaplasma urealyticum*.

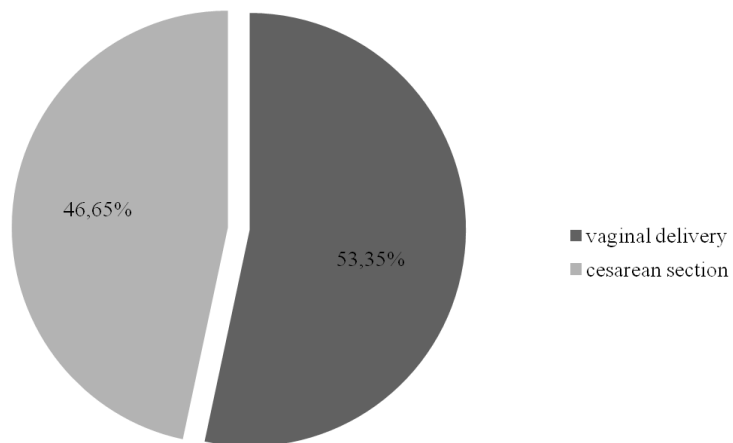
RESULTS

In the period between Jan 2013 and Dec 2013, 2406 patients were admitted to the Obstetrics Ward of the Medical University of Gdańsk in order to undergo labour. Amongst that group 253 women had positive microbiological cultures of the lower genital tract swab for *Ureaplasma urealyticum* this is 10,52% of the admitted women. Patients with positive cultures were divided into three groups according to their

age: less than 25 yr, 25–35 yr and those aged over 35 yr. Distinguished groups made up for following percentages: patients less than 25 years old - 20.95% (53 women), 25-35 years old - 70.75% (179 women), over 35 years old - 8.3% (21 women). Among the 253 studied patients 31 were diabetic (12.24%), 19 (7.51%) had PIH, 134 (53.35%) delivered vaginally and 118 (46.64%) had a cesarean section.



Graph 1. Age groups among patients with positive Ureaplasma urealyticum cultures



Graph 2. Way of delivery vaginal and cesarean section in patients with positive Ureaplasma urealyticum cultures

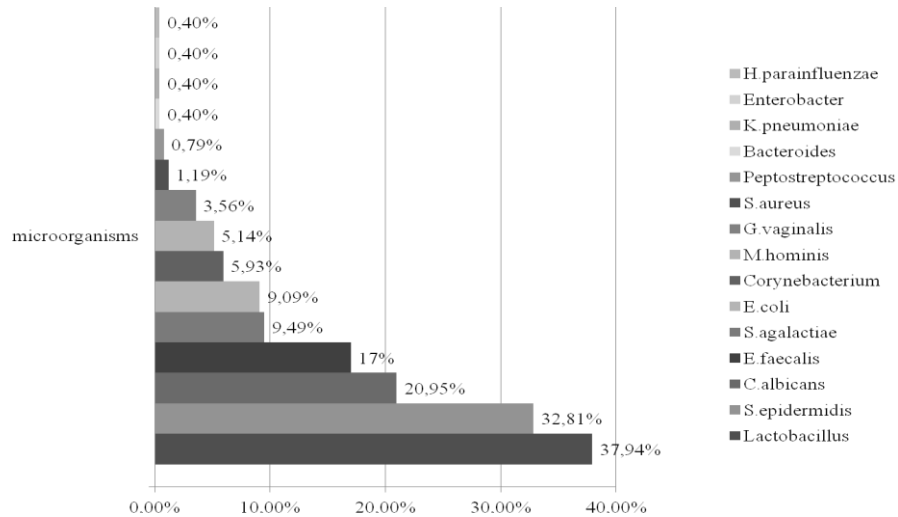
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Cultures of swabs acquired from the patients were described as follows: “+” a couple of colonies – 70 cultures (27.67%) were described like this, “++” substantial growth - 98 cultures (38.74%) and “+++” abundant growth – 85 cultures (33.60%). The levels of growth on the medium were compared with premature rupture of membranes (PROM) and preterm labour prevalence in the studied groups. Results: in patients with growth of *Ureaplasma urealyticum* described as abundant “+++” PROM occurred 11 times (39.56%), preterm labour - 15 times (35.71%). In patients with growth described as “++” PROM occurred 17 times (47.22%), a preterm labour 16 times (38.10%). In patients with colony growth described as “+” PROM occurred 8 times (35.10%) and a preterm labour - 11 times (26.19%).

Table I. Distribution of patients in accordance to the *Ureaplasma urealyticum* growth intensity on a medium

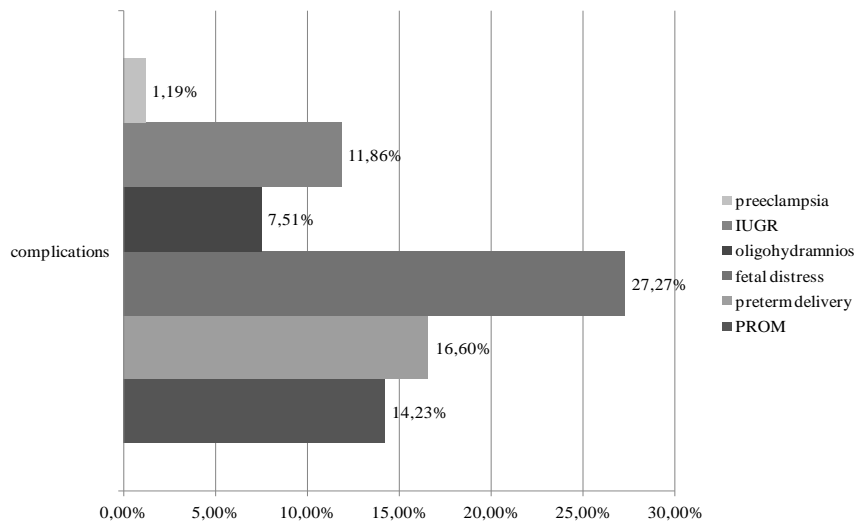
Culture description	Number of patients	Percentage
+	70	27,65%
++	98	38,74%
+++	85	33,60%

In the group of patients who had positive bacterial cultures of the lower genital tract swabs for *Ureaplasma urealyticum* other microbes were also isolated: *Lactobacillus* - 96 (37.94%), *Staphylococcus epidermidis* - 83 (32.81%), *Candida albicans* - 53 (20.95%), *Enterococcus faecalis* - 43 (17%), *Streptococcus agalactiae* - 24 (9.49%), *Escherichia coli* - 23 (9.09%), *Corynebacterium* - 15 (5.93%), *Mycoplasma hominis* - 13 (5.14%), *Gardnerella vaginalis* - 9 (3.56%), *Staphylococcus aureus* - 3 (1.19%), *Peptostreptococcus* - 2 (0.79%), *Bacteroides* - 1 (0.4%), *Klebsiella pneumoniae* - 1 (0.4%), *Enterobacter* - 1 (0.4%), *Haemophilus parainfluenzae* - 1 (0.4%).



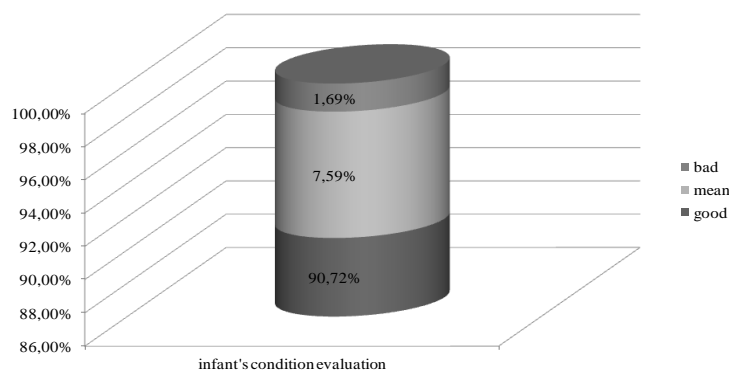
Graph 3. Mixed culture and pure culture occurrence

Women who had *Ureaplasma urealyticum* in their cultures had following obstetric complications: PROM - 36 patients (14.23%), preterm labour - 42 patients (16.6%), fetal distress - 69 women (27.27%), oligohydramnios - 19 women (7.51%), IUGR of the foetus - 30 patients (11.86%), preeclampsia - 3 patients (1.19%). Out of 36 patients with PROM, 20 delivered preterm (55.56%).



Graph 4. Prevalence of chosen obstetric complications in *Ureaplasma urealyticum* infected patients

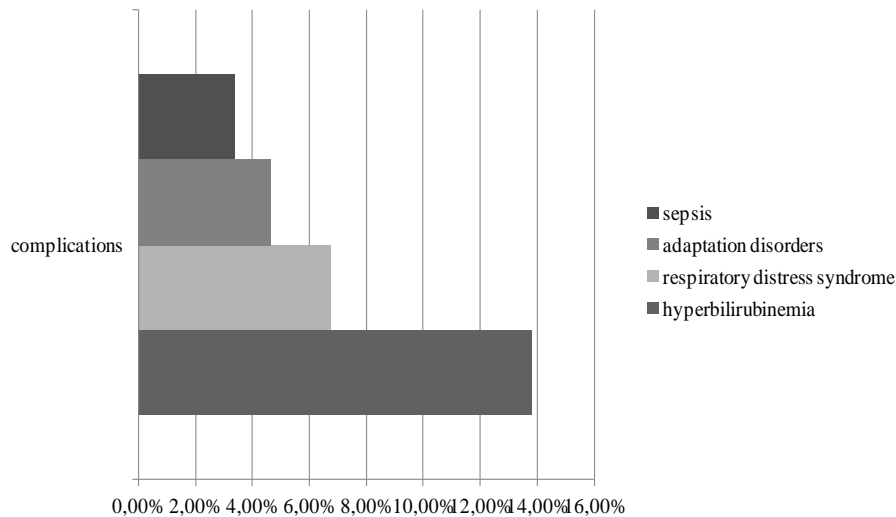
Infants of the studied patients were divided into 3 groups according to their Apgar score (assessed within the first minute following birth). General good state 8-10 points – 215 neonates (90.72%), fairly low score 4-7 points - 18 neonates (7.59%), low score 1-3 points - 4 neonates (1.69%). These infants were further divided into 3 groups according to their birth mass: those with birth mass below 1200g – 5 neonates (2.11%), birth mass between 1200 and 2500g – that group made up for 12.24% of all infants (29 neonates) and infants with birth mass exceeding 2500g – 203 (85.65%). Average infants' birth mass was 3252,93g. Infants of mothers with *Ureaplasma urealyticum* had suffered from the following complications: pathological jaundice – 31 (13.8%), infant respiratory distress syndrome (IRDS) - 16 (6.75%), adaptation disorders - 11 (4.64%), sepsis - 8 (3.38%).



Graph 5. Percentage of children of infected mothers according to their Apgar score.

Table II. Distribution of mothers with positive *Ureaplasma* cultures according to the birth mass of the neonates

Birthweight (g)	Number of neonates	Percentage
<1200	5	2,11%
1200-2500	29	12,24%
>2500	203	85,65%



Graph 6. Prevalence of chosen complications in the newborns of mothers with positive Ureaplasma cultures

DISCUSSION

Ureaplasma urealyticum is a bacterium belonging to the Mycoplasmataceae family that commonly inhabits the mucosa of the genital tract. Urogenital Mycoplasmas are isolated from women of all ethnical and racial groups [9]. Different sources give different prevalences of positive cultures of *Ureaplasma urealyticum* in pregnant women - Georgia USA: 60% [3], Mexico: 31% [6], Spain 32% [4]. The swabs from the lower genital tract of 2406 women admitted to undergo labour in the Obstetrics Clinic of the Medical University of Gdańsk were taken and had tested positive for *Ureaplasma urealyticum* in 253 women – 10.52%. In the year 2009 an epidemiological analysis of the genital tract swab cultures was performed and it showed that 12% of patients had *Ureaplasma urealyticum* infection [14]. *Ureaplasma urealyticum* infection is a sexually transmitted disease. The peak of infection occurrence happens between 15-25 years due to high sexual activity. In the conducted analysis the microbe was most often isolated from women aged 25-35 yr. The group aged over 35 constituted for the smallest percentage – 8.3%. It is probably due to better gynaecological care during pregnancy and higher awareness of STD prevention in older women.

A preterm labour is one of the main problems of modern obstetrics, being the cause of up to 70% deaths of the neonates and over a half of all neurological complications in that group [12]. In Poland about 6-8% of labours are preterm [5]. Inflammation of the vagina and the cervix are often listed by other authors as risk factors of a preterm labour. Among the women who delivered preterm endocervical swabs most often test positive for *Ureaplasma urealyticum*, *Mycoplasma hominis*,

Gardnerella vaginalis, *Peptostreptococcus*, *Bacteroides*, *Neisseria gonorrhoea*, *Chlamydia trachomatis* [12]. Worth mentioning is the fact, that *Ureaplasma urealyticum* is a microorganism most often present in the cultures from placentas and amniotic fluid of women who delivered preterm [19]. Among the patients admitted to the Obstetrics Clinic of the Medical University of Gdańsk who had positive cultures for *Ureaplasma urealyticum* a preterm labour occurred in 42 patients (16.7%). However there was no relation between the intensity of growth on a medium and the risk of a preterm labour.

Premature rupture of membranes is one of the commonest obstetric pathologies. It occurs in 2-4% of all pregnancies and is a reason of about one third of preterm labours [5]. PROM can be both – caused by and a cause of an intrauterine infection. Nowadays an infection seems to be the most common cause of premature rupture of membranes. In the analyzed material taken from patients' histories of patients of the Obstetrics Clinic of the Medical University of Gdańsk in the year 2013 who had positive cultures for *Ureaplasma urealyticum*, a premature rupture of membranes was diagnosed in 36 patients (14.23%), 20 of them had a preterm delivery (55.56%). There was no relation between the intensity of growth on a medium and the risk of a premature rupture of membranes in the studied group.

Ureaplasma urealyticum can colonize the foetus during delivery. The source of the microbe is the cervix or the vagina of the woman giving birth. It is believed that urogenital mycoplasmas that are transmitted to the foetus during delivery usually are not causing any serious consequences in the majority of neonates [19]. Although there are cases of meningitis, sepsis and bronchopulmonary dysplasia. The following abnormalities were taken into account: IRDS, increased bilirubin, adaptation disorders. The infant respiratory distress syndrome is not a separate disease but rather a set of symptoms usually occurring in a preterm neonate. It is caused by surfactant deficiency or insufficient maturity [15]. Among the studied infants 6.75% were diagnosed with IRDS. The relation between *Ureaplasma urealyticum* infection and bronchopulmonary dysplasia is an interesting subject. An infection with this microbe is not a proven risk factor of bronchopulmonary dysplasia and the link remains controversial. Many clinical and epidemiological studies suggest that *Ureaplasma urealyticum* can increase the risk of bronchopulmonary dysplasia by enhancing the injury of the lungs done by respiratory therapy [11]. None of the infected mothers' infants from the studied group had bronchopulmonary dysplasia.

In a prospective study, Brauni et al. announced that mothers who had *Ureaplasma urealyticum* isolated from their cervical and vaginal swabs delivered neonates of a mean birth mass of 3099g which is statistically significantly lower than the mean birth mass of healthy mothers' neonates, being 3297g [19]. In the analyzed material the mean mass of the neonate was 3252g, which is not no different from a mean birth masses of normal, healthy neonates of healthy mothers.

The most often complication in the studied group of neonates was increased bilirubin: 13.8%

CONCLUSIONS

1. Among the patients admitted to the Obstetrics Clinic of the Medical University of Gdańsk to deliver, 10.52% had positive bacterial cultures for *Ureaplasma urealyticum*.
2. Among the infected women who delivered in the Obstetrics Clinic, 16.6% were diagnosed with PROM and 14.23% had a preterm delivery.
3. In the analyzed group PROM and a preterm labour occurred more frequently than in the general population of Poland.
4. Intensity of growth on a medium of *Ureaplasma urealyticum* did not influence the prevalence of PROM and a preterm labour.
5. In the studied group a positive bacterial culture for *Ureaplasma urealyticum* did not influence the mean birth mass of the neonate.
6. The most common complication occurring in the infants of the infected mothers was increased bilirubin 13.8%.

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ABSTRACT

The goal of the study was to analyze the *U. urealyticum* colonization of the lower genital tract of patients admitted to the Obstetrics Clinic of the Medical University of Gdańsk to deliver. Patients' histories of 2406 patients admitted in 2013 were studied, 253 (10.52%) of which were infected with *U. urealyticum*. Women aged 25-35 were most frequently infected. It has been shown that in mixed cultures *Lactobacillus* spp. and *Staphylococcus epidermidis* were most commonly grown alongside *U. urealyticum*. Most common of the chosen obstetric complications were a preterm labour (14.23%) and PROM (16.6%). The intensity of growth on the medium was related neither to the prevalence of PROM nor to a preterm labour. The most common neonate complication in the infants of infected mothers was increased bilirubin – 31 infants (13.8%). In the studied group no relation between mother's positive swab culture and a neonate's birth mass has been observed.

STRESZCZENIE

Celem badania była analiza kolonizacji *U. urealyticum* dolnych dróg rodnych pacjentek przyjmowanych do Kliniki Położnictwa Gdańskiego Uniwersytetu Medycznego celem odbycia porodu. Przystudowano historie chorób 2406 pacjentek przyjętych na oddział w 2013 r. Zainfekowanych patogenem były 253 pacjentki - 10,52%. Kobiety należące do przedziału wiekowego 25-35, były najczęściej zainfekowaną grupą. Drobnoustrojami najczęściej izolowanymi łącznie z *U. urealyticum* były *Lactobacillus* i *Staphylococcus epidermidis*. Z wybranych powikłań położniczych najczęstszymi był poród przedwczesny - 14,23% i PROM - 16,6%. Powikłania te nie były związane ze stopniem wzrostu kolonii. Najczęstszym z powikłań u noworodków matek z dodatnim posiewem w kierunku *U. urealyticum* była hiperbilirubinemia - 31 dzieci (13,8%). Nie zaobserwowano wpływu dodatniego wyniku posiewu w kierunku *U. urealyticum* na średnią masę urodzeniową noworodka.

Artykuł zawiera 22803 znaki ze spacjami + grafika