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VAGINAL COLONIZATION AND PRETERM BIRTH

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ABSTRACT

Preterm birth is a significant cause of infant morbidity and mortality. Considerable evidence suggests that infections play a key role in causing women to have preterm labour and delivery. The specific bacteria found in the amniotic fluid and the placenta in association with premature birth are thought to come from the vagina. This is especially true in women with bacterial vaginosis. The aim of the study was to assess the association of vaginal colonization from *M. hominis* and *U. urealyticum* with preterm birth. We evaluated the genital mycoplasmas from a total of 172 vaginal swabs from pregnant and non women who admitted at the department of obstetrics in Obstetric Gynaecology University Hospital "Koco Gliozheni", Tirana, Albania, between 2015 and 2019. The mean age of women was 28.6 (±6.10) years with a range 16-57 years. 132 (76.7%) of them were pregnant. Independent risk factors for preterm birth in multivariate logistic regression resulted *U. urealyticum* (p=0.03), and mixed infections (p=0.001). U urealyticum, is an independent risk factor of preterm birth. The testing for bacterial vaginosis and its prompt treatment may reduce the risk of preterm labour.

Keywords: vaginal colonization, *M. hominis, U. Urealyticum*, preterm birth

INTRODUCTION

Several bacterial sexually transmitted infections (STI) during pregnancy have been reported to be associated with poor pregnancy outcomes (1). Chlamydia trachomatis (CT, chlamydia), Neisseria gonorrhoeae (NG), Trichomonas vaginalis (TV, trichomoniasis) and Mycoplasma genitalium (MG) have all been associated with one or more of the following: premature rupture of membranes (PROM), preterm birth and low birth weight (LBW)1–10; CT and NG are also recognised as causes of neonatal conjunctivitis and CT is a cause of neonatal pneumonia (2). Other genital mycoplasmas in the reproductive tract are M. hominis, Ureaplasma urealyticum and U. parvum (3).

Combined testing for these organisms is common and they are very frequently found in the vagina (4). Routine testing and treatment of asymptomatic non-pregnant women are discouraged because the evidence that they cause disease is questionable. Detection of these organisms during pregnancy has been reported in some studies, however, to be associated with spontaneous abortion, stillbirth, preterm birth, LBW and perinatal morbidity and mortality (5).

In a large cohort study in south Asia, Ureaplasma spp (U. urealyticum and U. parvum together) were the second most common organism identified in infants with signs of serious bacterial infection than from healthy babies and were more commonly isolated from sick than healthy infants(16).

Bacterial culture for U. urealyticum does not distinguish between two closely related species, U. urealyticum and U. parvum and associations with each of these subspecies and adverse pregnancy outcomes are not consistent (6). Comprehensive and systematic information about associations between STI, other genital infections in pregnancy and adverse pregnancy and perinatal outcomes is needed to improve understanding about the evidence for causal associations, to contribute to estimates of the global burden of STI and to determine the potential impact of preventive interventions. For example, associations between syphilis in pregnancy and preterm birth, LBW, stillbirth and systemic congenital infection are well-established, the burden of disease has been estimated and a global strategy for elimination of congenital syphilis is in place (7).
For other STI and reproductive tract infections, the consistency and causal nature of associations are not so clear. Much of the published works on STI, reproductive tract infections and their association with adverse birth outcomes comes from middle-income and high-income countries, with less evidence from low-income settings which have the highest prevalence rates of STI in pregnancy (1).

Spontaneous preterm labour (SPTL) leading to PTB is now recognized as a syndrome caused by a number of pathological processes resulting to activation of the common terminal pathway of parturition (8). The etiology of SPTL is multifactorial, but there is an abundant evidence that local or systemic infection or inflammation is a major cause, particularly of early PTB (9).

This involves interleukins, prostaglandins (PGs), pro - inflammatory chemokines and cytokines, as well as pattern recognition receptors known as toll-like receptors (10). In addition, there is a relationship between infection and PTB changes as pregnancy progresses. Infection in late PTB (34–36 weeks) is unusual but its presence in most cases of the third trimester is associated with PTB o before 34 weeks gestation. In addition, the earlier in pregnancy at which PTB occurs, the more likely it is to be due to infection (11). Between 26 and 34 completed weeks of gestation, women admitted in SPTL are more likely to have abnormal genital tract microflora and chorioamnionitis compared to women delivered electively at the same gestational age for feto-maternal indications (16–18). Systematic reviews that synthesise findings from different studies can help to examine the consistency and risk of bias of the body of evidence. To date, a systematic review about adverse pregnancy outcomes, by Lis et al (12), found that MG was associated with preterm birth and spontaneous abortion. Nucleic acid amplification tests (NAATs) for MG are only now becoming widely available, so a new systematic review of evidence about MG is warranted (25). For NG and adverse pregnancy and neonatal outcomes we are unaware of any systematic reviews. Multiplex NAATs now include targets for M. hominis, U. urealyticum and U. parvum. We are aware of a systematic review that has synthesised quantitative data about associations between these genital mycoplasmas and adverse pregnancy outcomes. M. hominis, in particular, is strongly associated with bacterial vaginosis (BV) which itself is strongly associated with adverse pregnancy outcomes (13).

The use of antibiotic therapy for treating BV in pregnancy has been found to eradicate BV during pregnancy but did not reduce the risk of preterm birth, or preterm, premature rupture of membranes (14). It would be useful to examine whether or not co-existing BV modifies any association between genital mycoplasmas and adverse pregnancy outcomes. STIs and genital mycoplasmas can co-occur and the use of multiplex NAATs means that findings about multiple organisms are increasingly presented together (15). A single search strategy that includes terms for different pathogens and outcomes could make the work of a systematic review more efficient. The aim of the study was to assess the association of vaginal colonization from *M. hominis* and *U. Urealyticum* with preterm birth.

MATERIAL AND METHODS

We evaluated the genital mycoplasmas from a total of 172 vaginal swabs from pregnant and non women who visited the department of obstetrics in Obstetrics – Gynaecology University Hospital “Koco Gliozheni”, Tirana, Albania, between June 2015-2019. A case record form was used to record maternal age, obstetric history, past medical/

surgical history, sexual history, socioeconomic status, history of drug and alcohol abuse, gestational age at admission, physical examination data, gestational age at delivery, the route of delivery, and the newborn birth weight and conditions. The gestational age was calculated from the first day of the last menstrual period and earliest available ultrasound scan. If the estimated gestational age by menstrual and ultrasound estimation showed a difference of more than seven days, the ultrasound estimation was used. Pelvic examination was performed. Using a sterile vaginal speculum vaginal swab was collected from lower one-third of the vaginal wall. Identification and antimicrobial susceptibilities of *U. urealyticum* and *M. hominis* were determined using a commercially available Mycoplasma IST-2 kit (bioMerieux, Marcy-l'Etoile, France), according to the manufacturer's instructions. Statistical analysis: Descriptive statistics were reported as frequencies and percentages for categorical variables and mean and standard deviation for continuous variables. Univariate and multivariate logistic regression was used to assess the risk factors for preterm birth.

RESULTS

The mean age of women was 28.6 (±6.10) years with a range 16-57 years. 132 (76.7%) of them were pregnant. Table 1 showas the Sociodemographic and clinical characteristics of women.

Table 1. Sociodemographic and clinical characteristics of women

Variables	N	%	P
Age M (SD)	28.6 (±6.10)	16-57	
Agegroup, years			<0.01
≤20	8	4.7	
21-30	105	61.0	
31-40	52	30.2	
41-50	5	2.9	
>50	2	1.2	
Parity			<0.01
Nulipara	99	57.6	
Primipara	46	26.7	
Multiparity	27	15.7	
Pregnancy			<0.01
No	40	23.3	
Yes	132	76.7	
Gestational age, weeks M (SD)	25.5 (±4.9)	14-35	

M. hominis was detected in 52.3% of the total women whereas *U. urealyticum in 69.2% (table 2).*

Table 2. Frequency of *M. hominis* and *U. urealyticum*

Genital mycoplasmas	N	%	95%CI
M. hominis	90	52.3	44.56 - 59.95
U. urealyticum	119	69.2	61.72 - 76.0

31 (18%) of women had a preterm birth. Independent risk factors for preterm birth in multivariate logistic regression resulted *U. urealyticum* (p=0.03), and mixed infections (p=0.001) *(table 3).*

Table 3. Association of independent risk factors for preterm birth. Multivariate logistic regression.

Variable	β	Std. Error	Wald	P
Age	-0.06	0.07	0.74	0.4
Gestational age	0.09	0.06	2.55	0.11
No. of births	0.30	0.40	0.54	0.4
M. hominis	-0.08	0.63	0.02	0.8
U. urealyticum	2.40	1.11	4.64	0.03*
Mixed infections	2.73	0.64	18.11	<0.001*

**significant association*

The results of this prospective study demonstrated that women with vaginal U. urealyticum infection, were at increased risk for preterm birth. There have been several previous studies of the association of the two *Ureaplasma* species with clinical disease and/or pregnancy outcome. The association of vaginal M. hominis with preterm birth has been reported as positive in some studies (10) but not in others.

In our study M. hominis was detected in 23 (25.6%) of women in the preterm birth group and in 67 (74.4%) women in term and was not a risk factor for preterm birth at 34 weeks of gestation in the present study.
However, in univariate logistic regression M. hominis was significantly associated with abortion, PROM and preterm birth In many studies, these microorganisms have been reported to cause adverse pregnancy outcomes, such as preterm labour, stillbirth, and chorioamnionitis (16).

On the other hand, they can be merely a part of normal genital flora, which makes the association of genital mycoplasmas with adverse pregnancy outcomes incomplete and confusing. Furthermore, the mechanism of how genital mycoplasma infections affect pregnancy has not been clearly identified. Only the identification of microbial stimuli causing inflammatory reactions in the gravid uterus, which initiates a cascade of events leading to precipitous delivery, has been described (17).

In a large prospective observational study, a significant correlation was found between preterm delivery and *Ureaplasma* colonization. However, Choi, et al (18) mentioned that despite a high prevalence of *Ureaplasma* colonization in preterm labour cases, the rate of preterm delivery did not reach statistical significance. One of the focal points of our study was the relationship between genital mycoplasma infections and adverse pregnancy outcomes. As vaginal colonization with M. hominis seemed to be independent of that with U. urealyticum, it is possible that M. hominis will become an independent risk factor for early preterm birth in future larger studies.

CONCLUSIONS

- ✓ U. urealyticum, is an independent risk factor preterm birth. There is evidence from literature that infection screening and treatment programs for pregnant women before 20 weeks' gestation reduce preterm birth and preterm low birth weight. Infection screening and treatment programs are associated with cost savings when used for the prevention of preterm birth.

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