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Chlamydia Infection in Pregnant Women with Preterm Premature Rupture of Membranes (PPROM) and Preterm Labour (PTL)

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ABSTRACT

Introduction: *Genital chlamydia infection is caused by Chlamydia trachomatis, an obligate intracellular bacterium. Genital chlamydia infection is known to result in serious problems, which include preterm premature rupture of membranes (PPROM), preterm labour (PTL), stillbirth, pelvic inflammatory disease, tubal factor infertility and neonatal infections such as conjunctivitis and pneumonia. This study aims to investigate the occurrence of genital chlamydia infection in pregnant women with PPROM and PTL in KK Women's and Children's Hospital (KKH) and identify risk factors for this group of women, in working towards formulation of a screening protocol.*

Methods: *This is a cross-sectional, prospective, single-centre study conducted at KKH on 83 consecutive pregnant women gestational age between 22 +0 weeks to 36 +6 weeks, age between 21 to 45 years, admitted to the labour ward with PPROM, defined by definite pool of liquor seen on speculum examination, positive AmnicatorTM test and/or Actim® PROM test; and PTL, defined by regular painful contractions with cervical changes. Women on antibiotics for any reason in the last one month, those diagnosed with fetal anomalies and/or placenta praevia were excluded from this study. A urine sample was collected for chlamydia polymerase chain reaction (PCR) analysis and these women were asked to complete a questionnaire to obtain information on socio-demographic and sexual history. Data collected was analysed using SPSS version 17.0.*

Results: *Out of the 83 women included in this study, 32.5% were diagnosed with PPROM alone, 62.7% with PTL alone whilst 4.8% of women were diagnosed with both PPROM and PTL. This study showed that there were no cases of genital chlamydia infection in our study population. Amongst our study group, 79.5% of women had post-secondary education and 97.6% of women were married, 97.6% had only one sexual partner in the year prior to their current pregnancy and 94.0% had never had history of STI.*

Conclusion: *Our study showed no genital chlamydia infection in women with PPROM and PTL. We should consider screening only high-risk women, such as those who are young, single and with multiple sexual partners. A larger study with a control group will provide more information to formulate a screening protocol.*

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INTRODUCTION

Genital chlamydia infection is caused by *Chlamydia trachomatis*, an obligate intracellular bacterium. It is prevalent in 4.2% of females and 2.7% of males globally[1]. It is also one of the most common sexually transmitted infections (STI) in Singapore[2]. The prevalence of genital chlamydia infection in pregnant women ranges from 2-35%[3] in the

American population, being highest amongst those age 15 to 25 years. For pregnant women with preterm premature rupture of membranes (PRROM) and preterm labour (PTL), the prevalence is variable across studies[4-6].

Genital chlamydia infection results in decreased quality of life and serious morbidity. It increases the risk of pelvic inflammatory disease[7,8], chronic pelvic pain[7], ectopic pregnancy[8] and tubal factor infertility[9]. It is also known to increase the risk of acquiring or transmitting human immunodeficiency virus[10]. During pregnancy, women with genital chlamydia infection can experience complications such as miscarriage[11], low birth weight[12], PPROM[7], PTL[3], chorioamnionitis[7], intrauterine fetal death[12] and postpartum endometritis[7]. Furthermore, it can also cause neonatal infection which includes conjunctivitis and pneumonia[1,7]. These complications are preventable by screening and treatment.

To date, there are no local studies investigating the prevalence of genital chlamydia infection in pregnant women, especially those whose pregnancies are complicated by PPROM and PTL. This study aims to investigate the occurrence of genital chlamydia infections in pregnant women with PPROM and PTL in KK Women's and Children's Hospital (KKH) and identify risk factors for genital chlamydia infection in this population. Furthermore, we aim to provide important local data to formulate a genital chlamydia infection screening protocol for pregnant women in KKH.

METHODS

A cross-sectional, prospective, single-centre study conducted at KKH on 83 consecutive pregnant women, age between 21 to 45 years, who were admitted to the labor ward with PPROM and PTL. These women were only recruited during working hours between 8AM and 5PM on the weekdays due to logistics issue. Recruitment period was between October 2013 and February 2015. We approached 83 eligible pregnant women and all consented to participate in our study.

KKH is a tertiary referral centre for obstetrics and gynaecology with over 12,000 deliveries annually. Pregnant women with gestational age between 22^{+0} weeks and 36^{+6} weeks were included in our study. PPROM was defined by definite pool of liquor seen on speculum examination, positive Amnicator™ test and/or Actim® PROM test, whereas, PTL was defined by regular painful contractions with cervical changes. Women taking antibiotics for any reason in the last one month, those with fetal anomalies and/or placenta praevia were excluded from this study.

All eligible women were provided with verbal and written information about genital chlamydia infection in pregnancy study and a written consent was obtained from those willing to participate in the study. A face-to-face interview was conducted by a study investigator for collection of socio-demographic data (maternal age, parity, race, education and marital status) and sexual data (number of sexual partners in the year prior to current pregnancy, number of sexual partners in her lifetime, age of first sexual intercourse and history of sexually transmitted infection (STI)). A urine sample was collected to test for *Chlamydia trachomatis* using the nucleic acid amplification testing (NAAT).

According to our study protocol, patients who were tested positive for genital chlamydia infection were to be treated with a single dose of oral Azithromycin 1g and referred to the Department of STI control (DSC) for contact tracing. In patients with allergy to Azithromycin, Amoxicillin 500mg three times a day dosage, for seven days was to be administered instead. Patients who had not delivered after one month were to be offered a post-treatment early morning urine test to confirm genital chlamydia eradication. In patients who had delivered before one month from diagnostic test, no post-treatment test was indicated.

Data collected were analysed using the SPSS-data entry statistical program (Statistical package for the Social Sciences) version 17.0. This research study was approved by the Singhealth Centralised Institutional Review Board (CIRB).

RESULTS

A total of 83 women were included in the cohort,

where 32.5% of study participants were diagnosed with PPROM alone, 62.7% were diagnosed with PTL alone, and 4.8% were diagnosed with both PPROM and PTL.

The majority of our study population (79.5%) were aged above 26 years and 62.7% were multipara. In our study group, 79.5% of women had post-secondary education and 97.6% of women were married. The majority of women (60.3%) presented between gestational age of 34 and 36 weeks. Table 1 shows the detailed demographic data of the women participating in our study. From sexual history obtained from these women, 97.6% had only one sexual partner in the year prior to their current pregnancy and 94.0% had never had a history of an STI, although interestingly the majority of women participating in the study were sexual active at a relatively young age. Our study showed that 37% (n=31) of the women commenced sexual activity between ages of 16-20, while approximately 36.1% (n=30) became sexually active between ages of 21-24 of age. The details of sexual history are shown in table 2. The results of the urine PCR analyses for chlamydia showed that there were no cases of genital chlamydia infection amongst our study population.

DISCUSSION

The effect of genital chlamydia infections on pregnancy outcomes, particularly PPROM and PTL, remains controversial. In our study, none of the pregnant women with PPROM and PTL aged between 21 to 45 years had genital chlamydia infection. One of the limitations with this study is that we have excluded women age below 21 years due to the difficulty in obtaining consent from their parents for participating in this study. This group of women is known to have a higher chlamydia infection rate. This is shown in an epidemiological study in Hungary, where the chlamydia infection rate in women under 20 years old was 11.41%, as compared to 5.42% in 20-28 year olds and 4.64% in women 29 years and above [13]. Moreover, the majority of our study population was also married in a monogamous relationship and has a high educational level. The negative result in our study might be associated with the exclusion of women with high-risk sexual behavior.

A review of literature revealed several case-control studies which concluded that genital chlamydia infection is not associated with increased risk of PTL [14-17]. This is supportive of our study findings. However, a retrospective case-control study suggested that this might be explained by early treatment [15]. Another case-control study by Cohen et al looking at serum specific antibodies for *Chlamydia trachomatis* also revealed that there was no significant difference in IgG and IgA levels across pregnant women with PPROM, healthy preterm pregnant women, and healthy term pregnant women [18].

In contrary, we also found several studies, which showed an increased risk of chlamydia infection amongst women with PPROM and PTL. A cross-sectional study performed in Brazil showed a 13.9% prevalence of chlamydia infection in women with preterm birth [6]. A population-based retrospective cohort study using Washington State birth certificate data revealed an increased risk of preterm delivery (RR of 1.46) and PPROM (RR of 1.50) in women with chlamydia infections as compared to non-infected women [19]. Several other studies, including one by Rours et al showed that Chlamydia infection was associated with preterm delivery before 32 weeks (OR 4.35) and 35 weeks' gestation (OR 2.66) [20], and another by Andrews et al. showed that genitourinary *Chlamydia trachomatis* infection at 24 weeks' gestation was associated with a 2-fold to 3-fold increased risk of preterm birth [21].

In conclusion, our study showed no genital chlamydia infection in women with PPROM and PTL. We have identified the possibility of bias in this study population where our study subjects were older, married in monogamous relationship and also highly educated, resulting in exclusion of high-risk women. In working towards formulating a screening protocol in KKH, a larger study with a control group will be able to provide us with more information. Perhaps, for cost effectiveness, we only need to screen high-risk women, such as those who are young, single and with multiple sexual partners.

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Table 1 Socio-demographic characteristics

Characteristics	n (%)
Age groups	
21-25 years	17 (20.5)
26-30 years	23 (27.7)
31-35 years	30 (36.1)
36-40 years	12 (14.5)
>40 years	1 (1.2)
Race	
Chinese	41 (49.4)
Malay	23 (27.7)
Indian	8 (9.6)
Others	10 (12.1)
Unknown	1 (1.2)
Education	
Below secondary	2 (2.4)
Secondary	15 (18.1)
Higher education	66 (79.5)
Marital status	
Single	1 (1.2)
Married	81 (97.6)
Divorced	1 (1.2)
Gravidity	
1	31 (37.3)
>1	52 (62.7)
Gestational age at diagnosis	
<28 weeks	6 (7.2)
28-33 weeks	27 (32.5)
34-36 weeks	50 (60.3)

Table 2 Sexual history of the study population

Characteristic	n (%)
Sexual partners in the year prior to pregnancy	
1	81 (97.6)
>1	2 (2.4)
Sexual partners in lifetime	
1	38 (45.8)
2-4	36 (43.4)
>/=5	9 (10.8)
Age at first sexual intercourse	
</=15	4 (4.8)
16-20	31 (37.4)
21-24	30 (36.1)
>/=25	18 (21.7)
History of STI	
Yes	5 (6.0)
No	78 (94.0)