UNIVERSITI PUTRA MALAYSIA

OCCURRENCE OF Chlamydia trachomatis INFECTION IN PREGNANT WOMEN WITH PRETERM COMPLICATIONS AND STILLBIRTHS

NURSHAHIRA BINTI SULAIMAN

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OCCURRENCE OF *Chlamydia trachomatis* INFECTION IN PREGNANT WOMEN WITH PRETERM COMPLICATIONS AND STILLBIRTHS

By

NURSHAHIRA BINTI SULAIMAN

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OCCURRENCE OF *Chlamydia trachomatis* INFECTION IN PREGNANT WOMEN WITH PRETERM COMPLICATIONS AND STILLBIRTHS

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NURSHAHIRA BINTI SULAIMAN

September 2012

Chairman : Chong Pei Pei, PhD

Faculty : Faculty of Medicine and Health Sciences

This study aims to determine the occurrence of *C. trachomatis* infection across a multi-ethnic cohort of pregnant women who presented with preterm complications and stillbirths and to determine the risk factors for *C. trachomatis* infection. This study also detects *C. trachomatis* using nested PCR and PCR ELISA as the screening tools.

A cross-sectional study on pregnant women less than 37 weeks of pregnancy who presented with preterm contractions, preterm premature rupture of membranes and stillbirths was carried out in two public hospitals in Southern Selangor, Malaysia. A total of 106 endocervical swabs obtained were subjected to DNA amplification using Nested PCR (BioSewoom, Korea) and PCR-ELISA (Roche, USA) for *C. trachomatis* detection.

Self-administered questionnaires were used to collect data on demographic and behavioural factors.

In addition, *C. trachomatis* was detected in 43% of women with preterm complications and in 62% of women with stillbirths. Multiple logistic regression analysis indicated that mothers who were less than 25 years old of age (OR 2.731; 95% CI: 1.139, 6.549) and Chinese ethnicity (OR 17.799; 95% CI: 1.406, 225.387) were significant independent risk factors for chlamydial infection ($p<0.05$).

High prevalence of *C. trachomatis* infection was observed among women with preterm complications and stillbirths. This study supports the essential need to screen pregnant women with preterm complications and stillbirths for infection with *C. trachomatis* using highly sensitive PCR ELISA. Thus, early intervention such as antibiotic therapy can be instituted at the earliest possible time with appropriate screening guidelines to reduce the adverse outcomes of *C. trachomatis* infection.

Abstrak tesis yang dikemukakan kepada Senat Universti Putra Malaysia sebagai memenuhi keperluan untuk ijazah Master Sains

KAJIAN JANGKITAN *Chlamydia trachomatis* DI KALANGAN WANITA HAMIL MENGALAMI KOMPLIKASI PRA-MATANG DAN KEMATIAN BAYI BARU LAHIR

Oleh

NURSHAHIRA BINTI SULAIMAN

September 2012

Pengerusi : Chong Pei Pei, PhD

Fakulti : Fakulti Perubatan dan Sains Kesihatan

Tujuan kajian ini dijalankan adalah untuk mengkaji kelaziman dan faktor risiko jangkitan bakteria *C. trachomatis* di kalangan ibu mengandung yang terdiri daripada pelbagai kaum yang mempunyai kontraksi pra-matang, pecah air ketuban pra-matang dan kematian bayi baru lahir. Di samping itu, kajian ini juga menggunakan 'nested PCR' and 'PCR ELISA' sebagai ujian diagnostik bagi jangkitan *C. trachomatis*.

Kajian rentas di kalangan ibu mengandung yang mempunyai usia kandungan kurang daripada 37 minggu dan mempunyai komplikasi pra-matang dan kematian bayi baru lahir telah dijalankan di dua buah hospital di Selangor. Seramai 106 responden telah bersetuju untuk menyertai kajian ini di mana pemeriksaan servik dilakukan oleh pegawai

perubatan bagi memperoleh sampel calitan servik. Pada masa yang sama, responden juga dikehendaki menjawab soalan kaji-selidik yang digunakan untuk mendapatkan maklumat demografi dan faktor tingkah-laku. Kehadiran bakteria *C. trachomatis* di dalam sampel tersebut kemudiannya diuji menggunakan nested PCR (BioSewoom, Korea) dan PCR-ELISA (Roche, USA).

Nested PCR menunjukkan prestasi yang kurang sensitif (10.81%) tetapi sangat spesifik (97.83%) berbanding dengan PCR ELISA. Nilai ramalan positif (PPV) dan nilai ramalan negatif (NPV) yang diperolehi dari kajian ini adalah 80% dan 57.7%. Di samping itu, *C. trachomatis* telah ditemui di kalangan 43% ibu yang mengalami komplikasi pra-matang dan 62% daripada ibu yang mengalami kematian bayi baru lahir. Ujian logistik regresi menunjukkan ibu yang berumur kurang daripada 25 tahun (OR 2.731; 95% CI: 1.139, 6.549) dan berbangsa Cina (OR 17.799; 95% CI: 1.406, 225.387) adalah faktor risiko penyebab jangkitan *C. trachomatis* (p<0.05).

Peratus jangkitan *C. trachomatis* di kalangan ibu mengandung yang mengalami komplikasi pra-matang dan kematian bayi baru lahir adalah tinggi. Justeru itu, kajian ini menyokong keperluan untuk ujian saringan *C. trachomatis* di kalangan ibu mengandung yang mengalami komplikasi pra-matang dan kematian bayi baru lahir.

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I certify that a Thesis Examination Committee has met on **14 September 2012** to conduct the final examination of Nurshahira Binti Sulaiman on her thesis entitled **"Occurrence of *Chlamydia trachomatis* infection in pregnant women with preterm complications and stillbirths"** in accordance with the Universities and University College Act 1971 and the Constitution of the Universiti Putra Malaysia [P.U.(A) 106] 15 March 1998. The Committee recommends that the student be awarded the Master of Science.

Members of the Thesis Examination Committee were as follows:

Zuraini Binti Ahmad, PhD
Associate Professor
Department of Biomedical Sciences
Faculty of Medicine and Health Sciences
Universiti Putra Malaysia
(Chairman)

Vasantha Kumari Neela, PhD
Associate Professor
Department of Medical Microbiology and Parasitology
Faculty of Medicine and Health Sciences
Universiti Putra Malaysia
(Internal Examiner)

Cheah Yoke Kqueen, PhD
Associate Professor
Department of Biomedical Sciences
Faculty of Medicine and Health Sciences
Universiti Putra Malaysia
(Internal Examiner)

Tang Thean Hock, PhD
Associate Professor
Advanced Medical and Dental Institute (AMDI)
Universiti Sains Malaysia
(External Examiner)

_____

SEOW HENG FONG, PhD
Professor and Deputy Dean
School of Graduate Studies
Universiti Putra Malaysia

Date:

This thesis was submitted to the Senate of Universiti Putra Malaysia and has been accepted as fulfillment of the requirement for the degree of **Master of Science**. The members of the Supervisory Committee were as follows:

Chong Pei Pei, PhD
Associate Professor
Department of Biomedical Sciences
Faculty of Medicine and Health Sciences
Universiti Putra Malaysia
(Chairman)

Rozita Binti Rosli, PhD
Professor
Department of Obstetrics and Gyneacology
Faculty of Medicine and Health Sciences
Universiti Putra Malaysia
(Member)

Rusinahayati Binti Mokhtarudin, MBBS (Malaya), MOG(Malaya)
Quality Department
University Malaya Medical Centre
University of Malaya
(Member)

_____

BUJANG BIN KIM HUAT, PhD
Professor and Dean
School of Graduate Studies
Universiti Putra Malaysia

Date:

DECLARATION

I declare that the thesis is my original work except for quotations and citations which have been dully acknowledged. I also declare that it has not been previously, and is not concurrently, submitted for any other degree at Universiti Putra Malaysia or at any other institution.

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NURSHAHIRA BINTI SULAIMAN

Date:

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APH	antepartum hemorrhage
ANC	antenatal clinic
bd	bis in die (twice daily)
Chlamydiae	trivial names (plural)
chlamydial	adjective
CDC	Centre for Disease Prevention and Control
CI	confidence interval
DFA	direct fluorescence antibody
DNA	deoxyribonuclease acid
DNase	deoxyribonuclease
ELISA	enzyme linked immunoassay assay
FEME	urine full examination and microcopic examination
FVU	first void urine
g	gravity
Gel. Liq.	gelatin liquefaction
HIV	human immunodeficiency virus
IUD	intrauterine device
κ	kappa
min	minutes
µl	microliter
ml	milliliter
MOMP	transmembrane protein with surface antigenic components which can be used to identify the different *C. trachomatis* serovar
NAAT	nucleic acid amplification test

O&G	obstetrics and gynaecology
ONPG	o-nitrophenyl-β-D-galactopyranoside (a test for β-galactosidase)
omp 1	gene that encodes outer major membrane protein
OR	odds ratio
PAC	patient administration centre
PCR	polymerase chain reaction
PID	pelvic inflammatory disease
PPROM	preterm prelabour rupture of membranes
RMB	Renminbi
sec	seconds
serovars	serological variance
SDA	strand displacement amplification
STI	sexually transmitted infections
TMA	transcription-mediated amplification
UTI	urinary tract infections
VP	Voges-Proskauer (a test for butanediol fermentation)
w/v	weight per volume
WHO	World Health Organization

CHAPTER 1

INTRODUCTION

1.1 Background

Identification of pregnant women infected with *Chlamydia trachomatis* is essential to allow early antibiotic treatment in order to prevent adverse pregnancy outcomes due to chlamydial invasion. Pregnant women may have contracted *C. trachomatis* endocervical infection before they conceive through sexual intercourse with infected partner (Mardh, 2002). Infection in women mostly occur when the sexually transmitted pathogen invade the single-layer columnar epithelium following receptive anal intercourse with infected partners (Hladik and McElrath, 2008). Maternal infections with *C. trachomatis* have been linked to perinatal morbidity and mortality as well as low birth weight (Rours et al., 2011, Borges-Costa et al., 2011, Johnson et al., 2011).

In Malaysia, the prevalence of chlamydial infection among patients with pelvic inflammatory disease admitted to Seremban General Hospital was found to be 22.7% (Ravindran et al., 1998). A *Chlamydia* surveillance conducted in Sweden revealed that the prevalence of *Chlamydia* is highest in females within the age group of 15-24 years old in which it reaches a rate of 976 cases per 100,000 (Riera-Montes and Velicko,

2011). In most countries, opportunistic chlamydial testing is offered to sexually active adolescents and young adolescents with multiple sexual partners (Maymon et al., 2000). On the other hand, guidelines for the treatment of sexually transmitted infections in Malaysia were based on the syndromic approach. Thus far, there is lack of a comprehensive study on the incidence rate of *C. trachomatis* infection among pregnant women with preterm complications and the associated risk factors.

Due to the fastidious growth requirement of *C. trachomatis* in culture and the lack of clinical value of serology tests, diagnosis of *C. trachomatis* infection is often missed. The development of nucleic acid amplification tests (NAATs) has resulted in a significant increase in sensitivity and specificity in the field of chlamydial diagnosis (Masek et al., 2009). Chapter 3 describes detection of *C. trachomatis* in endocervical specimens using two different nucleic acid amplification techniques which were Nested PCR (BioSeewoom, Korea) and PCR ELISA (Roche Diagnostics, USA). Nested PCR targets on the *omp 1* gene encoding *C. trachomatis* major outer membrane proteins while PCR ELISA targets on the cryptic plasmid. Evaluating the performance of commonly used nested PCR against the gold standard PCR ELISA is important to test the sensitivity and specificity of different target regions used for *C. trachomatis* detection.

Distributions of *C. trachomatis* infection across different types of preterm complications were observed in Chapter 4. Other symptoms and antenatal complications such as urinary tract infection, abnormal vaginal discharge, antepartum hemorrhage and past obstetrics history such as ectopic pregnancy and preterm delivery were also evaluated. In addition, postpartum progress, birth outcome and detection of other microorganisms among *Chlamydia* infected and non-infected women were compared. The final part of this study investigated the potential predictors affecting *C. trachomatis* infection among pregnant women.

Chapter 5 described the association of socio-demographic and behavioral factors with chlamydial infection. Respondents' demography de
status, multiple sexual partners and partner condom usage were obtained with the aid of self-administered questionnaires. All in all, this study supports the essential need to screen pregnant women with preterm complications and stillbirths for infection with *C. trachomatis* so that antibiotic therapy can be instituted at the earliest possible time to reduce the adverse outcomes of *C. trachomatis* infection.

1.2 General objective

To study the distribution and association of *C. trachomatis* endocervical infection in pregnant women presented with preterm contractions, preterm prelabour rupture of membranes (PPROM) and stillbirths using nested PCR and PCR ELISA as the screening tools.

1.3 Specific objectives

1. To detect *C. trachomatis* DNA by commercially available nested PCR and PCR ELISA.

2. To determine the distribution and association of preterm contractions, preterm prelabour rupture of membranes (PPROM) and unexplained stillbirths with *C. trachomatis* infection.

3. To identify the association of preterm delivery and low birth weight with *C. trachomatis* infection.

4. To determine the association of socio-demographic and behavioural factors with *C. trachomatis* infection among pregnant women.

1.4 Null hypothesis

1. There is no significant agreement in *C. trachomatis* detection using nested PCR and PCR ELISA.

2. There is no association between preterm complications and stillbirths with *C. trachomatis* infection.

3. There is no association between socio-demographic and behavioural factors with *C. trachomatis* infection.

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