Prevalence of genital *Chlamydia trachomatis* in Iran: a systematic review and meta-analysis

Mohammad Hossein Ahmadi, Akbar Mirsalehian, Abbas Bahador

Department of Microbiology, School of Medicine, Tehran University of Medical Sciences, Tehran, Iran

Objective: To determine the overall prevalence of *Chlamydia trachomatis* in Iranian males and females and to find out the effect of this bacterium on fertility potential and its association with urogenital symptoms.

Methods: We searched both English and Persian electronic databases using keywords '*Chlamydia*', '*Chlamydia trachomatis*', 'prevalence', 'incidence', 'frequency', 'epidemiology' and 'Iran'. Finally, after some exclusion, 34 studies from different regions of Iran were included in our study, and a meta-analysis was performed to determine pooled prevalence estimates for each group.

Results: *C. trachomatis* prevalence for women and men was high and ranged from 0 to 32.7% and 0 to 23.3%, respectively (95% CI). The pooled prevalence of the bacterium in the female population was 12.3% (95% CI: 10.6–14.2%) and in men was 10.9% (95% CI: 7.6–15.4%). A high level of heterogeneity was seen for both men ($I^2 = 77.4\%$; $P < 0.001$) and women ($I^2 = 77.5\%$; $P < 0.001$); but in men and not in women, some evidence for publication bias was observed [Egger's test (two-tailed $P = 0.013$); Begg's test (two-tailed $P = 0.025$)]. In females analysis of symptomatic/infertile group with asymptomatic/fertile group in females, the overall OR was above 1 and the overall P -value was below zero.

Conclusions: This bacterium may play a role in female infertility or be associated with clinical manifestations; thus, planning national programmes for adequate diagnosis of genital infections caused by this pathogen is necessary. Furthermore, screening strategies, particularly for asymptomatic individuals, and treatment of infected people can reduce consequent complications.

Keywords: *Chlamydia trachomatis*, Prevalence, Infertility, Urogenital Symptoms, Iran

Introduction

C. trachomatis is one of the most common pathogens that cause sexually transmitted infections (STIs).¹ Although as much as two-thirds of women and 50% of men who are infected with this organism develop asymptomatic infections,² in the remaining population, this bacterium can cause a broad spectrum of genitourinary infections, such as non- and post-gonococcal urethritis, epididymitis and prostatitis in males³ and cervicitis, salpingitis and pelvic inflammatory disease (PID) in females, which particularly in the chronic form may lead to ectopic pregnancy or exert negative effects on fertility. Furthermore, *in vitro* co-incubation of *C. trachomatis* with human spermatozoa can impair sperm motility and kill spermatozoa likely because of the bacterium lipopolysaccharide,⁴ although the role of this pathogen in male infertility remains controversial.^{3–5} However, symptomatic or asymptomatic infections by this pathogen have a profound impact on the female reproductive

system;⁶ ascending infections can cause PID, which may lead to infertility or ectopic pregnancy.^{7,8}

As mentioned above, most genital chlamydial infections are usually asymptomatic, which are capable of transmitting to sexual partner(s);⁹ therefore, screening is necessary to identify these infections¹⁰ and to know the relative frequencies of these agents in different populations.⁶ This involves screening programmes, which have been established in some industrialised countries to prevent reproductive complications.^{11–13}

In Iran, to date, several studies have reported the frequency of *C. trachomatis* infections in males and/or females, in which the frequency of this pathogen varies significantly in different studies. However, most of these studies are local and limited to an individual hospital or a special province, and a comprehensive analysis of the overall prevalence of this bacterium, as well as its association with infertility and urogenital symptoms, which may be useful to set up control programmes for the prevention of STIs, has not yet been performed.

Thus, the present study was designed to determine the prevalence of *C. trachomatis* infection, its impact

Correspondence to: Abbas Bahador, Department of Microbiology, School of Medicine, Tehran University of Medical Sciences, Keshavarz Blvd, 100 Poursina Ave., Tehran 14167-53955, Iran. Email: abahador@tums.ac.ir

on fertility potential, and its association with urogenital symptoms in the Islamic Republic of Iran (I.R.Iran) using a systematic review and meta-analysis according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) statement.¹⁴

Methods

Search strategy

Electronic databases, including OVID databases, PubMed, Web of Science, Scopus and Google Scholar, were searched for the prevalence of *C. trachomatis* infections in Iran from November 1998 to January 2015. The search was restricted to original articles published in English that present the prevalence, frequency or incidence of *C. trachomatis* infections in Iranian males or females using the following keywords with the help of Boolean operators (AND, OR): ‘*Chlamydia*’, ‘*Chlamydia trachomatis*’, ‘prevalence’, ‘incidence’, ‘frequency’, ‘epidemiology’ and ‘Iran’. In addition to articles published in English, we also looked for relevant articles in Persian published and indexed in Iranian databases, such as Scientific Information Database (SID) [<http://www.sid.ir/>], Magiran [<http://www.magiran.com/>], Irandoc [<http://www.irandoc.ac.ir/>], Regional Information Center for Science and Technology (RICST) [<http://en.ricest.ac.ir/>] and Iranian National Library [<http://www.nlai.ir/>], with similar strategies and related and appropriate Persian keywords. References from reviewed articles were also searched for more information.

Study selection

Included studies were all original articles presenting cross-sectional, case-control, or cohort studies on the prevalence of symptomatic or asymptomatic genital *C. trachomatis* infections in Iranian males/females in which the methods for diagnoses were molecular amplification techniques, such as polymerase chain reaction (PCR), multiplex PCR and plasmid PCR. Excluded studies were: (1) those that used detection methods other than molecular amplification techniques, including culture or serological methods, such as enzyme-linked immunosorbent assay (ELISA) or immunofluorescence (IF), (2) studies reporting combined prevalence data for male and female participants and (3) those that studied chlamydial infections in organs or body sites other than the genitourinary tract.

Review articles, congress abstracts, studies reported in languages other than English or Persian, meta-analyses or systematic reviews, duplicate publications of the same study and articles available only in abstract form were also excluded.

Data extraction

Variables extracted from each study included first author’s name, year of publication, study setting, geographical location, participants, gender, specimen type, number of patients investigated, bacterial species investigated, type of detection method and number of positive samples. The articles were reviewed and relevant data were extracted by two authors independently. Disagreements between reviewers were discussed to obtain consensus.

Statistical analysis

The data were analysed using Comprehensive Meta-Analysis Software Version 2.0 (Biostat, Englewood, NJ, USA). The prevalence was reported by 95% confidence intervals (CIs). Cochrane *Q*-statistic test and *I*² test were performed to estimate heterogeneity between studies, and random effect model was chosen to estimate the average prevalence because of its conservative summary estimate and because in all calculations, *I*² was above 50%. To assess the possible publication bias, a funnel plot along with Begg’s rank correlation and Egger’s weighted regression methods were used. Two-tailed *P* < 0.05 was considered indicative of a statistically significant publication bias.

Results

A total of 92 articles (64 in English and 28 in Persian) were collected. Through the first screening, 21 articles were excluded on the basis of the title evaluation, as eight of them were duplicate publications of the same study, and 13 have titles irrelevant to our study. After the second assessment, five papers were discarded because they had reported Chlamydial infections in organs or body sites other than the genitourinary tract. Finally, after full-text evaluation, 32 studies were ruled out on the basis of their detection methods (detection methods other than molecular amplification techniques), or status of reported prevalence data (combined prevalence data for males and females) (Fig. 1), and 34 articles (25 in English and nine in Persian) published between 2006 and 2014 were selected and included in our analysis (Table 1).

Of 34 articles included, 24 had studied the prevalence of *C. trachomatis* in women, seven in men and three in both genders; eight studies (six for women and two for men) were case-control (which investigated fertile-infertile or symptomatic-asymptomatic individuals) and the rest were cross-sectional. The participants of the cross-sectional studies were miscellaneous and varied from asymptomatic and fertile individuals to symptomatic men and women having urogenital infections and complications,

Figure 1 Flow chart of the literature search, systematic review and study selection. *Studies reporting combined prevalence data for male and female participants.

such as urethritis, cervicitis, PID, ectopic pregnancy and infertility.

The most commonly collected sample for detection was first-void urine for both men and women, but other samples included semen and urethral swabs for men and vaginal discharge, endocervical swabs and fallopian tube tissue for women. Six papers studied other agents in addition to *C. trachomatis*, such as *Neisseria gonorrhoeae* or *mycoplasma* spp., simultaneously.

Most of the studies were performed in Tehran ($n = 21$), which is the capital of Iran, in comparison with ones performed in central ($n = 7$), southwestern ($n = 3$), northeastern ($n = 2$) and western ($n = 1$) Iran. The prevalence of genital infections due to *C. trachomatis* in different regions of Iran is shown in Fig. 2.

The age for women ranged from 15–66 years (median: 40.5 years) and for men from 14–59 years

(median: 36.5 years). Four studies did not report ages of participants, and more than two-thirds of studies had neither age-stratified data nor usable information on patients' education and occupation.

C. trachomatis prevalence for women and men ranged from 0 to 32.7% and 0 to 23.3%, respectively (95% CI). The pooled prevalence of the bacterium in women was 12.3% (95% CI, range: 10.6–14.2%) and in men was 10.9% (95% CI, range: 7.6–15.4%); Figs. 3 and 4 show the forest plot of the meta-analysis of *C. trachomatis* prevalence for women and men, respectively. The funnel plot for meta-analysis of *C. trachomatis* prevalence in women suggests no evidence of publication bias (Fig. 5). Neither Egger's test (two-tailed $P = 0.053$) nor Begg's test (two-tailed $P = 0.069$) was statistically significant for the publication bias; however, a high level of heterogeneity was observed ($I^2 = 77.5\%$; $P < 0.001$). But, for men, in addition to heterogeneity

Table 1 Studies included in meta-analysis after final evaluation.

First author (reference)	Published year	Province/city	Sex	Sample(s)	Mean age	Total number of participants	Events number	Events rate (95% CI) (%)
Chamani-Tabriz (a) ¹⁵	2006	Tehran	F	First-void urine	28.5	1052	129	12.3
Zaeimi-Yazdi ¹⁶	2006	Tehran	F	Endocervical swabs	32.7	142	22	15.5
Meidani ¹⁷	2007	Tehran	M	First-void urine	32	140	1	0.7
Chamani-Tabriz (d) ¹⁸	2007	Tehran	F	First-void urine	28.5	1052	133	12.6
Golshani ¹⁹	2007	Tehran	M	Semen	35	200	36	16.3
Hashemi ²⁰	2007	Tehran	F	Endocervical swabs	37.5	123	21	17
Samarbaf-Zadeh ²¹	2007	Ahvaz	F	Vaginal discharge	ND	202	33	16.3
Kalantar ²²	2007	Yazd	F	Vaginal discharge	30.2	91	0	0
Chamani-Tabriz (c) ²³	2007	Tehran	F	First-void urine	26.1	340	38	11.2
Khalili ²⁴	2008	Kerman	M	Urethral swabs	ND	66	8	12.1
			F	Endocervical swabs	ND	64	4	6.3
Chamani-Tabriz(b) ²⁵	2008	Tehran	F	First-void urine	28.8	991	127	12.8
Rashidi (a) ²⁶	2009	Tehran	F	First-void urine	26.8	458	48	10.5
Jenab ²⁷	2009	Isfahan	F	Endocervical swabs	37.5	80	17	21.3
Taheri-Beni (b) ²⁸	2010	Ahvaz	F	Endocervical swabs	ND	620	108	17.4
Haghighi ²⁹	2011	Sabzevar	F	First-void urine	31	196	27	13.8
Asgari ³⁰	2011	Tehran	M	First-void urine	32.5	130	3	2.3
Naderi ³¹	2012	Kerman	F	Fallopian tube tissue	ND	129	5	3.9
			M	First-void urine	ND	129	19	14.7
Taheri-Beni (a) ³²	2012	Isfahan	F	Endocervical swabs	ND	80	17	21.3
Hassanzadeh ³³	2012	Shiraz	F	First-void urine	27	210	0	0
Ghazvinj ³⁴	2012	Mashhad	M	First-void urine, urethral swabs	38	178	19	10.6
Eslami ³⁵	2012	Tehran	F	Endocervical swabs	27.5	121	16	13.2
Fatholahzadeh (a) ³⁶	2012	Tehran	F	First-void urine	32.5	260	39	15
Mohammadzadeh ³⁷	2013	Tehran	F	Endocervical swabs	33.8	130	6	4.6
Sadrpour ³⁸	2013	Tehran	M	Semen	26.8	120	28	23.3
Ilami ³⁹	2013	Yasouj	M	First-void urine	34.9	28	2	7.1
			F	First-void urine	30.1	109	3	2.8
Zahirnia ⁴⁰	2013	Tehran	F	Endocervical swabs	28.6	121	16	13.2
Afrakteh ⁴¹	2013	Tehran	F	First-void urine	28.8	49	16	32.7
Hajikhani ⁴²	2013	Tehran	F	Endocervical swabs	32.5	51	6	11.7
Rashidi (b) ⁴³	2013	Tehran	F	First-void urine	28.3	457	48	10.5
Akya ⁴⁴	2013	Kermanshah	F	Endocervical swabs	32.6	255	8	3.1
Saeedzadeh ⁴⁵	2013	Shiraz	F	Endocervical swabs	ND	212	17	8
Yeganeh ⁴⁶	2013	Tehran	M	First-void urine	33.5	200	24	12
Fatholahzadeh (b) ⁴⁷	2013	Tehran	M	First-void urine	32.5	200	17	8.5
Marashi ⁴⁸	2014	Tehran	F	Endocervical swabs	24.8	350	61	17.4

M: males; F: females; ND: not determined
Lower-case letters inside the parentheses indicate the various studies performed by the same author

Figure 2 Prevalence of genital infections due to *C. trachomatis* in different regions (cities) of I.R.Iran. *There was only one study about females in Yazd which had reported no detection of the bacterium; the number of studies in other cities included: Yasouj: one (studied both males and females), Kermanshah: one (females), Sabzevar: one (females), Mashhad: one (males), Shiraz: two (females), Ahvaz: two (females), Kerman: two (each of them studied both males and females), Isfahan: two (females) and Tehran: 21 (15 females and six males); M: males; F: females.

($I^2 = 77.4\%$; $P < 0.001$), some evidence for publication bias was observed [Egger's test (two-tailed $P = 0.013$) and Begg's test (two-tailed $P = 0.025$); the resulting funnel plot is shown in Fig. 6.

The forest plot for six case-control studies about women is presented in Fig. 7; as seen in the plot, the odds ratios (ORs) for all these studies except one were above 1, P -values for three surveys were below 0.05, the overall OR was 2.3 (95% CI, range: 1.1–4.6), and the overall P -value was 0.02, indicating that the prevalence of *C. trachomatis* is significantly higher in the case group compared with that in the control group. However, the number of studies was fewer than 10 and insufficient for an accurate conclusion; the corresponding funnel plot is shown in Fig. 8.

Discussion

The role of *C. trachomatis* and some other bacteria as primary agents of genital infections and STIs both in men and women is unquestionable.⁶ Furthermore, a considerable amount of genital infections is asymptomatic and consequently remain undetected and untreated because most infected people do not seek

medical care and treatment, thereby transmitting the infection to their sexual partner(s). Thus, implementing national control programmes to interrupt the transmission chain and prevent the subsequent negative impact on the male and female reproductive system is thought to be necessary; in this regard, comprehensive analyses of the overall prevalence of this bacterium, particularly in developing countries (including Iran), may help to accomplish this strategy.

By performing this systematic review and meta-analysis, which is the first such study in Iran, we found that the prevalence and frequency of genital *C. trachomatis* in men as well as women was greatly variable in various studies. There was also a high grade of heterogeneity in participants' characteristics and conditions, kinds of samples taken for tests, detection methods, sample sizes and study settings.

Because men and women are distinct populations with different indicators of prevalence, corresponding data about each of them were analysed separately in the present study. Among articles finally included in this analysis, there were no studies conducted either in northern or southern Iran, and most of

Meta Analysis

Figure 3 Forest plot of the meta-analysis of *C. trachomatis* prevalence for women.

Meta Analysis

Figure 4 Forest plot of the meta-analysis of *C. trachomatis* prevalence for men.

them were performed in the capital, Tehran, and central Iran; this may relatively suggest some participation bias in generalisation of reported estimates. Another limitation of the present study is that

many papers conducted in different regions of the country had to be excluded from the analysis because their methods of detection were culture, or serology (for example, ELISA and IF), which have lower

Figure 5 Funnel plot of the meta-analysis of *C. trachomatis* prevalence for women.

Figure 6 Funnel plot of the meta-analysis of *C. trachomatis* prevalence for men.

sensitivity and specificity in comparison with molecular techniques.⁴⁹ Furthermore, different samples were used for detection, and the number of participants in included studies was different and ranged from 28–200 and 49–1052 for men and women, respectively.

We analysed six case-control studies among included articles; all were about females. As seen in Fig. 7, ORs for all these studies^{26,31,43,47,48} except one²⁷ were above 1, *P*-values for three surveys were below 0.05,^{31,47,48} the overall OR was 2.3 (95% CI, range: 1.1–4.6), and the overall *P*-value was 0.02;

indicating that the prevalence of *C. trachomatis* was significantly higher in the case group (infertile/symptomatic females) compared with that in the control group (fertile/asymptomatic ones); meaning that this bacterium may play a role in female infertility or be associated with clinical manifestations. However, the number of such studies was fewer than 10 and was not enough to perform a good meta-analysis, generalise the results, and make conclusions about them. In addition, more than two-thirds of the studies had reported neither age-stratified data

Meta Analysis

Figure 7 Forest plot of the meta-analysis of *C. trachomatis* prevalence for six case-control studies about women.

Figure 8 Funnel plot of the meta-analysis of *C. trachomatis* prevalence for six case-control studies about women.

nor usable information on patients' education and occupation to be analysed and compared with each other. Moreover, there were no randomised, controlled clinical trials assessing the effects of antibiotic therapy for genital *Chlamydia* on the improvement of infertility due to this bacterium among surveys included in this study.

As reported by the World Health Organization in 2005, approximately 101 million chlamydial infections are detected annually worldwide, and the prevalence rates of *C. trachomatis* among adults varies between different countries.⁵⁰ In a systematic review, 25 studies from several countries were analysed in which the prevalence of urogenital *C. trachomatis* for women varied from 1.1–10.6% and for men from 0.1 to 12.1%; the prevalence of this bacterium

was highly variable between countries and was higher in women than that in men, and the younger age groups (<25 years) had the highest prevalence rate.⁵¹ The results of our meta-analysis showed that the pooled prevalence of *C. trachomatis* in males and females was 10.9% (95% CI, range: 7.6–15.4%) and 12.3% (95% CI, range: 10.6–14.2%), respectively; this shows a higher prevalence rate in females rather than that in males and is in the range of the above study.

In a meta-analysis study conducted by Lewis *et al.* in Australia, the pooled prevalence estimates of *C. trachomatis* for indigenous women under 25 years was reported to be 22.1% (95% CI: 19.0–25.3; three studies) and for indigenous men under 25 years to be 14.6% (95% CI: 11.5–17.8; three studies).

They also reported a high level of heterogeneity among their included studies and a higher prevalence rate in younger populations, indigenous Australians and those attending sexual health centres.⁵²

In another systematic review and meta-analysis survey about females performed in the United Kingdom, healthcare settings had higher prevalence estimates than those in population-based studies because studies performed in general practice surgeries had an overall high chlamydia prevalence of 8.1% (95% CI; range: 6.5–9.9%) compared with 5.0% in population-based studies (95% CI; range: 3.2–7.6%). The authors also declared that age and study setting were variables with the most influence on the prevalence rate of this bacterium.⁵³

As mentioned above, more than two-thirds of studies included in our analysis had not reported age-stratified data; therefore, we could not make a comparison between age groups. However, some variability was seen in prevalence rates reported in different countries, which is perhaps due to differences in detection methods and protocols, types of samples studied, epidemiological aspects (different populations), hygiene issues and existence or non-existence of regular screening, treatment and control programmes, particularly in some of the developing countries, such as Iran, for dealing with this pathogen.

In conclusion, the results of the present study highlight the necessity of planning national programmes for adequate diagnosis of genitourinary infections due to *C. trachomatis*. Furthermore, our results denote the importance of screening strategies, particularly for asymptomatic individuals, and treating infected people (including sexual partners) to control STIs and their ensuing complications and to maintain fertility and reproductive health.

Disclaimer statements

Contributors

MHA and AB planned the overall study and wrote the protocol. MHA performed the bibliographical searches, identified the studies, extracted data, planned the analyses and produced the first draft of the manuscript. AB reviewed and revised the manuscript. AM participated in data collection and reviewing papers for the study. All authors read and approved the final manuscript.

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Conflict of interest

None declared.

Ethics approval

None.

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