Burden of *Chlamydia trachomatis* in India: a systematic literature review

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**ABSTRACT**

*Chlamydia trachomatis* (hereafter CT) is Gram-negative, obligate intracellular pathogen. It causes the world’s most common non-viral sexually transmitted disease. India is home to the world’s greatest burden of infectious diseases, yet information on prevalence rates of CT is scarce. This article systematically reviews the literature for the prevalence rates and testing methods in India. A total of 27 studies were included. Four main patients groups (symptomatic women, infertile women, pregnant women and asymptomatic population groups) could be identified with varying rates of CT (0.1%–32% using PCR, 2.4%–75% using ELISA serology). Most of the studies originated from urban settings, 11 of them from New Delhi. In-house PCR was the most common diagnostic technique used generating the following ranges in prevalence for the four group studies: symptomatic women 10%–50%, pregnant women 0.1%–2.5% and asymptomatic populations 0.9%–24.5%. The rates among infertile women were 9%–68% based on serology results. The prevalence rates featured in this paper are in line with other locations across the Indian subcontinent. This review highlights the extreme heterogeneity in the limited studies available in India on CT and the need for standardized guidelines for diagnosis and management of CT in India. The availability of resources should be considered in the formulation of recommendations.

**Keywords:** Chlamydia trachomatis, India, C. trachomatis, Sexually Transmitted Diseases, Infertility
INTRODUCTION

Chlamydia trachomatis is a Gram-negative, obligate intracellular pathogen that can lead to a broad spectrum of clinical diseases in human populations. It is known to cause a significant burden of preventable blindness in third world countries. Chlamydia trachomatis is also known as the most common bacterial sexually transmitted infection worldwide (Newman et al. 2015). With a total of over 130 million new cases per year worldwide in 2015, C. trachomatis infections represent a major problem worldwide. Latest trends furthermore seem to indicate that this number is likely to increase (WHO 2008). Urogenital infections with C. trachomatis have been associated with a wide range of genitourinary conditions including cervicitis and salpingitis in women as well as epididymitis and urethritis in men. Infection with the pathogen is however often asymptomatic and hence frequently remains undiagnosed, leading to an array of severe long-term consequences (Haggerty et al. 2010). Studies indicate that chlamydial infections can lead to severe impairments such as pelvic inflammatory disease, tubal damage and ultimately tubal factor infertility in women if they are not treated in a timely and adequate fashion (den Hartog, Morré and Land 2006; Haggerty et al. 2010). Additionally, infections with C. trachomatis can severely impact the reproductive health of women, causing severe conditions such as ectopic pregnancies, repeated and spontaneous abortions and stillbirths (Tiller 2002; Baud and Greub 2011). These features render timely identification and reliable diagnosis of C. trachomatis an issue of public health importance, as the disease can effectively be treated using antibiotics. This is particularly true in developing countries, where infectious disease already significantly burdens the populations and the healthcare systems (Gangolli, Duggal and Shukla 2005; John et al. 2011). The asymptomatic nature of the disease also requires evidence-based guidelines for the implementation of population-wide screening programs. In fact, studies have claimed that, due to the low prevalence of Chlamydia at the population level, screening in the general population may not be cost-effective (Low et al. 2007). The identification of high-risk groups or chlamydial infections is however a public health issue (Althaus et al. 2010). This aspect is particularly significant for low and middle-income countries, where healthcare resources and budgets are limited (CDC and World Bank 2008).

With a total population of approximately 1.2 billion inhabitants, India is after China the second most populous country in the world (Perianayagam and Goli 2012). It is similarly known to be home to one of the greatest burden of Infectious diseases in the world (John et al. 2011). There is however a paucity of data and a lack of overview concerning the burden of C. trachomatis infections in India. Insights regarding the strategies for diagnosis and management of C. trachomatis in healthcare settings are also limited (Malhotra et al. 2013). As a result of the varying levels of specificity and sensitivity of the diagnostic tools utilized in the clinical settings, the choice of method is of primordial importance (Chernesky 2005).

The aim of this paper is to systematically review the available scientific literature to investigate the urogenital C. trachomatis burden in India, across different regions and patient groups. The initial scope of this review is to provide an overview of the prevalence of the disease among the different patient groups. Additionally, the techniques used to identify C. trachomatis in patients need to be assessed, to lead the way for formulation of future best practices and potential evidence-based guidelines for diagnosis and management of C. trachomatis across the Indian subcontinent. Finally, in light of the significant impact of C. trachomatis on the female reproductive tract, and the importance of maternal and child health in India, the disease’s contributions to the national burden of reproductive health needs to be clarified (Inhorn and Bharadwaj 2007; Ganguly and Unisa 2010; Mahesh 2013) in order to aid policy decisions.

METHODS

Peer-reviewed articles included in this review were obtained from the major databases namely PubMed and Embase using the search headlines ‘Chlamydia trachomatis’ and ‘India’. Additionally, Google Scholar was screened with the same search criteria to include non-indexed articles and ‘gray’ literature (Mahood, Van Eerd and Irvin 2014). Lastly, all the references and work cited by the articles included in this review were screened to identify further articles to be included. The above databases were screened for available data from August 2015 until December 2015.

In light of the previously mentioned lack of consistent data originating from the Indian settings, the scope of the literature search was designed to include all the patient groups that are at a higher risk of infection or subsequent sequelae when considering C. trachomatis. Taking into account the exploratory nature of the review, the authors screened all articles based on the type of patient population, the diagnostic method utilized to test for a urogenital C. trachomatis and the geographical location of the study. All of the studies that suited the scope of the review were included for further analysis based on the abstract and reviewed by at least two of the authors and checked for duplicates. The included articles were then scrutinized individually in their full-text versions. The final inclusion of discordant studies was then discussed with the authors.

If the data screened did not feature population testing, described laboratory techniques in relation with C. trachomatis detection or Chlamydia typing of established positive samples, they were excluded from this review. Additionally, all duplicates were excluded.

RESULTS

The combined literature search yielded a total of 27 unique articles; the details of the inclusion are summarized in Fig. 1.

The literature search succeeded in unveiling scientific studies originating from a wide range of geographical locations.

Figure 1. Sources of included articles.
However, the city of New Delhi was over-represented, as over a third of all the included studies (11/27 = 40%) could be traced back to this location. Similarly, three studies originated from the city of Mumbai and three others from the city of Chennai, respectively. Additionally, it should be noted that most of the studies originated from urban settings, as only two studies were conducted in rural settings (2/27 = 7%). The locations of the different studies included are summarized in Fig. 2.

The differences in the testing methods used to diagnose Chlamydia trachomatis and the differences in patient populations enclosed in this review render a meta-analysis of the data difficult. Some distinct patient groups could however be consistently identified and grouped together for analysis. A total of four patient groups could be identified as listed below (see Table 1 for details):

1. Symptomatic patients presenting in healthcare settings: 13 identified studies.
2. Infertile and subfertile women: seven identified studies.
3. Pregnant women: two identified studies and four control groups.
4. Asymptomatic population groups: three studies and one control group included

**Symptomatic patients presenting at the gynecology outpatient department (OPD)**

The first patient population was the most represented in the review with a total of 13 studies identified. The details of the studies are featured in Table 2. The prevalence of C. trachomatis among the studies ranged from 10% in the study by Sood et al. (2012) to 50% in the study by Gopalkrishna et al. (2000) using polymerase chain reaction (PCR), both in New Delhi (Gopalkrishna et al. 2000; Sood et al. 2012). However, another study from Chennai by Pushpa Innocent (2010) using ELISA reported a prevalence of 75%. The predominance of studies from New Delhi could also be observed in this group. Eight of the studies conducted on symptomatic patients were in fact conducted in New Delhi.
A similar study testing on men attending the STD clinic in Mumbai was also identified. The authors however did not specify patient details. The study reported 2.2% C. trachomatis prevalence using first-void urine (FVU) PCR (Lindan et al. 2005).

Female patients (repeatedly) infected with C. trachomatis are known to be at an elevated risk for late complications, i.e. tubal factor infertility (den Hartog, Morré and Land 2006). Seven articles are included in this review.

### Table 1

The articles are color-coded based on the patient groups they feature: Group 1 (green): symptomatic women; Group 2 (blue): infertile and subfertile women; Group 3 (red): pregnant women; Group 4 (white): asymptomatic population groups.

| Main Author | Journal and Year | Location | Study population | Control group | Method of testing* | C. trachomatis prevalence |
|-------------|------------------|----------|------------------|---------------|-------------------|--------------------------|
| Choksi et al. (2015) | Annals of clinical microbiology and Antimicrobials | New Delhi (North) | Women attending the Gynecology OPD | | PCR (smear) | 5% |
| Mohan & Borthaker (2015) | Indian Journal of medical research | New Delhi (North) | Infertile and subfertile women | | PCR (In-House) | 13.5% (PCR) 6.5% (EIA) |
| Dhawan et al. (2014) | Indian Journal of medical research | New Delhi (North) | 208 infertility women | | In-house PCR DFA EIA COBAS Taqman | 13.5% (PCR) 6.5% (EIA) |
| Vidyasagar et al. (Vidyasagar et al. 2012) | Journal of reproductive infertility | Mumbai (West) | 896 women attending the gynecology OPD (symptomatic) | | PCR (In-House) | 12.1% |
| Dettai et al. (2011) | Male infertility | Chennai (South) | 3513 fertile married couples | | Roche AMPLICOR PCR | 0.9% at baseline |
| Cunha et al. (2011) | Infectious diseases in obstetrics and gynecology | New Delhi (North) | 2466 women under suspicion of C. trachomatis infections (PID, Cervicitis, Salpingitis etc) | | DFA Culture In-house PCR (Plasmid RFLP-based genotyping (MOMP) | 15.85% (19/1264 DFA) 12.5% (10/807 Culture) 12.2% (44/353 In-house PCR) 24.2% (22/90/MOMP RFLP) |
| Sood et al. (2012) | Indian Journal of dermatology, venereology and leprology | New Delhi (North) | 97 symptomatic women presenting at the STD clinic | | DFA PCR (plasmid) | 11.4% (DFA) 10.3% (PCR) |
| Patil et al. (2010) | Annals of clinical microbiology and Antimicrobials | New Delhi (North) | Women attending the Gynecology OPD Symptomatic (discharge) | | Group F: Direct fluorescent assay (N=273) Group 2: In-house PCR and AMPLICOR | 23% |
| Prabha et al. (2010) | Annals of biological research | Chennai (South) | 280 patients in 2 groups (discharge and irregular periods) | | IgG ELISA | 60.95% (75 patients) 9.5% (controls) |
| Savvitha, Madhavan, Vinodh Raj (2009) | Journal of Pharmaceutical Sciences and Research | Salem (South) | 200 women presenting at the Primary Health care center and private clinics | | Giemsa stain | 10.3% |
| Malik et al. (2009) | Fertility and Sterility | Aligarh (North) | 46 infertile women | | IgG ELISA Culture | 55% (IgG ELISA infertile women) 5.5% (IgG ELISA controls) |
| Dwivedi et al. (2009) | Indian Journal of Dermatology, Venereology and Leprology | Cuttack (East) | 108 symptomatic married women (71 tested) | | MOMP PCR (in-house) | 7.04% |
| Gupta, Sushil and Mittal (2009) | Journal of Infectious diseases in developing countries | New Delhi (North) | 355 symptomatic women attending the OPD | | IgG and IgM inclusion proteins ELISA MOMP ELISA | 30.2% (in which 62 % IgG+ and 59.25% IgM+) |
| Malhotra et al. (2008) | Indian Journal of Sexually Transmitted Diseases | New Delhi (North) | 276 women with genital discharge or ulcer (symptomatic) | | DFA test (Immuno PA) IgG and IgM ELISA | 19.9% (DFA) 10.9% (ELISA) |
| Malik et al. (2006) | Indian Journal of Medical Research | Aligarh (North) | 110 women suffering with primary or secondary infertility | | Culture and ELISA | 28.1% (infertile group) positive by one or more markers, 22% (culture) 13.3% (control Group) |
| Vinita et al (2005) | Journal of Obstetrics and Gynecology in India | Lucknow (North) | Women attending gynecology and Family planning (symptomatic and Asymptomatic) | | In-house urine PCR | 14% of symptomatic women 4% of asymptomatic women |
| Lindan et al. (2005) | Journal of clinical Microbiology | Mumbai (West) | 690 men attending the STI clinic | | Ferret Catch Urine PCR | 2.2% |
| Joyce et al. (2004) | International Journal of STD and AIDS | Tajour, Ramad and Digni district | Randomly selected adults aged 15-45 1849 participants (1066 females,783 males) | | AMPLICOR PCR IgM ELISA | 1.5% (PCR) 2.4% (IgM ELISA) |
Table 1. Chlamydia trachomatis prevalence among symptomatic patients (results given for PCR or most sensitive technique).

| Authors                      | Location       | Testing       | Cohort size | Prevalence                  |
|------------------------------|----------------|---------------|-------------|-----------------------------|
| Mania-Pramanik et al. (2012) | Mumbai         | PCR           | 896         | 12%                         |
| Sood et al. (2012)           | New Delhi (North) | DFA, PCR     | 97          | 10%                         |
| Gita et al. (2011)           | New Delhi       | DFA, PCR Culture, PCR | 2466      | 15% (DFA)/13.2% (PCR)       |
| Patel et al. (2010)          | New Delhi       | PCR           | 593         | 23%                         |
| Pushpa Innocent (2010)       | Chennai         | IgG ELISA     | 280         | 60%/75% (two cohorts)       |
| Dwibedi et al. (2009)        | Lucknow         | PCR           | 100         | 14%                         |
| Gupta, Salhan and Mittal (2009) | New Delhi     | IgG ELISA     | 355         | 30%                         |
| Malhotra et al. (2008)       | New Delhi       | DFA, IgG IgM ELISA | 276      | 19%                         |
| Vinita et al. (2006)         | New Delhi       | PCR           | 280         | 28%                         |
| Singh et al. (2003)          | Chennai         | Culture and PCR | 143      | 32%                         |
| George et al. (2003)         | Culture and PCR |               |             |                             |
| Singh et al. (2002)          | New Delhi       | DFA, PCR      | 350         | 43%                         |
| Gopalkrishna et al. (2000)   | New Delhi       | IgG ELISA, PCR | 50         | 50%                         |

Table 2. Chlamydia trachomatis prevalence among infertile and subfertile women (results given for PCR or most sensitive technique).

| Authors                       | Location     | Testing       | Cohort size | Prevalence                  |
|-------------------------------|--------------|---------------|-------------|-----------------------------|
| Mania-Pramanik et al. (2012)  | Kolkata      | IgG ELISA, PCR | 50         | 2.5%PCR 15% ELISA          |
| Mohan and Borthakur (2015)    | Guwahati     | IgG ELISA     | 40          | 25%                         |
| Baijai, Ganesh and Neellesh (2015) | Indore   | IgG ELISA     | 111         | 9%                          |
| Dhawan et al. (2014)          | New Delhi    | PCR,DFA, EIA  | 200         | 13.5%                       |
| Malik et al. (2009)           | Aligarh      | IgG ELISA     | 20          | 55%                         |
| Malik et al. (2006)           | Aligarh      | Culture, IgG ELISA | 110     | 28.1%                       |
| Sharma, Aggarwal and Arora (2002) | Amritsar | IgG ELISA     | 50          | 68%                         |

Table 3. Prevalence among infertile and subfertile women (results given for PCR or most sensitive technique).

| Authors                        | Location   | Testing     | Cohort size | Prevalence                  |
|--------------------------------|------------|-------------|-------------|-----------------------------|
| Ghosh et al. (2015)            | Kolkata   | IgG ELISA, PCR | 50         | 2.5%PCR 15% ELISA          |
| Mohan and Borthakur (2015)     | Guwahati  | IgG ELISA   | 40          | 25%                         |
| Baijai, Ganesh and Neellesh (2015) | Indore  | IgG ELISA   | 111         | 9%                          |
| Dhawan et al. (2014)           | New Delhi | PCR,DFA, EIA | 200        | 13.5%                       |
| Malik et al. (2009)            | Aligarh   | IgG ELISA   | 20          | 55%                         |
| Malik et al. (2006)            | Aligarh   | Culture, IgG ELISA | 110     | 28.1%                       |
| Sharma, Aggarwal and Arora (2002) | Amritsar | IgG ELISA   | 50          | 68%                         |

Studies conducted among infertile and subfertile women were included. The results are summarized in Table 3. The prevalence ranged from 9% in Indore in central region of India to 68% in a study performed in Amritsar, making use of enzyme immunoassay (Sharma, Aggarwal and Arora 2002; Baijai, Ganesh and Neellesh 2015). A further study from Kolkata in the eastern region of India reported an even lower prevalence using PCR (2.5%) (Ghosh et al. 2015). The same study nonetheless reported a seroprevalence of the pathogen of 15% while testing with ELISA (Ghosh et al. 2015).

Pregnant women

The third group of interest is pregnant women. Two studies were identified where testing was conducted in pregnant women. Pregnant women were also used as a control group in four previously mentioned studies (Sharma, Aggarwal and Arora 2002; Malik et al. 2006, 2009; Ghosh et al. 2015). All results are summarized in Table 4. The reported prevalence of C. trachomatis in this group for studies reporting the use of PCR ranged from 0.1% in Vellore, South India, to 2.5% in the study by Ghosh et al.
Table 4. Chlamydia trachomatis prevalence among pregnant women (results given for PCR or most sensitive technique).

| Authors            | Location    | Testing                | Cohort size | Prevalence |
|--------------------|-------------|------------------------|-------------|------------|
| Ghosh et al. (2015)| Kolkata     | ELISA, PCR             | 50          | 2.5%       |
| Vidwan et al. (2012)| Vellore     | PCR                    | 1198        | 0.1%       |
| Malik et al. (2009)| Aligarh     | IgG ELISA, culture     | 30          | 5.5%       |
| Malik et al. (2006)| Aligarh     | IgG ELISA, culture     | 30          | 3.3%       |
| Sharma, Aggarwal and Arora (2002) | Amritsar | IgG EIA                | 50          | 10%        |
| Paul et al. (1999) | New Delhi   | Enzyme immunoassay     | 94 and 172  | 17%/18.6%  |

Table 5. Prevalence of Chlamydia trachomatis in population screening (results given for PCR or most sensitive technique).

| Authors                      | Location                          | Testing        | Cohort size                  | Prevalence |
|------------------------------|-----------------------------------|----------------|------------------------------|------------|
| Detels et al. (2011)         | Chennai                           | PCR            | 3513 (males and females)     | 0.9%       |
| Savitha, Madhavan and Vinoth Raja (2009) | Tanjore district, Tamil Nadu | Giemsa Stain  | 200 (females)                | 10.5%      |
| Joyee et al. (2004)          | Tanjore, Ramnad and Dingidul districts, Tamil Nadu | PCR            | 1849 (males and females)     | 1.1%       |
| Singh et al. (2002)          | New Delhi                         | PCR            | 53 (males and females)       | 24.5%      |

in Kolkata, East India (Vidwan et al. 2012; Ghosh et al. 2015). The prevalence range is even greater in the studies utilizing ELISA tests. These results range from 3.3% in Aligarh reported by Malik et al. (2006) to 18.6% in the study by Paul et al. (1999). The results featured in this group also display higher prevalence in the studies utilizing serology-based testing.

Asymptomatic population groups

Data from studies performing testing at the population level could only be found in three studies and one control group. The population screening group is hence the least represented group, the results and prevalence of the study are summarized in Table 5. The populations screened in this patient group present with major differences in both sample size, origin and prevalence of C. trachomatis. The lowest prevalence (0.9%) was observed by Detels et al. among shop owners and commercial sex workers in Chennai, while the highest prevalence (24.5%) was reported for residents of slum areas in New Delhi by Singh et al. (2002). Both the aforementioned results were provided using PCR testing.

Testing and diagnostic methods

The methods used to diagnose the disease and identify the pathogen in clinical settings are of pivotal importance. In fact, C. trachomatis can be identified through different tests, all of which have different characteristics. Although PCR is currently the gold standard for the identification of the bacteria in human subjects, it however can also be identified through culture (Centers for Disease Control and Prevention 2014; Lanjouw et al. 2016). On the other hand, serology-based tests such as ELISA are only suitable for screening in subfertile women. Serology tests help to ascertain the presence of an immune response against the pathogen through the detection of specific antibodies. These antibodies highlight a previous infection which is particularly relevant in the case of C. trachomatis infections (Keltz, Gera and Moustakis 2006). Previous infections may in fact be the cause of tubal pathologies which can be traced back as the cause of infertility. Table 6 summarizes the testing methods featured in the studies included in this review. It should be noted that many of the studies made use of more than one diagnostic test.

The most commonly reported test in the review was in-house PCR testing, which was performed in 14 studies. ELISA immunological testing was the second most common test, present in 13 studies.

Table 6. Diagnostic and tests in the studies included in the review.

| Testing method                  | Number of studies |
|---------------------------------|-------------------|
| In-house PCR                    | 14                |
| ELISA                           | 13                |
| Commercial PCR tests            | 5                 |
| DFA                             | 4                 |
| Culture/Giemsa stain            | 3                 |

Material for PCR testing

Material for the conduction of (or sample for conducting the) PCR testing can be obtained from different parts of the body as well as different bodily fluids. Each of the products requires a specific sampling procedure which might be more or less invasive. The origin of the sampled material for PCR among the different studies is summarized below. It should be specified that some of the studies featured more than one PCR assays requiring different materials each.

It can be seen that the most commonly used biological material for the conduction of PCR assays were endocervical swabs. It can be seen that the most commonly used biological material for the conduction of PCR assays were endocervical swabs, As featured in Table 7. This method of sampling was used in 11 studies. Other methods included FVU and urine sampling, which were conducted in three studies each. Vaginal samples were used in only two studies.
**DISCUSSION**

This review provides the first overview on the Chlamydia trachomatis prevalence in the Indian subcontinent. Articles and studies on the subject could be traced back to various geographical regions of India, and the results could be classified into symptomatic women, infertile and subfertile women and asymptomatic population groups. All of them display varying values of C. trachomatis prevalence, which can be attributed to the different settings where testing was conducted, the different population characteristics, but most importantly the tools used to diagnose the pathogen. The findings of this constitute a first attempt at identifying existing discrepancies attributable to differences in population testing techniques and locations regarding the current situation surrounding C. trachomatis in India. In fact, in all patient groups investigated in this review, the prevalence results stemming from studies making use of serology-based testing such as ELISA were as expected higher when compared with the results of studies using PCR.

It was observed that, in patient groups 1 and 2, the prevalence reported using ELISA serology is higher than results obtained through PCR testing. This highlights that the seroprevalence is higher among symptomatic and infertile patients when compared to other groups. The presence of an immune response to the pathogen as supported by positive results of serological tests in fact suggests a past or chronic exposure to the pathogen (Horner et al. 2013). The high seroprevalences as compared to PCR prevalences suggest that previous Chlamydia trachomatis infection is related to long-term consequences. In fact, PCR detects bacterial DNA inside of the patient’s genital tract, which suggests a current infection rather than a past one. This finding underscores the role played by C. trachomatis in chronic infections leading to adverse health outcomes, and particularly, infertility.

Lack of studies featuring male participants could also be observed in group 1. In fact, only one study could be identified, where testing was conducted among men. This study could furthermore not be included in the tables, as the patients tested were not listed as asymptomatic, but as attendees of the STD clinic, who may be present only for information. The only testing group where accounts for both men and women could be obtained was the group regarding population screening. All of them display varying values of C. trachomatis prevalence, which can be attributed to differences in sensibility and specificity of testing, varied cultural backgrounds as well as healthcare practices and health-related beliefs. Additionally, the performance of local, state-run healthcare delivery systems varies greatly between the different states (Goli et al. 2014). Moreover, research in different settings has highlighted the role of host genetic markers in the development of symptoms and consequences related to pathogens such as C. trachomatis. Genetic and genomic differences present within the different ethnicities that inhabit the Indian subcontinent could lead to varying prevalence of C. trachomatis. Furthermore, it should be stated that, despite the various represented patient groups included in this review, only three individual studies featured male patient groups. It should be furthermore stated that the only patient group where only men were represented was part of the asymptomatic population groups category. This limited data representing the male populations not only questions the completeness of the picture regarding the prevalence of C. trachomatis in the population but also raises the question of public health relevance associated with an undetected reservoir of infections, which could be held accountable for propagation of the disease. In addition, there are no mentions of contact tracing and partner testing in the different studies. Nonetheless, the data regarding prevalence featured in this article, with the exception of some very high prevalence numbers, match to some extent the prevalence data from European countries, when considering similar patient groups (ECDC 2014; Redmond et al. 2015). Additionally, and in a similar fashion compared with the Indian scenario, data from neighboring countries in similar situations and geographical locations are scarce. Some studies from Sri Lanka and Bangladesh nonetheless seem to suggest similar results across comparable patient groups. A study from the Colombo district in Sri Lanka in fact highlighted a C. trachomatis prevalence of 8.3% using PCR amid women attending the STI clinics (Kamani Mangalika et al. 2014). In another study from Bangladesh, a prevalence rate of 23% from sexually active women was found using in-house PCR (Hoque et al. 2013). The results from these studies support the range of prevalence, which was observed in similar groups in India. These results support the idea that C. trachomatis is associated with a significant burden of disease on the Indian subcontinent, particularly among high-risk groups such as sex workers and patients at STI clinics.

An important factor that may render the Indian settings unique regarding testing and identification of C. trachomatis and other sexually transmittable diseases in the community is the cultural stigma. Stigma was briefly mentioned in the study by Dwibedi et al. (2009) as a significant factor hindering women for seeking assistance and medical care for STI-related symptoms. Although no work could be identified highlighting the stigma against C. trachomatis, there exists a body of evidence surrounding the stigma surrounding HIV/AIDS in India. Many articles in fact support the idea that stigma is a major factor, present at multiple levels which hinders proper and timely management of HIV/AIDS, and that impacts the daily life of people affected by the diseases (Bharat 2011; Ekstrand et al. 2012, 2013). It is hence plausible that many people in the community shy away from getting diagnosed and treated with a sexually transmitted infection, even in spite of the fact that treatments and cures may exist, like in the case of C. trachomatis. This is further supported by experience of co-authors (Indian researchers/medical doctors) in this paper. This highlights the need for additional research into psychosocial factors influencing the health-seeking behavior of Indian patients. Stigma might in fact cause many patients to renounce seeking care and hence expose themselves to long-term health impairments. The absence of acknowledgement of the role of stigma related to STIs may suggest that the issue is widely ignored.
Furthermore, there seems to be discrepancies between the internationally recognized gold standards for *C. trachomatis* detection in industrialized countries and the practices currently implemented in India. As a matter of fact, only slightly short of half of all the studies included in this review featured testing using PCR. Most the PCR tests were performed in-house, while only five studies featured commercially available and internationally acclaimed tests such as the Roche AMPLICOR assay. It should be stressed that, as per the co-authors’ experience, due to the elevated prices of some of the commercial PCR assays, in-house PCR tests might represent a valuable alternative for identification of *C. trachomatis* in healthcare settings. More research is nonetheless necessitated to better understand the properties of such tests. The values of specificity and sensitivity of in-house PCR tests ought to be judged against internationally acclaimed tests to ensure appropriate diagnosis. Additionally, there would be a need for evidence-based guidelines regarding the conduction of in-house PCR for the detection of *C. trachomatis*. Research conducted in Indian settings has highlighted that in-house PCR testing displays highly satisfactory results when compared to the AMPLICOR assay (Sachdeva et al. 2009). Research from Trinidad and Tobago has further highlighted the use of in-house PCR as a valuable option for settings where the availability of commercial testing kits is limited (Rampersad et al. 2007). Further research from South America has highlighted that a set of well-defined in-house PCR primers can be used for the detection of *C. trachomatis*, showcasing high levels of sensitivity and specificity when compared to gold standard kits (Aguilera-Areola et al. 2014).

Furthermore, many of the articles referred to cell culture as the gold standard for the detection and diagnosis of *C. trachomatis* in India. These aspects might be associated with the resource intensity of PCR when compared to more affordable testing methods such as culture, direct fluorescence assay (DFA) or ELISA. PCR testing in fact necessitates a vast array of equipment and expertise and can hence only be performed in some facilities and by trained staff. Identification through culture or serology can conversely be performed in traditional laboratory settings which are present in clinics and primary health centers. This further supports the need for cost-effective diagnostic tools for detection in resource-limited settings such as in India. It should hence be stated that research is needed for the implementation of novel testing and diagnosis methods for *C. trachomatis* and other pathogens in resource-limited settings.

Another important point brought up by the review is the discrepancies in research methodology among the included studies. The control group included in some of the studies did not match with the study populations. This holds in the article by Singh et al. (2002) for instance. The study in fact compares female patients in healthcare settings to randomly selected inhabitants of the slums. This also holds for the lack of information regarding the inclusion of these populations. Additionally, in the two studies by Malik et al. (2006, 2009), both testing groups composed of infertile women were compared to control groups that were smaller in size. The population tested for *C. trachomatis* ought to be thorough and representative of their populations in order to provide sound information to policy makers. This is especially true in studies aiming at screening populations, as they may guide future screening schemes for sexually transmitted diseases. Overall, there should be a drive towards high-quality research designs, in order to facilitate policy implementations aimed at addressing the burden of *C. trachomatis* among the Indian population. In fact, there is a need for high-quality research to enable the development of evidence-based guidelines for the management of *C. trachomatis* in Indian healthcare settings. The current standard operating procedure regarding the diagnosis and management of sexually transmissible diseases are in fact hard to identify and appear to be incomplete. The current guidelines issued by the government of India indeed miss *C. trachomatis* as a potential cause of vaginal discharge, although it is one of the most common manifestation of *C. trachomatis* infection once it presents with symptoms (Government of India 2014). There is thus a need for clarity at the policy level for the identification, screening, prevention and treatment of pathogens like *C. trachomatis*. In addition of the need for cost-effective and readily implementable testing solutions, there is a need for more research in the policy strata. There is in fact a need for an encompassing policy framework taking all the relevant variables into account in order to foster safe, effective and evidence-based management of *C. trachomatis* infections as well as the long-term consequences they may cause.

This paper touches upon the topic of female infertility in India. This topic remains vastly unexplored, although some accounts suggest that the burden might underreported in India (Jejeebhoy 1998; Malhotra et al. 2013). There has been an increase in the number of couples that make use of in vitro fertilization and other methods in order to conceive (Widge and Cleland 2009). Experts have also argued that the issue is not properly addressed and is not sufficiently investigated in Indian settings (Pande 2013). Results from national surveys suggest a rise in the number of infertile couples (Mahesh 2013). These factors ought to draw more attention on the burden of infertility, of which *Chlamydia trachomatis* is a major cause alongside other diseases such as *N. gonorrhoea*. In fact, not only is the detection of the pathogen straightforward, but a timely management and treatment of the infection may lead to a full recovery and replenished reproductive health.

**CONCLUSION**

This review is the first endeavor to systematically review the prevalence of *Chlamydia trachomatis* across India. The studies included for analysis differed greatly based on research methodology, patient populations and testing methods used to diagnose *C. trachomatis* highlighting a need for standardization and guidelines for the identification and diagnosis of *C. trachomatis* in India. The prevalence of the disease across states and patient groups has been shown to vary quite significantly, suggesting the influential role of a wide range of factors including diagnostic tools and perhaps the genetic makeup of the different populations on the Indian subcontinent. More research is needed to develop novel diagnosis tests which are cost-effective and which can be implemented in resource-limited settings such as India. This paper highlights in-house PCR as a technique yielding high levels of sensitivity and specificity for pathogen identification. Tools and techniques however ought to be streamlined. More research is also necessary to ascertain the role of *C. trachomatis* in primary and secondary infertility in India as well as in adverse pregnancy outcomes. Further research will also need to be conducted in order to identify population subgroups that are at a high risk for sexually transmitted diseases and, particularly, for *C. trachomatis*. Policies and guidelines defining the identification and management of *C. trachomatis* in India also ought to be updated to maximize patient outcomes.
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