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Review

Female urogenital chlamydia: Epidemiology, chlamydia on pregnancy, current diagnosis, and treatment

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ABSTRACT

Female urogenital chlamydia is a disease caused by *Chlamydia trachomatis* infection in the female urogenital tract. It is a common bacterial sexually transmitted disease. The bacteria is transmitted through sexual contact with an infected partner or from mother to newborn during vaginal delivery. The prevalence varies among studies and the number is possibly higher due to the lack of massive screening. Many patients were asymptomatic and still be able to transmit the disease. The undiagnosed and untreated disease could cause pelvic inflammatory disease, which leads to infertility, ectopic pregnancy, and chronic pelvic pain. The prevalence among pregnant women is similar to non-pregnant women, therefore chlamydia screening in pregnant women is highly recommended. The nucleic acid amplification test is the most reliable method for the diagnosis due to high sensitivity. The current treatment is given by prescribing antibiotics.

1. Introduction

Chlamydia is the most common bacterial sexually transmitted disease in females, caused by *Chlamydia trachomatis*, an obligate intracellular gram-negative bacterium [1]. It is estimated that 1 in 20 sexually active young women aged 14–24 years has chlamydia [2]. Chlamydial infections among youths aged 15–24 years accounted for two-thirds of the total new infections [3]. The highest prevalence was in the Region of America, followed by the region of Africa, while South East Asia had the lowest prevalence [4]. Chlamydia is transmitted through sexual contact with an infected partner and can also be transmitted from mother to newborn during vaginal delivery. The disease is commonly asymptomatic. It affects the urethra and cervix of the female urogenital tract. Ascending infection could lead to pelvic inflammatory disease, which leads to infertility, ectopic pregnancy, and chronic pelvic pain. Mass screening are recommended for sexually active women aged <25 years therefore, non-sexually-active female were mostly undiagnosed, unreported, and untreated. The diagnosis is generally based on nucleic acid amplification tests (NAATs) on the cervical or vaginal swabs and urine samples. Other methods such as cell culture and enzyme-linked immunosorbent assay (ELISA) could be used. The current treatment for Chlamydia infection is using antibiotics to treat patients and their sexual partners to prevent reinfection. This article reviews the current epidemiology, clinical presentation & effect on pregnancy, diagnosis, and treatment of female urogenital chlamydia which can be used as consideration to create health policy in the management of chlamydial infection.

2. Epidemiology

Epidemiological and clinical data of chlamydia cases are difficult to obtain. It was estimated that the prevalence of chlamydial infection among US men and women aged 15–39 years was 2.35% [5]. The characteristic of the study population and different methods used for diagnosis leads to a wide prevalence (Table 1). Several studies in Table 1 showed that the prevalences range from 1.7% to 24.3%. An estimation of the global prevalence and incidence of urogenital chlamydia in women aged 15–45 years in 2016 was 3.8% in prevalence and 127.2 million in the incident. The asymptomatic nature may cause undetectable disease transmission. About 75% of women and 50% of men are

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Table 1
Prevalence of female urogenital Chlamydia from several studies.

Study design	Population	Num. of participants	Chlamydia prevalence	Ref.
Cross-sectional survey	Female aged 14–39 years	4149	2%	[2]
cross-sectional survey	Female patients attending clinic	69	8.7%	[18]
Meta-analysis	General female population	89,886 (include male)	3.1%	[4]
a systematic review and meta-analysis	Reproductive age women	17,119	7.8%	[19]
a systematic review and meta-analysis	General population	NA	3.8%	[20]
Territory-wide STI and Sexual Health Survey (TeSSHS)	General population	535	1.7%	[21]
A retrospective study	Female patients attending clinic	338	24.3%	[22]
A retrospective study	Pregnant women	439	4.6%	[12]

asymptomatic.

Female urogenital Chlamydia primarily occurs between the ages of 14–24 years [3]. Young and sexually active females are primarily affected. Several key risk factors have been identified. Females have a 3.5-fold higher prevalence than men. The other risks include being under 25 years, having multiple or new sex partners, no or rare use of condoms or oral contraceptives, and prior or having sexually transmitted disease (STDs) [6–10]. The probability for chlamydia transmission varies depending on the type of sexual contact, the number of sexual acts, and partnership length [11]. It was estimated that transmission probability was 2.0% per vaginal sex act and 5.8% per anal sex act for both male-to-female and female-to-male [11].

A study among pregnant women in Pemba Island, Tanzania showed that the prevalence of chlamydia was 4.6% [12]. A cross-sectional survey among pregnant women, gynecology clinic attendees, and subfertile women in Guangdong, China showed that the prevalence of chlamydia was 6.7% in pregnant females and 5.9% in subfertility females [13]. A similar number (6.9%) was observed in a prospective study among pregnant women from Córdoba, Argentina [14]. 18% of pregnant women attending Primary Health Care services in Amazon, Brazil have chlamydia [15]. A study among Pregnant Women in the Tertiary Hospital in south-south Nigeria from January 2010 to December 2019 showed 7.3% of the population has chlamydia [16]. A Retrospective observational cohort study in the UK showed that being pregnant doubled the odds of having Chlamydia after controlling for age [17]. These studies showed that chlamydia screening among pregnant women is suggested.

3. Clinical presentation and effect on pregnancy

Chlamydia can be transmitted via oral, vaginal, or anal sexual contact. Therefore, clinical presentations reflect the sexual contact practices. Since chlamydia infections are asymptomatic in most females, the infections are often unnoticed, untreated, and under-reported. The common sign and symptoms associated with chlamydia infections in urogenital organs are cervicitis that causes vaginal discharge, abdominal pain, bleeding, and dysuria. The bacteria could migrate to the upper reproductive tract and cause pelvic inflammatory disease (PID). The PID could cause abdominal pain or pelvic pain, fever, low back pain, nausea, and chills.

Untreated chlamydia infection could lead to ascending infection to the fallopian tube which can damage the tube and cause infertility and ectopic pregnancy [23]. The immune system may stop the replication and growth of the bacteria, but the bacteria are still able to produce the heat shock protein hsp60, then secreted to the extracellular part of the milieu and induce inflammation in the fallopian tube. The inflammation results in scar formation and tubal occlusion. Since there is a similar region of hsp60 produced by the bacteria and hsp60 produced by the human body, there is a possibility to develop immune tolerance to the infection which leads to more tubal damage [24,25].

Chlamydia trachomatis specific antibodies could be used to detect tubal damage in infertile women [26–30]. The tubal damage was confirmed with laparoscopy or hysterosalpingography. These studies indicate that the history of chlamydia infection is associated with a significantly increased risk of infertility due to tubal damage even though the patients do not present any clinical symptoms.

A study in a subfertile woman with no sign of damage tubal pathology showed that chlamydia antibody was associated with a 33% lower spontaneous pregnancy rate compared to those without chlamydia antibody [23,27]. This might be due to the presence of persistent chlamydia infection which induces chlamydia hsp60 protein and impaired embryo development and implantation [27,31]. Therefore, chlamydia antibody testing could be useful as a valuable predictor for pregnancy failure.

A prospective observational study showed that positive serology screening could be used as predictive of tubal damage and a possibility of reduced cumulative pregnancy rate. The Serology-positive patients had significantly more tubal block, confirmed by hysterosalpingography and laparoscopically. If the fallopian tube has been damaged due to infection, in vitro fertilization may be an option to improve clinical pregnancy outcomes [32].

4. Diagnosis

Female urogenital chlamydia can be diagnosed by using both direct and indirect methods [33]. Vaginal swabs are the preferred specimens for the chlamydial test. It has similar sensitivity and specificity to cervical swabs [34,35]. Since the bacteria reside inside the host cell, a high sensitivity method is needed to detect the presence of bacteria biological samples. The direct methods include the cell culture method, which was considered to be a gold standard. The cell culture method examined the localized infection by antigen test and nucleic acid hybridization and amplification tests. This method needs to isolate the infectious bacteria and the mucosal cells. However, this method is rarely used in diagnostic laboratories. This method, whilst depending on the correct specimen collection, storage, and transportation, can be used to monitor antibiotic susceptibility and change of virulence. The indirect method comprises NAATs, ELISA, and rapid diagnostic tests (RDTs). NAATs are the most sensitive assays to detect the presence of the bacteria. The specificity was similar to cell cultures and is the recommended method for Chlamydia detection. NAATs can be performed on various biological specimens and do not require infectious bacteria. Detection of Chlamydia using ELISA and RDTs are insufficient due to the low sensitivity and specificity of the test. Serology tests to detect antibodies using ELISA may be useful to detect chronic infection but can not discriminate past and present infection and are inappropriate to diagnose acute infections [33]. However, a serology test might be used to study the prevalence of chlamydia and its correlation with infertility [36,37].

A meta-analysis study assessing the performance of point-of-care tests (POCTs) for the detection of chlamydia infections showed that NAAT-based tests have a significantly better sensitivity than antigen detection-based POCTs. Therefore, screening strategy with antigen detection-based POCTs may potentially result in a substantial underdetection of the infections [38].

5. Treatment

The usual treatment for treating chlamydia is by prescribing antibiotics. The goal is to prevent the complication associated with the infection and disease transmission. The 2015 European *C. trachomatis* guideline provides up-to-date guidance regarding the treatment of

C. trachomatis infections [35]. The recommended first-line treatment is Doxycycline for uncomplicated urogenital chlamydia. If the first-line treatment is unavailable and there is no *Mycoplasma genitalium* infection, Azithromycin is a viable alternative. Other alternatives include levofloxacin, erythromycin, and ofloxacin. The cure is verified three weeks after the treatment completion and repeat testing to detect the bacteria should be performed three months later.

In the IVF setting, one hundred ninety-four women under 40 years of age with positive serum Chlamydia underwent a total of 316 IVF cycles. All participants (including their partners) were prescribed doxycycline, 100 mg twice daily, for 10 days before the first IVF cycle. The study shows that when there was no active genital chlamydia infection, the chlamydia antibody was not associated with IVF outcome. This result was in agreement with other studies [39,40]. Therefore, IVF is an option to improve clinical pregnancy [41]. An observational study showed that IVF patients who have IgA antichlamydial antibody have significantly lower pregnancy and implantation rates, therefore patients should undergo IVF procedure after serum antichlamydial IgA tests negative [42,43].

6. Conclusion

The actual prevalence of female urogenital chlamydia disease is unknown yet likely to be of a significant burden. The prevalence in pregnant and non-pregnant women is similar. The disease is mostly asymptomatic. Several signs and symptoms may be observed including vaginal discharge, abdominal pain, bleeding, dysuria, abdominal pain, pelvic pain, fevers, low back pain, nausea, and chills. The most recommended method for the diagnosis is NAATs which give the highest sensitivity than the other methods. Undiagnosed and untreated chlamydia in females may lead to PID which causes ectopic pregnancy and infertility. Positive patients should be prescribed antibiotics and retested three months after completing the treatment. IVF may be an option for patients with tubal damage caused by chlamydia infection to improve pregnancy outcomes. The patients should undergo an IVF procedure after serum antichlamydial IgA tests negative.

Conflicts of interest

The authors declare that we have no conflicts of interest.

Sources of funding

The study did not receive external funding.

Ethical Approval

N/A as this is a review.

Consent

N/A as this study does not involve patient participation.

Author contribution

DT and BR conceived the study. DT, BR and TD determined the recruitment of other studies to be included in the manuscript. DT, BR and KDT wrote the manuscript. IP, TD and WP reviewed the manuscript. All authors approved of this version of the manuscript for publication.

Registration of Research Studies

Registrasion of research is not applicable in our case.

1. Name of the registry:
2. Unique Identifying number or registration ID:
3. Hyperlink to your specific registration (must be publicly accessible and will be checked):

Guarantor

The guarantors of this study is Dian Tjahyadi as the first author.

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