Chlamydia in female reproductive tract

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Citation

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Abstract

Chlamydia trachomatis today has become the most common bacterial sexually transmitted infection (STI), all over the world. Most of the times it is asymptomatic in female reproductive tract; but if left untreated leads to dreaded consequences like pelvic inflammatory disease (PID), infertility, ectopic pregnancy and chronic pelvic pain. Advent of nucleic acid amplification tests (NAATs) for diagnosis coupled with introduction of single dose azithromycin therapy for treatment has shown high promises to fight against Chlamydial infection as well as to prevent its long term sequels.

INTRODUCTION

Chlamydia trachomatis today has become the most common bacterial sexually transmitted infection (STI), all over the world. [1]

Most of the times it remains silent in female reproductive tract; but if left untreated leads to dreaded consequences like pelvic inflammatory disease (PID), infertility, ectopic pregnancy and chronic pelvic pain.

BURDEN OF SUFFERING

According to National Institute of Allergy and Infectious Diseases (NIAID) sexually transmitted diseases fact sheet, worldwide, an estimated four million new Chlamydial infections occur every year. Four million per year means 333,333 per month; 76,923 per week; 10,958 per day; 456 per hour; and around seven people every minute are getting infected by this organism. As many as one in ten adolescent girls tested for Chlamydia is infected with it. Moreover, what is visible to us is just the tip of an iceberg, as an estimated 3.4 million cases remain undiagnosed every year.

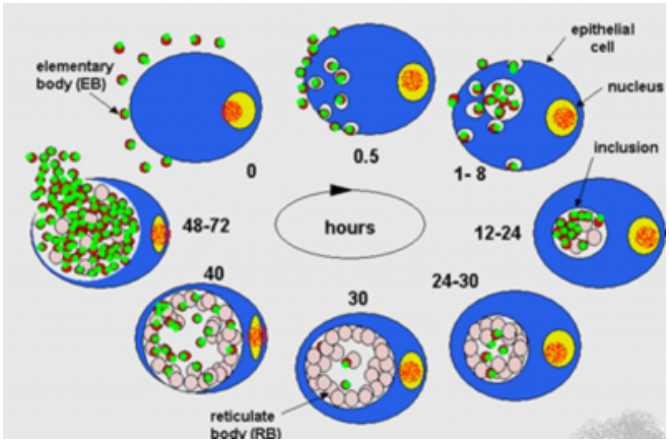
The prevalence of Chlamydia infection in our society varies from three per 100 in low risk population to 35 per 100 in high risk group.[2] 80% of this infected population is asymptomatic. Out of these 40% later on will develop pelvic Inflammatory disease (PID),[3] of which 20% will have infertility and 9% will ultimately land up with tubal ectopic pregnancy.[4]

MICROBIOLOGICAL ASPECT

Chlamydia is an obligate intracellular bacterium. Three different species of Chlamydia are pathogenic to human beings: Chlamydia trachomatis, Chlamydia psittaci, and Chlamydia pnemoniae. Out of these three, Chlamydia trachomatis has a special tropism for genital and conjunctival epithelium.

Figure 1

Figure 1: Life cycle of Chlamydia



The biphasic life cycle of this bacterium is unique, in which there are infectious but metabolically inactive elimentary bodies (EB) which when endocytosed by eukaryotic cells, reside within the cytoplasmic inclusions and get transformed into noninfectious but metabolically active reticulate bodies (RB). These reticulate bodies after an incubation period of 7-21 days begin to replicate every three hours; some of them get converted again into infectious EBs and are released to exterior of the cell, to infect the other cells.

TRANSMISSION OF INFECTION

EBs discharged from the cells are potentially infectious. Transmission of infection takes place either by sexual or by vertical transmission. Risk of sexual transmission varies from 40-60%. There is relatively high chance of bidirectional transmission in younger couples. This observation supports the hypothesis that biological factors in older women are protective for the development of infection and also for the promotion of clearance of infection, once it sets in.

The rate of vertical transmission is also 40-60%, which means if a pregnant lady is infected with Chlamydia the chances of her neonate getting the infection in- utero or at the time of delivery is around 50%.

NATURAL HISTORY

Once the Chlamydia reaches the reproductive tract of a woman, there is evidence that even in the absence of appropriate pharmacotherapy at least 20-30% of women clear the infection spontaneously.2 In the Remaining 70-80% it not only persists, but ascends up, to cause endometritis, inflammation of the tubes, and at times also peritonitis with Fitz Hugh Curtis syndrome. Fitz Hugh Curtis syndrome is a rare condition where perihepatitis sets in, following PID, presenting as right upper quadrant abdominal pain and liver tenderness with signs and symptoms of PID.

The dreaded long term squeals, as a result of PID caused by Chamydia are infertility and ectopic pregnancy. It has been estimated that 50% of all cases of salpingitis and infertility in the United Kingdom are caused by Chlamydial infection.[5]

Moreover, Chlamydia trachomatis has been proposed as an independent risk factor for the development of cancer cervix.[6]

CLINICAL PRESENTATION

More than 80% of women infected with chlamydia are asymptomatic. Speculum examination in these women might reveal cervicitis with a yellow or cloudy mucoid discharge from the external cervical os. The cervix tends to bleed easily when rubbed with a cotton swab or scraped with a spatula. In addition, to be kept in mind is the fact that chlamydial infection in the lower genital tract does not cause vaginitis; thus, if vaginal findings are present, they usually indicate a different diagnosis or a co-infection.

Some women might have chlamydial urethritis, again most of the times a diagnosis of suspicion. Dysuria but no urgency and frequency; or sterile culture when routine examination is showing plenty of pus cells, point towards the possibility of Chlamydia urethritis.

At times patient can directly present with PID, infertility, chronic pelvic pain or rarely with ectopic pregnancy.

EFFECTS ON PREGNANCY

Though many of the women infected with Chlamydia present in infertility clinic, if pregnancy occurs, it usually is not a very pleasant experience, as it might end up with ectopic pregnancy or spontaneous abortion. Even if pregnancy escapes, all these first trimester complications, there are high chances of preterm rupture of membranes, preterm birth, intrauterine infection and intrauterine death. In the postpartum period these women are at high risk of developing puerperal sepsis and secondary post partum hemorrhage (PPH).

EFFECTS ON THE NEONATE

Other than prematurity, at the time of delivery, if the fetus encounters Chlamydial infection it can acquire conjunctivitis, pneumonia, or ear infections. During the first few days after birth, episodes of unexplained apnea might occur that can cause sudden infant death syndrome (SIDS). Long term sequels like asthma and chronic obstructive pulmonary disease (COPD) are like a complimentary gift with the infection acquired during intrauterine life.

LABORATORY DIAGNOSIS

Serology is not of much value in clinical decision making as far as infection with Chlamydia is concerned. Sensitivity and specificity of light microscopy is also not satisfactory.

Culture is 100% specific,[7] the sensitivity is however, not optimal, it is time consuming and laborious. So, the practical use is only to compare the validity of new diagnostic tests.

Antigen detection can be done by enzyme immuno-assay (EIA) or direct flouroscent assay (DFA). Based on these techniques rapid-in-office tests are also available. But the diagnostic efficacy of these tests is not high enough to warrant clinical use unless the need of fast test results outweighs the lower diagnostic accuracy.

The advent of NAAT has revolutionized the laboratory diagnosis of Chlamydial infection with sensitivity of more than 90% and specificity of around 99%. Because of its high sensitivity even self obtained vaginal secretion or urine samples can be sent through mail to the laboratory, without

revealing personal identity. In the early 1990s, the usefulness of polymerase chain reaction (PCR) was recognized for its ability to detect difficult-to-grow pathogens and Chlamydia trachomatis was the first organism for which there was a commercially available PCR assay.[8] Now there are many more varieties of NAATs available for detection of Chlamydia other than PCR, those include – ligase chain reaction (LCR), transcription mediated amplification (TMA), standard displacement amplification (SDA). All these methods offer expanded sensitivities of detection, while maintaining high specificity.

ROUTINE SCREENING

As most of the times Chlamydial infections are asymptomatic, it is well understood that these patients will never have the urge to consult a health care provider for diagnosis. That is the reason; screening plays an important role when Chlamydial infection is of concern. There is level A evidence for proven benefits with annual screening of all sexually active women less than 25 years of age, and also for high risk women even if they are more than 25 years of age.[9] Risk factors include a new male sex partner or two or more partners during the preceding year, inconsistent use of barrier contraception, history of a prior STI, African-American race, and cervical erosions.

Whether the screening should be performed in all pregnant women less than 25 years and high risk pregnant women even more than 25 years, the evidence is only of level B.9

Though according to American College of Preventive Medicine Practice Policy Statement, one time screening in pregnancy either during their first trimester or at their first prenatal visit is sufficient in low risk population, those with risk factors should be re-screened during their third trimester.[10]

Use of noninvasive samples, such as urine or self-obtained vaginal swabs is being recommended for routine screening of a low risk population. This method eliminates need for a visit to the hospital, long waiting hours, and is cost-effective as well as time saving. Only a NAAT test can be used with these kinds of self obtained samples to screen asymptomatic Chlamydial infection.

Keeping in mind the potential for false positive tests because of lower positive predictive values (PPV) of NAATs in low prevalence populations, Centre of Disease Control (CDC) has recommended that a confirmatory test should be performed, if the individual belongs to a low risk group.[11]

TREATMENT

Currently many effective drugs are available to treat Chlamydia populating female reproductive tract.

Tetracyclines are being recommended as effective treatment modality for more than 20 years. Efficacy of various tetracyclines are similar, difference is in half life and thus in dosing schedule; and also in terms of adverse effects. Current CDC treatment guideline[12] recommends doxycycline, 100 mg two times a day for seven days, as the primary therapy for Chlamydia infection, in non-pregnant women.

For years macrolides continued as an alternative to tetracyclines. However, erythromycin could never become popular because of its side effects. The introduction of newer macrolide, single dose azitromycin therapy constituted an important step forward in the treatment of Chlamydial infection. It's long half life of 50-68 h coupled with high bioavailability permits it to become an effective single dose treatment for a pathogen having long replication time of 48-72 h.

In pregnancy amoxicillin 500 mg thrice a day for 7-14 days, is the drug of choice.12

Though treatment of the lady infected with chlamydia is the primary aim, the strongest predictor for preventing re-infection and infection sequels is - treatment of sexual partner simultaneously or at least before the resumption of coital activity.[13]

CONCLUSION

Chlamydial infection can be described as ‘3Cs' – Common, Crooked, yet Curable. Though it is the most common bacterial sexually transmitted infection worldwide and most of time in female reproductive tract it multiplies and damages tissues silently, only to present later on with long term, difficult to manage sequels. The only sigh of relief however is its easy detection with NAAT and simple treatment with single dose azithromycin therapy.

References

1. Kaveh Manavi. A review on infection with Chlamydia trachomatis. Best Practice & Research Clinical Obstetrics and Gynaecology. 2006; Vol. 20: No. 6, 941-951
2. Jane Norman. Epidemiology of female genital Chlamydia trachomatis infection. Best Practice & Research Clinical Obstetrics and Gynecology. 2002; Vol. 16: No. 6, 775-787
3. Rees E. Treatment of pelvic inflammatory disease. Am J Obstet Gynecol 1980;138:1042-7
4. Westrom L, Joesoef R, Reynolds G, Hadgu A, Thompson SE. Pelvic inflammatory disease and fertility: a cohort study

of 1,844 women with laparoscopically verified disease and 657 control women with normal laparoscopy results. Sex Transm Dis 1992;19:185-92
5. Bevan CD, Johal BJ, Mumtaz G, Ridgway GL, Siddle NC. Clinical, laparoscopic and microbiological findings in acute salpingitis: report on a United Kingdom cohort. Br J of Obstet Gynecol 1995 May;102(5):407-14
5. Jonathan M. Zenilman. Chlamydia and Cervical Cancer - A Real Association? JAMA. 2001;285:81-83
6. C.M. Black, Current methods of laboratory diagnosis of Chlamydia trachomatis infections, Clin Microbiol Rev 10 (1997), pp. 160-184
7. Jaschek G., Gaydos C., Welsh L., Direct detection of Chlamydia trachomatis in urine specimens from symptomatic and asymptomatic men by using a rapid polymerase chain reaction assay. J Clin Microbiol 1993; 31:1209-1212
8. Screening for Chlamydial Infection: U.S. Preventive Services Task Force Recommendation Statement. U.S. Preventive Services task force. 17 July 2007;Volume 147: Issue 1
9. Katerina Hollblad-Fadiman, Samuel M. Goldman. Screening for Chlamydia trachomatis. American College of Preventive Medicine Practice Policy Statement. Am J Prev Med 2003;24:3
10. Clarke L.M., Sierra M.F., Daidone B.J., Comparison of the Syva MicroTrak enzyme immunoassay and Gen-Probe PACE 2 with cell culture for diagnosis of cervical Chlamydia trachomatis infection in a high-prevalence female population. J Clin Microbiol 1993; 31: 968-971
11. Kimberly A. Workowski, William C. Levine, Sexually Transmitted Diseases Treatment Guidelines 2002: Vol. 51 / No. RR-6
12. McCormack WM, Martin DH, Hook III EW et al. daily oral grepafloxin vs twice daily oral doxycycline in the treatment of Chlamydia trachomatis endocervical infection. Infectious diseases in Obstetrics and Gynecology 1998; 6;109-15

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