The relationship between male factor infertility and Chlamydia infection, still an undecided issue

Shakeela Ishrat*, Marufa Hossain, Shirin Jahan, Sohely Nazneen, Fahmida Chowdhury, Satu Farhana Karim

INTRODUCTION

According to World Health Organization (WHO), Chlamydia trachomatis infection is the most prevalent sexually transmitted bacterial infection. Urogenital infection accounts for about 15% of male factor infertility. Sexually transmitted infections can impair fertility in men by organ damage, cell damage via mediators of inflammation, obstruction, binding to spermatozoa. There may be inflammation of the tissues of testis and genital tract such as orchitis and epididymitis, partial or complete obstruction of genital tract, reduced viability and motility of spermatozoa.

Chlamydia trachomatis is an obligate intercellular gram negative bacteria having two phases in development. The elementary body is infectious but extracellular and non-replicating. On internalization, it becomes intracellular reticulate body and replicating. Infections of C. trachomatis in males are mostly asymptomatic and can cause urethritis, prostatitis, epididymitis and epididymo-orchitis. Penile urethra is the primary site of infection with C. trachomatis in males. The most common clinical...
presentation is urethritis. There is a chronic silent genitourinary infection leading to retrograde epididymitis, epididymo-orchitis and most probably prostatitis. Epididymitis in men appears to be caused by *Chlamydia* in 40-50% cases. Symptoms are reported by about 50% of those men who are *Chlamydia* positive. Exposure of spermatozoa in infected males to *C. trachomatis* during spermatogenesis and epididymal storage and transport may alter the sperm parameters. The infection has been variably associated with poor semen quality. Others have said that semen is active carrier of elementary bodies of *Chlamydia* and transmits the infection to female partner. The quality of semen is not directly affected.

Seropositivity of *C. trachomatis* in men is suggestive of chronic and recurrent infection with this sexually transmitted organism. Sero-discordance warrants careful counseling. Men infected with *C. trachomatis* can transmit the infection to female partner and cause pelvic inflammatory disease and tubal obstruction. The risk of reinfection can be minimized by timely treatment of the couple, once *Chlamydia* seropositivity is detected in any partner, male or female.

Most males with urogenital *Chlamydia* infection have serum IgG antibodies to *C. trachomatis* that persist for years. Serologic studies linking *C. trachomatis* to male infertility and sperm quality lead to highly variable results. The median number of progressively motile spermatozoa was lower in seropositive males than those who are seronegative. Seropositivity was not associated with any other semen parameters. One more similar study could help decide whether *Chlamydia* antibody testing of the male partner could contribute beyond being a marker of tubal factor infertility in the female partner.

The objective of the study was to examine the effect of *Chlamydia* infection on semen parameters. *Chlamydia* antibody test is done as part of infertility workup to predict sexually transmitted infection. Detection of *Chlamydia* infection in semen needs expensive and complicated molecular technologies. Since *Chlamydia* antibody test is done often to screen sexually transmitted infection in the infertile couples, it appears prudent to search for any remote association between *Chlamydia* seropositivity and semen quality.

**METHODS**

The cross sectional study was carried out on a total 100 men in the Department of Reproductive Endocrinology and Infertility of the Bangabandhu Sheikh Mujib Medical University over one year from January 2019 to December 2019. The participants were male partners of the women who failed to conceive after one year of unprotected sexual intercourse. They had semen analysis as part of their infertility work up and had some form of abnormal semen parameters. Those who had sexual dysfunction, family history of male infertility, heavy smoking (more than 10 sticks per day), history of genital trauma, hernia repair, chemotherapy, radiotherapy, low testosterone (less than 300 ng/ml or 1040.15 nmol/L), high/low follicle stimulating hormone or luteinizing hormone were excluded. The men had *Chlamydia* antibody test at the same time. None of them had symptoms of urogenital infections.

**Semen analysis**

The men were asked for 2-5 days abstinence before providing semen for analysis. The semen was collected on site into standard containers. The sample was allowed to liquefy for up to 30 minutes. The analysis including sperm morphology and quantification of round cells was done on Makler counting chamber. The WHO (1999) guidelines was used for assessing semen quality. Thresholds for normozoospermia was sperm concentration 20 million/ml, progressive motility 50% for asthenozoospermia, normal morphology 30% for teratozoospermia.

**Chlamydia antibody test**

Blood sample was drawn and analyzed for *Chlamydia* antibody. Five ml of venous blood was collected from each subject into a plain specimen bottle, properly labelled and send to Department of Virology for analysis. The blood specimen was allowed to clot and then centrifuged to obtain clear sera. The specimen was analyzed for serum *Chlamydia* antibodies.

*C. trachomatis* specific IgG antibody in serum was detected by IgG enzyme-linked immunosorbent assay (ELISA) kit manufactured by DRG instruments GmbH, Germany. *C. trachomatis* specific antibodies of positive specimen and control were bound to the immobilized antigens. Samples with (Optical density (OD) values more than 10% above cut off control (CO) were regarded as positive as per kits instructions.

**Scrotal sonogram**

Men with azoospermia and severe oligospermia had scrotal ultrasonogram at the Department of Radiology and Imaging of Bangabandhu Sheikh Mujib Medical University. Epididymal cyst, a surrogate finding of epididymal obstruction were noted for the participants.

**Statistical analysis**

The men were grouped into those who were seropositive for *Chlamydia* antibody IgG and those who were not. The continuous variables were compared with unpaired t test and the categorical variables with Chi square test or Fishers exact test where appropriate.

**RESULTS**

The baseline characteristics of the participants are described in Table 1. There were no significant difference...
in age, type of infertility and other factors between the two groups.

Table 2 describes the sperm parameters and prevalence of different semen abnormalities in the two groups, *Chlamydia* positive and *Chlamydia* negative. There were no significant difference between the two groups.

None of the men, *Chlamydia* positive or negative had leukocytospermia (round cells more than 10/HPF). Regarding the sonographical variable in those with azoospermia and severe oligospermia, the presence of epididymal cyst is 45.8% in *Chlamydia* positive compared to 12.2% in *Chlamydia* negative; the difference is significant.

Table 1: General characteristics of the participants.

<table>
<thead>
<tr>
<th>Parameters</th>
<th>Chlamydia seropositive (n=59) (%)</th>
<th>Chlamydia seronegative (n=41) (%)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years), mean, SD</td>
<td>33.56±5.083</td>
<td>33.85±4.720</td>
<td>0.587</td>
</tr>
<tr>
<td>Residence (%)</td>
<td>Urban 33.9</td>
<td>43.9</td>
<td>0.311</td>
</tr>
<tr>
<td></td>
<td>Rural 66.1</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Socio economic condition (%)</td>
<td>Low 45.8</td>
<td>46.3</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Middle 45.8</td>
<td>43.9</td>
<td>0.805</td>
</tr>
<tr>
<td></td>
<td>High 6.8</td>
<td>9.8</td>
<td></td>
</tr>
<tr>
<td>Duration of infertility (years)</td>
<td>6.91±3.748</td>
<td>6.05±3.451</td>
<td>0.728</td>
</tr>
</tbody>
</table>

Table 2: Semen parameters of the participants.

<table>
<thead>
<tr>
<th>Parameters</th>
<th>Chlamydia seropositive (n=59) (%)</th>
<th>Chlamydia seronegative (n=41) (%)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Semen volume (ml)</td>
<td>2.14±1.53</td>
<td>2.66±2.28</td>
<td>0.449</td>
</tr>
<tr>
<td>Sperm concentration (million/ml)</td>
<td>0.50, 0-15.0*</td>
<td>2.0, 0-17.5*</td>
<td>0.870</td>
</tr>
<tr>
<td>Progressive motility (%)</td>
<td>0, 0-25.0*</td>
<td>0, 0-27.5*</td>
<td>0.934</td>
</tr>
<tr>
<td>Normal morphology (%)</td>
<td>15.0, 0-15.0*</td>
<td>0, 0-16.50*</td>
<td>0.839</td>
</tr>
<tr>
<td>Severe oligospermia</td>
<td>15.3</td>
<td>14.6</td>
<td>0.932</td>
</tr>
<tr>
<td>Azoospermia</td>
<td>42.4</td>
<td>43.9</td>
<td>0.879</td>
</tr>
<tr>
<td>Asthenozoospermia</td>
<td>37.3</td>
<td>39.0</td>
<td>0.860</td>
</tr>
<tr>
<td>Teratozoospermia</td>
<td>5.1</td>
<td>2.4</td>
<td>0.507</td>
</tr>
</tbody>
</table>

*Non Gaussian distribution, so described as median, interquartile range, and *analysis done by Mann Whitney U test.

DISCUSSION

The objective of the study was to explore if there is any association of *Chlamydia* seropositivity with abnormal serum parameters. The findings were inconclusive as no significant association was established.

Hosseinzadeh et al examined the ejaculation of 642 infertile men. In addition to semen analysis (WHO guidelines 1999) nested plasmid polymerase chain reaction was done to detect the presence of *C. trachomatis* DNA. There was significant difference in semen volume but not in sperm concentration, sperm motility, sperm morphology or concentration of leukocytes between the groups *Chlamydia* DNA positive and *Chlamydia* DNA negative.¹

There are studies describing the relation of *C. trachomatis* infection with reduction of sperm concentration, sperm motility, sperm morphology and viability and increased likelihood of leukocytospermia, sperm DNA fragmentation. Chronic or recurrent infection with *C. trachomatis* lead to chronic inflammation like epididymitis, prostatitis and orchitis in men. The activation of macrophages and immune mediated release of mediators such as IL-1, TNF-α and prostaglandins perpetuate the tissue and cell damage.¹⁰

A prospective study was done on one hundred and forty three infertile men, diagnosed as having genitourinary infection with *Chlamydia trachomatis* and *Mycoplasma* and fifty fertile men. They were assessed for sperm concentration, motility and morphology as well as sperm DNA fragmentation. Infertile men having genitourinary infection with *Chlamydia trachomatis* had sperm DNA fragmentation enhanced compared to fertile controls. The change in serum parameters were proportionately less.¹¹

The study by Veznik et al examined a total of 627 sperm samples. *Chlamydia* was detected in the semen by immunofluorescence reaction. Semen analysis showed that normal sperm morphology was 14.4% lower, volume 6.4% lower, concentration 8.3% lower, motility 7.8% lower in *Chlamydia* positive semen than in semen which are *Chlamydia* negative.⁷
The study by Mazzoli et al investigated men with diagnosis of chronic prostatitis who had semen analysis and serological test for Chlamydia antibody. Who had chronic prostatitis from Chlamydia infection had significant difference in sperm concentration, percentage of motile sperm, normal morphology from those with prostatitis from other bacterial infections.

Positivity of mucosal IgA antibody and/or C. trachomatis-DNA amplifications in expressed prostatic secretions and/or post prostatic massage urine, not serum IgG was considered to define C. trachomatis infection. There was no correlation between serum IgG and semen parameters.12

Al-Sweih et al had an study where the semen of a total of 127 infertile and 188 fertile men were examined for the presence of C. trachomatis by polymerase chain reaction. There was no significant difference in the prevalence of the pathogen between infertile and fertile men. The Chlamydia infection had negative impact on semen quality. There was low sperm count and vitality in those who were infected, though the difference was not significant from infertile men who were not infected.13

Hamdad-Daoudi et al examined three specimens, namely first void urine, urine obtained after prostatic massage and semen, from 111 infertile men for the presence of C. trachomatis by polymerase chain reaction (PCR) and found positive in 5.4%, 0.9% and 2.7% samples respectively. C. trachomatis IgG antibodies were detected in 4.5% by microimmunofluorescence (MIF) test and 0.9% by pELISA (peptide based ELISA). The men who had detection of C. trachomatis by PCR had negative serological test. The possible reasons speculated include absence of organisms in upper genital tract, or inaccessibility of systemic immune system to the areas harboring the organism.8

There are few studies linking serological test of C. trachomatis to semen parameters. In the study by Joki-Korpela et al the median number of progressively motile spermatozoa was lower in seropositive males than those who are seronegative. Seropositivity was not associated with any other semen parameters.9

Seropositivity of Chlamydia is not an unequivocal evidence of Chlamydia infection because individuals differ in immune response and an elevated antibody titer is not clearly indicative of current active or previous quiescent infection. The antibody response may be a cross reaction to closely related organisms such as Chlamydia pneumoniae. Due to blood-testis/epididymal barrier, serum antibody titer may not reflect the actual infection inside testis or epididymis.8

Chlamydia antibodies in serum do not differentiate past and present C. trachomatis infection of urogenital tract. Antibodies persist a long time after the infection has resolved. High or persisting antibody titer may not correlate with current or persistent infection.8

There was significant association of epididymal cyst with Chlamydia seropositivity. Epididymal cyst at scrotal sonogram is suggestive of epididymal obstruction which may result from Chlamydia infection, leading to inflammation and scarring.14

Limitations

The study is limited by small sample size and absence of random sampling. The sperm morphology and concentration of leukocytes were assessed in Makler chamber.

CONCLUSION

Seropositivity of Chlamydia infection in infertile male is not predictive of semen abnormalities. Serological screening of the male partner for Chlamydia trachomatis provides no more benefit than identifying the female partner at risk of tubal factor infertility and males at risk of epididymal obstruction.

ACKNOWLEDGMENTS

Authors would like to thank FCPS trainees in reproductive endocrinology and infertility who provided service in the male infertility clinic, the men who have been part of the study and to those who supported the investigation facilities in the allied Departments of Bangabandhu Sheikh Mujib Medical University.

Funding: No funding sources
Conflict of interest: None declared
Ethical approval: The study was approved by the Institutional Ethics Committee

REFERENCES


