Original Article

The relationship between chlamydia infection and infertility at the Lagos University Teaching Hospital, Lagos, Nigeria

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ABSTRACT

Context: Infertility affects 10–15% of couples worldwide and tubal factor is a major component in sub-Saharan Africa. Pelvic inflammatory disease due to chlamydia infection is a known risk factor for tubal infertility.

Objective: This case-control study was carried out to determine the relationship between chlamydial infection and infertility as seen at the Lagos University Teaching Hospital, Lagos, Nigeria.

Methodology: This was a case-controlled study of 180 participants recruited from the Gynaecology Outpatient and Family Planning Clinics of the Lagos University Teaching Hospital, Lagos, Nigeria (LUTH). The cases were 60 females diagnosed to have tubal infertility and 60 other infertile females with patent tubes. The control group comprised of 60 females attending the family planning clinic. The females were tested for serum chlamydia IgG antibody using a kit that detects serovar specific *Chlamydia trachomatis* antibody. Endocervical swab samples were also tested for chlamydial antigen using a kit that detects *C. trachomatis* genus specific lipopolysaccharide antigen. The results were collated and analyzed using the statistical package for the social sciences (SPSS) version 18.

Results: All the females tested negative for chlamydia antigen. The odd ratio for having a case testing positive for chlamydial antibody compared to control was 4.0 [95% CI = 1.47–10.88]. The odd ratio for infertile females with blocked tubes compared with those who had patent tubes testing positive for chlamydia antibody was 3.52 (95% CI: 1.46–8.49).

Conclusion: This study suggests an etiological relationship between chlamydial infection and infertility in general and tubal infertility in particular.

Key words: Chlamydia; hysterosalpingography; infertility; tubal blockage.

Introduction

The clinical, financial, and psychological burden of infertility, in any society is enormous. The psychological burden is more pronounced in traditional societies like Nigeria where much premium is placed on child bearing. The contribution of tubal pathology to infertility varies across populations. Genital *C. trachomatis* infection is one of the most prevalent sexually transmitted infections and pelvic inflammatory disease (PID) from chlamydia infection is a major risk factor for tubal infertility.[1] Chlamydial cervicitis has also been suggested to contribute to unexplained infertility by yet to be fully determined mechanism.[2] In males, genital chlamydial infection is asymptomatic in about 50% of cases[1] and is associated with male infertility.[3] Chlamydial infection is thus probably the most important preventable cause of infertility.

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Owing to the increasing prevalence of chlamydial infection, its often asymptomatic course and the potential for serious complications especially infertility, screening programs have been developed in industrialized nations to reduce the rate of PID and other reproductive sequelae.[1,4] Ironically in Africa where the prevalence of infection and tubal infertility is perceived to be high, there are no population screening programs. Females attending for gynecological procedures and work-up for infertility like hysterosalpingogram (HSG) and laparoscopy and chromotubation are not routinely screened for chlamydia. This makes the magnitude of the problem unclear but potentially huge. Furthermore, procedures like dilatation and curettage and insertion of intrauterine devices are carried out without screening or prophylactic treatment for chlamydia. This may disseminate existing cervical infection to the pelvis or worsen preexisting pelvic infection.

Despite the high prevalence of infertility in Nigeria and the recognised contribution of PID to tubal infertility, very limited local data exist on the contribution of genital chlamydia infection to infertility generally and tubal infertility in particular. Elsewhere, studies have demonstrated significant correlation between past chlamydia infection and infertility[5,6] and some studies have shown an association between active infection and infertility.[7]

This study was carried out to determine the relationship between chlamydial infection and tubal infertility as seen at the Lagos University Teaching Hospital, Lagos, Nigeria (LUTH). The study aims to determine the prevalence of current and past chlamydial infection in females with and without infertility and establish any relationship between chlamydia infection and tubal infertility.

Methodology

The study was a case-controlled study carried out at the Lagos University Teaching Hospital between 1st March and 30 September 2012. A total of 180 participants were recruited from the Gynaecology Outpatient and Family Planning Clinics of the Lagos University Teaching Hospital, Lagos, Nigeria (LUTH). The participants consisted of 60 females diagnosed to have tubal infertility and 60 other infertile females with patent tubes attending the gynecology clinic. The control group comprised of 60 females without history of infertility attending the family planning clinic but not yet on any contraceptive method. Ethical approval for the study was obtained from the Lagos University Teaching Hospital Health Research and Ethics Committee (LUTH-HREC). All consecutive females attending the gynecology clinic and the family planning clinic, respectively, during the study period who met the inclusion criteria were approached and requested to participate in the study. A written informed consent was obtained from each participant.

A pro forma was used to collect relevant sociobiological and clinical data for each participant including age, parity, and clinical diagnosis. The results of laboratory tests carried out were later entered into the pro forma.

Five milliliters of venous blood was drawn from each patient and serum was prepared from each sample using standard techniques. The serum samples were stored in the Central Research Laboratory at –20°C till it was time for analysis. Chlamydia antibody (IgG) testing was carried out on sera collected from each participant using the DIA. PRO kit. This detects serovar specific *Chlamydia trachomatis* antibody using microplate coated with immuno-dominant species-specific *C. trachomatis* major outer-membrane protein antigen (MOMP). An optical signal that was proportional to the level of antibody present was generated using this kit. The optical density (OD) was measured at 450 nm. The OD cutoff value of 0.3 was determined using the calibrators provided with the kit. The samples were considered positive when the absorption value was higher than the cutoff.

An endocervical swab was also collected from each participant using standard technique. Chlamydia antigen testing was carried out on the endocervical sample using the DiaSpot Chlamydia kit. This works on the principle of detection of *C. trachomatis* genus specific lipopolysaccharide (LPS) antigen. The method employs the principle of monoclonal antibody testing with high specificity (97%) and sensitivity (90%). The results were entered into the pro forma for each participant.

Data from the pro forma were fed into an electronic database designed on Microsoft Access. Data analysis was carried out using the SPSS Statistics for Windows Version 18.0, (SPSS Inc., Chicago, USA). Frequency analysis was run and cross tables constructed. Significance in the outcome was verified using the Chi-square test.

Results

The females with infertility (cases) were aged between 22 and 45 years, their mean age was 33.2 (±2.1) years. Females in the control group were aged between 27 and 42 years, their mean age was 36.3 (±2.3) years. Table 1 shows the distribution of the cases of infertility according to whether they were primary or secondary; and whether the tubes were patent or blocked. Among the females with infertility, 89 (74.2%) had secondary infertility whereas the remaining 31 (25.8%) had primary infertility. Majority (56.2%) of the females with

secondary infertility had tubal blockage whereas only 32.3% of those with primary infertility had tubal blockage. The odd ratio for having blocked tubes in females with secondary infertility compared to those with primary infertility was 2.692 (95% CI = 1.137–6.373).

Table 2 shows the results of chlamydial antibody test for the cases and control groups. Thirty-two (26.7%) of the cases tested positive for chlamydial antibody whereas only five (8.3%) of the control group were positive for antibody. The odd ratio for having a case positive for chlamydial antibody compared to control was 4.0 (95% CI = 1.47–10.88). The odd ratio of positive chlamydia antibody in secondary compared with primary infertility was 1.45 (95% CI = 0.6–3.5) [Table 3]. Table 4 shows distribution of chlamydial antibody in infertility patients with blocked and patent tubes, respectively. Twenty-three (38.3%) of patients with tubal blockage and nine (15.0%) of those with patent tubes, respectively, tested positive for chlamydial antibody. The odd ratio for infertile females with blocked tubes compared with those who had patent tubes testing positive for chlamydia antibody was 3.52 (95% CI: 1.46–8.49).

It is notable that none of the females (in both cases and control groups) tested positive for chlamydial antigen indicating zero prevalence of active chlamydial infection.

Table 1: Tubal status in primary and secondary infertilities

Tubal status	Primary infertility (%)	Secondary infertility (%)
Tubes patent	21 (67.7)	39 (43.8)
Tubes blocked	10 (32.3)	50 (56.2)
Total	31	89

Table 2: Chlamydia antibody in infertility and control groups

Chlamydia antibody	Infertility cases (%)	Control group (%)
Positive	32 (26.7)	5 (8.3)
Negative	88 (73.3)	55 (91.7)
Total	120	60

Table 3: Chlamydia antibody and type of infertility

Chlamydia antibody	Primary infertility (%)	Secondary infertility (%)
Positive	10 (32.3)	22 (24.7)
Negative	21 (67.7)	67 (75.3)
Total	31	89

Table 4: Chlamydia antibody in infertile females with patent and blocked fallopian tubes

Chlamydia antibody	Blocked tubes (%)	Patent tubes (%)
Positive	23 (38.3)	9 (15.0)
Negative	37 (61.7)	51 (85.0)
Total	60	60

Discussion

This study showed that none of the females attending the infertility clinic (cases) or family planning clinic (control group) had evidence of active chlamydial infection as they tested negative for chlamydia antigen. This is not surprising giving that the mean age of the females were 33.2 (±2.1) years and 36.3 (±3.2) years, respectively. However, the study demonstrated that 37 (20.6%) of the females tested positive for chlamydia antibody. It also found that 26.7% of the females with infertility tested positive for chlamydia antibody compared with 8.3% of the control group. Furthermore, among the infertility group, 38.3% of those with tubal infertility tested positive compared with 15% of those with patent tubes.

It is notable that all the females in the study (both cases and controls) tested negative for chlamydial antigen. This is consistent with very low prevalence rates that have been reported in similar populations elsewhere.[8-11] Although the principle of antigen detection using the enzyme linked immunosorbent assay (ELISA) against specific lipopolysaccharides was used in this study, different techniques were used in other studies reviewed. Siemer and colleagues recorded a prevalence of 1.6% among infertile females using the nucleic acid amplification technique of polymerase chain reaction (PCR) in Ghana.[8] Using both ELISA and PCR in Iran, researchers observed a 0% prevalence rate of chlamydia.[9] Similarly, no antigen was detected by culture technique among 105 infertile females in Norway in whom fallopian tube specimens were collected at laparoscopy.[10] In Aberdeen, in which 427 infertile females were tested, no antigen was detected using ELISA technique among 217 females, but 4 of the remaining 210 females (1.9%) tested positive using PCR.[11] The variations in the rates recorded may be attributable to the difference in laboratory techniques and sociodemographic characteristics of the different populations studied.

Nucleic acid amplification tests (NAAT) are expensive and not readily available in Nigeria. Similarly, culture techniques are expensive and very laborious and have low sensitivity but high specificity.[12] Considering the limitations of culture and nucleic amplification techniques, the use of ELISA for antigen detection can be justified in screening for chlamydial infection. It is a more readily available test modality in Nigeria, it is cheaper and the expertise required is readily available. The kit used in this study (DiaSpot Chlamydia) has a quoted sensitivity of 90% and a specificity of 97% relative to PCR.

Studies in Nigeria that have examined the prevalence of active genital chlamydia infection are few and have used diverse

study population. Researchers working in northern Nigeria, reported a prevalence rate of 9% in a population of females with an average age of 24 years attending gynecology and antenatal clinics whereas a prevalence of 11% was reported among sexually active undergraduates less than 30 years in the south.[13,14] A prevalence rate of 6.5% was reported in Lagos by Aladesanmi and coworkers among antenatal patients with mean age of 25 years.[15] Age is an important risk factor for genital chlamydial infection.[1,4] The Centre for Disease Control (CDC) reported the peak age of infection as 15–24 years.[4] This age-related risk is probably associated with having new sexual partners, multiple sexual partners, and inconsistent use or outright failure to use barrier contraceptives. The mean age of the study population (infertile females) was 33.2 years and 36.3 years for the control group. The mean age in this study is similar to that of the Iranian study where the average age of the 96 infertile females studied was 30 years and none of them tested positive for chlamydial antigen by both ELISA and PCR techniques.[9] The populations in which some antigen positivity was recorded tend to be younger.[13-15] It is probable therefore that genital chlamydial infection acquired in the adolescent/earlier years had resolved leaving behind the sequelae of tubal damage and/or infertility. Also all females studied were married and presumably in restricted sexual relationships. These may substantially reduce the risk of active genital chlamydial infection.

This study found that females in the infertility group had a higher prevalence of chlamydia antibody compared with the control group. An infertile female was four times more likely to have chlamydial antibody than a female without infertility (95% CI: 1.47–10.88). This supports an etiological role for chlamydia infection.[6,16,17] It also further showed that females with tubal infertility had a higher prevalence of chlamydia antibody compared with those with patent tubes. Females with tubal infertility were three and a half times more likely to have evidence of past chlamydia infection than infertile females with patent tubes. This finding lays credence to the observations that *C. trachomatis* infection is a major etiological agent in tubal infertility.[5,6]

It is observed from this study that even infertility patients with patent tubes had a higher prevalence of chlamydia seropositivity (15.0%) compared with the control group (8.3%). This may suggest that apart from gross tubal blockage, chlamydia infection affect fertility in other ways, for example, by effecting other subtle damages in the cervix and on tubal architectural and functional integrity.[2]

Secondary infertility was the predominant type in this study accounting for 74.2% of the infertility group. Chlamydial antibody seropositivity was higher in those with primary infertility (32.3%) compared with the secondary type (24.7%). This suggests that chlamydial infection plays a more prominent role in the etiology of primary than secondary infertility.

Conclusion

The findings from this study suggest that chlamydia infection represents a major etiological factor for infertility particularly tubal infertility. It appears that affected individuals contract the infection in the early reproductive years. The reproductive health needs of young adults therefore should address the prevention, detection, and effective treatment of sexually transmitted infection alongside the need for effective contraception.

Limitations of the study

This was a facility-based study. Majority of participants in this study were referred and may have had different treatments especially antibiotic therapy before presentation in LUTH. The results obtained may therefore not be truly representative of prevalence of chlamydial antigen or antibody in infertile females in the community.

The most sensitive tests for chlamydial antigen are the nucleic acid amplification techniques (NAAT), for example, with PCR. The prohibitive costs of these however make them inappropriate as a screening tool in our environment hence the use of ELISA. The possibility of a few false negative results can therefore be speculated because of the lower sensitivity of ELISA. Laparoscopy is the gold-standard for the assessment of tubal patency. Its cost and invasiveness however limit its routine use. Hysterosalpingography (HSG), a cheaper, less invasive, and generally acceptable practical method of diagnosis was used in this study.

Recommendation

Reducing the burden of tubal infertility demands adequate attention to the predisposing events, which are largely preventable causes like chlamydial infection. However, noting that high sero-prevalence is often associated with low-antigen prevalence among infertile females with tubal diseases, effective preventive strategies should focus on detection and eradication of lower genital tract infection in adolescent girls and young females among whom the risk of infection is highest.

This study has not found any need for routine screening or prophylactic treatment for genital *C. trachomatis* infection among infertile females before procedures like HSG. However, a large community-based study of genital chlamydial infection

among infertile females will be required to fully address this issue.

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Conflicts of interest

There are no conflicts of interest.

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