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**Original Research Article**

# Burden of *Chlamydia trachomatis* infection amongst infertile women compared with pregnant controls in North-central Nigeria

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## ABSTRACT

**Background:** Female infertility due to tubal damage resulting from pelvic infections including *Chlamydia trachomatis* is common among women in our environment. The study aimed at determining the prevalence of *Chlamydia trachomatis* antibody amongst infertile women and to assess the relationship between exposure to *Chlamydia trachomatis* infection and tubal infertility in Garki Hospital, Abuja, Nigeria.
**Methods:** This was a case control study among 76 infertile patients with tubal occlusion diagnosed with hysterosalpingography and confirmed by laparoscopy compared with 81 pregnant women recruited from the antenatal clinic. Both cases and control were investigated with a study protocol which solicited information on socio-demographic variables, sexual and reproductive risk factors and history of previous pelvic infection. Each subject and control had 5 ml of blood collected for serological assay for Chlamydial antibody titre using the immunocomb *Chlamydia trachomatis* 1gG kit. The data was analyzed using the SPSS version 20 (IBM, Armonk, NY, USA). A p-value of $< 0.05$ was considered statistically significant.
**Results:** The prevalence of serum Chlamydial antibody was 57 (75.0%) and 19 (23.5%) among the cases and the pregnant controls respectively (P-value $< 0.001$). The results showed statistically significant associations between tubal infertility and early age at sexual debut, three or more sexual partners, nulliparity and positive *Chlamydia trachomatis* antibody titre (P-values $< 0.001$).
**Conclusions:** The prevalence of *Chlamydia trachomatis* antibody titre was higher among women with infertility compared to the pregnant controls. The findings suggest that tubal infertility is associated with exposure to *Chlamydial trachomatis* infection.

**Keywords:** *Chlamydia trachomatis*, Infection, Nigeria, Tubal infertility

## INTRODUCTION

*Chlamydia Trachomatis* is one of the most prevalent sexually transmitted diseases (STD) worldwide and according to center for disease control and prevention (CDC), about one million reported *Chlamydia trachomatis* infections occur annually among active young people in the United States[1]. Based on antigenic reactivity, *Chlamydia trachomatis* is divided into 15 serovars, with "d" through "k" typically cause non-gonococcal urethritis in men and cervicitis in women.[1-3] This obligate intracellular bacterium has two phases of developmental cycle comprising an extracellular

infectious form (elementary body EB) and an intracellular replicative form (reticulate body RB).[4-7] This bacterial infection is highly prevalent among economically disadvantaged young individuals less than 25 years of age.[4,5,8-13] It is the most predominant infectious organism causing pelvic inflammatory disease (PID). Its association with PID, tubal factor infertility and ectopic pregnancy have also been noted to be increasing.[3,5,7,8,14]

Most of the infections are salient and asymptomatic and most infected people do not seek medical attention. When untreated, the organism may migrate to female upper genital tracts cause PID with the risk of severe reproductive sequalae, such as tubal factor infertility and ectopic pregnancy.[3,14,15] After an episode of PID, the risk of infertility is about 11% and it increases to 23% and 54% after 2 and 3 episodes respectively.[3,15,16] It is the most prevalent and most active in causing tubal damage of all sexually transmitted diseases.[7,16-19]

Presumably the increasing incidence of infertility is consequent to a rising incidence of tubal infection with C. trachomatis and other sexually transmitted pathogens. It is estimated that in western countries and Nigeria by the end of one year of unprotected sexual intercourse, 10-15% and about 30% respectively of couples will fail to conceive.[20,21] Infertility is a worldwide gynaecological problem with devastating psychological effects on affected couples.[22]

Their emotional problems are compounded by monetary cost for investigation and treatment.[23] Infertility constitutes 50% of all gynaecological consultations in developing countries.[24]

It has been found that 37% and 85% respectively of infertility in developed and developing countries is due to tubal factor.[25] *Chlamydia trachomatis* has received significant attention as a primary etiological factor for approximately 40-50% of PID and salpingitis, 25% of ectopic pregnancies, 50% of tubal infertility and 50% of epididymitis in men.[26,27]

In a series of Swedish studies, 17.2% of women with pelvic inflammatory disease were infertile because of tubal blockage after one or more episodes of Chlamydial infections.[28] Investigations from at least 13 different cities around the world have documented that tubal blockage is strongly associated with the presence of Chlamydial antibodies and when this study is combined, 70% of women with tubal infertility had antibodies to Chlamydia compared with 26% of controls.[28]

Clinical history is not reliable in making a diagnosis of Chlamydial infection.[29,30] and WHO estimate that 70-75% of women with *Chlamydia trachomatis* infection are asymptomatic.[6] Since, this organism is highly prevalent and asymptomatic, a screening programme has been established in some industrialized countries to reduce the rate of PID and its reproductive sequelae.[14,31] Infertility as a result of *Chlamydia trachomatis* is a preventable type of infertility when detected early.[32] Therefore, it is now mandatory in most developed countries for routine *Chlamydia* screening with serology at the beginning of infertility routine serological screening for *Chlamydia trachomatis* at the beginning diagnostic investigation in order to ensure adequate management.[33,34]

With recent advances in the field of science, it is now believed that by using Chlamydia antibody titre assay, the need for laparoscopy could be reduced.[34,35] Disappointingly, despite the profuse works in literatures on this important cause of a number of gynaecological and obstetric morbidities, little has been done in our environment. This however is due to the fact that reliable assays are too expensive and too complex for routine use in resource limited setting.[3,36] This underscores the rate and significance of *Chlamydia trachomatis*, being one of the commonest bacterial infections of the genital tract associated with tubal blockage.[36] Some authors have shown in the past that Chlamydia is commoner in infertile population than fertile pregnant controls.[20,23,36]

The reported prevalence of Chlamydia infection varies with clinical setting and population sample.[19,37] In United Kingdom, values of 10.7% have been reported for asymptomatic women in general practice and 19% and 9% respectively for symptomatic and asymptomatic gynaecological patients.[3,12,19,22] National and local estimates are lacking in Nigeria but it is suspected that the prevalence may not be different or even higher than that of developed countries as most of the risk factors for Chlamydial infection are prevalent in Nigeria.[23,37,38]

Pelvic inflammatory disease and infertility which may result from Chlamydial infection constitute a major part of our gynaecological cases in this environment. This study therefore was designed to compare the prevalence of *Chlamydia trachomatis* antibody titres among infertile patients at Garki hospital Abuja, Federal Capital Territory and to determine the association between tubal infertility and sexual variables as well as exposure to *Chlamydia trachomatis* in the population.

## METHODS

This was a case control study conducted among women with tubal infertility over 16 weeks period between May to August 2013 at Garki hospital located in the central district of Abuja in the federal capital territory of Nigeria. The hospital is one of the largest in Abuja with about 200 bed capacity attending to most of the gynecological and obstetric populations with referrals from other area councils like Abaji, Kwali, Bwari, Karu and neighboring states of Nasarawa, Niger and Kaduna.

The subjects were consecutive infertile patients with proven tubal infertility detectable by hysterosalpingography and confirmed by laparoscopy

within the study period in the gynecological clinic. The controls were pregnant women recruited during the study period as they presented in the antenatal clinic. All patients found not to have tubal occlusion in laparoscopy were excluded from the study. Also excluded were women that were pregnant after infertility treatment including assisted reproductive techniques and those that declined consent for the study.

Upon recruitment, each participant was administered a questionnaire which contained sections on socio-demographic characteristics, sexual and reproductive risk factors. Other information that was obtained included age at sexual debut, number of sexual partners and history suggestive of previous pelvic infections. Also, the source from which previous pelvic infection if any was treated was elicited.

The sample size of 81 each for cases and controls was calculated using the formula $n=Z^2pq/d^2$ based on *Chlamydia trachomatis* prevalence rate of 12% in Benin city as reported by Azenabor et al.[39] Then venous blood of 5 ml was collected from the cases and control into a clean and sterile plastic bottle container. The blood specimens were allowed to retract at 6$^o$c and subsequently centrifuged over five minutes to obtain the sera, which was needed for the assay. All specimens were analyzed by the hospital's medical microbiologist and laboratory technologist.

Specimens (sera) which were not immediately analyzed were stored in deep freezer and this was allowed to subsequent analysis. The serological assay was done using the solid phase enzymes immune assay (EIA), immunocomb *Chlamydia trachomatis* 1gG kit, which is a test for the semi quantitative determination of 1gG antibodies to *Chlamydia trachomatis* in human serum or plasma.[40] The reagent test kit was brought to room temperature after removal from the refrigerator and then 10 micro liter of pipette serum was assayed with reagents and control samples for *Chlamydia trachomatis* 1gG antibody. The procedure was run via a number of timed steps as outlined by the manufacturer.[40]

This study was approved by the ethical committee of the Garki hospital, Abuja. The data was analyzed using SPSS version 20 (IBM, Armonk, NY, USA). Descriptive statistics was done and test of association between variables and tubal infertility was carried out using Chi square test. P value of $< 0.05$ was considered statistically significant.

## RESULTS

A total of 156 respondents who met the inclusion criteria and provided informed consent were recruited into the study. The numbers of cases were 76 (48.4%) while controls were 81 (51.6%).

**Table 1: Socio-demographic characteristics of cases and controls.**

| Variables | Cases N = 76 (%) | Controls N = 81(%) | Total N = 157 (%) |
|---|---|---|---|
| **Age group in years** | | | |
| < 20 | 16 (21.1) | 0 (0.0) | 16 (21.1) |
| 20-24 | 37 (48.7) | 24 (29.6) | 61 (38.9) |
| 25-29 | 22 (28.9) | 32 (39.5) | 54 (34.4) |
| 30-34 | 1 (1.3) | 20 (24.7) | 21 (13.3) |
| > 35 | 0 (0.0) | 5 (6.2) | 5 (0.3) |
| **Educational level** | | | |
| Primary | 17 (22.4) | 11 (13.6) | 28 (17.8) |
| Secondary | 37 (48.7) | 26 (32.1) | 63 (40.2) |
| Tertiary | 22 (29.1) | 44 (54.3) | 66 (42.0) |
| **Marital status** | | | |
| Single | 7 (9.2) | 0 (0.0) | 7 (4.5) |
| Married | 69 (90.8) | 81 (100.0) | 150 (95.5) |

The mean ages of respondents were 22.5±3.5 years and 27.3±4.3 years for cases and controls respectively. Majority of the cases were in the age group 20-24 years [37 (48.7%)] while majority of the controls were 25-29 years [32 (39.5%)]. Concerning level of education attained, most of the cases had secondary education [37 (48.7%)] while most of the controls attained tertiary education [44 (54.3%)]. Furthermore, less than a tenth of the cases were single while, all the controls were married. About two-third of the cases were nulliparous [47 (61.8%)] while about a quarter of the controls were nulliparous [21 (25.9%)]. Conversely, multiparity was higher among controls [38 (46.9%)] compared to cases [5 (6.6%)].

Concerning age at sexual debut, a higher proportion of the cases attained sexual debut earlier than controls; in 10-14 years age group, sexual debut among cases was 25 (32.9%) compared with control 5 (6.2%) while among age group 15-19 years, it was 31 (40.8%) among cases while controls were 22 (27.2%). With respect to number of sexual partners, more than half of the had three or more sexual partners [39 (51.3%)] compared to controls 12 (14.8%). The commonest gynecological symptoms reported by cases and controls were vaginal discharge with 35 (24.5%) among cases compared to 20 (18.0%) among controls, followed by dysmenorrhea, 35 (24.5%) among cases versus 44 (39.6%) among controls, and lower abdominal pain, 33 (23.1%) among cases against 20 (18.0%) among control.

**Table 2: Obstetrics and gynecological history of cases and controls.**

| Variables | Cases, N = 76 (%) | Controls, N = 81 (%) | Total, N = 157 (%) |
|---|---|---|---|
| **Parity** | | | |
| Nulliparity | 47 (61.8) | 21 (25.9) | 68 (43.3) |
| Primiparity | 24 (31.6) | 22 (27.2) | 46 (29.3) |
| Multiparity | 5 (6.6) | 38 (46.9) | 43 (27.4) |
| **Age at sexual debut** | | | |
| 10-14 | 25 (32.9) | 5 (6.2) | 30 (19.1) |
| 15-19 | 31 (40.8) | 22 (27.2) | 53 (33.8) |
| 20-24 | 4 (5.3) | 48 (59.3) | 52 (33.1) |
| 25-29 | 16 (21.1) | 6 (7.4) | 22 (14.0) |
| **Number of sexual partners** | | | |
| One | 17 (22.4) | 21 (25.9) | 38 (24.2) |
| Two | 20 (26.3) | 48 (59.3) | 68 (43.3) |
| ≥ Three | 39 (51.3) | 12 (14.8) | 51 (32.5) |

**Table 3: History of gynecological symptoms among cases and controls.**

| Variables | Cases, N = 76 (%) | Controls, N = 81(%) | Total, N = 157 (%) |
|---|---|---|---|
| Dysuria | 12 (8.3) | 1 (0.0) | 13 (5.1) |
| Vaginal discharge | 35 (24.5) | 20 (18.0) | 55 (21.7) |
| Lower abdominal pain | 33 (23.1) | 20 (18.0) | 53 (20.9) |
| Dysmenorrhea | 35 (24.5) | 44 (39.6) | 79 (31.1) |
| Intermenstrual bleeding | 5 (3.5) | 0 (0.0) | 5 (2.0) |
| Abdominal discomfort | 0 (0.0) | 0 (0.0) | 0 (0.0) |
| No Symptom | 23 (16.1) | 26 (24.4) | 49 (19.3) |
| Total | 143 (100.0) | 111 (100.0) | 254 (100.0) |

*Some participants disclosed more than one symptom.

**Table 4: Sources of treatment among cases and controls.**

| Variables | Cases, N = 76 (%) | Controls, N = 81 (%) | Total, N = 157 (%) |
|---|---|---|---|
| Teaching hospital | 15 (12.9) | 33 (40.7) | 48 (24.4) |
| General hospital | 5 (4.3) | 7 (8.6) | 12 (6.1) |
| National hospital | 0 (0.0) | 2 (2.5) | 2 (1.0) |
| Private hospital | 12 (10.3) | 15 (18.5) | 27 (13.7) |
| Medical diagnostic lab | 13 (11.2) | 2 (2.5) | 15 (7.6) |
| Pharmacy | 6 (5.2) | 0 (0.0) | 6 (3.0) |
| Chemist | 50 (43.2) | 19 (23.5) | 69 (35.1) |
| Traditional practitioner | 0 (0.0) | 0 (0.0) | 0 (0.0) |
| Friends | 15 (12.9) | 3 (3.7) | 18 (9.1) |

With regards to the sources of treatment for pelvic infection sought by respondents, chemist stores were the most utilized by cases 50 (43.2%) compared to controls 19 (23.5%). Similarly, a higher proportion of cases

consulted friends for treatment than controls, 15 (12.9%) cases versus 3 (3.7%) controls (Table 4). The prevalence of Chlamydia trachomatis infection revealed a higher prevalence among cases compared to controls. Three-quarter of the cases 57 (75.0%) had a positive result while about a quarter of the controls 18 (22.2%) had a positive *Chlamydia trachomatis* titre test results. Table 5 below shows results of test of association between tubal factor infertility and exposure to *Chlamydia trachomatis* when compared with pregnant controls. The early age at sexual debut among cases was found to be significantly associated with tubal factor infertility (P < 0.001). Those with three or more sexual partners was found to be significantly associated with tubal factor infertility among cases than their control counterparts, 39 (51.3%) versus 12 (14.8%) (P- < 0.001).

**Table 5: Association between tubal infertility and some risk factors of past exposure to *Chlamydia trachomatis*.**

| Risk factors | Cases, N = 76 (%) | Controls, N = 81 (%) | Total, N = 157 (%) | Chi square | P value |
|---|---|---|---|---|---|
| **Age at sexual debut** | | | | | |
| 10-14 | 26 (34.2) | 5 (6.2) | 31 (19.7) | 57.132 | < 0.001 |
| 15-19 | 30 (39.5) | 22 (27.2) | 52 (33.1) | | |
| 20-24 | 4 (5.3) | 48 (59.3) | 52 (33.1) | | |
| 25-29 | 16 (21.1) | 6 (7.4) | 22 (14.0) | | |
| **Number of sexual partners** | | | | | |
| 1 | 17 (22.4) | 21 (25.9) | 38 (24.2) | 26.112 | < 0.001 |
| 2 | 20 (26.3) | 48 (59.3) | 68 (43.3) | | |
| > 3 | 39 (51.3) | 12 (14.8) | 51 (32.5) | | |
| **Parity** | | | | | |
| Nulliparity | 48 (63.2) | 20 (24.7) | 68 (43.3) | 36.733 | < 0.001 |
| Primiparity | 23 (30.3) | 23 (28.4) | 46 (29.3) | | |
| Multiparity | 5 (6.6) | 38 (46.9) | 43 (27.4) | | |
| ***Chlamydia trachomatis* test result** | | | | | |
| Positive | 57 (75.0) | 18 (22.2) | 75 (47.8) | 43.775 | < 0.001 |
| Negative | 19 (25.0) | 63 (77.8) | 82 (52.2) | | |

Also, nulliparity was significantly associated with tubal infertility among cases, nulliparity among cases was 48 (63.2%) compared to controls 20 (24.7%) [(P < 0.001)]. Analysis of the relationship between *Chlamydia trachomatis* titre test and tubal factor infertility showed a statistically significant relationship between positive results among cases 57 (75%) and tubal factor infertility compared with controls with positive results [18 (22.2%)] (P < 0.001).

## DISCUSSION

The prevalence of *Chlamydia trachomatis* antibody among women with tubal infertility was 75.0% while it was 23.5% among the controls and this was statistically significant. This tends to be in agreement with earlier reports in Nigeria which showed *Chlamydial* antibody to be commoner in infertile women compared with pregnant controls.[19,36] This demonstrates the role played by *Chlamydia* trachomatis in causation of infertility. Studies in Nigeria and other West African countries show prevalence between 23.4% 65.8% among the female infertile population and 17.3% among pregnant women.[41] Based on these findings, the *Chlamydial* antibody prevalence in this study was expected. The "e" antibody prevalence studies mirrors past infection in the women and this tend to suggest a trend toward increasing *C. trachomatis* infection worldwide.[19,23,41,42] This high prevalence of Chlamydial infection amongst infertile women probably is responsible for tubal factor infertility which accounts for up to 85% of cases of female infertility in developing countries, Nigeria inclusive.[23]

This finding is also similar to the investigation from at least 13 cities around the world which have documented that tubal blockage are strongly associated with the presence of Chlamydial antibodies.[28] When these studies were combined, 70% of the women with tubal factor infertility had antibodies to *Chlamydia trachomatis* compared with 26% of the controls.[28]

In this study, majority of young women aged less than 25 years had positive antibody test result for *Chlamydia trachomatis* infection. This is in consonance with earlier report in which the isolation rate for *Chlamydia* was highest in the 15-19 years age group and 90% of reported cases among individuals under 25 years.[13,43] To some extent these trend among the youths may be a marker for sexual activity and also the possibility of acquired immunity to *Chlamydia* with age.[12] In this study marriage In this study, marriage did not significantly influenced the rate of *Chlamydia trachomatis* infection and this is

because the study population of infertile women and pregnant control were mostly married.

This study shows that women with lower level of education have higher risk for chlamydial infection. Those with positive Chlamydial antibodies were mostly in the primary and secondary school education category while tertiary level of education offers significant risk reduction. This may be ascribed to that fact that women with higher level of education are more enlightened about reproductive health issues than the less educated individuals and may also have the financial capacity to seek medical assistance where necessary. Most of those who are negative for the chlamydial antibody had tertiary level education.

Nulliparity was an associated risk factor for chlamydial infection in which 63.2% of the cases had positive antibody for chlamydial infection. In this study, it was found that age at sexual debut below 20 years has an associated risk factor for *Chlamydia trachomatis* infection and in the study about 73% of those positive for Chlamydial infection are in this age group. Dedicated school girls may not have time for sexual practices until later in life and this will result in a higher age at sexual debut. Therefore, higher educational level may lead to higher age at sexual debut and so higher chances of being negative for *trachomatis* infection. Looking at the prevalence age at sexual debut, 73% of cases had sexual debut at age less than 19 years while those who are negative had a higher prevalence of 84.2% at above 25 years. This is in agreement earlier reports.[12-15]

This report has shown that having multiple sexual partners is associated with significant risk of *Chlamydial* infection. This is especially so when the woman has greater than three sexual partners as the prevalence was 51.3% among the cases with multiple sexual partners compared with 14.8% among those without multiple sexual partners. This is also in agreement with earlier reports.[13,44] Generally speaking the presence of multiple sexual partners is a biological risk factor and presumably relates to the increased likelihood of having sexual intercourse with an infected partner.

Based on the findings from this study clinical feature that have the potential of identifying woman at high risk for *Chlamydia* infection are dysuria, vaginal discharge, lower abdominal pain and dysmenorrhea. These features were also reported in earlier research work and these are evidences of pelvic inflammatory disease of which tubal blockage is a sequalae.[4,20]

Finally, this study suggests that poor health seeking behavior was one of the indicators for *Chlamydial* infection. Poor health seeking behavior was exemplified by majority of those attending chemist (66.8%) and those who sought care from friends (16.6%) and these had *Chlamydial infection* compared to those who sought care at more appropriate places like teaching hospitals (40.7%) and private hospitals (18.5%) respectively. Those with poor health seeking behavior may end up with the use of wrong medications or inappropriate dosage with resultant tubal damage due to poorly treated pelvic infection.

This study was limited by sample size. This was essentially due to the prohibitive cost of chlamydial antigen test kit. This study was hospital based and so may not be a true reflection of the situation in the general population.

Also, the information obtained was based on self-reporting of events and problem of recall bias may be present. Furthermore, pregnant women were reluctant in disclosing previous history of pelvic infections and sexual activities compared to the infertile women. The test kit used for the study was qualitative and so results were either positive or negative for antibodies to *Chlamydia trachomatis*. A quantitative test that determines the titre level of the antibodies may show differences in titre ranges for the positive results among the controls and cases. So, antibody titre levels that correlate with tubal disease could not be determined.

## CONCLUSION

The prevalence of *Chlamydia trachomatis* was higher in the study group with infertility when compared to the pregnant controls. There was a strong association between chlamydial antibody positivity and tubal occlusion. Also, early coitarche, multiple sexual partners and nulliparity are associated with risk of tubal infertility and so a possible reflection of previous exposure to chlamydial infection.

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