Original Article

The Prevalence and Outcome of Asymptomatic Chlamydial Infection Screening Among Infertile Women Attending Gynecological Clinic in Ibadan, South West Nigeria

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Abstract

Background: Chlamydial trachomatis infection is the most common cause of tubal infertility among women world-wide. Serological diagnosis of Chlamydial infection that may suggest previous, persistent or on-going infection is now incorporated into routine pre-treatment evaluation of infertile women including assisted conception. **Aim:** The aim of this study is to determine the prevalence and predictors of asymptomatic Chlamydial infection screening among infertile women and also to compare the screening outcome with findings on hysterosalpingogram (HSG). **Subjects and Methods:** This was an observational study conducted among 132 infertile women that were attending Adeoyo Maternity Hospital Ibadan. A total volume of 2-3 ml of venous blood was collected for Chlamydia serology using ImmunoComb Bivalent immunoglobulin G kit (Code 50416002) and the results were compared with their HSG. Other information collected was socio-demographics and clinical parameters. Descriptive, bivariate and multivariate tests were performed using Statistical Package for the Social Sciences 15.0 (Chicago, IL USA) and statistical significance was set at ($P < 0.05$). **Results:** A total of 130 women were studied with a mean age of 31.6 years (standard deviation = 4.7). Majority - 72.0% (95/132) - had been infertile for 5 years or less. The prevalence of Chlamydial trachomatis was 20.5% (27/132). Bivariate analysis between the biosocial variables and serology result showed a significant association with education ($P < 0.01$) and religion ($P < 0.01$). Logistic regression analysis revealed that Muslim women were 3.6 times more likely than Christians to have positive Chlamydial serology result (95% confidence interval odds ratio = 1.18-11.11). Of those with HSG result (64), the accuracy of the test kit showed low sensitivity - 44.2% (19/43) and negative predictive value 40.0% (16/40) (but, high specificity - 76.2%(16/21), and positive predictive value - 79.2% (19/24). **Conclusion:** Asymptomatic Chlamydial infection is common among infertile women and it positively predict HSG blockage. The serological test may prove invaluable in predicting the presence of tubal blockage; therefore, prophylactic antibiotics may be justified to be included in their care.

Keywords: Africa, Chlamydial infection, Infertile women

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Introduction

Infertility is a socially distressing medical condition that remains a public health concern in many developing countries including Nigeria.[1] Tubal diseases are the most common cause of female infertility in Africa[2,3] and it is usually a resultant outcome of repeated infections of the upper genital tracts.[4] This often culminates in the destruction of cilia within the

tubes and consequently leads to bilateral tubal blockage of various degrees. These tubal infections may arise from poorly treated sexually transmitted infections (STIs), post-abortal and puerperal infections.[4,5]

Tubal blockage is commonly associated with persistence of a sub-clinical genital Chlamydial infection and it is usually asymptomatic in over 70% of women. Therefore, majority would not have had treatment. Apart from this challenge, objective diagnosis of Chlamydia infection is by tissue culture.[6] It is expensive and often time consuming.[6]

Use of rapid serological methods that rely on immunology of the infection as proxy determinants of either an on-going or previous infections were developed.[7] It involves use of immunoglobulin G (IgG), A and M detections in either the serum or urine samples. Several studies have confirmed the reliability of using this simple serological test as a predictor of tubal blockage in different settings.[8,9] In addition, many infertility units have incorporated this technique as part of the routine evaluation before embarking on any invasive diagnostic test.[10]

Furthermore, there had been series of debates on whether the use of serological Chlamydial test is enough as a screening tool for tubal infertility alone.[9,11] The aim is to reduce the financial burden on clients and also to assist in prioritizing those with possible tubal blockage for hysterosalpingography (HSG) and or laparoscopy for definitive diagnosis.

Routine screening of infertile couples is reported by various regulatory bodies to be cost-effective in any setting whenever the prevalence of asymptomatic *Chlamydia trachomatis* is more than or equal to 3%.[12,13] They argued that such screening will assist in further evaluation of the patient's previous STIs and also prevent flaring of a sub-clinical infection after instrumentation procedures such as HSG, laparoscopy and or endometrial biopsy.[12,14,15] This flaring effect may further compromise the reproductive chance of such women including assisted reproductive conception methods.[16] Those found to have evidence of *Chlamydia trachomatis* infection are offered treatment and their partner before proceeding with any invasive investigation or treatment.

As interesting as all these proposition sounds, there is a dearth of scientific research evidence in Nigeria that have explored the burden of Chlamydial trachomatis infections and its association with the outcome of tubal infertility investigation in our settings with a view to developing an informed protocol during client's evaluation. The aim of this study is determine the prevalence and possible predictors of asymptomatic Chlamydial infection among infertile women population and also to compare the screening outcome with results of their HSG.

Subjects and Methods

Study design

This was an observational study conducted among consenting women seeking infertility treatment at the Gynaecological out-patient clinic of the Adeoyo Maternity Hospital, Ibadan (a public secondary health care).

Procedure

At each gynecological clinic, all infertile women present were individually interviewed by trained research assistants for any features of the exclusion criteria before their recruitment into the study. The exclusion criteria included previous clinical or laboratory evidence of pelvic infection in the last 6 months and use of any form of antibiotics in the last 6 weeks.

The socio-demographic parameters (age, educational level, religion and tribe) and clinical variables (duration of infertility and previous abortion/miscarriages) were recorded in a proforma form for each of the woman recruited. The result of the HSG performed was also recorded. Thereafter, about 2-3 ml of venous blood was collected from each patient into an ethylenediaminetetraacetic acid bottle and the specimens were refrigerated and stored at 2-8°C.

The screening protocol

The principle of the screening test

The Chlamydia serology was performed using ImmunoComb Bivalent IgG kit (Code 50416002) – it is an indirect solid-phase enzyme immunoassay technique for *Chlamydia trachomatis* (L2 serovar strain) and *Chlamydia pneumoniae* (IOL 207).[17]

The interpretation of results

The results were read using comparison of specific colors of the middle and lower spot with the measuring scale. The color change is based on the level of specie-specific anti-Chlamydial IgG in each specimen. The middle color change signifies *C. pneumoniae* infection while the lower spot color change revealed Chlamydial trachomatis infection. The manufacturer grades the intensity of the lower spot color change on the comb as 1:32 and 1:8 for anti-Chlamydial. Trachomatis active and previous infections respectively while the middle spot color change were graded as 1:512 and 1:16 for anti-*C. pneumoniae* active and previous infections respectively. Any color intensity that is less than 1:8 for C trachomatis and 1:16 for anti-*C. pneumoniae* were regarded as negative result. In this study, cut-off values of 1:32 and 1:512 were taken for evidence of infection.

The result of each woman was recorded into the proforma for data analysis.

Sample size determination

A total of 132 women were studied using an assumption of 5% prevalence from previous similar study[18] at 5% level of

significance using a Leslie Kish formula for estimating single proportions. Ethical approval was secured from the Oyo state ethical review committee through the management of the study site.

Data analysis

The data obtained were entered into the Statistical Package for Social Science 11 software (Chicago, IL USA) and statistical significance was set at ($P < 0.05$). Variables were summarized using frequencies, mean, median and standard deviation (SD). Bivariate analysis was performed between the socio-demographics and the outcome of the Chlamydial infection screening using the Chi-square test. Logistic regression analysis was used to identify the significant predictors after adjusting for cofounders. The sensitivity, specificity, positive predictive and negative predictive values of the test kits was calculated by comparing with HSG results. The level of the statistical significance was set at 5%.

Results

A total of 132 women were studied with a mean age of 31.6 (4.7) years). Majority 90% (118/132) were between the ages of 25 and 39 years. 43 (32.6%) had tertiary level of education, 38.6% (51/132) had secondary while the remainder 25.7% (34/132) had primary education or less. There were more Christians 56.8% (75/132) than Muslims 43.2% (57/132) [Table 1] and almost all 97% (128/132) were of the local Yoruba tribe.

Table 1: Distribution of socio-demographic profile and duration of infertility (*n*=132)

Variables	Frequency (%)
Age range	
20-24	4 (3.0)
25-29	45 (34.1)
30-34	45 (34.1)
35-39	28 (21.2)
40-44	8 (6.1)
Missing	2 (1.5)
Educational level	
None	6 (4.5)
Primary	28 (21.2)
Secondary	51 (38.6)
Tertiary	43 (32.6)
Missing	4 (3.0)
Religion	
Christianity	75 (56.8)
Islam	57 (43.2)
Duration of infertility (years)	
1	19 (14.4)
2-5	76 (57.6)
6-10	27 (20.5)
≥11	9 (6.8)
Missing	1 (0.1)

95 (72.0%) had been infertile for 5 years or less, another 20% (27/132) for 6-10 years while the remaining 6.8% (9/132) had been infertile for more than 10 years.

Concerning Chlamydia serology, ½ (66/132) of the women were negative to the test. C. trachomatis alone was found in 3 (2.3%), *C. ete* in 31 (23.5%), both C. trachomatis and *C. pneumoniae* in 24 (18.2%) while the remaining 8 (6.1%) were indeterminate. The prevalence of Chlamydial trachomatis was 20.5% (27/132).

The relationship between Chlamydia results and some patient's characteristics is shown in Table 2. The proportion of women with primary education or less 44.1% (15/34) with positive results was significantly higher than in those with higher education ($P < 0.001$). Furthermore, Muslims had significantly higher prevalence 35.1% (20/57) of positive results compared with Christians ($P < 0.001$). Age or previous abortions were not significantly related. Logistic regression analysis of Chlamydia results on variables significant at 10% on bivariate analysis showed that Muslims were about 3.6 times more likely than Christians to have positive Chlamydia results (95% of the confidence interval odds ratio = 1.18-11.11) [Table 2].

Of the 132 subjects, HSG results were available for 64 women and this was the sample size used for accuracy measures. The accuracy of the Chlamydia serology tests using the HSG results as standard revealed low sensitivity - 44.2%(19/43), and high specificity 76.2% (16/21). The positive predictive value was 79.2% (16/21) while the negative predictive value was 40% (16/40).

Discussion

In this study, the prevalence of asymptomatic *Chlamydia trachomatis* was 20.5%. This is far higher than similar studies conducted in the UK and other western countries that reported figures of up to 10.4%.[19] The high prevalence recorded in this study may be related to the poor diagnostic facility and health-seeking behavior of Nigerian women especially on sexually transmitted infection. The fear of possible stigma and accusation of marital infidelity may be an added barrier to accessing care for STIs by the womenfolk in our setting.

The higher proportion of Chlamydial infection among infertile women in this study population may be a reflection of higher rate of tubal infertility that has been consistently documented in Nigeria when compared to other developed countries. Furthermore, detection of *C. pneumoniae*, which is often associated with cardiac disorder in this bivalent test kit, offers additional opportunity. Hence, its occurrence amongst infertile women may suggest the need for more thorough cardiovascular examination to either rule out or discover silent heart diseases. Use of prophylactic anti-Chlamydial agents for women with tubal infertility in Nigeria may be justified judging by the higher prevalence rate and such prescription should be given

Table 2: Bivariate and multivariable analysis of positive Chlamydia serology and variables

Variables	Cross-tabulations			Multiple logistic regression	
	% positive for chlamydia	Total	*P* value	OR	95% CI OR
Age group (years)					
20-29	8 (16.3)	49	0.60		
30-34	10 (22.2)	45			
Above 35	9 (25.0)	36			
Educational level					
None and primary	15 (44.1)	34	<0.001*	1.89	0.55-6.67
Secondary	5 (9.8)	51		0.45	0.12-1.61
Tertiary	7 (16.3)	43			
Religion					
Christianity	7 (9.3)	75	<0.001*	3.64	1.18-11.11
Islam	20 (35.1)	57			
Previous abortions					
Yes	17 (21.8)	78	0.19		
No	6 (12.5)	48			

*Statistically significant at 5%. CI: Confidence interval, OR: Odds ratio

prior to tubal patency tests to avert "flaring-up effect" of the infection. In spite of this suggestion, it will still be desirable to conduct operational studies in our setting so as to gather more convincing evidence including those with equivocal result, as prescription of antibiotic prophylaxis may be a challenge.

Identification of at-risk group of women allows for prudent prophylactic prescription of anti-Chlamydial agent as well as easy evaluation and this exercise has been encouraged. Some experts even advocated for routine screening of at-risk groups before embarking on any pelvic instrumentation to prevent iatrogenic spread of the infection.[10] Analysis from this study suggests that women with lower educational level or none and those with Islam as a religion are more likely to be at risk of Chlamydial infection. The lower education level of women is related to lower social class, risky sexual behavior, poor health awareness and health seeking behavior and this may explain the possibility of the association with STIs generally. However, this finding was not found to independently predict the likelihood of Chlamydial infection on regression analysis.

Although, the Muslim women in this study were not stratified into either a monogamous or polygamous family structure, however, polygamy is more permissible in Islam than other religions. Therefore, the sexual networking within a polygamous structure poses a risk of genital infections. However, this association should be cautiously interpreted because of the likelihood of other confounders such as culture, sexual discipline and so on. Therefore, there is the need to conduct research to identify the possible role of family setting as an independent predictor variable. More so, that religion independently predicts the possibility of Chlamydial trachomatis infection on regression analysis.

Just as in previous studies, the accuracy of Chlamydia serology using HSG as standard was found to be highly specific and to have good positive predictive value.[20] This suggests that the detection of positive serological results is highly suggestive of tubal blockage and could easily be used as either a proxy evaluation of tubal patency as being recently suggested or complement the standard evaluation protocol of infertile women. Surprisingly, in this study, the serological screening method used was found to have low sensitivity and low negative predictive value. Therefore, it means that negative Chlamydial screening result does not rule out the possibility of tubal blockage. Laparoscopy was not done in this study and this may have accounted for this result, as some reported tubal blockage on HSG might be due to tubal spasm. Therefore, where laparoscopy is not available, it is advised that health care practitioners effectively combine their clinical acumen and other ancillary investigations of detecting tubal blockage to be able to rule out tubal infertility in women testing negative.

The results should be interpreted with caution because the confirmatory test of Chlamydial infection was not done for those that are positive to the screening test in this study. There may be possibility of some false positive results. Nucleic acid amplification testing (NAAT) remains the goal standard for Chlamydia infections due to its high sensitivity and specificity which was not used in this study.[21] Another benefit of NAAT is that vaginal, urine and rectal samples could be used for the test.[21] However, NAAT is expensive and this has made its availability limited especially in resource poor settings.[20] It is advised that future studies should incorporate it. Another limitation is the small sample size of women that were screened for Chlamydial infection and positive to the test. This may also have implication on the interpretation of the result.

Conclusion

This study revealed a high prevalence of C. trachomatis infection among infertile women, as one in five is likely to harbor the infection and that its occurrence may be associated

with level of education and religious affiliation. The serological test fairly predicts the tubal blockage. We therefore recommend that Chlamydia serological test should be incorporated into the routine infertility investigation and where this is not possible; use of prophylactic anti-Chlamydial agent may be useful.

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