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Association Between Exposure History, Antichlamydia Antibody Positivity, and Testicular Abnormalities in Azoospermic Male Infertile Patients

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Abstract **Original Research Article**

Background*:** Male infertility is a global concern, with azoospermia contributing to 10–15% of cases. Chlamydia trachomatis, a common sexually transmitted infection (STI), is linked to male infertility through inflammation, testicular damage, and impaired spermatogenesis. However, its association with exposure history, antichlamydia antibody positivity, and testicular abnormalities in azoospermic men remains underexplored. This study aimed to assess the prevalence of antichlamydia antibody positivity in azoospermic males and its association with exposure history (multiple sexual partners), hormonal disturbances, and testicular abnormalities. ***Methods: A cross-sectional study was conducted at Bangabandhu Sheikh Mujib Medical University (BSMMU), Dhaka, Bangladesh, from March 1, 2022, to February 28, 2023. A total of 64 azoospermic male patients were recruited through purposive sampling. Structured interviews assessed exposure history. Serological testing for IgG and IgA antichlamydia antibodies was performed using ELISA kits. Hormonal analysis (FSH, LH, testosterone, prolactin) and testicular ultrasonography evaluated endocrine and structural abnormalities. Statistical analysis was conducted using Chi-square and Fisher's exact tests, with $p < 0.05$ considered statistically significant. ***Results:*** Antichlamydia antibody positivity was detected in 15.63% of patients. Those with multiple sexual partners had a significantly higher antibody positivity rate (50%) compared to those without such history (9%) ($p = 0.002$). Testicular abnormalities were more frequent in antichlamydia-positive patients (40%) than antibody-negative individuals (9.26%) ($p = 0.015$). No significant association was found between antibody positivity and hormonal disturbances ($p = 0.07$). ***Conclusion:*** This study highlights a strong link between exposure history and antichlamydia antibody positivity in azoospermic men. The high prevalence of testicular abnormalities in antibody-positive patients suggests Chlamydia trachomatis may contribute to testicular damage. Routine STI screening should be included in male infertility evaluations, especially for high-risk individuals. Further research with longitudinal studies and molecular diagnostics is needed to confirm a causal relationship with azoospermia.

Keywords: Azoospermia, Male Infertility, Chlamydia trachomatis, Antichlamydia Antibody, Exposure History.

INTRODUCTION

Male infertility is a significant global health concern, contributing to approximately 40–50% of all infertility cases [1]. Among its various causes, azoospermia, the complete absence of sperm in the ejaculate, affects approximately 1% of all men and up to 10–15% of infertile men [2]. This condition is classified into obstructive azoospermia (OA), caused by physical blockages in the reproductive tract, and non-obstructive azoospermia (NOA), which results from genetic, hormonal, or infectious factors [2]. Among infectious causes, Chlamydia trachomatis is one of the most prevalent sexually transmitted infections (STIs) worldwide and has been linked to spermatogenic failure, reproductive tract inflammation, and obstruction, all of which may contribute to male infertility [3].

Chlamydia trachomatis accounts for 20–30% of all bacterial STIs globally, often remaining asymptomatic in men [4]. However, untreated infections can lead to epididymitis, prostatitis, and vas deferens obstruction, impairing sperm transport and function [4]. Studies suggest that the presence of antichlamydia antibodies in serum can indicate previous or ongoing infections, making them a potential biomarker for chlamydia-induced infertility [5]. Additionally, chronic chlamydia infections have been associated with oxidative stress, increased inflammatory cytokines, sperm DNA damage, and the production of anti-sperm

antibodies, all of which negatively impact male fertility [6].

The risk of acquiring Chlamydia trachomatis is closely linked to sexual behaviors, particularly multiple sexual partners, unprotected intercourse, and lack of STI screening [7]. Several studies have reported that men with a history of multiple sexual partners are at a higher risk of persistent or recurrent chlamydia infections, which can contribute to long-term reproductive complications [8]. Despite the established role of chlamydia infections in male infertility, limited research has specifically examined the association between exposure history and chlamydia-related immune responses in azoospermic males [5].

Given the global burden of male infertility and the recognized role of STIs, particularly Chlamydia trachomatis, in azoospermia, investigating the relationship between sexual exposure history and antichlamydia antibody positivity is essential. Establishing this association could facilitate early STI screening, prevention, and targeted interventions for high-risk individuals [5].

This study aims to assess the prevalence of antichlamydia antibody positivity in azoospermic male infertile patients and examine its association with exposure history (multiple sexual partners). Additionally, it explores potential correlations with hormonal disturbances and testicular abnormalities, providing insights into the impact of Chlamydia trachomatis on male infertility.

METHODOLOGY

Study Design: This cross-sectional descriptive study investigated the association between exposure history and antichlamydia antibody positivity among Bangladeshi azoospermic male infertile patients.

Study Setting and Duration: The study was conducted in Department of Anatomy, Bangabandhu Sheikh Mujib Medical University (BSMMU), Dhaka, Bangladesh. Data collection and laboratory analyses took place between March 1, 2022, and February 28, 2023.

Study Population and Sampling: A total of 64 azoospermic male patients were recruited from the Outpatient Department of Reproductive Endocrinology and Infertility, BSMMU, using purposive sampling. The inclusion criteria required participants to be Bangladeshi residents aged 21–60 years, with a confirmed diagnosis of azoospermia and a history of primary or secondary infertility. Patients with co-morbid conditions such as diabetes, hypertension, known genetic disorders, or previous vasectomy were excluded. Additionally, individuals with ongoing infections, recent antibiotic use, or medication history affecting fertility were not considered for the study. Selection was based on detailed clinical evaluations, semen analysis, and confirmed azoospermia through laboratory reports.

Ethical Considerations: Ethical approval was obtained from the Institutional Review Board (IRB) of BSMMU. Written informed consent was secured from each participant, ensuring confidentiality and anonymity through unique patient ID numbers. The study adhered to the ethical principles outlined in the Declaration of Helsinki (7th revision, 2013).

Laboratory Procedures: For serological testing of antichlamydia antibodies, 5 mL of venous blood was collected from each participant in sterile vacutainer tubes. The blood samples were then centrifuged at 3000 rpm for 10 minutes, and the serum was separated and stored at −20°C until further testing. The presence of IgG and IgA antichlamydia antibodies was detected using Enzyme-Linked Immunosorbent Assay (ELISA) kits, following the manufacturer's instructions. To ensure test accuracy and reliability, positive and negative controls were included in each run.

For hormonal and testicular assessments, serum levels of Testosterone, Follicle-Stimulating Hormone (FSH), Luteinizing Hormone (LH), and Prolactin were measured using chemiluminescent immunoassay (CLIA). Additionally, scrotal ultrasonography was performed to evaluate testicular volume, echotexture, and structural abnormalities, providing further insight into potential testicular dysfunction.

Data Analysis: Statistical analyses were performed using IBM SPSS Statistics (version 25, 2017). Descriptive statistics were used to summarize the sociodemographic characteristics of the study population, with results expressed as frequencies and percentages. To determine the association between exposure history and antichlamydia antibody positivity, a Chi-square test (χ^2 test) was conducted. Fisher's exact test was applied when the expected count in any cell was less than 5, ensuring the reliability of statistical comparisons. The results were presented highlighting the significant relationship between exposure history and antichlamydia antibody positivity ($p = 0.002$). Further, the association between antichlamydia antibody positivity and hormonal disturbances or testicular abnormalities was evaluated using the Chi-square test, with findings summarized. A p-value <0.05 was considered statistically significant.

Quality Control and Assurance: All laboratory procedures followed standard operating protocols (SOPs) to ensure accuracy and reliability. To prevent contamination, tests were conducted in a Class II biosafety cabinet under sterile conditions. Reagents, pipettes, and ELISA kits were validated before use to maintain precision. Duplicate testing was performed on 10% of randomly selected samples, and borderline

results were reanalyzed to ensure reproducibility and eliminate errors.

RESULT

Table I shows that, about 36 (56.3%) patients lies between 31 years to 40 years. Mean ± SD of the patients age was 33.53 ± 6.37 years.

Table 1: Sociodemographic Characteristics of the Study Population (n = 64)

Characteristic	Number of Patients (n = 64)	Percentage (%)
Age at Diagnosis		
21-30 years	20	31.3
31-40 years	36	56.3
41-50 years	8	12.5
BMI		
Normal (18.5–25)	34	53.1
Overweight (25-30)	26	40.6
Obese (>30)	4	6.25
Education		
Secondary School	38	59.38
Higher Education	26	40.63
Occupation		
Service Holder	26	40.63
Businessman	24	37.5
Worker (e.g., factory)	14	21.88
Exposure History		
Positive	8	12.5
Negative	56	87.5
Family History of Infertility		
Positive	4	6.25
Negative	60	93.75

Table 2: Association Between Exposure History and Antichlamydia Antibody Positivity

Exposure History	Antichlamydia Antibody Positive (n=10) (%)	Antichlamydia Antibody Negative (n=54) (%)	Total (n=64)	p-value
Positive (Yes)	5 (50.0)	3 (5.36)	8 (12.5)	0.002*
Negative (No)	5 (9.0)	51 (91.0)	56 (87.5)	
Total	10 (15.63)	54 (84.38)	64 (100)	

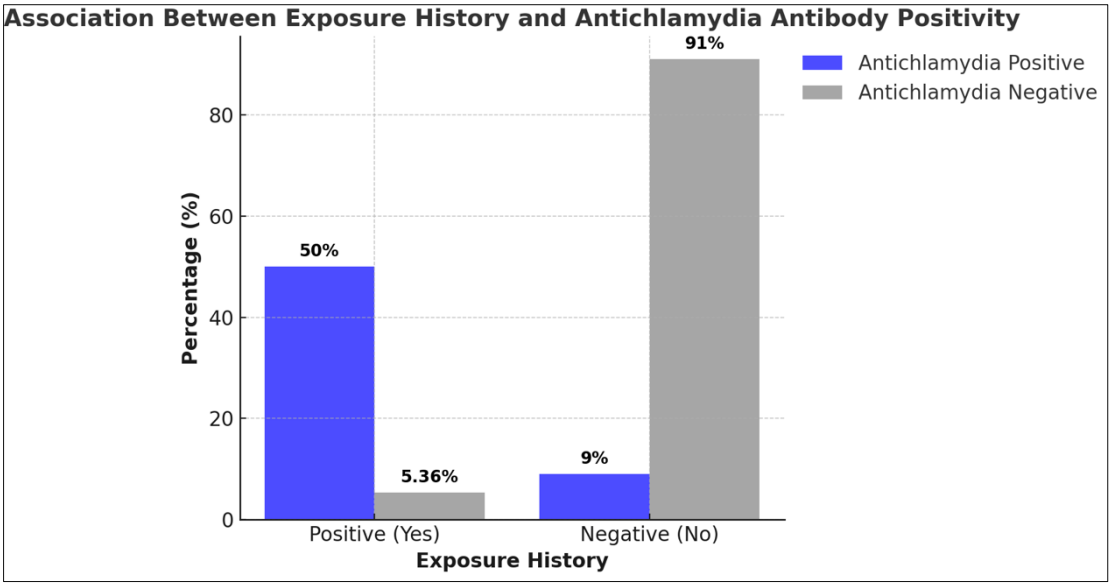

Figure 1: Association Between Exposure History and Antichlamydia Antibody Positivity

Figure 1 illustrates the association between exposure history and antichlamydia antibody positivity among azoospermic male infertile patients. The antichlamydia antibody positivity rate was significantly higher (50%) among individuals with a history of multiple sexual partners, compared to only 9% among those without such a history. Conversely, 91% of participants with no exposure history tested negative, while only 5.36% of exposed individuals were antibody-negative. These findings indicate a strong association between exposure history and chlamydia infection, suggesting that individuals with multiple sexual partners are at a higher risk of acquiring Chlamydia trachomatis, which may contribute to male infertility. The statistically significant difference ($p = 0.002$) reinforces the importance of STI screening in high-risk groups to prevent complications related to chlamydia-induced azoospermia. (Figure 1)

Table 3: Association of Antichlamydia Antibody Positivity with Hormone Profiles and Testicular Abnormalities)

Category	Antichlamydia Antibody Positive (n=10) (%)	Antichlamydia Antibody Negative (n=54) (%)	p-value
Abnormal Hormone Levels	2 (20.0)	2 (3.7)	0.07
Normal Hormone Levels	8 (80.0)	52 (96.3)	
Testicular Abnormalities	4 (40.0)	5 (9.26)	0.015
No Testicular Abnormalities	6 (60.0)	49 (90.74)	

Table 3 examines the association between antichlamydia antibody positivity and hormonal as well as testicular abnormalities in azoospermic male infertile patients. The prevalence of abnormal hormone levels was higher (20%) in antichlamydia-positive patients compared to 3.7% in antibody-negative individuals, though this difference was not statistically significant ($p = 0.07$). While this suggests a possible link between chlamydia infection and hormonal disturbances, a larger sample size may be needed for confirmation. However, testicular abnormalities were significantly more frequent in antichlamydia-positive patients (40%) compared to 9.26% in antibody-negative individuals, with a statistically significant p-value of 0.015. This indicates a strong correlation between chlamydia infection and structural testicular damage, which may contribute to spermatogenic failure and azoospermia. These findings highlight the potential role of chlamydia infection in both testicular abnormalities and endocrine dysfunction, emphasizing the importance of STI screening and testicular evaluations in infertile males, particularly those with a history of multiple sexual partners. (Table 3)

DISCUSSION

This study aimed to explore the association between exposure history and antichlamydia antibody positivity among azoospermic male infertile patients. The findings demonstrated that 50% of patients with a history of multiple sexual partners tested positive for antichlamydia antibodies, compared to only 9% among those with no such history ($p = 0.002$). These results suggest a strong correlation between high-risk sexual behavior and chlamydia-related infertility, supporting existing evidence that Chlamydia trachomatis is one of the most common sexually transmitted infections (STIs) associated with male infertility [9].

Additionally, 40% of antichlamydia-positive patients exhibited testicular abnormalities, compared to 9.26% in antibody-negative individuals ($p = 0.015$), reinforcing prior studies demonstrating that chronic Chlamydia trachomatis infections contribute to testicular inflammation, epididymal obstruction, and sperm DNA fragmentation [10]. Although the association between antichlamydia antibody positivity and hormonal disturbances was not statistically significant ($p = 0.07$), the higher prevalence of hormonal abnormalities (20%) in infected individuals suggests that chlamydia infections may disrupt the hypothalamic-pituitary-testicular axis, which is consistent with previous findings [11,7].

The prevalence of antichlamydia antibody positivity (15.63%) in this study aligns with prior research conducted in Bangladesh, which reported a similar prevalence of chlamydia infections among infertile males [4]. Similarly, global studies have documented that chlamydia infections frequently remain asymptomatic but significantly impact sperm function, leading to oxidative stress and inflammatory responses in the reproductive tract [12].

The strong correlation between exposure history and antichlamydia antibody positivity observed in this study is supported by a meta-analysis, which found that men with multiple sexual partners had a higher likelihood of recurrent chlamydia infections, leading to long-term reproductive complications [13]. A study by Close *et al.*, also indicated that chlamydia infections contribute to the development of anti-sperm antibodies, further impairing fertility [10]. Furthermore, research from Central Africa has highlighted the high prevalence of chlamydia-related infertility in regions with increased STI transmission rates, emphasizing the need for early screening and treatment [9].

The findings of this study underscore the importance of routine STI screening in men undergoing infertility evaluations, particularly those with a history of multiple sexual partners. Despite existing recommendations for chlamydia testing in asymptomatic men at high risk, STI screening is often excluded from standard male infertility assessments [1]. Given the significant association observed in this study, serological testing for chlamydia antibodies should be incorporated into azoospermia evaluations, as early detection and treatment may prevent irreversible reproductive damage [10].

Moreover, the strong correlation between antichlamydia antibody positivity and testicular abnormalities suggests that scrotal ultrasonography should be considered a routine diagnostic tool in STI-exposed men. Chronic chlamydia infections have been associated with testicular fibrosis, epididymal obstruction, and inflammatory damage, highlighting the necessity for early intervention [12].

CONCLUSION

This study provides strong evidence of an association between exposure history and antichlamydia antibody positivity in azoospermic male infertile patients. The high prevalence of testicular abnormalities among antibody-positive individuals suggests that chronic chlamydia infections may contribute to structural testicular damage. Given these findings, routine STI screening should be incorporated into infertility assessments, particularly for men with multiple sexual partners. Future research using longitudinal study designs and molecular diagnostic techniques (e.g., PCR-based testing) is needed to establish a definitive causal relationship between chlamydia infections and azoospermia, ultimately guiding evidence-based reproductive health strategies.

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