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Serum Levels of Immunoglobulin A, G & M in *Chlamydia trachomatis* Infection among Primary and Secondary Infertility Patients

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Authors' contributions

This work was carried out in collaboration between all authors. Author DOPE designed the study, performed the statistical analysis, wrote the protocol, wrote the first draft of the manuscript and managed literature searches. Authors IMO, NAM, ILC and EE managed the analyses of the study and literature searches. All authors read and approved the final manuscript.

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ABSTRACT

Background: *Chlamydia trachomatis* is a well- known sexually transmitted bacteria that is capable of damaging female reproductive tract leading to infertility. *Chlamydia trachomatis* infection in men can mechanically hinder sperm from reaching female reproductive tract.
Aim: The aim of this study is to determine the serum levels of immunoglobulin (Ig) IgA, IgG & IgM in clinically diagnosed primary and secondary infertile patients that tested positive to *Chlamydia trachomatis* IgG antigen.

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Study Design: In this case control study, two hundred male and female patients that visited Government hospital Ekpan due to inability to achieve pregnancy after a period of one year unprotected sexual intercourse were randomly selected for the study.
Place and Duration of Study: Government Hospital Ekpan, Delta state, between June, 2013 and August, 2013.
Methodology: Two hundred patients (104 men, 96 women; age range 18-45 years) that are clinically diagnosed with primary and secondary infertility and hospital staff (23 men, 27 women; age range 18-45 years) with no history of infertility were included. *Chlamydia* assay was done by Enzyme Immunosorbent Assay (EIA). IgA, IgG & IgM determination were done by Immunoturbidimetric method.
Results: The result of this study showed that the mean +/- SD of IgG g/dl in male infertility due to positive *Chlamydia trachomatis* infections; 301.22 +/- 43.86 g/dl, negative *Chlamydia trachomatis* infections; 333.14 +/- 40.08 g/dl and fertile male 337.09 +/- 40.89 g/dl were compared. The result showed statistically significant difference (F= 9.96; P= 0.05). Also the mean +/- SD of Immunoglobulin G (IgG) in female infertility due to combined effect of positive *Chlamydia trachomatis* infection; 154.81 +/- 60.12 g/dl, negative *Chlamydia trachomatis* infection; 184.54 +/- 63.33 g/dl, and fertile female control; 137.96 +/- 87.11 g/dl without infertility were compared. The result showed statistically significant difference (F= 3.32; P= 0.05).
Conclusion: *Chlamydia trachomatis* bacteria are one of the causes of infertility in patients diagnosed of primary and secondary infertility at Government Hospital Ekpan.

Keywords: Chlamydia trachomatis; infertility; IgA; IgG; IgM.

1. INTRODUCTION

Chlamydia trachomatis (Ct) infection is a major and increasing public health problem worldwide and is currently the main cause of sexually-transmitted infections (STIs). The incidence of this infection is highest in young women and men, and is especially important in this population group due to the potential consequences in the female and male reproductive tract, such as pelvic inflammatory disease, tubal damage, and infertility [1]. Transmission of *Chlamydia trachomatis* infection is thought to be direct contact between the mucous membranes of two individuals during sexual activity or through an infected birth canal because of the anatomical characteristics of the female genital tract, the risk of contracting a sexually transmitted disease (STI) is higher in women than in men [2]. Considering other sexually transmitted disease, the risk of *Chlamydia trachomatis* transmission is directly related to certain sexual activities, such as starting sexual relations at an early age, their frequent sexual activity without protection or incorrect condom use, multiple sexual partners and promiscuity. Pregnant women are not free of these risks [3]. High risk of infection has been described in persons with a low socioeconomic position and in substance abusers, due to low awareness in these population groups. Adolescents are the group most likely to engage in high-risk behaviours, such as unprotected sex, especially when they are under the influence of drugs or alcohol [4]. A major feature of the epidemiology of *Chlamydia trachomatis* infection is the high percentage of the infected population that may be asymptomatic, often for several months. While the percentage of asymptomatic infected men is estimated to be up to 50%, in women this percentage may be as high as 70-75% [2]. Asymptomatic infected individuals may spread undiagnosed infection among the sexually active population. Transmission of *Chlamydia trachomatis* infection among the population can also be facilitated by the emergence of mutated strains, as occurred in Sweden in 2006 with the new variant of *Chlamydia trachomatis (*nvCt), which was not detected with the molecular techniques used in some regions due to a 377 bp deletion in the cryptic plasmid [5]. The nvCt caused many false negative diagnoses, allowing this variant to spread to other northern European countries [6]. Another important issue is that other micro organisms causing sexually transmitted infection, including HIV, hepatitis B virus, herpes simplex viruses, *Neisseria gonorrhoeae*, *Treponema pallidum*, can be transmitted in the same episode as that leading to *Chlamydia trachomatis* infection. Moreover, in *Chlamydia trachomatis* - infected individuals, there is a greater risk of acquiring and, in the case of co infection, of transmitting other sexually transmitted infection due to the inflammatory alterations produced in affected genital mucous membranes [7]. The

Chlamydia trachomatis infected individuals might have some changes in their humoral immune response; for instance immunization of animal with *Chlamydia trachomatis* has been shown to elevate, although in an irregular manner [8]. Some previous studies also evaluated the dynamic, alterations in indices of specific and nonspecific as well as in haematological and serological variables in rabbits (the standard animal in biological studies on human and animal immunization with *Chlamydia* spp [8]. According to author, there were elevated levels of serum IgA, IgG and IgM classes of Immunoglobulin. Deptula et al. [8] confirmed that serum Immunoglobulin play principal role in protecting against the infection with *Chlamydia trachomatis*. The result of the researchers [8] found practical confirmation in diagnosis of *Chlamydia* in human in whom the antibodies particularly those IgG and IgM classes represent a specific diagnostic element of the *Chlamydia trachomatis* infection alteration in the haematological parameters. In most parts of Nigeria, *trachomatis* are not routinely screened for, and hence relative information about frequencies of the organisms is sparse [9]. Malik et al. [10] reported prevalence of past *Chlamydia trachomatis infection* as strongly statistically significant in women with secondary infertility. According to their finding current infection may also be statistically significant in these women. IgG antibody detection was effective tool for detecting *Chlamydia*. It has been observed that persistent *Chlamydia trachomatis* infection can result in the scaring of ejaculatory ducts or loss of stereocilia [1]. Recent studies have implicated *Chlamydia trachomatis* as one of the major cause of pelvic inflammatory disease which may lead to subsequent infertility [11]. Infertility could result from tubular damage due to chronic infection or as a result of acute salpingitis. Since antibodies to *Chlamydia trachomatis* were found in female patients with tubal factor infertility, by some Authors [12]. It is suggestive that *Chlamydia* is involved in other pathogenesis of pelvic inflammatory disease which may cause infertility due to compromised function of the uterine tubes [13]. Paavonen [14] discovered that more than 70% of women with signs of tubal damage had circulating antibody to *Chlamydia trachomatis* compared to non in a group of control with normal fallopian tubes. The implication is that the organism has a prediction for inducing inflammatory changes of the deep pelvic organs in female. The above implications lead us to carry out study on *Chlamydia trachomatis* antibody pattern in male and female infertility.

2. MATERIALS AND METHODS

2.1 Study Area

This study was carried out at Government hospital Ekpan Delta State. Ekpan in Delta State (region) is a town located in Nigeria- about 412 km south west of Abuja, the country′s capital place. Ekpan is one of the densely populated crude oil refining towns in Delta State Mid West Nigeria. It is predominately inhabited by crude oil workers.

2.2 Study Design

A total of two hundred patients and fifty apparently healthy men and women were used for this study. The age of these Participants ranges between 18-45years. Patients and control subjects were screened for *Chlamydia trachomatis* by Immunocomb *Chlamydia trachomatis* IgG test. Serum levels of IgA, IgG and IgM were determined by Immunoturbidimetric method. The detail of the study was explained to each subject and informed consent was obtained before specimen was collected for analysis. This study took a period of Two (2) Months. Those included in this study are clinically confirmed patients that had infertility problem. Ethical approval for this study was obtained from Government Hospital Ekpan Warri, Delta State.

2.3 Sample Collection

A total of 2 ml of venous blood was collected by venipuncture under aseptic condition using a sterile disposable syringe and needle from each of the patients into Plain container and labeled. The blood sample in plain container was allowed to clot and after clot retraction the sample was spun with bucket centrifuge and sample separated into a plain container for *Chlamydia* assay, IgA, IgG & IgM serum level. *Chlamydia trachomatis* antibody was determined by Immunocomb *Chlamydia trachomatis* IgG test (ORGENIC PRODUCT, ISREAL). The principle of the test is based on antibody antigen reaction in which when serum is introduced into the well containing *Chlamydia trachomatis* antigen a chromogenic component formed resulting in a gray-blue spots on the teeth of the card. Serum levels of IgA, IgG & IgM antibody were determined by immunoturbidimetric method as described by Linear Chemical S.L (2013, Spain). The principle of the assay of immunoglobulin classes (IgA, IgG & IgM) is based on

turbidimetric measurement. Turbidity is caused by the formation of antigen antibody insoluble immune complexes enhanced by polyethylene glycol (PEG) and the concentration is read spectrophotometrically at 340 nm.

3. RESULTS AND DISCUSSION

Table 1 show mean +/- SD IgA (g/dl) level in female infertility and *Chlamydia* point; 104.53+/- 45.64, female infertility with negative *Chlamydia trachomatis*; 108.39 +/- 36.41 and fertile female (normal control); 108.52 +/- 38.53, when compared statistically, there was no significant differences. Also mean +/- IgG in *Chlamydia trichomatis* positive infertile female; 291.57 +/- 64.08, infertile female with negative *Chlamydia trichomatis*; 282.43 +/- 66.77 and fertile female with *Chlamydia* negative, 278.41 +/- 78.53, compared statistically, showed no significant difference, (F= 0.43, P= 0.65). However, the ANOVA comparison of mean +/- IgM serum level, 157.81 +/- 60.12, 184.54 +/- 63.33 and 137.96 +/- 87.11 for infertile female with *Chlamydia trichomatis* positive, infertile female with negative *Chlamydia* and control fertile female respectively. When they were compared, there was statistical significant difference (F= 3.32, P=0.04). Comparison to mean serum level of IgM in infertile female with positive *Chlamydia* and infertile female with negative as well as comparison between IgM level of infertile female with *Chlamydia* sero positive and fertile female showed no significant difference (P=0.15, P=0.53) respectively.

Table 2 Compared mean +/- SD levels of IgA, IgG and IgM among male infertility and positive *Chlamydia trichomatis*; male infertility with negative *Chlamydia trichomatis* and fertile (control) male using ANOVA and post hoc. The mean +/- SD serum of IgA (g/dL); 143.91 +/- 47.31 for infertile male with sero positive *Chlamydia trichomatis*, 160.65 +/- 50.57 for infertile male with negative *Chlamydia trichomatis*, 165.65 +/- 49.21 for normal control fertile male, compared, showed no statistical significant difference (F= 2.41, P= 0.09). Similarly the mean level of IgM in infertile with *Chlamydia* seropositive; 251.58 +/- 57.90, in fertile male with *Chlamydia trichomatis* seronegative; 262.70 +/- 77.12 and in fertile (control) male compared showed no significant difference (F= 0.31, P= 0.73). However, the comparison of mean serum level of IgG in infertile male with *Chlaymydia* seropositive, 01.32 +/- 40.08 and fertile (control) male 337.09 +/- 40.80 showed statistically significant difference (F= 9.96, P= 0.00). The in-between comparison using post hoc analysis showed that mean serum level of IgG in infertile male with *Chlamydia* was significant in each case lower than infertile male with seropositive *Chlamydia* and fertile (control) male (P= 0.00, P= 0.00) respectively. Out of 200 patients, 135 patients (67.5%) tested positive to *Chlamydia trachomatis* antigen by ELISA technique.

The study is aimed at evaluating patterns of IgA, IgG & IgM in infertility with *Chlamydia trachomatis* infection in Ekpan, Uwvie local Government Area of Delta State. The immunoglobulin M (IgM) level in female infertility with sero positive *Chlamydia trachomatis*, sero negative *Chlamydia trachomatis* were higher than the fertile normal females. The finding may agree with the report of researchers that immunization of animal with bacteria has been shown to elevate, although in an irregular fashion levels of IgG and IgM and IgA classes of immunoglobulin in serum and secretions [8]. However, the IgG level in male infertility with seropositive *Chlamydia trachomatis* and

Table 1. Compared mean +/- SD of IgA, IgG & IgM among female infertility due to positive *Chlamydia trachomatis* infection (*Ct*) (1), negative *Chlamydia trachomatis* (*Ct)* 2 and fertile female (3) using ANOVA

***Ct* status**	**IgA (g/dl)**	**IgG (g/dl)**	**IgM (g/dl)**
(1) +ve *Ct*(n=68)	104.53+/- 45.64	291.57+/- 64.08	157.81+/- 60.12
(2) –ve *Ct* (n=28)	108.39+/- 36.41	282.43+/- 66.77	184.54+/- 63.33
(3) Fertile female (n=27)	108.52+/- 38.53	278.41+/-78.53	137.96+/- 87.11
F (P) value	0.13(0.88)	0.43 (0.65)	3.32 (0.04)
1v2	0.90	0.81	0.15
1v3	0.90	0.72	0.53
2v3	1.0	0.98	0.05

*Key: *Level of significant, SD= Standard Deviation, -ve =negative, +ve= positive and v= versus*

Table 2. Compared Mean +/- SD of IgA, IgG & IgM among male infertility due to positive *Chlamydia trachomatis* infection (*Ct*) 1, negative *Chlamydia trachomatis* (*Ct*) 2 and fertile male (3)using ANOVA

Ct status	IgA (g/dl)	IgG (g/dl)	IgM (g/dl)
(1) +ve *Ct* (n=67)	143.91 +/- 47.31	301.22 +/- 43.86	251.58 +/- 57.90
(2) –ve *Ct* (n=37)	160.65 +/- 50.57	333.41 +/- 40.08	262.70 +/- 77.12
(3) Fertile (n=23)	165.65 +/- 49.21	337.09 +/- 40.80	253.43 +/- 86.
F (p) value	2.41 (0.09)	9.96 (0.00*)	0.31 (0.73)
1v2	0.23	0.00*	0.73
1v3	0.17	0.00*	1.00
2v3	0.92	0.93	0.91

*Key=*Level of significance, v=versus, SD=standard deviation, +ve =positive and –ve =negative*

seronegative *Chlamydia trachomatis* were significantly lower than the normal males without infertility. This also agrees with the findings of researchers [8], that immunization of animal with bacteria has shown to have elevated although in an irregular fashion levels of IgG, IgM and IgA class of immunoglobulin in serum or secretions. The significant differences seen in IgM and IgG in both male and female may be associated with persistence infection which has been shown to occur in *Chlamydia trchomatis* infection [15]. All IgA parameters serum levels in all the groups in both male and female studied compared with the normal were insignificant. Deptula et al. [8] confirmed this finding.

4. CONCLUSION

From the findings and observations in this study, the following conclusions were deduced. Immunoglobulin G, (IgG) was involved in male infertility while IgM is in female infertility, with or without seropositive *Chlamydia trachomatis*. The level of immunoglobulin A (IgA) were insignificant in both male and female infertility.

COMPETING INTERESTS

Authors have declared that no competing interests exist.

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