Research Article

iMedPub Journals
www.imedpub.com

Health Science Journal
ISSN 1791-809X

2021
Vol. 15 No. 5: 837

Sero-prevalence of IgG and IgA Antisperm Antibodies in Men with Infertility Attending Two Major Hospitals in Zaria, Nigeria

Oduma Audu[1,3]*, Bolanle Olufunke Priscilla Musa[1], Mukhtar Abdulmajid Adeiza[1], Ahmad Muhammed[2], Abdurrahman El-fulaty Ahmad[3], Bawa Ega[3], Suraju Ahmad Opaluwa[3] and Bukhari Isah Shuaib[4]

1Department of Medicine, Ahmadu Bello University Teaching Hospital, Zaria, Nigeria

2Department of Surgery, Division of Urology, Ahmadu Bello University Teaching Hospital, Zaria, Nigeria

3Department of Medical Microbiology, Ahmadu Bello University Teaching Hospital, Zaria, Nigeria

4Anti-Retroviral Therapy (ART) Laboratory, Ahmadu Bello University Teaching Hospital, Zaria Nigeria

***Corresponding author:**
Oduma Audu

Tel: +2348039771422

imam02803@gmail.com

Department of Medicine, Ahmadu Bello University Teaching Hospital, Zaria, Nigeria.

Citation: Audu O, Musa BOP, Adeiza MA, Muhammed A, Ahmad AE, et al. (2021) Sero-prevalence of IgG and IgA Antisperm Antibodies in Men with Infertility Attending Two Major Hospitals in Zaria, Nigeria. Health Sci J. 15 No. 5: 837.

Abstract

Background: Antisperm antibodies (ASA) have been implicated in some male with infertility especially those in which a definite cause could not be found. Also, some studies have attributed a causal relationship to the presence of antisperm antibodies and male infertility.

Objective: This study investigated the prevalence of serum antisperm antibodies in men with infertility seen in two Hospitals in Zaria, Nigeria

Materials and Methods: A total of 91 infertile men and 45 fertile men (as controls) were enrolled and follow up for 5 months. Blood samples and semen were collected, processed and analysed for serum IgA and IgG ASA using ELISA kits.

Results: The study revealed the sero-prevalence of antisperm antibodies among infertile men in Zaria to be 57.1%, which varied significantly with that of the fertile male (11.1%). The prevalence of IgA and IgG antisperm antibodies were significantly higher in infertile male compared to fertile male (27.5% vs 4.4% for IgA ASA; 53.8% vs 8.9% for IgG ASA).

Conclusion: The study demonstrated that IgA and IgG ASA are associated with male infertility in Zaria and as such screening for serum antisperm antibodies in the evaluation of men infertility is recommended in our environment.

Keywords: Antisperm antibodies; Male infertility; Fertile male; Sperm count; Zaria

Received with Revision May 14, 2021, **Accepted:** May 18, 2021, **Published:** June 03, 2021

Introduction

Infertility is the failure of a couple to achieve clinical pregnancy after 12 months or more of regular unprotected sexual intercourse [1]. Primary infertility is said to exist if an individual has never had an established pregnancy irrespective of the outcome. On the other hand secondary infertility is when an individual who was previously able to bear a child becomes subsequently unable to do so [1].

Many medical conditions have been implicated in infertility, however occasionally no cause is identifiable [2]. Overall, one third of infertility cases are attributed to male factors, one third to female reproductive pathologies and one third to both male and female factors [2]. Antisperm antibodies (ASA) have been implicated in some cases of infertility.The humoral immune response involving ASA formation could be induced in men during infectious and non-infectious inflammation, or by obstruction of the testicular efferent duct [3,4]. ASA can also be induced after accidental and or surgical injury of testicles, exposure to very low temperatures or cryptorchidism [5,6].

The presence of ASA reacting with antigens on the sperm is considered typical and specific for immunological infertility [7]. ASA can impair fertilization by several mechanisms. They can interfere with sperm motility by immobilizing or agglutinating the sperm, or interfere with sperm cervical mucus interaction and disturb sperm transport [8]. ASA mediated impairment of fertilization can also occur as interference with sperm penetration into the oocyte, and perhaps affect zygote development by impairing early cleavage, or even damaging the implantation process [9,10]. Subsequently,

infertility can result from antibodies directly binding the sperm, or cell and impeding motility by impairment of spermatogenesis due to allergic orchitis. Most affected men develop epididymal sperm granulomas and testicular degeneration associated with the formation of antisperm antibodies [6,7].

The relevance of ASA in the diagnosis and treatment of infertility is still controversial [11], as sperm antibodies have been found in 3-7% of infertile men [12]. These include immunoglobulins of the IgG, IgA and or IgM isotypes that are directed at various aspects of the spermatozoa (head, tail, mid-piece or a combination) and are proposed as an immunological cause of male infertility when 50% or more of motile spermatozoa are found to be coated with antibodies [3]. Such immunoglobulins can be found in semen, serum and cervical mucus [3]. This study was therefore undertaken to evaluate IgG and IgA Antisperm Antibodies in Men with Infertility Attending Two Major Hospitals in Zaria, Nigeria.

Materials and Methods

Study area and design

This was a cross sectional comparative study of serum antisperm antibodies in men with infertility carried out at Ahmadu Bello University Teaching Hospital (ABUTH) and Hajia Gambo Sawaba General Hospital (HGSGH), Zaria, Kaduna State, Nigeria. The participants include 91 men with diagnosed infertility and 45 men with proven fertility (in the last 1 year).

The selection of the participants was done with the support of the physician. Participants who were found to be eligible were selected and recruited for 5 months. The participant's case records were reviewed and pertinent data documented.

Ethical consideration

Ethical approval for this study was obtained from the Health Research Ethics Committee (HREC) of ABUTH (HREC/TRG/36) and the Ministry of Health, Kaduna state and written informed consent was obtained from all the participants before enrollment into the study.

Specimenscollection and laboratory analysis

Five milliliters of venous blood were collected from each participant into a plain bottle. Serum was obtained from the blood collected in plain bottles and used for ASA assay. Samples that could not be processed immediately were preserved at -20^{0}C until analysis within 48 hours [13]. Semen samples were aseptically collected into sterile containers from each participant and transported to the laboratory for analysis within 1 hour of collection [14]. All protocols were strictly followed according to the standard operative procedure.

Examination of semen

The volume of the seminal fluid and pH were measured. The viscosity of the sample was determined with the aid of Pasteur pipette. Seminal fluid analysis (SFA) parameters were performed, such as sperm count, semen agglutination and coagulation after waiting for liquefaction of the seminal coagulum, by a single examiner using the protocol of WHO[1].

Estimation of antispermantigen

The ASA was assayed using the enzyme-linked immunosorbent assay (ELISA) WKEAMED ™ ASA KIT according to the method described by Shibahara and Koriyama [7]. All protocols were strictly followed according to the manufacturer's instructions.

Data analysis

Data obtained were analysed using Graph pad prism version 6.0 statistical software. Descriptive statistics were computed and presented in frequency tables. The difference between groups was analysed using student t-test and chi square for qualitative variables. Statistical significance (p) was set at <0.05 with 95% confidence interval.

Results

Study characteristics and age distribution among the study participants

Table 1 show the characteristics of the study population. There were a total of 136 participants '69 years (range 20-69 years) which comprises of two groups; viz, 91 infertile male and 45 fertile male which served as control. The ratio of infertile male to fertile male was 2:1. Mean age for infertile male was 37.3 ± 8.0 while the mean age for fertile males was 36.0 ±7.5 respectively **(Table 1).**

Overall Prevalence of IgA and IgG antisperm antibodies among the study participants

The overall prevalence of IgA and IgG antisperm antibodies is depicted in **Table 2**. The overall prevalence of antisperm antibodies in infertile male (both IgG and IgA) was 52(57.1%) while; the prevalence of antisperm antibodies in fertile male (both IgG and IgA) was 5(11.1%).

Prevalence of serum IgA antisperm antibodies among the study participants

Prevalence of IgA antisperm antibodies in infertile male was 27.5% while in fertile men it was 4.4%. The difference between the prevalence of IgA antisperm antibodies in infertile male when compared to fertile male was significant (p<0.011, OR: 10.98; 95% CI: 2.493-48.41) **(Table 3).**

Table 1 Study Characteristics and Age Distribution among the Study participants.

Variable Age group (years)	Infertile male (%) (n=91)	Fertile male (%) (n=45)
20 – 29	13(9.6)	9(6.6)
30 – 39	42(30.9)	22(16.2)
40 – 49	26(19.1)	11(8.1)
50 – 59	9(6.6)	3(2.2)
60 – 69	1(0.7)	0(0.0)
Mean(± SD) Age	37.8 ± 8.0	36.0±7.5
Ratio	2	1

Table 2 Overall Prevalence of IgA and IgG ASA among the Study Participants.

Variable	Infertile male (%) n=91	Fertile male (%) n=45	Total N=136
Anti-Sperm Antibody Positive	52(57.1)	5(11.1)	57(41.9)
Anti-Sperm Antibody Negative	39(42.9)	40(88.9)	79(58.1)
Total	91(100.0)	45(100.0)	136(100.0)

Table 3 Prevalence of serum IgA antisperm antibodies among the study participants.

Variable	Infertile Male (%) n-=91	Fertile Males (%) n=45	Total	p-value
IgA Positive	25(27.5)	2(4.4)	27(19.9)	0.0011*
IgA Negative	66(72.5)	43(95.6)	109(80.1)	
Total	91(100.0)	45(100.0)	136(100.0)	

OR: 8.144; 95% CI: 1.834 – 36.17, *Significant relationship by Fisher's exact test

Table 4 Prevalence of serum IgG antisperm antibodies among the study participants.

Variable	Infertile Male (%) n-=91	Fertile Males (%) n=45	Total	p-value
IgG Positive	49(53.8)	4(8.9)	53(39.0)	< 0.0001*
IgG Negative	42(46.2)	41(91.1)	83(61.0)	
Total	91(100.0)	45(100.0)	136(100.0)	

OR: 11.96; 95% CI: 3.95 – 36.16, *Significant relationship by Fisher's exact test

Table 5 IgA and IgG Antisperm Antibodies in Relation to Type of Infertility.

Variable	10 Infertility	20 Infertility	Total	P-value	95% CI
IgA=25/91	18(19.8)	7(7.7)	25(100.0)	0.057	1.256-6.709
IgG=49/91	29(31.9)	20(22.0)	49(100.0)	0.372	0.794-0.3205

CI: Confidence Interval; 10 (Primary): infertility; 20 (Secondary): infertility

Table 6 Distribution of IgA and IgG ASA in Relation to Sperm Count.

Variable	Oligospermia	Normozoospermia	P-value	95% CI, OR
IgA=25/91	20(22.0)	5(5.5)	0.7849	0.413-3.964, 1.280 IgA
IgG=49/91	39(42.9)	10(11.0)	0.6868	0.5205-3.679, 1.384

OR: Odd Ratio; CI: Confidence Interval

Prevalence of serum IgG antisperm antibodies among the study participants

Prevalence of IgG antisperm antibodies in infertile male was 53.8% while among the fertile male it was 8.9%. The difference between the prevalence of IgG antisperm antibodies in infertile male and fertile male was statistically significant (p<0.0001, OR: 11.96; 95% CI: 3.95–36.16) **(Table 4).**

IgA and IgG antisperm antibodies in relation to type of infertility

Out of 25(27.5%) infertile male with IgA antisperm antibodies 18(19.8%) had primary infertility, while 7(7.7%) had secondary infertility. There was a trend between IgA antisperm antibodies and types of infertility but it did not attain significance on statistical scrutiny (p =0.0571, 95% CI=1.256-6.709).

Of the 49(53.8%) male with IgG antisperm antibody, 29(31.9%) had primary infertility, while 20(40.8%) had secondary infertility. There was no significant relationship between IgG antisperm antibodies and types of infertility (p=0.3722, 95% CI=0.794–0.3205) **(Table 5).**

Distribution of IgG and IgA antisperm in relation to sperm count

Considering the distribution of IgG and IgA antisperm antibodies and total sperm count**,** there was low sperm count in 39 (42.9%) of 49 participants with IgG antisperm antibodies (p=0.6868, OR=1.384 (95% CI: 0.5205-3.679). While in 25(27.5%) participants with IgA antisperm antibodies, 20(22.0%) had low sperm count; there was also no significant relationship between IgA antisperm antibodies and low sperm count (p=0.7849, OR: 1.280 (95% CI: 0.4133-3.964).

Discussion

Several studies have suggested that the presence of ASAs may be primarily responsible for infertility, since they can affect sperm motility. ASAs have been implicated to cause sperm agglutination, hindering sperm motility and interposing between sperm-mucus interactions [15,16].

In this study, we observed the overall prevalence of serum antisperm antibodies (IgG and IgA) among infertile male and fertile male in Zaria to be 57.1% and 11.1% respectively. This is

comparable with the prevalence of ≥50% antipserm antibodies as threshold of clinically relevance [1,3]. This result is higher than that obtained in the study done by Adejumo et al. [17], which obtained 22.7% prevalence in infertile men. However, the study done by Ekwere et al. [18], obtained a prevalence of 44% which is slightly lower than our study. The differences in the prevalence rate observed could be due to different assay techniques used Ekwere [18].

The prevalence of ASA was observed to be higher among infertile male compared to fertile male and is thought to be due to a breach in the blood- testis barrier by several disease conditions and with concomitant immunologic response to exposed sperm antigens. Sperm antigens are proteins which appear on the outer sperm membrane as the young sperm cells develop within the testes. Such antigens can only stimulate antibody production when they come in contact with components of the blood [7]. Under normal conditions blood and sperm do not mix. However the blood-testis barrier can be broken by infection, trauma, toxins and radiation. When this barrier is breached, sperm antigens escape from their immunologically protected environment and come in direct contact with blood elements that launch an immunological attack [11].

The prevalence of IgG antisperm antibodies in infertile males and fertile male showed that IgG ASA accounted for 53.8% in infertile males, while in fertile male it was 8.9%. This difference was statistically significant and indicates some form of chronicity in the conditions driving infertility. This is consistent with the work done by Rowe et al. [19].

The prevalence of IgA serum antisperm antibodies in males with infertility were 27.5%, while in fertile male it was 4.4%. This difference was statistically significant. Sperm antibodies may be found in the blood of both fertile and infertile men [12] but it achieves relevance as an immunological cause of male infertility when 50% or more of motile spermatozoa are found to be coated with antibodies [3]. IgA anti sperm antibodies are known to block the sperm's ability to bind to the zone pellucid of the egg [7].

Our literature search shows that IgA is more relevant clinically than IgG. IgG hardly occurs without IgA [20-22]. Therefore, IgA and IgG testing are adequate as a routine screening method for antisperm antibodies.

The relationship of serum antisperm antibodies (IgG and IgA) with type of infertility in infertile males shows that males with primary infertility had the highest IgA and IgG profiles (51.4%) while ASA (IgG and IgA) with secondary infertility had the least IgA and IgG profiles (29.7%), though this difference was not statistically significant. This agrees with the work done by Ahmad et al. [23], where primary infertility was found to be higher in than secondary infertility in northern Nigeria. The implications of these findings with IgG and IgA ASA being more prevalent in primary infertility are profound as it could mean that many young males at the age of marriage are inadvertently exposed to conditions which induce immunological and irreparable sperm damage such as infections, trauma and ionizing radiation and may never be able to bear children. Indeed, infertility was higher in the age group of 30-39 yrs in this study and this was more of primary than secondary infertility.

The relationship between sperm count and presence of antisperm antibodies in this study revealed that men with infertility, participants with low sperm count had the highest percentage of antisperm antibodies, while those with normal sperm count had the least antisperm antibodies. Though this difference did not attain statistical significance; an association of ASA with oligospermia is implied. Antibodies mark the sperm for attack by natural killer (NK) cells of the body's immune system in a process described as antibody dependent cellular cytotoxicity; thus reducing the sperm concentration and quality [15].

Concerning the relationship between sperm agglutination with serum IgA and IgG ASA in this study; IgG ASA was more associated with sperm agglutination compared to IgA ASA in males with infertility though it did not reach statistical significance. IgG ASA were more prevalent in males with infertility and clumping of sperm on semen analysis compared to IgA ASA. These findings agree with the study carried out by Shibahara et al. [7], where IgG ASA was more prevalent in infertility than IgA ASA. A possible reason could be that IgA is mostly found in secretions and less in the blood serum [7].

This study is not without limitations. We did not include the duration of infertility in our study, we therefore suggest further studies involving the duration of infertility, *invitro* cervical mucus penetration tests and testosterone levels are advocated to add robustness to the role of ASA in the infertility work up.

Conclusion

This study observed an increase in antisperm antibodies in infertile males when compared to fertile male, which suggests a significant proportion of infertility cases in males may have ASA as the possible aetiology or a complication of the primary cause of their infertility. Incorporation of ASA testing in the evaluation of couples with infertility, associated with oligospermia or of unknown causes is recommended especially in our environment.

Acknowledgements

The authors wish to express their gratitude to the study participants that consented & participated in this study. The logistics support given by the staff of Ahmadu Bello University Teaching Hospital (ABUTH) and Hajia Gambo Sawaba General Hospital (HGSGH) is highly appreciated.

Competing Interests

Authors declared no competing interest.

Funding

None received.

Authors' Contributions

This work was carried out in collaboration among all authors. Author AO conceived and designed the study. Authors AO, AEA, SAO and BE were involved in samples collection and laboratory investigations. Authors AO, BIS and AEA analyzed the data obtained. Author AO and BIS prepared the draft manuscript while authors BOP, MAA and AM provided ideas during draft writing. All authors read, reviewed and approved the final manuscript.

References

1 World Health Organisation (2013) Laboratory Manual for the Examination and Processing of Human Semen.

2 Centres for Disease control and prevention (2009) Infertility FAQ, From National Public Health Action Plan for the Detection, Prevention, and Management of Infertility, Atlanta, Georgia.

3 Naz RK, Menge RC (1994) Antisperm Antibodies. Origin, Regulation and Sperm Reactivity in Human Infertility. Fertility and Sterility 61: 1001-1013.

4 Almagor M, Dan-Goor M, Hovav Y, Kafka I (1998) Antisperm Antibodies in Men with Psychogenic and Ejaculation. Andrologia 41: 1-4.

5 Sakamoto Y, Matsumoto T, Mizunoe Y, Haraoka M, Sakumoto M, et al. (1995) Testicular Injury Induces Cell-Mediated Autoimmune Response to Testis. Journal of Urology 153: 1316-1320

6 McDonald SW (2006) Cellular Responses to Vasectomy. International Review Cytology 199:295-339.

7 Shibahara H, Koriyama J (2013): Methods for direct and indirect antisperm antibody testing. Journal of Methods for Molecular Biology 927: 51-60.

8 Marshburn PB, Kutteh WH (1994) The role of Antisperm Antibodies in Infertility. Fertility and Sterility 61:799-811.

9 Lombardo F, Gandini L, Dondero F, Lenzi A (2001) Immunology and Immunopathology of the male Genital Tract; Antisperm Immunity in Natural and Assisted Reproduction. Human Reproductive update 7:450-456A.

10 Swan SH (2004)Your Fertility, your Environment. Journal of infertility 1: 13-19.

11 Matsumoto (1995) Pathophysiology of Male Infertility. Journal of infertility pp: 555-579.

12 Hjort T (1999) Antisperm Antibodies and Infertility: an Unsolvable Question? Human Reproduction 14:2423–2429.

13 Cheesbrough M (2006) District laboratory Practice in Tropical Countries.Cambridge University Press.

14 Jones WR (1994) Gamete Immunology. Human Reproduction 9:828-841.

15 Razzak AH, Wais SA (2002)The infertile couple: a cohort study in Duhok, Iraq. East Mediterr Health J 8:234-238.

16 Nagaria T, Patra PK, Sahu JP (2011) Evaluation of serum anti-sperm anti-bodies in infertility. J Obstet Gynaecol India 61: 307-316.

17 AdejumoBI,Oke AA, Emokpae MA, Oyeleke AA, Erhebor TA, et al. (2014)Antisperm Antibodies Among Infertile Subject Investigated for Infertility in Lagos. Nigeria Journal of Clinical Practice 13: 1-4.

18 Ekwere PD (1995) Immunological infertility among Nigerian men: incidence of circulating anti-sperm auto-anti-bodies and some clinical observations: a preliminary report. Br J Urol 76:366-370.

19 Rowe PJ, Comhair FH, Hargreave TB, Mahmoud AM (2002) WHO manual for the standardized investigation and diagnosis of the infertile male. UK: Cambrige university press.

20 Rumke P (1976)The origin of immunoglobulin in semen. Clin ExpImmunol 17: 287-297.

21 Jager S, Kremer J, Kuiken J, Van Slochteren-Draaisma T (1980) Immunoglobulin class of anti-spermatozoal anti-bodies from infertile men and inhibition of in vitro sperm penetration into cervical mucus. Int J Androl 3: 1-14.

22 Kay DJ,Boettcher B (1992) Comparison of the Sperm Mar test with currently accepted procedures for detecting human sperm anti-bodies. Reprod Fertil Dev 4: 175-181.

23 Ahmed A, Bello A, Mbibu NH, Maitama HY, Kalayi GD (2010) Epidemiological and Aetiological Factors of Male Infertility in Northern Nigeria. Nigeria Journal of Clinical Practice 13: 205-209.