

Antisperms antibodies in infertile males attending a Tertiary Care Hospital in Karachi

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ABSTRACT

Objective: To estimate the levels of anti-sperm antibodies in infertile males attending a tertiary care hospital in Karachi.

Methodology: Out of 160 males studied, 132 met the criteria and were included in the study. Semen analysis was done by proper standardized procedures as mentioned in WHO manual for examination of human semen and sperm cervical mucus interaction. A blood sample was drawn to detect the presence of anti-sperm antibodies.

Results: Antisperm antibodies were found positive in 8 males suggesting that antisperm antibodies are the etiologic factor causing infertility in 6% infertile male subjects. A positive correlation was found between the ages of patients and antisperm antibodies greater than 70 IU/ml.

Conclusion: Direct correlation of circulating antisperm antibodies with male infertility suggests the role of immunologic infertility as an etiologic cause of infertility in idiopathic infertile males of Pakistan.

KEYWORD: Primary infertility, Azoospermia, Oligospermia, Antisperm antibody.

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INTRODUCTION

Infertility is defined as a failure to conceive despite one year of unprotected intercourse. 13%-18% of

the couples are affected by infertility of which male factor is considered responsible for almost half of all the cases.¹ In reproductive age group, around 40 – 50% men have some defect in sperm production that can be qualitative or quantitative.²

Immunologic factors are one of the several mechanisms proposed for male infertility.³ Although advancements of contemporary molecular medicine and diagnostic tools have helped a great deal in understanding the etiology of male infertility during the last two decades but the exact mechanism involved in the pathogenicity of male infertility by Immunologic factors particularly Antisperm Antibodies (ASA) is still poorly understood. ASA to human spermatozoa from infertile men was first described by Rumke⁴ and independently by Wilson in 1954.⁵ Antisperm antibodies have been isolated from the seminal fluid, cervical mucus, oviductal fluid or follicular fluid of women or in blood serum of men and women.⁶ The presence of antibodies against sperm can cause infertility only

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if the circulating antibodies are present within the reproductive tract and on the living sperm surface⁷ and when the degree of antibody binding is high enough (>50%).^{8,9}

Autoantibodies to sperms are present approximately in 10% of infertile males¹⁰ and in (24.6% and 32%) among patients with varicocele.^{11,12} Further, around 70% of men, who have had their vasectomy reversed will develop antisperm antibodies. Variety of mechanisms have been proposed for the formation of antisperm antibodies including injury to the testicles, undescended testicles, testicular torsion, infection, testicular cancer, testicular biopsy, varicocele and vasectomy reversal. It has been observed that the antisperm antibodies are responsible for reduced motility, decreased penetration of cervical mucus by sperm and blockage of acrosome reaction and thus intercepting sperm egg interaction.¹³

Although, couples with antisperm antibodies have been reported to achieve pregnancy naturally, due to its subsequent infection of the genital tract following initial pregnancy can also lead to development of antisperm antibodies.⁶ Currently, there is no information about the status of antisperm antibodies in Pakistani population so the aim of this study was to find out the incidence of antisperm antibodies in primary and secondary infertile couples of Pakistani origin.

METHODOLOGY

A cross sectional study with convenient sample of 160 infertile males attending OPD at a tertiary care hospital in Karachi was conducted. After explaining the purpose of the study and taking informed consent, the subjects were asked to fill a questionnaire.

The questionnaire was designed after thorough literature review and included findings obtained from detailed clinical history and physical examination to exclude the subjects with secondary infertility.

Inclusion Criteria: Oligospermic and normospermic infertile males with age ranging from 21 to 50 years.

Exclusion Criteria: Subjects undergone pelvic surgery or hernia repairs, patients with diabetic neuropathy or with psychiatric disorders, injury to the testicles, undescended testicles, testicular torsion, infection, testicular cancer, testicular biopsy, varicocele and vasectomy reversal.

Out of 160 infertile males seen, 132 met the criteria. Semen analysis was done by properly standardized

procedures as mentioned in WHO laboratory manual (1998) for the examination of human semen and sperm cervical mucus interaction. A blood sample of 3ml was drawn to determine the antisperm antibodies in the serum. The test was performed by ELISA to estimate the levels of ASA.

Subjects were divided into two groups based on sperm count following the WHO guidelines. Forty five subjects who had sperm count less than 20 million per ml were labeled oligospermics whereas 87 subjects who had sperm counts greater than 20 million and were labeled normospermics. Beside sperm count motility of sperms were also noted either they were actively motile or the movement was sluggish only at one point.

Data were analyzed using Statistical Package for the Social Sciences (SPSS version 16.0). Mean, standard deviation and correlation studies were performed using the descriptive statistics and Pearson's correlation respectively. Ethical approval was obtained and the project was approved by Institutional Review Board (IRB) of the institute.

RESULTS

The mean age of the patients included in the study was 33.4 SD years. The mean duration of infertility was 4.7 SD years, with a range of 2-10 years for all couples. Out of 132 cases, 104 (78.8%) were suffering from primary infertility whereas 28 (21.2%) were of secondary infertility. Amongst the 104 primary infertility males 6 (5.8%) were positive for ASA and in secondary infertility couples the incidence of ASA was 7.1% (2 out of 28 patients). (Table-I)

A positive correlation ($r = 0.05$) (0.039) at $p < 0.05$ was found between the ages of patients and antisperm antibodies greater than 70 IU/ml and actively motile sperms of the patients respectively. Antisperm antibodies greater than 70 IU/ml were also found positively correlated (0.021) at $p < 0.05$ with the sperm counts of the oligospermic (less than 20 million/ml) and normospermic patients (0.001) at $p < 0.01$ and with actively motile sperms of patients and as shown in Table-II.

Table-I: Incidence of Antisperm Antibodies in Primary and Secondary Infertile men.

Type of Infertility (n)	ASA Positivity	% Incidence
Primary (104)	6	5.8
Secondary (28)	2	7.1
Total (132)	8	6.06

Table-II: Correlation coefficient among different variables of infertile males in a Pakistani population.

	Age	ASA > 70 IU/ml	SP count < 20 million/ml	Actively motile	Normospermic
Age	1.000	0.05*	0.026*	0.039*	0.480
ASA > 70 IU/ml		1.000	0.021*	0.038*	0.001**
SP count < 20 million/ml			1.000	0.52	0.56
Actively motile				1.000	0.49
Normospermic					1.000

* (P < 0.05 = significant, **P < 0.01 = highly significant)

DISCUSSION

In the present study, 132 infertile males were screened out of which 8 were found positive for antisperm antibodies indicating that antisperm antibodies can be the etiologic factor in 6% of idiopathic infertile male population. Our results are similar with the other study having 8-21% cases positive for ASA.¹⁴ The prevalence of ASA among infertile males in our study corresponds to the expected prevalence presented in other studies.^{15,16} However, a recent study in India reported a very high prevalence (47.71%) of antisperm antibodies in primary (52.12%) and secondary infertile couples (39.47%) which is not consistent with our findings.¹⁷ The possible reason for this difference might be the ethnic and cultural variation among the two countries.

Our study showed no significant difference in the incidence of circulating antisperm antibodies among primary and secondary infertility which is consistent with the finding of an Indian study.¹⁷ However, this contradict with another study¹⁸, that reported a high incidence of sperm antibodies amongst patients with primary unexplained infertility in subjects attending a program for assisted reproduction by various test (ELISA, TAT, SIT and GAT).

Several studies have shown ASA to be the causative factor behind immunologic infertility. Although, ASA has been shown to affect sperm function at various levels, it is difficult to ascertain the extent to which these interfering effects occur in each individual patient. The major problem is the inability of current diagnostic tests to quantify the antibody density on the sperm surface and to define the antigenic specificities of ASA, main determinants of their anti-fertility effect.

There are number of questions which still remain unclear, such as the exact role of ASA in infertility, best method for screening and final determination of ASA, threshold levels of ASA which have significant effects, parts on spermatozoa targeted by the

ASA for binding, interference of ASA with different steps of fertilization process, and the best method for treatment of cases with ASA-related infertility.

The lack of a standardized and universally accepted assay for the detection of ASA directed against known antigens has been repeatedly claimed as the main reason of the confusion over the actual role of ASA as well as their treatment in male infertility.¹⁹⁻²¹ ICSI has been claimed as the primary choice of treatment in immunological infertility, as it overcomes any potential interference of ASA with sperm fertilizing ability.^{22,23} However, given its high cost and invasive nature, as well as the heterogeneity of infertile male patients with ASA, ISCI should rather be reserved for patients for whom achieving a pregnancy with less invasive techniques would be very unlikely.

CONCLUSION

The presence of circulating antisperm antibodies can be a reason for infertility in idiopathic infertile males of Pakistan and circulating antisperm antibodies directly correlates with male infertility. After detecting antisperm antibodies in serum it will be treated and if only this cause is their then fertility can be assure after treatment.

REFERENCES

1. Iammarrone E, Balet R, Lower AM, Gillott C, Grudzinskas JG. Male infertility. Best Practice & Research Clinical Obstetrics & Gynaecology. 2003;17(2):211-229.
2. Bohring C, Krause E, Habermann B, Krause W. Isolation and identification of sperm membrane antigens recognized by antisperm antibodies, and their possible role in immunological infertility disease. Molecular Human Reproduction. 2001;7(2):113-118.
3. Lu JC, Huang YF, Lu NQ. Antisperm immunity and infertility. Expert Review of Clinical Immunology. 2008;4(1):113-26.
4. Rumke PH. The presence of sperm antibodies in the serum of two patients with oligozoospermia. Vox Sang. 1954;4:135-140.
5. Wilson L. Sperm agglutinins in human semen and blood. Experimental Biology and Medicine. 1954;85(4):652-654.

6. Karimi F, Khazaei S, Ala AF. Serum antisperm antibodies in fertile and infertile individuals. *Iran J Med Sci.* 2008;33(2):88-93.
7. Bronson R, Cooper G, Rosenfeld D. Sperm antibodies: their role in infertility. *Fertil steril.* 1984;42(2):171-83.
8. Barratt CLR, Dunphy BC, McLeod I, Cooke ID. The poor prognostic value of low to moderate levels of sperm surface-bound antibodies. *Hum Reprod.* 1992;7(1):95-98.
9. Fallick ML, Lin WW, Lipshultz LI. Leydig cell tumors presenting as azoospermia. *The J Urology.* 1999;161(5):1571-1572.
10. Kuhn JM, Lefebvre H, Duparc C, Pellerin A, Luton JP, Strauch G. Co-secretion of estrogen and inhibin B by a feminizing adrenocortical adenoma: impact on gonadotropin secretion. *J Clin Endocrinol Metab.* 2002;87(5):2367-2375.
11. Akman H, Ege G, Yildiz S, Cakiroglu G. Incidental bilateral Leydig cell tumor of the testes. *Urologia internationalis.* 2000;71(3):316-318.
12. Steiner H, Hörtl L, Maneschg C, Berger AP, Rogatsch H, Bartsch G, et al. Frozen section analysis-guided organ-sparing approach in testicular tumors: technique, feasibility, and long-term results. *Urology.* 2003;62(3):508-513.
13. Menge AC, Christman GM, Ohl DA, Naz RK. Fertilization antigen-1 removes antisperm autoantibodies from spermatozoa of infertile men and results in increased rates of acrosome reaction. *Fertil Steril.* 1999;71(2):256-260.
14. Vazquez-Levin MH, Notrica JA, de Fried EP. Male immunologic infertility: Sperm performance on in vitro fertilization. *Fertil Steril.* 1997;68(4):675-681.
15. Ozen H, Asar G, Gungor S, Peker AF. Varicocele and antisperm antibodies. *Int Urology and Nephrology.* 1985;17(1):97-101.
16. Gilbert BR, Witkin SS, Goldstein M. Correlation of sperm-bound immunoglobulins with impaired semen analysis in infertile men with varicoceles. *Fertil Steril.* 1989;52(3):469-473.
17. Khatoon M, Chaudhari AR, Singh R, Prajapati S. Antisperm Antibodies in Primary and Secondary Infertile Couples of Central India. *Biomedical Research.* 2011;22(3):295-298.
18. Damianova V, Dimitrova-Dikanarova D, Kala dzhiev S, Vatev I. The incidence of sperm antibodies in patients included in a program of assisted reproduction]. *Akusherstvoi Ginekologiya* 1999;38(2):31-3.
19. Helmerhorst FM, Finken MJJ, Erwich JJ. Antisperm antibodies. *Hum Reprod.* 1999;14(7):1669-1671.
20. Bohring C, Krause W. Immune infertility: towards a better understanding of sperm (auto) immunity. *Hum Reprod.* 2003;18(5):915-924.
21. Chiu WW, Chamley LW. Clinical associations and mechanisms of action of antisperm antibodies. *Fertil Steril.* 2004;82(3):529-535.
22. Lombardo F, Gandini L, Dondero F, Lenzi A. Immunology and immunopathology of the male genital tract: Antisperm immunity in natural and assisted reproduction. *Hum Reprod.* 2001;7(5):450-456.
23. Lombardo F, Gandini L, Lenzi A, Dondero F. Antisperm immunity in assisted reproduction. *J Reprod Immunol.* 2004;62(1-2):101-109.

Authors Contribution:

FI did Statistical analysis and Final Review of manuscript.
 NA Patient selection and did the manuscript writing.
 FK Data collection and laboratory work.
 AM Data collection and laboratory work.