
Anti sperm Antibody in a Sample of 50 Infertile couples

Areej-A-Jabbar

MBChB, MSc, DGO

Summary

Background: Human immunological infertility may be caused by different factors but the major factor is the presence of anti sperm antibodies, this might be then a cause of unexplained infertility; alternatively it might be an additional factor in cases of explained infertility

Patients & Methods: A cross sectional study was carried out during the last six months of 2009 for 50 infertile couples they were examined clinically and investigated for assessment of their infertility state, Their sera were tested for positive anti sperm anti body titer by ELISA test, the results were statistically analyzed to evaluate the association of the positive results with the age in years ,duration and cause of infertility ,previous exposure to surgery and poly cystic ovarian syndrome in wives.

Results: The percentage of positive serial anti sperm anti body wives in the sample was equal to what was found in husbands (22%). An obvious association was found with the secondary infertility in both genders, in previous exposure to surgery and with long duration of infertility although statistically not significant. The husbands with unexplained infertility had a higher significant association (32.1%) than other infertile husbands. The wives with poly cystic ovarian syndrome showed for the first time (up to our knowledge) a strong association with positive anti sperm anti body titer although statistically not significant. The immunological infertility had no significant association with age although it was higher with old age wives 40 years and more (33.8%) and between 30-39 years husbands (31.8%).

Conclusion: The immunological type of infertility is an important finding in unexplained infertility. Infertility nowadays had an obvious correlation with the positive anti sperm anti body titer that can ring a bell to consider the immunological factor an important cause to investigate in both infertile wives & husbands, and to encourage arrangement of further researches with increased sample size and related parameters.

Key words:-Immunological infertility. Anti Sperm Anti Body

Introduction

It has become clear after many decades of work, that an adverse immune response to certain tissues of the reproductive system can cause infertility^[1].

Human immunological infertility may be caused by many different factors but the major factor is the presence of antibodies to spermatozoa this might be then a cause of unexplained infertility; alternatively it might be an additional factor in cases of explained infertility^[2].

It is well established that both men & women can make antibodies which react with human spermatozoa & that this immune reaction may interfere with reproductive success^[1].

The sperm as a cell can be agglutinated or immobilized by antibodies & will be deterrent to reproduction even before the cervical area is reached^[3].

Also if sperm antibodies are present, the attached antibodies become involved in non specific attachment strands of mucus and many of the sperm cells are trapped causing a problem in cervical mucus penetration^[3].

And certain harmful effects of the sperm antibodies on the capacitating process found by Bandoh et al.1992^[4], by inhibition of the acrosome reaction. Other mechanisms occur at the level of the gamete interaction that needed for spermatozoa

progress to the ovum then ovum penetration is prevented & fertilization fails^[5].

On sperm cells, antibodies can specifically coat the sperm cell in specific region, such as head, mid-piece, tail-shaft or tail-tip; these locations represent different antigenic determinant groups⁽¹⁾.

In males the anti body to sperm can frequently be found in a seminal plasma although present in a lower titer than that found in blood probably because of the process of transudation from the blood or because of the presence of antibodies sink in the semen, the antibodies quantity will depend on how high is the initial titer & on how low is the sperm count in the testis^[1], although it may be not found because of the blood – testis barrier to the passage of immunoglobulin. Sperm antibodies themselves can arise from either systemic or local immune responses, most causes of auto immunity are spontaneous, or idiopathic, this condition has also been found in homosexual men, in testicular trauma, such as improper biopsy, in varicocele in mumps orchitis in spinal cord injury in congenital absence of the vas & in vasectomy^[6-9].

But in females; anti sperm antibodies can arise from either systemic or local immune responses & can occur in a number of compartments^[6]. They can be found in:-

- a- The cervical mucus were most frequently studied the component of the female reproductive system^[1].

- b- In other genital fluids, these include, the endometrial fluid and the follicular fluid,
 c- In the blood were sperm antibodies are very frequently found in the blood of women who have these antibodies^[2].

The clinical findings associate with a history of anal or oral intercourse^[10] & with unexplained infertility^[13].

The aim of this study was:

TO evaluate the immunological infertility in both husbands & wives.

TO find the association between positive serial anti sperm antibody titers in infertile couples & other related variables.

Patients & Methods

During last 6 months of 2009 a cross sectional study was carried out for 50 infertile Iraqi couples. The evaluation criteria were inability to conceive for more than one year with unprotected intercourse. Age distribution was from <30->40 years.

In addition to the standard clinical evaluation the reproductive hormones (Follicle stimulating hormone, Luteinizing hormones, prolactin & testosterone + Progesterone hormones) were assessed for each member and a post coital test for each couple after routine seminal fluid analysis for the husbands. To ensure tubal patency for wives hystero salpingogram performed for each. Then the polycystic ovarian wives were diagnosed depending on ultra sound evidence of cystic ovary with disturbance in Follicle stimulating hormone to Luteinizing hormone ratio, in addition to the history of oligomenorrhea (menses interval more than 42 days).

The unexplained infertility based on normal results of all the above investigations but failure to conceive.

Then 5 milliliter of blood were examined from each member after agglutination & centrifugation (2500 round/min.) for 10 min, then separation for serum and mixing with special ELIZA (Enzyme – Linked – Immunosorbent Assay). Biotip Kit wait

for half hour for detection of positive serial Anti Sperm Antibody titer by ELIZA (Enzyme linked immuno sorbent)technique, that was>20 u/ml.(as fixed on the applied kits).

The results were statistically analyzed against the type of infertility (primary or secondary), cause of infertility (depending on investigations), age of members, duration of infertility & history of surgical exposure

The data analysis performed by computer aids using SPSS.Ver13 frequency distribution for selective variables mentioned. The statistical significance of difference in mean of normal distribution variables between two groups was assessed by T-test. The prevalence ratio was used to assess the magnitude of association between two categorical variables. The 95%CI (confidence interval) of prevalence rates was calculated by natural logarithm method, P value <0.05 considered statistically significant^[20].

Results

Among 50 couples involved in our research **table 1** revealed that 20 wives (40%) had poly cystic ovarian syndrome. The same number of wives & husbands 11 (22%) showed positive results of Anti sperm Antibodies in their sera .The wives with previous exposure to surgery were 13 (26%) and the husbands were 11 (22%) But those with a known cause of infertility were 26 (72%) wives & 22 (44%) husbands.

The young wives in the sample (<30 years) were 23(46%) while the husbands were 12(24%). Those between 30-39 years of age were 21(42%) wives & 22(44%) husbands, the members above 40 years of age were only 6(12%) wives & 16(32%) husbands.

The primary infertile wives constituted (44%) 22 & husbands (42%) 21. While those with secondary infertility were 28 wives (56%) & 29(58%)

The range of infertility duration in wives was 1-20 years with a Mean±SD 4.7±3.9. While in husbands was 1-17 years, the Mean±SD 4.3±3 Table 3.

Table 1: The data of the studied parameters in the sample of both husbands & wives.

Total (n=50)	Wife		Husband	
	N	%	N	%
PCO (polycystic ovary)	20	40		
Serial ASAb (Antis perm Ab)	11	22	11	22
History of surgery	13	26	11	22
Infertility attributed to a possible medical condition	36	27	22	44

Tables 2: The percentage of the studied age groups in years and the type of infertility (Primary & Secondary) in husbands and wives of the sample.

Total (n = 50)	Wife		Husband	
	N	%	N	%
Age group (years)				
< 30	23	46	12	24
30 – 39	21	42	22	44
40+	6	12	16	32
Type of infertility				
Primary	22	44	21	42
Secondary	28	56	29	58

Table 3: The range, Mean and Standard deviation of the duration of infertility in husbands and wives included in the studied sample.

Infertile groups	Range	Mean	SD
Duration of infertility (years) in wives	1 to 20	4.7	3.9
Duration of infertility (years) in Husband	1 to 17	4.3	3

The associated factors with positive Anti sperm Anti Body titer in wives were explained by **table 4:**

Wives of 40 years age & above had highest non significant association (33.3%) while those between 30-39 years had lowest non significant association (19%).

The secondary infertile wives had higher non significant association (28.6%) than those with primary infertility (13.6%).

Also the wives with a known cause of infertility had a non significant association (22.2%) than those with unexplained infertility (21.4%). Then the wives with previous exposure to surgery had higher non significant association (30.8%). than others (18.9%).

But the wives with poly cystic ovarian syndrome showed a well defined association with positive Anti Sperm anti Body titer in their sera (30%), although that was statistically not significant.

In table 5: the duration of infertility (2-20) year's .mean, (7.2) had more association (SD.6.3) than shorter durations mean (4) (SD.2.6).

The factors associated with positive serial Anti Sperm anti Body titer in husbands were found in **table 6:**

The husbands in between 30-39 years of age had highest non significant association (31.8%) than younger members (<30years), (8.3%).

Also the secondary infertile husbands showed higher non significant association (27.6%) than those with primary infertility (14.3%).

But the husbands with unexplained infertility had higher significant association (32.1%).with positive serial Anti Sperm Anti Body titer than those with diagnosed cause of infertility(9.1%).Also the husbands who had previous exposure to surgery showed higher association (27.3%),than others(20.5%).although that relation was statistically non significant..

The long duration of infertility (2-7) years mean (5.1) had a higher association (SD 4.3) than shorter duration mean (4), (SD 26) as shown by **table 7.**

Table 4: The association of serial Anti sperm Antibody titer with other studied variables among wives.

studied variables among wives	Total No.	Positive serial Antis perm Ab titer in wives		P-Values
		N	%	
Age group of wife				
< 30	23	5	21.7	
30-39	21	4	19	0.28(NS)
40	6	2	33.3	0.32 (NS)
Type of infertility – wife				
Primary	22	3	13.6	
Secondary	28	8	28.6	0.13 (NS)
Infertility (possible medical causes)				
Condition in wife				
Unexplained	14	3	21.4	
Explained	36	8	22.2	0.29(NS)
History of surgery				
Negative	37	7	18.9	
Positive	13	4	30.8	0.2(NS)
PCO (Poly cystic ovary)				
Negative	30	5	16.7	
Positive	20	6	30	0.15(NS)

Table 5: The association of serial Anti sperm Antibody titer in wives with their duration of infertility.

Duration of infertility (years) wife	serial Anti sperm Antibodies in wives		P(t-test)
	Negative	Positive	
Range	(1 to 12)	(2 to 20)	0.13 (NS)
Mean	4	7.2	
SD	2.6	6.3	
SE	0.42	19	
N	39	11	

Table 6: The association of serial Anti sperm Antibody titer with other studied variables among husbands.

Studied variables among husbands	Total No.	Positive Anti sperm Ab titer in Husbands		P-Values
		N	%	
Age group of Husbands (years)				
< 30	12	1	8.3	
30 – 39	22	7	31.8	0.11(NS)
40-	16	3	18.8	0.33(NS)
Type of infertility				
Primary	21	3	14.3	
Secondary	29	8	27.6	0.15(NS)
Infertility (possible medical causes)				
Unexplained	28	9	32.1	
Explained	22	2	9.1	0.043
History of surgery				
Negative	39	8	20.5	
Positive	11	3	27.3	0.27(NS)

Table 7: The association of serial Anti sperm Antibody titer in husbands with their duration of infertility.

Duration of infertility (years) in Husbands	Serial Anti sperm Antibody titer in husbands		P(t-test)
	Negative	Positive	
Range	(1 to 12)	(2 to 17)	0.45(NS)
Mean	4	5.1	
SD	2.6	4.3	
SE	0.42	1.29	
N	39	11	

Discussion

This cross sectional study from June to December of 2009 included fifty infertile couples (wives and husbands) out of 50 wives 11 (22%) were immunologically infertile equal to what was found among the husbands involved in the sample. Similar results was documented by many previous studies from 1975 to 1985 by (Shulman, Fjallbrant, Hjort & Husted) were the incidence of positive Anti sperm antibody titer in the serum of infertile males and females was higher than in the fertile people^[1].

Our results were near to the range (5%-25%) discovered by Kuttch in 1992 & by Marsh burn pb in 1994, also a higher frequencies of Anti sperm antibodies occurrence in infertile women sera & lower frequencies in the sera obtained from women

who were fertile as documented by Shulman et al in 1978^[6].

The age factor in both wives & husbands had no significant correlation with the immunological infertility although the old wives (40 years & more) and husbands between (30-39) years had higher association (33.3%), (31.8%) respectively, the same result was obtained by Zhe, Juino, Zhong, Yi Za Zhi research during treatment of 115 cases of infertility due to presence of serial Anti sperm anti Body in 2008.^[11]

The secondary infertile wives & husbands had higher non significant association (28.6%) (27.6%) respectively than the primarily infertile members, the same found with those exposed to surgery (30.8%) wives & (32.1%) husbands.

As we know the secondary infertility in wives is defined as a preceding pregnancy irrespective of the outcome (12) that may expose them to more complications including inflammatory processes leading to increased immunological reactions.

The secondary infertile husbands could be due to medical problems like Diabetes & Hypertension in spite of exposure to surgical interference (Vasectomy & Vasectomy, testicular biopsy, & other injuries) may correlate to immunological infertility^[1]. Even the increase in kidney vacuity with blood stasis & damp, heat were the fundamental diseases mechanisms associated with high Anti sperm anti Body titers in both genders as revealed by ZheJang, YiZa Zhi in 2008^[11].

The long duration of failure to conceive found to associate significantly with positive Anti sperm anti Body titers in infertile people & also high titers in serum is strongly associated with delayed pregnancy in both wives & husbands^[2], this fact is documented in our research were the long duration of infertility (2-20) years, mean 7.2 (SD 6.3) in wives & (2-17) years mean 5.1 (SD 4.3) in husbands showed higher association than short duration although it was statistically non significant.

But the unexplained infertility in husbands was significantly associated with positive serial Anti sperm anti Body finding (32.1%) & not in wives. The association of unexplained infertility in male and female with the frequency of their serial Anti sperm antibodies were studied previously since 1964 by Robert R, Franklin & C. Dean, Dukes and a positive correlations obtained^[13], that may indicate a need for increasing our sample size especially for wives.

The poly cystic ovarian syndrome (PCO) is the most common hormonal disorder of young women, estimated to affect (5-10%) of women through & beyond their reproductive years^[14], it is multi systemic disorder which is associated with hyperinsulinemia, hyperlipidemia, Diabetes mellitus, obesity, hyperandrogenaemia, hirsutism, acne, & increase incidence of endometrial cancer^[15], it has also been reported that polycystic ovarian patients exhibit chronic low grade inflammation manifested as an elevated levels of C-reactive protein^[12] the fact that immune modulating treatment such as dexamethasone often used to attenuate poly cystic ovarian (PCO) symptoms, & as revealed by Palaces JR et al in 2006 work the (PCO) affect (5-10%) of women in reproductive age. Free radicals a product of oxidative stress impair cells & tissues properties related to human fertility. These free radicals together with oxidized molecules may have cytotoxic or deleterious effects on sperm & oocytes even on early embryo development or on endometrial^[17]. Also Anti sperm anti Body positive titer can be found in females, however in a number

of compartments & can arise from either local or systemic immune responses^[1].

All the above facts can explain the most important result found in this research that is the presence of high association between the infertile wives with (PCO) & positive Anti sperm anti Body titer in their sera (30%), although it was statically non significant which encourage arrangement of further researches with increased sample size.

References

1. Kwrpysz M, & Fernanez. Immunological reactions and infertility by Sidney Shulman. Immunology of Human Reproduction Textbook, 1994 Chap. 4: p 53
2. Kobayashis, Rsshot, Shegeta M, Koyomak, Isojimas, .Correlation between quantitative anti body titers of sperm immobilizing antibodies and pregnancy rates treatments, Ferti. Steril. 1990. 54; 1107-1113.
3. Steeny, Forssmon I, Lonnersteds E, Jonasson K, Wassen AC, Lycke E. Anti sperm Ig A antibodies against the equatorial segment of the human spermatozoa are associated with impaired sperm penetration & subfertility Fertil. Steril. 1994;39: 52-56.
4. Bandon R, Yamano S, Kamada M, Dairoh R, Aono T. Effect of sperm -immobilizing antibodies on the acrosome reaction of human spermatozoa. Fertil. Steril. 1992; 57:387-392.
5. Geva E, Vardinon, N, Lessing J. Organ specific auto antibodies are possible markers for reproductive failure: a prospective study in an IVF fertilization-embryo transfer program. Human. Reprod. 1996; 11:1627-1631.
6. Karen D, Brandshow, Samuwl J, Chontil S, and Bruce R, Corr. Diagnostic evaluation and Treatment Algorithms for the infertile couple. Text book of Reproductive Medicine, (second edition) 1998.
7. Shulman A, Shohoat B, Gillis D, Yavet ZH, H Hommonal ZT, Paz G. Mumps orchitis among soldiers frequency, effect on sperm quality, and sperm antibodies Fertil. Steril. 1992, 57; 1344-1346.
8. Siostean A, Steen Y, Forssmon L, Sullivan L. Auto-immunity to spermatozoa and quality of semen in men with spinal cord injury, Int. J. Fertil. 1993; 38:117-122.
9. Patrizio P, Bronson R, Silber SJ, Ord T, Asch R H. Testicular origin of immunobead-reacting anti gens in human sperm Fertil. Steril. 1992; 57:183-186.
10. Marshburn P B, Kuttch WH. The role of antis perms antibodies in infertility. Fertil. Steril. , 1994, 61; 799-811.
11. Zhe Jiang Zhang Yiza Zhi. The treatment of 115 cases of anti sperm anti body infertility with Xiao Kang Zhejiang Journal of Chinese Medicine. 2008; 711.

12. I Cooke D. Infertility. Dewhurst's Text book of Obstetrics & Gynecology 1998. Chapter 36: P433-440.
13. Robert R, Franklin and C. Dean Dukes. Anti sperm anti body and unexplained infertility Am. J. Obst. & gynec. 1994. 89:6.
14. Crosignoni PG and Nicolasi AE Poly cystic ovarian disease: heritability and hetero genitil. Hum. Reprod. Update 2001. 7, 3-7.
15. Norman RJ. Obesity, poly cystic ovarian syndrome & anovulation, how are they interrelated. Curr Opin Obstet. Gynecol. 2001; 3:323-327.
16. Kelly CC, Lyall H, Petrio JR, Gould GW, Connell JM and Satton N. Low grade chronic inflammation in women with polycystic ovarian syndrome J. clin. Endocrinol. Metab. 2001; 86:2453-2455.
17. Palacio. JR, Iborra. A, Icova. ZU. The presence of antibodies to oxidative modified proteins in serum from poly cystic ovarian syndrome patients. British .Soc. for Immunology. 2006. May 144(2):217-227.
18. Kuttch WH, Alkister. MC, Byrd W, Mestechy J, Anti sperm antibodies Current knowledge & new horizons Mol. Androl. 1992; 4:183, 1992.
19. March PB, Kuttch WH. The role of Anti sperm antibodies in infertility. Fertil. Steril. 1994. 61:799.1994.
20. Michael de Swiet. Geoffrey Chamberlain, Phillip Bennet. Statistic & evidence – based health care. Basic Science in Obstetrics & gynecology a text book for MRCOG. Part 1 Cambridge. London. Printed in Spain 2002.