

Original Article

Association of ABO Blood Group System and Anti-Sperm Antibody with Male Infertility

Elham Abdollahi¹M.S., Fataneh Tavasolian²M.S., Mohammad Ali Esmaili³M.S., Amir Abbas Momtazi Broujeni⁴ M.S., Ali Amini^{3*} Ph.D.

¹ Department of Immunology, School of Medicine, Mashhad University of Medical Sciences, Mashhad, Iran

² Department of Immunology, School of Medical Sciences, Tarbiat Modares University, Tehran, Iran

³ Department of Hematology, School of Allied Medical Sciences, Iran University of Medical Sciences, Tehran, Iran

⁴ Department of Medical Biotechnology, School of Medicine, Mashhad University of Medical Sciences, Mashhad, Iran

A B S T R A C T

Article history

Received 5 Sep 2014

Accepted 9 Oct 2014

Available online 15 Dec 2014

Keywords

ABO blood group
Anti-sperm antibody
Male infertility

Background and Aims: The ABO blood group system is recognized as major and clinically significant blood group. This group is not only important in terms of blood transfusion and organ transplantation, but also has been utilized in genetic, fertility and infertility researches. The objective of the present study was to evaluate a possible relationship between ABO blood group system and ASA with male infertility.

Materials and Methods: This is a retrospective, case-control study. Our study was carried out on samples referred to Research and Clinical Center for Infertility, Yazd, Iran. ABO blood group, titer of ASA and sperm analysis data of 150 infertile males (case group) and 150 fertile males (control group) was evaluated based on medical records of the patients. Data were then analyzed with SPSS 16 software using t-test and chi-square tests.

Results: Our results indicated that there is a significant relationship between male infertility and O blood group ($p=0.02$) whereas no significant relationship was observed between O blood group and fertility in the control group ($p=0.08$). In both groups the amount of ASA agglutination was statistically significant ($p=0.001$) whereas no significant relationship was detected between blood group and ASA in infertile males ($p=0.18$).

Conclusion: The present study revealed that there is a significant relationship between blood group O and male infertility as well as sperm agglutination and thus the concentration of ASA in infertile males is higher than of fertile males thereby demanding appropriate intervention strategies.

* **Corresponding Author:** Department of Hematology, School of Allied Medical Sciences, Iran University of Medical Sciences, Tehran, Iran. **Tel:** +982188622576, **E-mail address:** Aminia2010@gmail.com

Introduction

Karl Landsteiner was the first to find the ABO blood group system in 1901. According to the International Society of Blood Transfusion (ISBT), there are about 250 blood antigens which have been divided into 29 blood group systems [1, 2]. The ABO blood group antigens are considered as the clinically significant blood group system. After the discovery of an association between stomach cancer and blood type A in 1953, there have been several studies on the possible relationship between blood types and certain diseases [3, 4]. With regard to the importance of ABO blood group in blood transfusion, this blood group has been associated with several diseases (Table 1). It is possible that there exists a relationship between the type of blood group and men infertility. Recent works demonstrate that spermatozoa have detectable blood group antigens A or B. The presence of group-specific substances in the female's cervical secretions may prevent fertilization [5, 6]. Meiotic drive, in which certain sperm from a heterozygous male is favored for fertilization for their blood group, may also be significant. However, once fertilization has occurred, the mother's natural antibody reacts against father's blood group antigens on spermatozoa. Theoretically, the fertilized zygote should have a definable blood group. If there is sufficient antigenic stimulus, the mother's antibody titer will determine the degree and time of the reaction. A higher titer may prevent fertilization and caused infertility, a lower titer

(but one that is still relatively high) may cause loss of the fetus at an early age [7].

Evaluate of the ability of sperm to stimulate the immune system and research on anti-sperm antibodies (ASA) were first described in 1899 by Landsteiner and colleagues. According to these pioneer researchers, if the sperm of one species was injected into another, it can act as antigenic. Subsequently, the researchers found that when the sperms are exposed to the immune system of the same species, there would be antigenic power. In general, the blood-testis barrier may be damaged by different mechanisms and sperm antigens can be exposure to the immune system and eventually lead to the formation of immune response and the ASA [8]. Several studies indicate that about 6-26% of infertility can be due to the formation of ASA in men and women [8-10]. ASA effects on human fertility is diverse including the disruption of progressive sperm motility, sperm trapped in cervical mucus, reducing sperm penetration in the zona pellucida, acrosome reaction inhibition and inhibition of binding of sperm to oocyte plasma membrane and finally fertilization. So, ASA as an immunological factor can be the cause for male infertility [11-13]. The aim of this study was to evaluate a possible relationship between ABO blood group system and ASA with male infertility.

Table 1. ABO blood group and disease

Disease associated	Type of associated risk	Blood group
Squamous cell carcinoma of skin [6]	Low	O
Pancreatic cancer [7,8]	Low	O
Ovarian cancer [9]	High	B
Gastric cancer [10]	High / Low	A&O
Breast cancer [11]	High	O
Cervix cancer [11]	High	B & O
Lung cancer [11]	High	B
Buccal cancer [11]	High	B
Cholera & GI infections by E.coli [12]	High	O
H. pylori infection & GI Ulceration [12]	High	O
Ischemic heart disease [13]	High	AB
Otitis media with effusion [14]	Low	O

Materials and Methods

Cases and controls

This is a retrospective, case-control study carried out on samples referred to the Research and Clinical Center for Infertility in Yazd, Iran. The study was approved by the Ethics committee of Shahid Sadoughi University of Medical Sciences and signed informed consent was obtained from each sample. Patients consisted of 150 infertile males their female partners of whom were without any anatomical, microbial, viral, genetically disease. Hormone profile tests and tests for ovulation and tubal patency of female partners were normal in the patients. Also, according to medical evidences, female partners were healthy and fertile.

The control group consisted of 150 fertile males the partners of whom were infertile and had one or more of the anatomical, microbial, viral, genetically disease. Also some of the hormone profile tests and tests for ovulation and tubal patency were abnormal.

The investigations included semen analysis. A detailed sexual, occupational, medical and, surgical history was recorded.

Blood group typing

ABO and Rh blood group typing was done by cell and back type (only for ABO) methods (IBTO, Iran).

Evaluation of ASA

Evaluation of ASA was conducted by mixed agglutination reaction method (Sperm Mar™ IgA, Fertipro, Belgium) based on percentage of sperm aggregation with anti-sperm antibodies in serum or semen.

Statistical analysis

Data were analyzed with SPSS 16 software using t-test and Chi-square tests. The result was considered significant when p value was < 0.05.

Results

The mean age of the infertile males (case) was 36.1 and fertile male (control) was 36.7years; the difference was not significant ($p=0.42$). The overall distribution of the blood groups in the studied population (cases and controls) has been shown in table 2. Our results indicated that there was a significant relationship between male infertility and O blood group

($p=0.02$) whereas not significant relationship was observed in the control group ($p=0.08$). In addition, as shown in Table 2, there was no significant relationship between A, B and AB blood groups in both the case ($p= 0.6, 0.4$ and 0.3 respectively) and the control groups with infertility and fertility ($p=0.2, 0.2$ and 0.5 respectively). The results also suggested that there was no significant relationship between Rh blood group and male infertility ($p=0.09$).

According to Table 3, in both groups the amount of ASA agglutination (also its concentration) was statistically significant ($p=0.001$) whereas no significant relationship was detected between blood group and ASA in infertile males ($p=0.18$). Moreover the results showed no significant relationship between ASA and sperm quality [(motion ($p=0.08$) and number ($p=0.2$)).

Table 2. Frequency of ABO and Rh blood groups in fertile and infertile male.

Type of blood group	Frequency of ABO blood group (%) in Case group		Frequency of ABO blood group (%) in Control group		Frequency of Rh blood group (%) in Case group		Frequency of Rh blood group (%) in Control group	
		P value		P value				
					positive	negative	positive	Negative
A	26	0.6	29	0.2	22	3	30	2
B	14	0.4	23	0.2	14	2	23	1
AB	7	0.3	6	0.5	6	0	7	0
O	53	0.02	42	0.08	43	7	31	6
Total	100		100		88	12	91	9

Table 3. Mean sperm count and motility in the case and control groups

	Mean number of sperm (/ml)	Mean percentage of sperm motility
Control group	$66 \pm 49 \times 10^6$	49 ± 12
Case group	37.3 ± 9.04	45.17 ± 8.02

Discussion

Many studies have reported the association of ABO blood groups with several diseases [6-14]. This study was conducted to find any possible relationship between ABO blood groups and ASA with infertility in male. This study showed that there is a strong relationship between blood group O and male infertility while the relationship between the presence of ASA and blood groups was found to be

statistically insignificant. In addition, this study did not found a relationship between the antibodies against sperm with sperm count and motility. In other words, anti-sperm antibody had no effect on sperm motility and count in infertile males. In line with our study, Shoaib Khan et al. detected that blood group O is strongly related to male infertility [14]. The basis for this finding may be due to the presence of blood group antigens in seminal

fluid in secretor persons which react with natural antibodies in female uterus that can lead to infertility [7]. Several studies have been carried out to evaluate the association of ABO incompatibility in couples with infertility. One survey showed that 30-40% of infertile couples have ABO incompatibility thus concluding that ABO incompatibility between partners is a significant contributor to infertility [15]. In contrast, another study showed that women may have little tolerance to the A or B antigens on spermatozoa, so the ABO blood group incompatibility is not associated with infertility [16]. Some studies indicated that there is no relationship between ABO blood groups and human fertility [17, 18]. The relationship between ABO blood group incompatibilities in couples with recurrent miscarriages is highly controversial. These studies suggest that there is no association between ABO blood group incompatibility and recurrent spontaneous abortions probably due to tolerance [15, 19]. However, some studies have shown that in couples with recurrent spontaneous abortion compared to the normal fertile couples, ABO blood group incompatibility is significantly higher [20]. Studies on the ASA and infertility have shown that antibodies against sperm have negative effects on fertilizing ability of spermatozoa [21]. Although ASA can reduce the motility and sperm count, there are other functional mechanisms in ASA that can cause lack of fertilization due to disturbances in the reaction of acrosome with ovule. In addition, ASA can disrupt progressive sperm motility, trap sperm in cervical mucus, reduce sperm

penetration in the zona pellucida, induce acrosome reaction inhibition and inhibition of binding of sperm to oocyte plasma membrane, and finally fertilization [11-13].

Our study indicated that the percentage of sperm antibodies in infertile male with percentage of sperm antibodies in infertile male was significantly different while the ASA, sperm count and sperm motility did not show any significant relationship. This can suggest that the functional role of ASA in male infertility is higher than other mechanisms mentioned above. In this regard, a study showed that there is no significant relationship between sperm concentration and poor sperm quality [11]. In agreement with our results, some studies have shown that men with high concentration of ASA have lower fertility than men with lower concentrations of it (ASA inverse correlation with fertility) [22-24]. In disagreement with our results, some studies have, however, shown that there is no relation between ASA and ability of sperm to fertilize the oocyte [25]. Another survey was carried out to determine the association between ABO blood group and production of ASA in infertile couples and it was finally shown that blood group antigens with production of antibodies to sperm in the cervix has no relationship thereby confirming our findings in this regard [18].

This study suggests that blood group O proves a significant relationship with male infertility. This finding is in line with the previous researches conducted on the subjects similar to those our study and confirms the results. However, as aforementioned, there are some

contrary results on the relationship between ABO blood groups and fertility or infertility. It is possible that these differences are caused by genetic diversity in different populations. Future studies can be conducted with greater sample size as well as more focus on other blood groups and infertility or fertility in men and women.

Conclusion

The present study revealed that prevalence of male infertility in blood group O is invariably higher than that in all other blood groups.

References

- [1]. Chudley AE. Genetic landmarks through philately – Karl Landsteiner: the father of blood grouping. *Clin Genet* 2000; 57:267-269.
- [2]. Ganitha G, Bhumkar S, Bhuvaneshwari J. Association of ABO Blood Groups and Infertility. *Int J* 2012; 2(5):72-77
- [3]. Meade T, Cooper J, Stirling Y, Howarth D, Ruddock V, Miller G. Factor VIII, ABO blood group and the incidence of ischaemic heart disease. *Br J Haematol* 1994; 88(3):601-607.
- [4]. Apostolopoulos K, Labropoulou E, Konstantinos B, Rhageed S, Ferekidis E. Blood group in otitis media with effusion. *J Otolaryngol* 2002; 64(6):433-435.
- [5]. Shahani S, Southam A. Immunofluorescent study of the ABO blood group antigens in human spermatozoa. *Am J Obstet Gynecol* 1962; 84:660.
- [6]. Matsunaga E, Hiraizumi Y. Prezygotic selection in ABO blood groups. *Science (New York, NY)* 1962; 135(3502):432.
- [7]. Allen CM. Blood groups and abortions. *J Chronic Dis* 1964; 17(7):619-626.
- [8]. Rumke P, Hellings G. Autoantibodies against spermatozoa in sterile men. *Am J Clin Pathol* 1959; 332-357
- [9]. Tsuji Y, Clausen H, Nudelman E, Kaizu T, Hakomori S, Isojima S. Human sperm carbohydrate antigens defined by an antisperm human monoclonal antibody derived from an infertile woman bearing antisperm antibodies in her serum. *J Exp Med* 1988; 168(1):343-356.
- [10]. Check J, Adelson H, Bollendorf A. Effect of antisperm antibodies on computerized semen analysis. *Syst Biol Reprod Med* 1991; 27(1):61-63.
- [11]. Munuce M, Berta C, Pauluzzi F, Caille A. Association of antisperm antibodies, sperm movement, and semen quality *Urol Int*. 2000;65(4):200-203.
- [12]. Taneichi A, Shibahara H, Hirano Y, Suzuki T, Obara H, Fujiwara H, et al. Sperm immobilizing antibodies in the sera of infertile women cause low fertilization rates and poor embryo quality in vitro *Am J Reprod Immunol*. 2002; 47(1):46-51.
- [13]. Hadinedoushan H, Ghafourzadeh M. A survey of anti-sperm antibodies in infertile couples. *Iranian Journal of Reproductive Medicine* 2007; 5(1):39-40.
- [14]. Khan MS, Ahmed Z, Hanif R, Zaman S, Ali I. Association of blood groups and male infertility. *J Ayub Med Coll Abbottabad* 2010; 22(1):154-156.
- [15]. SJ B, WL T. ABO (H) blood incompatibility as a cause of infertility: a new concept. *Am J Obstet Gynecol* 1960; 79:847-55.
- [16]. Ogbimi A, Oyeyinka G, Omu A. ABO blood group incompatibility and infertility in Nigerian couples. *Immunol Lett* 1987;14(4):299-301.
- [17]. Allan T. ABO blood groups and human fertility. *Br J Prev Soc Med* 1953; 7(4):220-226.

Moreover, it was observed that ABO blood groups showing a strong relationship between blood group O and male infertility and ASA have a significant association with male infertility.

Conflict of Interest

The authors declare that they have no conflicts of interest.

Acknowledgement

The researchers would like to thank the staff of Yazd Research and Clinical Center for Infertility, in Yazd, Iran, especially Dr. Ali Mohammad Abdoli, for their cooperation.

- [18]. Omu AE, Al-Mutawa M, Al-Qattan F. ABO blood group and expression of antisperm antibodies in infertile couples in Kuwait. *Gynecol Obstet Invest* 1998; 45(1): 49-53.
- [19]. Lauritsen JG, Jørgensen J, Kissmeyer-Nielsen F. Significance of HLA and blood-group incompatibility in spontaneous abortion. *Clin Genet* 1976; 9(6):575-582.
- [20]. Ghasemi N, Sheikhha M, Davar R, Soleimani S. ABO Bloods group incompatibility in recurrent abortion. *IJPHO* 2011; 1(2):62-66.
- [21]. Bronson R, Cooper G, Rosenfeld D. Sperm-specific isoantibodies and autoantibodies inhibit the binding of human sperm to the human zona pellucida. *Fertil Steril* 1982; 8(6):724-739.
- [22]. Lähteenmäki A. In-vitro fertilization in the presence of antisperm antibodies detected by the mixed antiglobulin reaction (MAR) and the tray agglutination test (TAT). *Hum Reprod* 1993; 8(1):84-88.
- [23]. Rajah S, Parslow J, Howell R, Hendry W. The effects on in-vitro fertilization of autoantibodies to spermatozoa in subfertile men. *Hum Reprod* 1993; 8(7):1079-1082.
- [24]. Ford W, Willians K, McLaughlin E, Harrison S, Ray B, Hull M. Immunology: The indirect immunobead test for seminal antisperm antibodies and fertilization rates at in-vitro fertilization. *Hum Reprod* 1996; 11(7):1418-1422.
- [25]. Mandelbaum S, Diamond M, DeCherney A. Relationship of antisperm antibodies to oocyte fertilization in in vitro fertilization-embryo transfer. *Fertil Steril* 1987; 47(4):644.