

ORIGINAL RESEARCH

Implication of ABO Blood Type on Ovarian Reserve in Indian Women

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ABSTRACT

Background: To explore the association between ABO blood type and ovarian reserve, as reflected by early follicular phase follicle stimulating hormone (FSH) levels.

Materials and methods: In this cross-sectional observational study, early follicular phase (day 3) serum levels of FSH (IU/L) and information on blood types (O, A, B, AB), patient age, and body mass index (BMI) were collected from 300 female patients, who were undergoing fertility evaluation at Vydehi Institute of Medical Sciences and Research Centre (VIMS & RC), Bengaluru. Serum FSH > 10 IU/L was taken as a measure of decreased ovarian reserve (DOR). Data distribution for FSH, age, BMI were analyzed and nonparametric tests were used for comparison across blood groups. Pearson's correlation test was used to determine the relationship between elevated FSH and blood types after adjusting for age and BMI.

Results: Proportions of blood types O, A, B, and AB were 42, 24.3, 28.7, and 5% respectively. Mean age (years) and BMI (kg/m²) among study group were 34.08 ± 3.48 and 24.34 ± 2.56 respectively. Out of 300 women, 240 women had serum FSH < 10 IU/L and 60 women had serum FSH > 10 IU/L. Women with blood type "O" (32 out of 60) were twice as likely to exhibit FSH > 10 IU/L (p=0.02) compared to "A" and "B" blood type.

Conclusion: Our results have shown that there is an association between ABO blood type and DOR among Indian women. Blood group "O" appears to be associated with DOR that is independent of advancing age and BMI.

Keywords: Blood type, Decreased ovarian reserve, Follicle stimulating hormone.

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INTRODUCTION

Ovarian reserve is an important measure of woman's remaining oocyte available for achieving pregnancy. The concept "ovarian reserve" reflects the quantity and possibly the quality of residual oocytes available for procreation.¹⁻³ As women age, ovarian reserve decreases naturally. Despite mounting evidence identifying anti-mullarian hormone (AMH) and antral follicular count as sensitive prognostic markers of ovarian reserve, in clinical practice the early follicular phase serum follicle stimulating hormone (FSH) level appears to be the most commonly utilized parameter for assessment of ovarian reserve.⁴ In general, an early follicular phase serum FSH level > 10 IU/L has been accepted as a predictor of decreased ovarian reserve (DOR).⁵⁻⁷ In a recent article by Nejat et al,⁸ it has been reported that a novel association exists between blood type and DOR, suggesting that blood type "O" is a predictor for lower ovarian reserve compared with other blood groups that is independent of age. In their study, women with blood type "O" were observed to be twice as likely to have elevated FSH levels compared with those with blood type "A" or "AB." Another recent report by Binder et al,⁹ relating blood group antigens and ovarian hyper stimulation syndrome (OHSS), observed that OHSS was more likely during the course of ovarian stimulation in women with blood type "A" compared to those with blood type "O."

MATERIALS AND METHODS

Patients attending the Vydehi Institute of Medical Sciences and Research Centre Infertility clinic for fertility-related evaluation were randomly allocated in the study. The study was approved by the Vydehi Institute Ethical Committee (VICE). In this study, we included patients between 25 and 40 years. The data included the age, ABO blood type, and body mass index (BMI). Excluded were obese infertile women and patients with thyroid disorders. The early follicular phase serum FSH on day 3 of the menstrual cycle was estimated by immunoassay. Serum FSH > 10 IU/L was taken to indicate DOR.

Statistical Analysis

Statistical analysis was performed with software named SAS 9.2, SPSS 15.0, STATS 10.1, MEDCALC 9.0.1, SYSTAT 12.0 and R. Environment version 2.11.1 was used for the analysis of the data and Microsoft Word and Excel have been used to generate graphs, tables, etc. [Results on continuous measurements are presented as mean \pm SD (min – max).] Results on categorical measurements are presented in number (%). Significance was assessed at 5% level of significance. Chi-square/Fisher's exact test has been used to find the association between independent variables and DOR. Pearson's correlation between study variables is performed to find the degree of relationship. Student's t-test (two-tailed, independent) has been used and $p < 0.05$ was considered to be statistically significant.

RESULTS

Results on continuous measurements are presented as mean \pm SD (min–max) and results on categorical measurements are presented as percentage (%). Significance is assessed at 5% level of power of confidence. Informative data were available for 300 women aged ≤ 40 (mean age 34.08 ± 3.48). Average BMI of study population was 24.34 ± 2.56 . The prevalence of blood type among study population were 126 (42%) in "O" blood type, 73 (24.3%) in "A" blood type, 86 (28.7%) in "B" blood type, and 15 (5%) in "AB" blood type (Table 1).

The relationship between blood type and serum FSH levels is shown in Table 2.

Table 1: Descriptive statistics of population and prevalence of blood group

Parameter	n=300
Age (years)	34.08 ± 3.48 (25–40)
BMI (kg/m ²)	24.34 ± 2.56 (20–29)
FSH (IU/L)	7.90 ± 3.34 (3.00–19.80)
Blood type	
"O"	126 (42%)
"A"	73 (24.3%)
"B"	86 (28.7%)
"AB"	15 (5%)

BMI: Body mass index; FSH: Follicle stimulating hormone

Table 2: Relationship between blood type and serum FSH levels

Blood type	FSH ≤ 10 IU/L (n=240)	FSH ≥ 10 IU/L (n=60)	p-value
"O"	94 (39.2%)	32 (53.3%)	0.02
"A"	62 (25.8%)	11 (18.3%)	0.49
"B"	71 (29.6%)	15 (25%)	0.48
"AB"	13 (5.4%)	2 (3.3%)	0.50

FSH: Follicle stimulating hormone; p-value < 0.05 was considered as statistically significant

After adjusting for age, patients with blood type "O" were twice as likely to exhibit FSH > 10 IU/L (p -value = 0.02; which is statistically significant) compared to those with "A" and "B" blood types. Conversely, women with the "A," "B," and "AB" blood groups, antigens were significantly less likely to manifest FSH > 10 IU/L compared to those with blood type "O" (Table 2).

DISCUSSION

Our study findings have shown association between blood group antigen and DOR in Indian women seeking fertility treatment. Our study results show that blood type "O" relates to biochemical evidence of DOR (p -value = 0.02). Women with blood type "O" were observed to be twice likely to have elevated baseline FSH levels compared with those of "A" and "B" blood types. Nejat et al⁸ reported a similar finding of association between blood type and DOR, suggesting that blood type "O" is a predictor for lower ovarian reserve compared with other blood groups, i.e., independent of age.

Numerous etiological factors affect ovarian reserve, including age, autoimmune condition, ovarian surgery, genetics, chemotherapy, and radiotherapy. While numerous surrogate markers are recognized to reflect ovarian reserve, female age remains the strongest predictor of reproductive success in couples undergoing fertility treatment.¹⁰⁻¹³

The ABO gene locus is located on chromosome 9q34 and has three main allelic forms: "A," "B," and "O." The gene products of the ABO system are glycotransferases that catalyze the transfer of carbohydrates to the H antigen, which is a precursor of the ABO blood group antigens.^{14,15} The A allele encodes for a glycosyl transferase (A transferase) that catalyzes the transfer of N-acetyl galactosamine to the H antigen, producing the A antigen. Similarly, the B allele encodes for a glycosyl transferase (B transferase) that catalyzes the transfer of galactose to the H antigen, producing the B antigen. The product of the O allele is an enzymatically inactive protein leaving the H antigen unchanged on the red blood cell of those with blood group O lack the transferase enzyme.¹⁴ The red blood cell antigen, A and B antigens can be found on the cell membranes of various cell types, including epithelial cells.¹⁶ It is unknown whether that antigen is present in ovarian cells. Several proteins crucial for follicle development and maturation, such as FSH-receptor (FSH-R) and LH receptor (LH-R) are heavily glycosylated proteins, whose activity is influenced by A-transferase (A) and B-transferase (B).¹⁷ The circulatory half-life and biological activity of LH at the hormone receptor level are strongly affected by glycosylation.

Considering the protective effect of A-transferase (A) and B-transferase (B), it appears to exhibit against DOR,

one may speculate that those enzymes may be relevant to the process of gamete accrual or attrition, and the absence of A-transferase and B-transferase activity, as in case of blood type O, may be detrimental to these processes.

Another possible explanation for the observed relationship between blood type and ovarian reserve may include genetic inheritance. The nuclear receptor 5A1 (NR5A1) and transforming growth factor β receptor (TGFB1) genes, which are located on chromosome 9q34 and 9q22 near the ABO locus, are related to ovarian function. Therefore, recombination may occur between these genes and the ABO type genes at a relatively high rate, which would increase the likelihood of these genes being inherited together with ABO.¹⁸

Ovarian hyperstimulation syndrome is a potential life-threatening complication during controlled ovarian stimulation for fertility treatment. Binder et al⁹ and Bellver et al¹⁹ observed in their study that OHSS was more likely during the course of ovarian stimulation in women with blood type "A" compared to those with blood type "O."

The present study had some noteworthy limitations; first, the relatively small sample size from a single institute. Second, study population being exclusively comprised of infertile women, limiting the applicability of our findings to the general female population. Finally, FSH level alone was used to define DOR. The AMH levels were not evaluated in our study.

In summary, our findings have shown that there is an association between ABO blood type and DOR among Indian women. Blood group "O" appears to be associated with DOR that is independent of advancing age and BMI. The exact mechanism that relates blood type to ovarian reserve is unknown. Further studies are warranted to validate this association and to determine the underlying mechanisms.

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