Medical Sciences

Association of ABO blood type with ovarian reserve

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To investigate the relationship between ABO blood type and serum antimüllerian hormone (AMH) as a marker of ovarian reserve. Retrospective chart review of all potential in vitro fertilization (IVF) patients between 2010 and 2013. The percentage of patients belonging to each ABO blood type with an AMH ≤ 1 ng/ml, ≤ 0.5 ng/ml and ≤ 0.16 ng/ml was calculated. Within each AMH group, means and standard deviations for age and body mass index (BMI) were also calculated. Chi-square and Student's *t* tests were used to compare percentages and means between AMH groups. Complete data was available for 2394 patients. The overall distribution of ABO blood types was: 37% (A), 18.1% (B), 5% (AB), and 39.9% (O). Of the 2394 patients, 2146 (89.6%) patients were Rhesus factor positive, while 248 (10.4%) patients were Rhesus factor negative. There was no difference in the percentage of patients belonging to each ABO blood type, or mean age and BMI in the AMH ≤ 1 ng/ml group. The AMH ≤ 0.5 ng/ml and ≤ 0.16 ng/ml groups had a higher percentage of older patients, but there was no difference in mean BMI. No association between blood type and AMH ≤ 0.5 ng/ml or ≤ 0.16 ng/ml was found, even after controlling for age. Contrary to initial investigations, our study reveals no relationship between ABO blood type and ovarian reserve. The predictive value of ABO blood type for the evaluation of ovarian reserve remains questionable. *Journal of Nature and Science, 1(2):e40, 2015.*

ABO | blood type | ovarian reserve | antimüllerian hormone

Ovarian reserve is a widely used term that reflects the reproductive potential of a woman, primarily based on the quantity of remaining oocytes.[1-4] Ultrasonographic measurements of an antral follicle count (AFC), measurement of early follicular serum levels of follicle-stimulating hormone (FSH), anti-mullerian hormone (AMH) and inhibin-B have often been used as clinical markers for ovarian reserve.[5] Many of these tests have become part of the routine evaluation of infertility, particularly in patients undergoing assisted reproductive techniques.[6] These markers have also been used in clinical settings to predict ovarian response and in vitro fertilization (IVF) outcomes.[7] While different physiologic and pathologic conditions have been known to influence these markers of ovarian reserve, there has been a recent interest in exploring the relationship between ABO blood types and serum markers of ovarian reserve.[4,8 and 9] Initial investigations have suggested that certain blood types may be associated with diminished ovarian reserve, with others being protective.[4] To address this hypothesis, we aim to investigate the relationship between ABO blood type and AMH as a marker of ovarian reserve.

Materials and Methods

Inclusion Criteria

The institutional review board at Weill Cornell Medical College approved our study protocol. The Ronald O. Perelman and Claudia Cohen Center for Reproductive Medicine began using the second-generation AMH assay [GenII Beckman ELISA assay (Beckman Coulter, Inc)] as part of the evaluation of infertility in April 2010. Thus, all potential IVF patients at our center between May 2010 and January 2013 were analyzed for inclusion.

Laboratory Protocols

Serum AMH measurements were performed at our center's laboratory. All serum samples were assayed using the GenII Beckman ELISA assay (Beckman Coulter, Inc). The intra- and interassay variability were 5.8% and 13.4%, respectively, for AMH.[10]

Study Variables

Demographic characteristics extracted from patient charts included age, BMI (kg/m^2), ABO blood type, Rhesus factor type, and serum AMH levels. The percentage of patients belonging to each ABO blood type with an AMH ≤ 1 ng/ml, ≤ 0.5 ng/ml and ≤ 0.16 ng/ml was determined. At our center, serum AMH levels ≤ 1 ng/ml, ≤ 0.5 ng/ml, and ≤ 0.16 ng/ml are considered the cut-offs for diminished, very low, and undetectable ovarian reserve, respectively. Within each AMH group, means and standard deviations for age and BMI were also calculated.

Statistical analysis

Continuous variables were expressed as mean ± standard deviation (SD), and categorical variables were expressed as number of cases (n) and percentage of occurrence (%). Chi-square and Student's *t* tests were used to compare percentages and means between AMH groups, respectively. As initial investigations have suggested that blood type O is associated with diminished ovarian reserve while blood type A is protective,[4] odds ratios (OR) with 95% confidence intervals (CI) for the percentage of patients with blood type A versus blood type O and blood type A or AB versus blood type O within each AMH group were calculated. When indicated, adjusted odds ratios (aOR) were also calculated. Statistical significance was set at $P<0.05$. All statistical analyses were performed using STATA version 13 (College Station, TX: StataCorp LP).

Results

Complete demographic data was available for 2394 patients during the study period. The overall mean (± SD) age, BMI and AMH of the study cohort was 37.1 (±4.7) years, 23.5 (±5.9) kg/m^2, and 1.4 (±1.9) ng/ml, respectively. The overall distribution of ABO blood types in the cohort was as follows: 37% (A), 18.1% (B), 5% (AB), and 39.9% (O). Of the 2394 patients, 2146 (89.6%) patients were Rhesus factor positive, while 248 (10.4%) patients were Rhesus factor negative.

Table 1 shows the distribution of ABO blood types in patients with AMH ≤ 1 ng/ml and > 1 ng/ml. There was no statistical difference in the mean age, mean BMI, distribution of ABO blood types, or distribution of Rhesus factor types. There was no diffidence in the percentage of patients with blood type A versus blood type O (OR 0.97, 95% CI 0.81-1.20) and blood type A or AB versus blood type O (OR 0.96, 95% CI 0.80-1.10) when comparing patients with AMH ≤ 1 ng/ml with > 1 ng/ml.

Table 2 shows the distribution of ABO blood types in patients with AMH ≤ 0.5 ng/ml and > 0.5 ng/ml. The mean age of patients with AMH ≤ 0.5 ng/ml was higher than patients with AMH > 0.5 ng/ml i.e., 39.1 (±4.2) years versus 37.9 (±4.9) years ($P<.001$). No difference in the mean BMI or distribution of Rhesus factor type was noted. In the AMH ≤ 0.5 ng/ml group, there was no difference in the percentage of patients with blood type A versus blood type O (OR 0.99, 95% CI 0.53-1.87) and blood type A or AB versus blood

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Table 1: Distribution of ABO blood types in patients with AMH ≤1 ng/ml

Parameter	AMH ≤ 1 ng/ml (n=1351)	AMH > 1 ng/ml (n=1043)	*P*-value
Age (years)	38.4 (±4.2)	38.1 (±5.1)	0.11
BMI (kg/m^2)	23.3 (±6.2)	23.7 (±5.6)	0.10
Blood Type			0.99
A	499 (36.9%)	386 (37%)	
B	242 (17.9%)	191 (18.3%)	
AB	64 (4.7%)	56 (5.4%)	
O	546 (40.4%)	410 (39.3%)	
Rhesus factor			0.97
Positive	1204 (89.1%)	930 (89.2%)	
Negative	147 (10.9%)	113 (10.8%)	

AMH: Anti-Mullerian Hormone; BMI: Body Mass Index. Data are presented as mean ± standard deviation and n (%)

Table 2: Distribution of ABO blood types in patients with AMH ≤0.5 ng/ml

Parameter	AMH ≤ 0.5 ng/ml (n=830)	AMH > 0.5 ng/ml (n=1564)	*P*-value
Age (years)	39.1 (±4.2)	37.9 (±4.9)	<0.001
BMI (kg/m^2)	23.3 (±5.9)	23.6 (±5.9)	0.24
Blood Type			0.99*
A	307 (36.9%)	578 (36.9%)	
B	149 (18%)	290 (18.5%)	
AB	42 (5.1%)	78 (5%)	
O	332 (40%)	410 (39.6%)	
Rhesus factor			0.89*
Positive	742 (89.4%)	1401 (89.6%)	
Negative	88 (10.6%)	163 (10.4%)	

AMH: Anti-Mullerian Hormone; BMI: Body Mass Index. Data are presented as mean ± standard deviation and n (%)
*Data adjusted for age remains non-significant

Table 3: Distribution of ABO blood types in patients with AMH ≤ 0.16 ng/ml

Parameter	AMH ≤ 0.16 ng/ml (n=128)	AMH > 0.16 ng/ml (n=2266)	*P*-value
Age (years)	40.1 (±3.7)	37.2 (±4.9)	<0.001
BMI (kg/m^2)	23.7 (±5.8)	23.5 (±5.9)	0.71
Blood Type			0.99*
A	46 (35.9%)	839 (37%)	
B	25 (19.6%)	417 (18.4%)	
AB	6 (4.7%)	114 (5%)	
O	51 (39.8%)	896 (39.5%)	
Rhesus factor			0.86*
Positive	114 (89.1%)	2029 (89.5%)	
Negative	14 (10.9%)	237 (10.4%)	

AMH: Anti-Mullerian Hormone; BMI: Body Mass Index. Data are presented as mean ± standard deviation and n (%)
*Data adjusted for age remains non-significant

type O (OR 0.99, 95% CI 0.54-1.83). When controlling for age, these results remained unchanged; there was no difference in the percentage of patients with blood type A versus blood type O (aOR 0.88, 95% CI 0.78-1.03) and blood type A or AB versus blood type O (aOR 0.91, 95% CI 0.79-1.10)

Table 3 shows the distribution of ABO blood types in patients with AMH ≤ 0.16 ng/ml and > 0.16 ng/ml. The mean age of patients with AMH ≤ 0.16 ng/ml was 40.1 (±3.7) years, which was higher than the mean age of 37.9 (±4.9) years of patients with AMH > 0.16 ng/ml (*P*<.001). There was no difference in the mean BMI or distribution of Rhesus factor type. There was no difference in the percentage of patients with blood type A versus blood type O (OR 0.96, 95% CI 0.64-1.45) and blood type A or AB versus blood type O (OR 0.96, 95% CI 0.64-1.43). These results remained unchanged after controlling for age: blood type A versus blood type O (aOR 0.93, 95% CI 0.62-1.41) and blood type A or AB versus blood type O (aOR 0.99, 95% CI 0.66-1.48).

Discussion

Our findings suggest no relationship between ABO blood type and serum AMH as a marker of ovarian reserve in patients at our center. Furthermore, our analysis holds true at serum AMH levels ≤ 1 ng/ml, ≤ 0.5 ng/ml and ≤ 0.16 ng/ml, which are considered the cut-offs for diminished, very low, and undetectable ovarian reserve at our center, respectively.

Nejat et al. were the first to report an association between ABO blood type and diminished ovarian reserve.[4] The authors found a significantly higher representation of blood type O in patients with serum FSH levels > 10 mIU/ml (OR 2.36, 95% CI 1.27-4.41). Furthermore, they found that this relationship was magnified in patients with serum FSH levels > 12 mIU/ml (OR 3.48, 95% CI 1.46-7.32). In contrast, they found a significantly higher representation of the A antigen in patients with normal ovarian reserve. The authors postulated that patients with blood type O, unlike patients with the A antigen, lack a vital enzyme called glycosyltransferase (A transferase), which may be involved in the process of oocyte attrition or accrual.[4]

Subsequent investigations have failed to highlight any association between blood type and serum FSH as a marker of ovarian reserve. In their detailed multivariate analysis of 305 patients undergoing IVF, Timberlake et al. found no association between a woman's blood type and a serum FSH level > 10 mIU/ml, after controlling for race, ethnicity, BMI, smoking status, history of endometriosis, ovarian surgery, or previous pregnancy.[9] The authors, however, did find that older age was associated with greater odds for diminished ovarian reserve (OR 1.07, 95% CI 1.01-1.13). In another study involving 500 patients, Şengül et al. found no statistical difference in the distribution of blood groups in

patients with a serum FSH level > 10 mIU/ml compared to patients with a FSH level < 10 mIU/ml.[11]

Although a serum FSH level > 10 mIU/ml is commonly accepted as a cut-off for diminished ovarian reserve,[9,11 and 12] cycle-to-cycle variations in FSH levels are frequently encountered in the early follicular phase.[9] AMH levels better correlate with the number of early antral follicles compared to other hormonal markers,[13] and are more specific than FSH levels at predicting oocyte yield and IVF response.[5,14 and 15] Given these advantages of AMH over FSH, we chose AMH as a marker of ovarian reserve in our study cohort. Our findings are consistent with the results from de Mouzon et al.'s retrospective study of 1020 women, in which no relationship was found between blood groups and AMH as a marker of ovarian reserve.[8] Our findings are also consistent Timberlake et al.'s study showing an inverse relationship between increasing age and serum AMH levels.[9]

A major strength of our study is its large sample size. Furthermore, it is the largest study to date investigating the relationship between ABO blood type and serum AMH as a marker of ovarian reserve. In contrast, the retrospective nature of our study and the lack of analysis of potential confounders such as race, ethnicity, smoking status and prior ovarian surgery can be considered as weakness of this study. However, it is encouraging to note that our results remain consistent with other studies involving multivariate analysis of potential confounders.[9] We postulate that the association of ABO blood type with ovarian reserve, if any, is weak at best.

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