Association between ABO and Rh Blood Groups and Risk of Preeclampsia: A Case-Control Study from Iran

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Abstract

AIM: Preeclampsia (PE) is a major cause of maternal and neonatal morbidity and mortality. There is a genetic component in the development of PE with estimated heritability around 0.47. Several studies have investigated the association between maternal ABO blood groups (OMIM: 110300) and risk of PE, with contradictory results have emerged. Considering that there is no study in this filed from Iranian population, the present case-control study was carried out at Shiraz (south-west Iran).

MATERIAL AND METHODS: In this study 331 women; 121 pregnant with PE and 210 normotensive pregnant women were included. Using blood group O (for ABO blood groups) or Rh+ (for Rh blood groups) as a reference, odds ratios (ORs) and its 95% confidence intervals (95% CI) of PE risk were estimated from logistic regression analysis.

RESULTS: Although the A (OR = 0.67, 95% CI = 0.39-1.17, P = 0.165), AB (OR = 0.86, 95% CI = 0.48-1.53, P = 0.615) and AB (OR = 1.14, 95% CI = 0.37-3.45, P = 0.812) phenotypes showed lower risks compared with the O blood group, statistical analysis indicated that there was no significant association between ABO phenotypes and risk of PE. The frequency of Rh- phenotype was higher among PE patients compared with the control group. However, the association was not significant (OR = 1.79, 95% CI = 0.69-4.65, P = 0.229). Adjusted ORs for age of participants and parity did not change the above-mentioned associations.

CONCLUSION: Our present findings indicate that there is no association between ABO and Rh blood groups and risk of PE in Iranian population.

Introduction

Preeclampsia (PE) is a major cause of maternal and neonatal morbidity and mortality in humans. It is characterised by the presence of high blood pressure and proteinuria after the 20th week of pregnancy. It has been reported that PE is one of the top four causes of maternal mortality and morbidity worldwide [1]. For decades many studies investigate the pathogenesis and risk factors of PE with hopes of finding ways for prevention, early detection and effective management. It is well established that there is a genetic component in the development of PE [2-4].

Its heritability was estimated around 0.47 [2]. Genome-wide scans indicate that several chromosomal segments are associated with risk of PE [5, 6]. Consanguineous marriages are associated with increased risk of PE [7], indicating that homozygosity for variant alleles involved in PE.

The ABO blood group was discovered in 1900 by Karl Landsteiner. It is one of best known genetic traits because of its importance in transfusion medicine. In this blood group system, there are four major phenotypic groups named by A, B, AB, and O that result from 3 major alleles (A, B, and O) of the ABO gene (OMIM: 110300). The ABO gene encodes a glycosyltransferase that catalyses the transfer of carbohydrates to the H antigen (FUT1; OMIM: 211100), forming the antigenic structures of the ABO phenotypes. The proteins were encoded by the A and B alleles of ABO catalyse the transfer of different carbohydrates onto the H antigen to form the A or B
Antigens. In the O blood group, the A and B antigens did not produce. The gene encoding ABO blood group was localised on human chromosome 9q34 [8]. The ABO antigens are highly expressed by some human cells and tissues including epithelia, platelets, vascular endothelia and neurons [9, 10]. There is a large body of evidence supporting the notion that ABO antigens are involved in the pathogenesis of various systemic multifactorial traits, including cancers, infectious, neurological and cardiovascular disorders [10-12].

It should be noted that although the exact mechanism of PE pathogenesis remains unknown, it seems that placenta plays the main role. Overall the pathogenesis consists of decreasing placental circulation which causes increasing maternal endothelial dysfunction all of which leads to clinical presentations of preeclampsia such as hypertension and protein urea [13]. It is reported that genes responsible for thrombophilia are associated with an increased risk of preeclampsia [14].

Over many years, studies have investigated the association between maternal ABO blood groups and risk of PE, although contradictory results have emerged [15-21]. Based on our knowledge there is no study in this filed from Iranian population. Therefore present study was carried out.

Material and Methods

Study design

The present case-control study was conducted at Hafez Hospital (Shiraz, Iran) by reviewing medical files for pregnant women. PE was defined as pregnancy-induced hypertension (systolic blood pressure > 140 mmHg and diastolic blood pressure > 90 mm Hg) plus significant proteinuria (repeatedly ≥ 0.3 g/l or ≥ 0.5 g/24 hours or dipstick ≥++; representing values ≥ 0.3 g/l) after 20 weeks of gestational age in an earlier normotensive woman. The controls were pregnant women presented for delivery, with blood pressure values < 139/89 mmHg and no proteinuria recorded during the antenatal visits or at the time of delivery. Women with a twin pregnancy were excluded from PE and control groups. This study included 331 women; 121 pregnant with PE and 210 normotensive pregnant women. The ABO and Rh phenotypes were determined by standard serology methods.

Because Iranian population is one of the most heterogeneous populations [22-24], we select our participants (patients and controls) from Persian (Caucasians) Muslims living in Shiraz (Fars Province, South-West Iran).

Statistical analysis

For the control group, the observed frequencies of the ABO phenotypes were assessed for Hardy-Weinberg equilibrium using the \( \chi^2 \) statistic [25]. To analyse differences between cases and controls, we used t-test (for continuous variables), logistic regression (for categorical variables). Using blood group O (for ABO blood groups) or Rh\(^{+} \) (for Rh blood groups) as a reference, odds ratios (ORs) and its 95% confidence intervals (95% CI) of PE risk were estimated from logistic regression analysis. Also, logistic regression models were used to ORs adjusted for potential confounding factors. Statistical analysis was performed using the Statistical Package for Social Sciences (SPSS Inc., Chicago, IL, USA; version 11.5). Values of P<0.05 were considered as statistically significant.

Results

Table 1 shows selected characteristics factors in study groups. There was significant difference between cases and control group for age (t = 4.7, df = 329, P < 0.001). It should be noted that there was no association between parity and PE (OR = 0.76, 95% CI: 0.48-1.20, P = 0.241).

Table 1: Selective characteristic and blood groups among healthy pregnant women controls and preeclamptic patients

| Characteristic Number | Controls 210 | Cases 121 | Results of comparison |
|-----------------------|--------------|-----------|-----------------------|
| Age (years)           | 27.4 ± 5.6*  | 30.5 ± 6.1| P = 0.001             |
| Systolic BP (mmHg)    | 109.9 ± 7.8  | 154.7 ± 17.4| P = 0.001             |
| Diastolic BP (mmHg)   | 71.2 ± 7.1   | 97.6 ± 9.5 | P = 0.001             |
| Parity                |              |           |                       |
| Nulliparity           | 110 (52.4 %) | 73 (60.3 %)| P = 0.282             |
| Other parities        | 95 (45.2 %)  | 48 (39.7 %)|                       |
| Missing               | 5 (2.4 %)    | 0         |                       |
| ABO blood groups      |              |           |                       |
| O                     | 93 (44.3 %)  | 61 (50.4 %)| P = 0.536             |
| A                     | 63 (30.0 %)  | 28 (23.1 %)|                       |
| B                     | 46 (21.9 %)  | 26 (21.5 %)|                       |
| AB                    | 8 (3.8 %)    | 6 (5.0 %) |                       |
| Rh Blood Groups       |              |           |                       |
| Rh\(^{+} \)           | 201 (95.7 %) | 112 (92.6 %)| P = 0.223             |
| Rh\(^{-} \)           | 9 (4.3 %)    | 9 (7.4 %) |                       |

* Expressed as mean ± standard deviation (SD).

Table 1 also shows the prevalence of the ABO and Rh phenotypes in PE patients and healthy control pregnant women. The phenotypic frequencies of the ABO were in accordance with Hardy–Weinberg equilibrium in control group (\( \chi^2 = 1.47, df = 1, P = 0.223 \)). Although the A (OR = 0.67, 95% CI = 0.39-1.17, P = 0.165), B (OR = 0.86, 95% CI = 0.48-1.53, P = 0.615) and AB (OR = 1.14, 95% CI = 0.37-3.45, P = 0.812) phenotypes showed lower risks compared with the O blood group, statistical analysis indicated that there was no significant association between ABO phenotypes and risk of PE. To further evaluate the possible influence of difference of age of participants
and parity between the patient and control groups, as two confounding factors on the relationship between ABO blood groups and risk of PE, multiple logistic regression analysis was used. After adjustment for age of participants and parity, the same result was revealed (Table 2). Our present finding of no association between ABO blood groups and risk of PE is consistent with some reports [16, 17]. It should be noted that some researchers find the significant association between ABO blood groups and risk of PE [15, 18-21, 27].

Table 2: Association between ABO and Rh blood groups and risk of preeclampsia

| Phenytopes         | Crude OR (95% CI) | Adjusted OR (95% CI) | P      |
|--------------------|------------------|----------------------|--------|
| ABO blood groups   | P                |                      |        |
| O                  | 1.0              | -                    | -      |
| A                  | 0.57 (0.39-0.81) | 0.57 (0.39-0.81)     | 0.012  |
| B                  | 0.78 (0.54-1.13) | 0.78 (0.54-1.13)     | 0.326  |
| AB                 | 1.14 (0.73-1.75) | 1.14 (0.73-1.75)     | 0.583  |
| Rh*                | 1.0              | -                    | -      |
| Rh                 | 1.0              | -                    | -      |

Adjusted ORs for the age of participants and parity. On the other hand, the Rh* phenotype showed the higher risk for PE compared with the Rh phenotype. However, the association was no significant (OR = 1.79, 95% CI = 0.69-4.65, P = 0.229). Adjusted OR for the age of participants and parity did not change the above-mentioned association (Table 2). This finding is not consistent with previous reports [19].

Discussion

It has been reported that the A [20], AB [15, 18, 19, 27] and O [21] blood groups were the risk factor for PE. It is suspected that PE may result from changes in ischaemic vascular function [26] which can be influenced by ABO blood groups [27]. It should be noted that previous studies exploring ABO blood groups in women with PE revealed a great controversy between published studies [15-21]. While some studies reported the associations of ABO blood groups with PE [15, 18-20, 27], other studies failed to reach similar conclusions [16, 17]. Previously it has been reported that several genetic polymorphisms showed dissimilar associations with multifactorial complex traits among different ethnic populations [28-32]. Finally, it should mention that small sample size in studies and ethnicity are potential sources of heterogeneity between studies.

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