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Original Article

The prevalence and clinical manifestations of IgA deficiency among blood donors at transfusion centers in Shiraz, Southern Iran

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Abstract: Background: IgA deficiency is the most common immunodeficiency disorder. Most affected individuals are asymptomatic, and since there are no routine diagnostic screening programs the prevalence of this disease has remained uncertain. Methods and materials: Seven thousand blood donors who attended Fars Blood Transfusion Center, from September 2017 to March 2018, were selected randomly, and their serum IgA levels were checked by Immunoturbidimetry method. Cases with IgA levels <10 mg/dL were considered as serum IgA deficient patients. Serum IgM and IgG levels of IgA deficient cases were measured to determine selective IgA deficiency. The prevalent clinical findings of IgA deficiency were also investigated. Results: Ten blood donors had selective IgA deficiency: 0.14% (CI 95%: 0.001, 0.002). All cases were male, with a mean age of 36.10±9.70 years. Investigating common clinical findings in the IgA deficient cases revealed the most prevalent symptoms were recurrent upper respiratory tract infections (50%) which were significantly higher in the study group compared to the control group (*P*-value =0.008) and allergic disorders (40%) with no statistical difference from the control cases. Conclusion: The prevalence of selective IgA deficiency (SIgAD) among blood donors at Fars Transfusion Center was 0.14%. The most common clinical finding among the patients with SIgAD was recurrent upper respiratory infections, followed by allergic diseases.

Keywords: Selective IgA deficiency, blood donors, transfusion center, immunodeficiency, blood transfusion

Introduction

Selective IgA deficiency (SIgAD) is the most common immunodeficiency disorder which is defined as a serum IgA level less than 10 mg/dl, with normal to elevated IgM and IgG levels, in people over four years of age. To diagnose a patient with selective IgA deficiency, secondary causes of hypogammaglobulinemia should be excluded [1].

Although most IgA deficient individuals are asymptomatic and might be found among blood bank donors, the most common disease presentation in symptomatic patients is recurrent infections, especially recurrent respiratory infections [2-4]. The disease is also assumed to be strongly associated with atopic diseases [5]. This condition is also associated with various autoimmune and collagen vascular diseases, probably due to their genetic predisposition to such conditions [6].

Anti-IgA antibodies can be directed against IgA1 and IgA2 and might be detected in IgA deficient individuals. Although most Anti-IgA antibodies are IgG1 in nature, they might also be of IgE isotype, which can cause type 1 hypersensitivity and anaphylactic reactions during a blood transfusion. The exact incidence of IgE antibodies against IgA in SIgAD is not clear, however, studies have reported an overall incidence of 9/6% to 44% [7, 8].

The prevalence of SIgA disorder is unknown mainly due to its asymptomatic nature and lack

of diagnostic screening programs. Studies conducted worldwide to evaluate the prevalence of SIgAD in the normal population and mostly in healthy blood donors have provided different results, most probably due to ethnic variability. The prevalence can be as low as 1:18500 in the Japanese, to 1:163 in the Spanish population. In Iran, a study performed in 2008 showed the prevalence of SIgAD to be 1:651 in healthy volunteer blood donors in Tehran [9].

In the present study, we aimed to determine the prevalence of SIgAD in healthy blood donors at Fars Blood Transfusion Center. Moreover, clinical findings and medical history in IgA deficient individuals, including recurrent infections, allergies, autoimmune, endocrine and Celiac diseases were evaluated and compared with other studies.

Methods and materials

This cross-sectional retrospective study was performed on 7000 blood donors who attended one of the main blood transfusion centers in Shiraz which is responsible for about 75% of the whole blood donations in Fars. Samples were collected over six months from September 2017 to March 2018. This study received the approval of Shiraz University of Medical Sciences Committee of Ethics on Biomedical Research by the code IR.SUMS.MED.REC.1396.s53.

Exclusion criteria

According to the blood transfusion center protocol, donors need to carry certain criteria to get accepted for blood donation, including: age between 18 and 60 years old, weight over 50 Kg, blood pressure lower than 180/100 mmHg and higher than 90/50 mmHg, Hemoglobin level more than 12 g/dL in women, and more than 13 g/dL in men. There are also special health conditions and medical disorders which cause temporary or permanent contraindication for blood donation. All blood donors go through history taking, physical examination, and blood pressure measurement by a general practitioner for determining blood donation eligibility, and exclusion of individuals with contraindication for blood donation.

Sampling

A volume of 9 milliliters of each blood sample was centrifuged and stored in 2-8°C to be analyzed for viral markers and blood group. IgA levels were checked by immunoturbidimetry method. Individuals with IgA levels lower than 10 mg/dl were considered IgA deficient. Results were reported by the identification code of each blood donor, and similar codes were excluded.

Evaluation of IgA deficient cases

Individuals with IgA levels <10 mg/dl were called and rechecked for IgA level to confirm SIgAD. To investigate the clinical findings of SIgAD, a questionnaire including the most common clinical findings of IgA deficiency was filled for each IgA deficient blood donor as well as for 40 blood donors with normal IgA levels, as the control group. Since all IgA deficient cases were male, the control group was also selected amongst males.

The clinical findings mentioned in the questionnaire were autoimmune, allergic and endocrine disorders, recurrent infections, Celiac disease along with history and family history of immunodeficiency disorders.

In addition, hypothyroidism and type 2 diabetes mellitus were assessed in those cases due to their reported association with SIgAD, which is assumed to be because of their autoimmune natures [10].

Statistical analysis

SPSS version 16.0 was used for statistical analysis and prevalence measurement. Chi-square and Fisher-exact tests were applied for comparison between two or more groups. *P* values less than 0.05 were considered to be statistically significant.

Results

Among the 7000 participants in the study, 6855 (97.92%) were male and 145 (2.07%) were female, ranging from 20 to 59 years of age (mean age 34.83±7.35). Ten (0.14%) participants (CI 95%: 0.0001, 0.0002) had serum IgA levels less than 10 mg/dL. All of them were male, aging between 28 to 55 years old (mean age 36.10±9.70). Five cases (0.07%) (CI 95%: 0.0001, 0.004) showed serum IgA levels less than 5 mg/dL which is the definition for severe SIgAD.

Table 1 summarizes the prevalent clinical findings in IgA deficient and control (non-IgA defi-

Table 1. The prevalence of abnormal clinical findings in healthy blood donors with SIgAD

group		IgA deficient (%)	Normal IgA (%)	*P*-value
Allergic disorder	No allergy	6 (60%)	34 (85%)	0.080
	Allergic rhinitis or asthma	4 (40%)	6 (15%)	
Endocrine disease	No disease	8 (80%)	33 (82.5%)	0.855
	Type 2 diabetes or hypothyroidism	2 (20%)	7 (17.5%)	
Recurrent respiratory tract infections	No recurrent respiratory infections	5 (50%)	35 (87.5%)	0.008
	Recurrent respiratory infections	5 (50%)	5 (12.5%)	
Aphthous lesions	No recurrent aphthous lesions	8 (80%)	37 (92.5%)	0.243
	Recurrent aphthous lesions	2 (20%)	3 (7.5%)	

Table 2. The prevalence of SIgAD in healthy blood donors in different studies

	IgA<10 mg/dL	IgA<5 mg/dL
Present study	1:7000 (0.14%)	1:1400 (0.07%)
Australia		1:422 (0.23%)
Canada		1:545 (0.18%)
England		1:875 (0.11%)
Spain		1:163 (0.61%)
Brazil		1:965 (0.10%)
The USA		1:328 (0.30%)
Nigeria	1:250 (0.4%)	
Japan	1:14840 (0.006%)	
China		1:4100 (0.024%)
Zahedan		1:3837 (0.026%)
Tehran		1:651 (0.15%)

cient) groups. Recurrent infections (6-10 times per year) were evaluated in both groups. Recurrent upper respiratory tract infections were detected in 50% of the subjects in the case group, and 12.5% of the control group; the difference was statistically significant (*P*-value =0.008). Repeated GI and urinary tract infections were not detected in either group. The prevalence of recurrent aphthous lesions (5-10 times per year) in the IgA deficient group was 20% and 7.5% in the control group which was not statistically significant (*P*-value =0.243). The prevalence of allergic disorders including asthma and allergic rhinitis, diagnosed according to ARIA criteria, was 40% in the IgA deficient group and 15% in the control group, with no statistically significant difference (*P*-value =0.080). The prevalence of endocrine diseases, including diabetes and hypothyroidism was 20% and 17.5% in the IgA deficiency and the control groups, respectively, with no significant statistical difference (*P*-value =0.855). None of the groups had a history or a family history of immunodeficiency disorders or autoimmune, malabsorption and celiac diseases.

Discussion

According to this study, the prevalence of SIgAD (IgA level <10 mg/dl) among healthy blood donors at Fars blood transfusion Center is 1:700 (0.14%). Also, the prevalence of severe SIgAD (IgA level <5 mg/dl) is 1:1400 (0.07%). All cases were male since 97.92% of the participants were male. This result may not represent the prevalence in the general population as there are limitations for blood donation. Firstly, 95% of the blood donors are male, so the gender distribution is not homogenous. Secondly, some medical conditions and diseases which may exist in IgA deficient individuals, have a contraindication for blood donation. So, the result of this research measured the prevalence of SIgAD in healthy and asymptomatic individuals. In a study conducted in Tehran the mean age of participants was 38.6±11, and 89.1% of the subjects were male [11]. Considering previous studies on healthy blood donors worldwide, the prevalence of SIgAD in the current investigation was lower compared to Europe, Canada, Australia, the United States of America, and Nigeria [12-17], but higher than other parts of Asia, including China and Japan [10-19], and relatively similar to the other regions of Iran [4, 9, 12-17, 19-26], as shown in **Table 2**.

The most common clinical finding of IgA deficient cases was repeated upper respiratory tract infections (50%), which were mild in all cases, meaning that they never lead to hospitalization. In a study conducted by *Feng et al.* in china, the most common clinical finding of SIgAD was recurrent respiratory infections in 50% of the study group which was similar to our

findings [22]. Also, another case-control study conducted by Jorgensen et al. viral respiratory tract infections were shown to be common [4].

The second most common clinical finding in IgA deficient individuals was allergic disorders (40%), including asthma, allergic rhinitis, or both. In a study by Janzi et al. conducted on Swedish cases, 33% of IgAD patients experienced food hypersensitivity at 4 years of age which was significantly higher than the normal population, however, no statistically significant association was observed between IgAD and asthma, eczema, or sensitization [27]. In another study by Erkocoglu et al. on Turkish cases, 45.7% of patients had at least one type of allergic diseases [28].

Since immunodeficiency, autoimmune and collagen vascular diseases have contraindications for blood donation, none of the cases of either group had these diseases. But in the study conducted by Erkocoglu et al., 17.3% of the patients had at least one type of autoimmune disorders, such as Celiac disease, or type 1 diabetes mellitus [28]. Overall, IgAD patients show a higher prevalence of autoimmunity and collagen vascular diseases for which we did not carry out any investigations [6].

Conclusion

The results of this study indicate that the prevalence of SIgAD in healthy and asymptomatic blood donors is low. However, although most IgA deficient individuals are asymptomatic, this condition might be associated with significant medical conditions and the patients might even develop anaphylactic reactions if they receive a blood transfusion. Therefore, it is important to consider measuring the IgA level of blood donors and blood recipients, especially those with common underlying diseases in selective IgA deficiency.

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Disclosure of conflict of interest

None.

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