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ORIGINAL: The Role of ABO and Rh Blood Groups in Tuberculosis: A 10-year Study in Mazandaran, Iran

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ABSTRACT

Background: Tuberculosis (TB) remains a major global health concern, especially in low- and middle-income countries. Some studies have suggested a possible link between blood groups and susceptibility to TB, but findings remain inconsistent. Given the limited evidence from Iran, particularly in Mazandaran province, this study aimed to investigate the possible association between ABO/Rh blood groups and TB.

Methods: This descriptive cross-sectional study aimed to examine the association between ABO and Rh blood groups and the prevalence of TB in Mazandaran province, Iran, over a ten-year period (2008-2018). A total of 420 TB patients were included, and their blood group data were compared with those of the general population in the region. Data were collected from patient records and confirmed through laboratory tests using the direct agglutination method. Statistical analysis was performed using SPSS software, with Chi-square and Fisher's exact tests employed to assess any significant associations.

Results: Among the TB patients, blood group O was the most common (41.18%), followed by A (28.33%), B (23.05%), and AB (7.38%). Rh-positive individuals comprised 91.43% of the sample. No significant association was observed between blood group and TB prevalence ($p>0.05$). The distribution of blood groups in the TB patients closely mirrored that of the general population. Additionally, no significant differences were found in the distribution of blood groups between pulmonary and extrapulmonary TB cases.

Conclusion: This study did not find any significant association between ABO/Rh blood groups and TB susceptibility in Mazandaran province. Thus, blood type is unlikely to represent a reliable risk factor for TB in this setting. Larger multi-center studies with more rigorous designs are recommended to confirm these findings and to explore other potential host-related determinants of TB.

Introduction

Tuberculosis (TB), caused by Mycobacterium tuberculosis, remains a leading cause of death from infectious diseases globally, second only to AIDS [1,2]. This disease disproportionately affects developing countries, which account for 90% of all cases [1]. Despite the availability of effective anti-tuberculosis drugs, TB remains a significant global challenge, with an estimated 9 million new cases and 1.5 million deaths reported annually [3]. 80% of the world's TB cases are reported in 22 countries, with Pakistan and Afghanistan being among the most important of these countries. In Iran, TB cases are reported in all provinces, but higher rates have been observed in Sistan and Baluchestan,

Golestan, Razavi Khorasan, Khuzestan, Hormozgan, Qom, Kermanshah, and Gilan provinces [4]. According to the 2015 World Health Organization (WHO) report, the incidence rate of tuberculosis in Iran was 21 per 100,000 people[3].

Today, researchers are striving to find tools to control the spread of this pandemic disease. One of the most powerful tools in controlling TB is identifying the risk factors for the disease. From a clinical perspective, identifying TB risk factors can help in recognizing individuals at higher risk, allowing for targeted interventions to prevent the disease. Socioeconomic conditions, HIV infection, diabetes, and immune system disorders are among the predisposing factors. One of the risk factors in human susceptibility to tuberculosis that requires further research is blood type [5, 6].

Blood group antigens are present on the surface of red blood cells and include dozens of types. The most important blood group antigens are the A and B antigens. Some individuals have the A antigen, some have the B antigen, some have both A and B antigens, and some have neither, which is known as blood type O. Thus, individuals are classified into blood groups A, B, AB, and O [7].

In 1940, Landsteiner, the discoverer of the main blood groups, along with his assistant Wiener, demonstrated that in addition to the A, B, and O blood groups, there is another system called Rh. Anyone who has the Rh factor on their red blood cells is Rh-positive, and those who do not are Rh-negative. About 85-90% of Iranians are Rh-positive, and the rest are Rh-negative [7] .

So far, studies have been conducted in various parts of the world to examine the role of blood groups in tuberculosis. For example, one study showed a relationship between genetic defects in RBCs, such as sickle cell anemia, and tuberculosis [5]. In another study by Saha, examining ABO and Rh blood groups in patients with pulmonary tuberculosis of different ethnicities (Chinese, Malaysian, Indian) showed no significant association between blood group and tuberculosis among Malaysians and Indians. However, Chinese individuals with blood group O demonstrated more resistance to the disease [8] .Some reports also indicate that Rh-negative individuals may be more susceptible to TB than Rh-positive individuals[9] .Despite these studies, there are still many contradictions regarding the relationship between blood groups and TB risk factors, and the potential or influencing mechanisms for this association have not yet been fully identified. In general, factors such as the ethnicity of patients, differences in the distribution of ABO genes across various populations, and the number of individuals studied may affect the determination of the relationship between blood group and tuberculosis. Therefore, further large-scale studies are needed to establish the link between Rh-ABO and tuberculosis. Given the aforementioned points, as well as the relatively high prevalence of TB and its associated complications, which sometimes lead to death and reduced quality of life, and the importance of identifying risk factors, this study was designed to assess the frequency of blood groups in patients with tuberculosis in Mazandaran province from 2008 to 2018. Considering the unique ethnic composition of Mazandaran and the potential influence of genetic background on blood group distribution, evaluating this association in the region could provide valuable insights and contribute to more effective healthcare planning efforts.

Material and Methods

This descriptive-cross-sectional study was conducted on patients with tuberculosis in Mazandaran province who had visited healthcare centers in the province between 2008 and 2018. The minimum required sample size was determined using the PASS software. Based on an odds ratio (OR) of 1.97 according to the Ganguly et al. study and a power of 80%, the minimum required sample size was 420 individuals. Inclusion criteria included patients with tuberculosis, residency in Mazandaran province, and complete medical records. Patients with underlying diseases or pulmonary conditions were

excluded from the study. For comparison between blood groups of TB patients and healthy individuals, data on blood groups of the general population residing in Mazandaran province were collected from the Ministry of Health's databases, healthcare centers, and the Iranian Blood Transfusion Organization.

For data collection, demographic information of patients, including age, gender, place of residence, blood group, and type of tuberculosis, was extracted from their medical records. The relevant data were recorded in a pre-designed checklist. Trained interviewers completed the questionnaires. In cases where the blood group of the patient was not specified, patients were contacted by phone, and after obtaining consent, they were asked to attend a healthcare center.

Blood group antigens on the surface of red blood cells were then evaluated using specific anti-A, anti-B, and anti-D antibodies obtained from the Iranian Blood Transfusion Organization through the standard direct agglutination method. ABO and Rh blood groups were determined. The procedure was as follows: the individual's middle finger was sterilized, and a small prick was made using a lancet. Three separate drops of blood were placed on a clean slide, and then a drop of anti-A serum was added to the first drop of blood, anti-B serum to the second, and anti-D serum to the third. Each blood drop was mixed with the adjacent serum using disposable mixing sticks and spread over a 7-10 cm area. Agglutination was observed within two minutes, and the results were recorded.

At the end of the study, the data from the information forms were extracted and categorized, and the prevalence of each blood group in patients with tuberculosis was determined. Finally, the extracted data were analyzed using descriptive statistics, including the mean and standard deviation for quantitative variables and frequency and percentage for qualitative variables. The Chi-square test, Fisher's exact test, and independent t-test were used for statistical analysis in SPSS version 20, with a significance level of 0.05.

Results

Based on the study conducted in Mazandaran Province, out of the 420 patients examined, 237 (56.42%) were men and 183 (43.57%) were women (Figure 1). Among the total patients, 409 (97.38%) were Iranian.

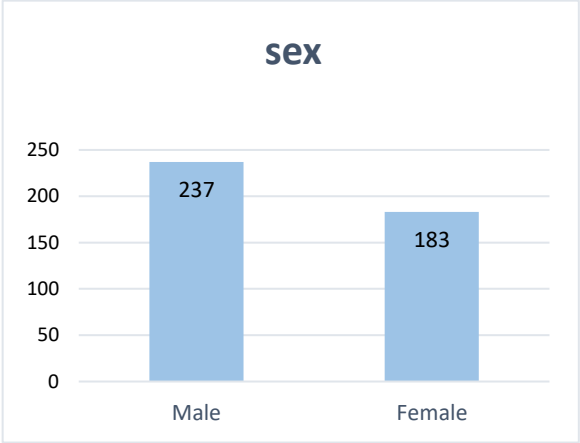

Figure 1. Distribution of tuberculosis cases by gender among patients presenting to healthcare centers in Mazandaran province.

The average age of men with tuberculosis was 46.6 ± 21 years, and for women, it was 45.7 ± 19 years. The distribution of patients based on age range is shown in the chart (Figure 2), indicating a significant relationship between age and tuberculosis ($p<0.05$).

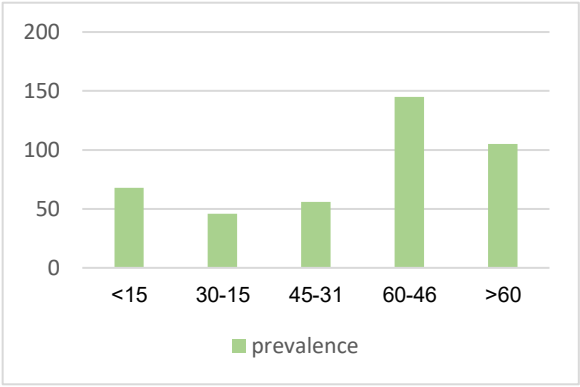

Figure 2 . Age distribution of tuberculosis cases among patients at healthcare centers in Mazandaran province.

Regarding blood types (ABO), 173 patients (41.18%) had blood group O, 119 patients (28.33%) had blood group A, 97 patients (23.05%) had blood group B, and 31 patients (7.38%) had blood group AB. In terms of Rh factor, 386 patients were Rh-positive and 34 were Rh-negative (Figure 3).

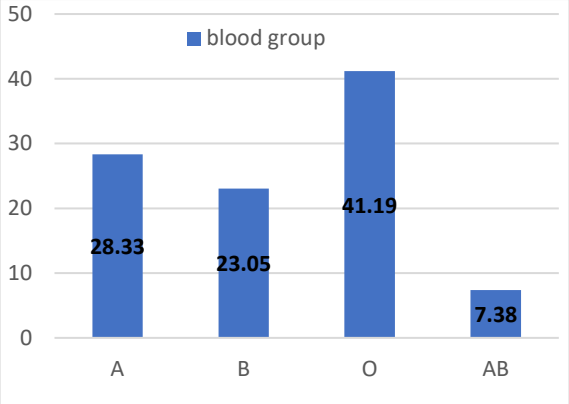

Figure 3. Frequency of tuberculosis infection by ABO blood type in patients at Mazandaran province health centers.

According to the data obtained from the blood transfusion organization, the distribution of blood groups in the general population is as follows: O (41.18%), A (28.33%), B (21.11%), and AB (7.34%), with Rh-positive at 89.67% and Rh-negative at 10.33%.

In this study, tuberculosis was reported more frequently in patients with blood group O compared to other blood groups. However, since blood group O is also more common in the general population of this region, no significant difference was observed (p>0.05) (Table 1).

Furthermore, the clinical characteristics of patients with tuberculosis were evaluated. The results showed that 376 patients (89.52%) had pulmonary tuberculosis, and 44 patients (10.47%) had extrapulmonary tuberculosis. When the patients with pulmonary and extrapulmonary tuberculosis were examined according to their ABO and Rh blood groups, the results indicated that both forms of tuberculosis occurred equally across different blood groups (p>0.05) (Table 2).

Table 1. Frequency of ABO blood groups in patients with pulmonary and extrapulmonary tuberculosis referring to health centers in Mazandaran province

	Pulmonary tuberculosis	Extrapulmonary tuberculosis	P-Value
O	42%	34%	P>0. 05
A	28%	29%	
B	23.4%	20.45%	
AB	6.3%	15.9%	

Table 2. Frequency of ABO blood groups in patients with pulmonary and extrapulmonary tuberculosis referring to health centers in Mazandaran province

Blood group	Pulmonary tuberculosis		Extrapulmonary tuberculosis		P-Value
	Frequency	Percentage	Frequency	Percentage	
RH+	347	93.15%	38	91.43%	P>0.05
RH-	29	6.85%	6	8.57%	
Total	367	100%	44	100%	

Discussion

In this study, the frequency of different blood groups, including the ABO blood group system and the Rh blood group system, among patients infected with Mycobacterium tuberculosis who had visited healthcare centers in Mazandaran province was investigated. A total of 420 patients were studied, and for comparison, 420 healthy individuals, matched for age, gender, and place of residence with the patient group, were also analyzed.

Of the patients analyzed in this study, 237 (56.42%) were male and 183 (43.57%) were female, which is consistent with other studies. In the study by Jafari and colleagues conducted in 2016, 238 tuberculosis patients were examined, showing that 150 were men and 148 were women. In some studies, the number of women infected with Mycobacterium tuberculosis has been higher than men. In the study by Farazi and colleagues in 2013, 241 cases of extrapulmonary tuberculosis were female and 192 were male, with a female-to-male ratio of 3 to 1.[10]

In the study by Valizadeh and colleagues in Shahriar, extrapulmonary tuberculosis was reported in 32.3% of cases, with a female-to-male ratio of 6 to 1, and the average age was 34 years for men and 37 years for women. The incidence of the disease was highest in the 31-40 age group. In most studies, the prevalence of Mycobacterium tuberculosis in women is lower than in men, which may be due to greater exposure of men to the causative agent [11].

Regarding different age groups, in this study, 68 individuals were under the age of 15, 46 were aged 15 to 30, 56 were aged 31 to 45,

145 were aged 46 to 60, and 105 were above 60 years old. In a similar study, Farazi and colleagues, who examined the prevalence of pulmonary tuberculosis in Markazi province, reported that 51.6% of the patients were over 55 years old[10].

The results of this study showed that among the patient group, regarding the ABO blood group system, 173 patients had blood group O, 119 had blood group A, 97 had blood group B, and 31 had blood group AB. Regarding the Rh system, 385 were Rh-positive, and 35 were Rh-negative. In comparison with the general population, based on a study conducted in Mazandaran province and data obtained from the blood transfusion organization, the blood groups O, A, B, and AB were reported to be 41.18%, 28.33%, 21.11%, and 7.4%, respectively, and Rh+ and Rh- were reported as 89.67% and 10.33%, respectively. No statistically significant difference was observed between the patient group and the general population. In a similar study by Tiwari and colleagues in 2015, the distribution of ABO and Rh blood groups in tuberculosis patients was examined. They reported that among the control group, most patients had blood group B positive, followed by O positive, whereas in the test group, the majority of patients had blood group B positive, followed by A positive and then O positive. However, no significant association between tuberculosis and Rh-ABO was observed[12].Although various researchers in studies conducted in different parts of India reported a significant association between chronic diseases like tuberculosis and the Rh-ABO system[13], no significant association was observed in this study.

Additionally, Rao and colleagues in 2012 examined the distribution of ABO blood groups and tuberculosis in India and observed a significant association between the prevalence of tuberculosis and blood groups B and AB, but no association was found between the prevalence of tuberculosis and blood groups A and O. A significant association between tuberculosis prevalence and Rh-positive in blood group A was observed, but no significant association was found between tuberculosis incidence and Rh-positive in blood groups B, AB, and O [13] .

In 1968, SAHA investigated the incidence of ABO and Rh blood groups in pulmonary tuberculosis among different ethnic groups (Chinese, Malaysian, Indian). The results of this study showed no significant difference between blood group and tuberculosis in Malaysian and Indian ethnicities, but Chinese individuals with blood group O showed more resistance to this disease[8] .In contrast to the recent study results, Ganguly and colleagues in 2016 examined the association between ABO blood group polymorphisms and tuberculosis in the Hindu Bengali population in southern Bengal, India, and found that individuals with non-O blood groups were 1.97 times more likely to develop tuberculosis than those with blood group O[14]. The results of recent studies provide contradictory information regarding the association between the blood group system and tuberculosis, indicating that more studies with larger sample sizes are needed to establish this association. Moreover, the results may vary across different ethnicities. Additionally, the diagnostic tests used to detect Mycobacterium tuberculosis have varied across different studies, and since different tests have different sensitivities, future studies should use more sensitive diagnostic methods, such as molecular techniques.

Conclusion

The present study aimed to investigate the association between blood groups and tuberculosis. Despite a thorough examination of the data and studied samples, no significant relationship was found between different blood groups and the risk of tuberculosis. These findings suggest that, contrary to some initial hypotheses, blood type cannot be considered a risk factor or predictor for this disease. It is recommended that future studies with larger sample sizes and in diverse populations be conducted to assess any other potential associations.

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Authorship
All authors contributed to the study's conception and design, conducted the literature review, and participated in drafting and critically revising the manuscript. All authors reviewed and approved the final version for submission.

Conflicts of interest
No potential conflict of interest relevant to this article was reported.

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