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Relationship of multiple myeloma with ABO blood groups

Multipl miyelomun ABO kan grupları ile ilişkisi

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ABSTRACT

Aim: Multiple myeloma is a heterogeneous, incurable haematological cancer that occurs as a result of the clonal proliferation of plasma cells. The impact of blood groups on human diseases and/or their role in the prognosis of the disease has attracted the attention of scientists since the discovery of blood groups. We investigated the blood group distribution of multiple myeloma patients and whether their blood groups are related to immunoglobulin type.

Materials and Methods: 75 multiple myeloma patients and 73128 control group were included in the study, which was planned retrospectively. The statistical evaluation was performed by using Statistical Package for Social Sciences (SPSS) software for Windows 20 (IBM SPSS Inc., Chicago, IL). The normal distribution of the data was evaluated with the Kolmogorov-Smirnov test.

Results: In multiple myeloma patients, the rate of A and B blood groups was low, and the rate of O and AB blood groups was high. Heavy chain IgA ratio was higher in B blood group compared to other blood groups. On the other hand, IgG ratio was found higher in O blood group compared to other blood groups.

Conclusion: A relationship has been found between immunoglobulin type and blood types in multiple myeloma. More comprehensive studies are needed on this subject.

Keywords: Multiple myeloma; ABO blood group; monoclonal gammopathy.

ÖZ

Amaç: *Multipl myelom plazma hücrelerinin klonal proliferasyonu sonucu oluşan, heterojen, kür sağlanamayan hematolojik bir kanserdir. Kan gruplarının insan hastalıklarına katkısı ve/veya hastalık seyrindeki rolü kan gruplarının keşfinden bu yana bilim insanlarının ilgisini çekmiştir. Multipl myelom hastalarının kan grubu dağılımını ve kan gruplarının immunglobulin tipi ile ilişkisinin olup olmadığını araştırdık.*

Gereç ve Yöntem: *Retrospektif planlanan çalışmaya 75 multipl myelom hastası ve 73128 kontrol grubu dahil edildi. İstatistiksel değerlendirme Statistical Package for Social Sciences (SPSS) for Windows 20 (IBM SPSS Inc., Chicago, IL) programı kullanılarak yapıldı. Verilerin normal dağılımı Kolmogorov-Smirnov testi ile değerlendirildi.*

Bulgular: *Multipl myelom hastalarında A ve B kan grupları oranı düşük, O ve AB kan grupları oranı yüksek saptandı. B kan grubunda ağır zincir IgA oranı diğer kan gruplarına kıyasla daha yüksek saptandı. IgG oranı ise O kan grubunda diğer kan gruplarına kıyasla daha yüksek saptandı.*

Sonuç: *Multipl myelomda immunoglobulin tipi ile kan grupları arasında bir ilişki bulunmuştur. Bu konuda yapılacak daha kapsamlı çalışmalara ihtiyaç vardır.*

Anahtar Sözcükler: *Multipl myelom, ABO kan grubu, monoklonal gammopati.*

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INTRODUCTION

Multiple myeloma (MM) is a heterogeneous, incurable haematological cancer that occurs as a result of the clonal proliferation of plasma cells (1). Various risk factors such as old age, male sex, positive family history, black race, and genetic factors increase the incidence of MM (2, 3).

Blood group antigens are found on the surface of many cells and tissues as well as erythrocytes. The impact of blood groups on human diseases and/or their role in the prognosis of the disease has attracted the attention of scientists since the discovery of blood groups. Contributions of ABO blood group system to human life have been investigated, in addition to the role of the ABO system in cardiovascular, infectious, and neoplastic diseases (4-9).

The connections of molecules such as sICAM, p-selectin, IL-6, which have been shown to have roles in cancer metastasis and/or development, with blood groups have been confirmed in many studies (10-12). There have also been studies showing that the correlation between MM and these molecules (13, 14). Based on this mechanism, we investigated the blood group distribution of MM patients and whether their blood groups are related to the type of MM.

MATERIALS and METHODS

75 multiple myeloma patients diagnosed with MM according to the International Myeloma Working Group (IMWG) diagnostic criteria (15) and control group with 73128 individuals were included in the study. The study was conducted as a single-centre and retrospective study with the approval of the ethics committee.

75 patients who were followed up in our clinic between September 2013 and December 2020 were retrospectively scanned using electronic database. Age, gender, blood type, type of multiple myeloma, heavy chain type, light chain type, presence of lytic lesions and laboratory findings, follow-up times, and prognosis of patients were recorded. The control group consisted of 73128 patients who did not have any malignant disease and who came to our hospital for any reason between 2018-2019. The blood groups of all patients were collected from the electronic database and the distribution of their blood group was determined.

We investigated the relationship between blood groups and MM by comparing the blood groups of the patients and the control group. We also examined whether blood groups in multiple myeloma patients are associated with the type of monoclonal immunoglobulin.

Statistical Analysis

The statistical evaluation was performed by using Statistical Package for Social Sciences (SPSS) software for Windows 20 (IBM SPSS Inc., Chicago, IL). The normal distribution of the data was evaluated with the Kolmogorov-Smirnov test. Numerical variables with normal distribution were presented as mean±standard deviation, while numerical variables that were not normally distributed were presented as median (minimum, maximum). Categorical variables are expressed as counts and percentages. Chi-square and Fisher's Exact Chi-Square test was performed to compare categorical data. ANOVA test was used for comparing normally distributed numerical variables among ABO groups. Kruskal Wallis H test was used to compare numerical variables that were not normally distributed. Cox regression analysis was used to evaluate risk factors associated with prognosis. Survival analysis according to blood groups was determined by Kaplan-Meier analysis.

RESULTS

The study population comprised 22 women (31.9%) and 47 men (68.1%), a total of 69 patients aged between 37-82 years (mean:64.0±10.9 years). Rates of blood types were determined as A blood type 34.8% (n: 24), B blood type 15.9% (n: 11), O blood type 40.6% and AB blood type 8.7% (n: 6). The distribution of blood groups of multiple myeloma patients compared to the blood groups of the control group is shown in (Table-1). As stated in the Table 1, the rate of A and B blood group is low in MM patients (34.8% and 40.0%; 15.9% and 18.4%; p = 0.005). The proportion of O and AB blood groups is high (40.6% and 34.8%; 8.7% and 6.8%; p = 0.005) in patients with MM.

The distribution of demographic characteristics according to blood groups was not significantly different (Table-2). IgA heavy chain ratio was higher in B blood group compared to other blood groups (A: 37.5%, B: 54.5%, 0: 21.4%, AB:0%; p=0.014). IgG ratio was higher in O blood group than other blood groups (A: 58.3%, B:36.4%,

0:60.7% and AB:33.3%; p = 0.014). Other clinical findings were not significantly different compared to blood groups (Table-2).

Between 2 and 103 months of follow-up, 29% of the patients died. Blood groups, demographic findings, and clinical findings did not correlate with mortality (Table-3).

Table-1. Distribution of blood groups of multiple myeloma patients.

ABO group	MM n=69	Control n=73128	p
A	24(34.8)	29210(40.0)	0.005*
B	11(15.9)	13439(18.4)	
O	28(40.6)	25540(34.8)	
AB	6(8.7)	4939(6.8)	

Categorical variables were presented as number (%).

* p <0.05 shows statistical significance.

Table-2. Distribution of demographic and clinical findings according to blood groups.

Clinical findings	Total n=68	A n=24	B n=11	0 n=28	AB n=6	p
Gender						
Female	22(31.9)	8(33.3)	3(27.3)	9(32.1)	2(33.3)	0.0999
Male	47(68.1)	16(66.7)	8(72.7)	19(67.9)	4(66.7)	
Age, years	63.0±11.0	60.7±12.0	62.5±9.8	63.0±10.7	71.3±7.2	0.207
Rh, n (%)						
Positive	62(89.9)	23(95.8)	10(90.9)	25(89.3)	4(66.7)	0.190
Negative	7(10.1)	1(4.2)	1(9.1)	3(10.7)	2(33.3)	
Diagnosis, n (%)						
MM	56(81.2)	20(83.3)	9(81.8)	22(78.6)	5(83.3)	0.964
MM+ Plasmacytoma	13(18.8)	4(16.7)	2(18.2)	6(21.4)	1(16.7)	
Heavy chain type, n (%)						
IgA	21(30.4)	9(37.5)	6(54.5)	6(21.4)	-	
IgG	37(53.6)	14(58.3)	4(36.4)	17(60.7)	2(33.3)	0.014*
Non-secretory	11(15.9)	1(4.2)	1(9.1)	5(17.9)	4(66.7)	
Light chain type, n (%)						
Kappa	48(69.6)	15(62.5)	9(81.8)	18(64.3)	6(100.0)	
Lambda	18(26.1)	9(37.5)	2(18.2)	7(25.0)	-	0.286
Non-secretory	3(4.3)	-	-	3(10.7)	-	
Lytic lesion, n (%)						
No	12(17.4)	5(20.8)	1(9.1)	4(14.3)	2(33.3)	0.554
Yes	57(82.6)	19(79.2)	10(90.9)	24(85.7)	4(66.7)	
Prognosis, n (%)						
Survived	49(71.0)	17(70.8)	8(72.7)	19(67.9)	5(83.3)	0.977
Died	20(29.0)	7(29.2)	3(27.3)	9(32.1)	1(16.7)	
Follow-up time (months)	17(2-103)	16(3-97)	14(4-103)	17(2-48)	36(11-48)	0.142

Numerical variables with normal distribution were shown as mean±standard deviation, whereas numeric variables that were not normally distributed were shown as median (minimum, maximum).

Categorical variables were presented as number (%).

* p <0.05 shows statistical significance.

Table-3. Relationship between demographic and clinical findings and mortality.

Clinical findings	Survival		Univariable Cox regresyon	
	Survived n=49	Died n=20	HR (%95 GA)	p
Gender				
Female	18(36.7)	4(20.0)	ref	
Male	31(63.3)	16(80.0)	3.21(0.93-11.08)	0.064
Age, years	61.3±11.1	66.6±9.6	1.03(0.98-1.08)	0.271
ABO group, n (%)				
A	17(34.7)	7(35.0)	ref	
B	8(16.3)	3(15.0)	0.48(0.10-2.38)	0.373
0	19(38.8)	9(45.0)	1.35(0.50-3.68)	0.558
AB	5(10.2)	1(5.0)	0.30(0.04-2.45)	0.258
Rh, n (%)				
Positive	43(87.8)	19(95.0)	ref	
Negative	6(12.2)	1(5.0)	0.64(0.08-4.89)	0.669
Diagnosis, n (%)				
MM	37(75.5)	19(95.0)	ref	
MM+ Plasmacytoma	12(24.5)	1(5.0)	0.26(0.04-1.97)	0.193
Heavy chain, n (%)				
IgA	15(30.6)	6(30.0)	ref	
IgG	25(51.0)	12(60.0)	0.71(0.26-1.95)	0.508
Non-secretory	9(18.4)	2(10.0)	0.32(0.06-1.64)	0.171
Light chain n (%)				
Kappa	34(69.4)	14(70.0)	ref	
Lambda	13(26.5)	5(25.0)	1.28(0.44-3.70)	0.65
Non-secretory	2(4.1)	1(5.0)	0.87(0.11-6.78)	0.9
Lytic lesion, n (%)				
No	8(16,3)	4(20.0)	ref	
Yes	41(83.7)	16(80.0)	0.76(0.25-2.28)	0.618
Follow-up time (months)	18(2-97)	15(3-103)	-	

Numerical variables with normal distribution were shown as mean±standard deviation, whereas numeric variables that were not normally distributed were shown as median (minimum, maximum).

Categorical variables were presented as number (%).

* p <0.05 shows statistical significance.

Abbreviations: ref: reference, HR: hazard ratio, CI: confidence interval

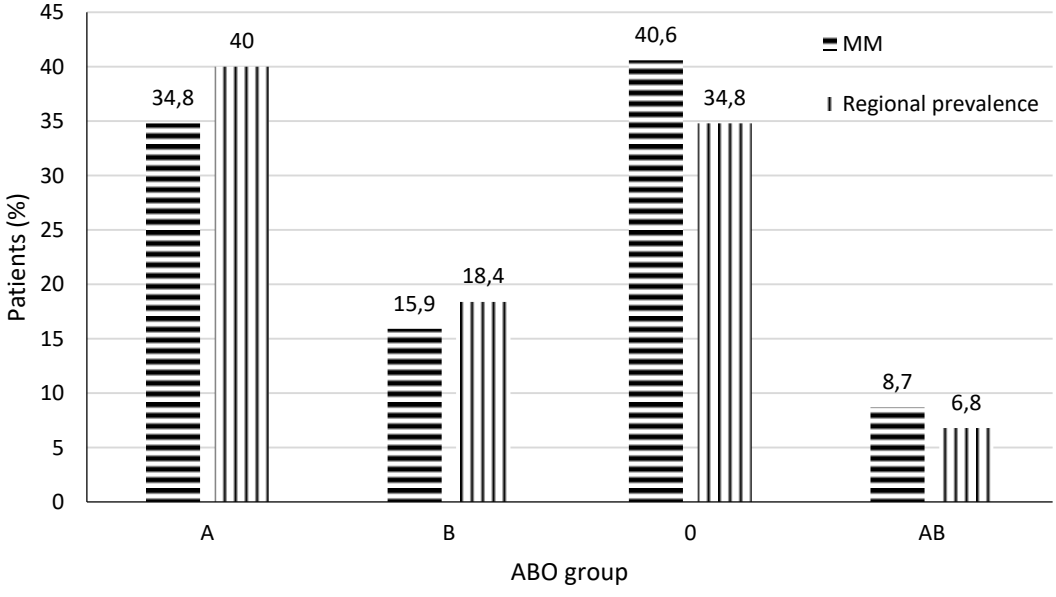

Figure-1. Distribution of blood groups.

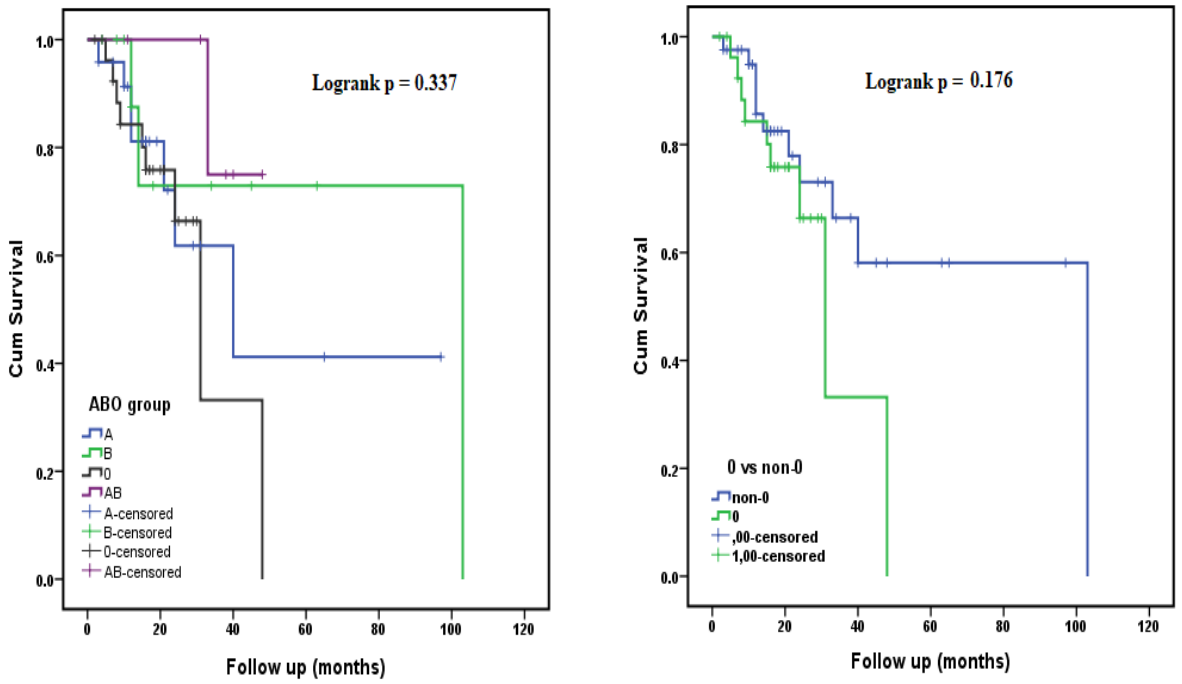

Figure-2. Overall survival curves of multiple myeloma patients according to blood groups AB0 group (A), and 0 versus non-0 group (B).

DISCUSSION

Environmental factors play an important role in the development of many types of cancer and other diseases (16, 17). Similarly, environmental factors determine the distribution of blood groups in that region (18, 19). Thereby, the results of studies investigating the relationship between diseases and blood groups are mostly inconsistent. Only two cancer studies have yielded consistent results among the studies on cancer and blood groups. The relation of the stomach and pancreatic cancer with blood groups is almost certain (20, 21).

Results are also contradictory in haematological cancer researches. Tavasolian F. et al. showed in their study that patients with AB blood group had a higher rate of acute lymphoblastic leukemia (ALL) (22). In one study, an increase in the rate of O blood group was demonstrated among female patients with acute leukemia (23). In contrast, Jackson et al. reported a decrease in the rate of O blood group among female patients with acute leukemia (24). In another study, they could not find a difference in the distribution of ABO blood group among patients with acute leukemia compared to the general population (25). In a recent study investigating the relationship between multiple myeloma and blood groups, they found that the frequency of O blood group in MM patients was significantly lower than in the normal population. In the same study, they determined that the O blood group was a predisposing factor for the development of extramedullary lesions and also showed that the O blood group was associated with more aggressive disease (26). In contrast to the previous study, the rate of A and B blood groups was low, and the rate of O and AB blood groups was high in MM patients in our study. A remarkable relationship was found between blood groups and immunoglobulin class. The proportion of IgA type multiple myeloma was found higher in B blood group compared to other blood groups, and IgG ratio was higher in O blood group compared to other blood groups. There was no relationship between blood types and life expectancy. With the fact that it is not known which mechanism plays a role in the relationship between blood groups and immunoglobulin class, it can be hypothesized that infectious agents and/or chemical agents play a role in this mechanism. The correlation between infectious agents and blood groups has been shown in many studies (27, 28, 29). IgA is involved in mucosal defence while IgG provides a long-lasting defence against infectious agents. Their chronic stimulation can lead to the clonal

evolution of plasma cells. Multiple myeloma is more common in farmer population. Farmers are chronically exposed to infectious agents, animals, and pesticides more than people in industrialized areas (30).

In haematological malignancies, the red blood cell antigen may undergo variation. The most common cause of ABO antigen variation is acute myelogenous leukemia (31, 32). There are two possible mechanisms for the weakening of ABO antigens in hematopoietic diseases. The first mechanism is the inactivation of A/B transferases and the second is the inactivation of H transferase (33-36). Loss of ABO antigens have also been demonstrated in multiple myeloma cases (32).

The relationship between integrins and von Willebrand factor (vWF) levels, which have been shown to play a role in cancer pathogenesis, with blood groups have been demonstrated in several studies (10, 37-40). Studies have shown that both vWF and intercellular adhesion factors play a role in multiple myeloma (41, 42).

We can associate the relationship between multiple myeloma and blood groups with infections, chromosomal abnormalities, integrins, and coagulation factors. However, the underlying mechanism is not yet clear, and extensive researches are needed on this topic.

Limitations

The limitations of our study are the small number of patients and short follow-up periods. Follow-up periods of the patients are not sufficient to indicate the effects of ABO blood group on MM prognosis.

Conflict of interest

There is no conflict of interest between the authors.

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