

# Blood Groups Distributions of Donors/Patients in a Tertiary Hospital

## Üçüncü Basamak Bir Hastanedeki Donör/Hastaların Kan Gruplarının Dağılımı

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### Abstract

|                             |   |
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| <b>Aim</b>                  | To demonstrate the distribution of ABO, and Rh blood groups in the blood, and blood products donated by volunteered blood donors living in a city in Turkey. ( <b>Sakarya Med J 2018, 8(4):753-758</b> )  |
| <b>Material and Methods</b> | Data of blood, and blood products donated by 13116 volunteered blood donors who admitted to our hospital between January 2009, and September 2013 were retrospectively analyzed. Blood typing was performed with EDTA-added blood samples using tube agglutination method, and gel card agglutination techniques in an automated blood grouping device.   |
| <b>Results</b>              | According to our results distribution of blood groups among our study participants was as follows:0 Rh(+) 30.2%; 0 Rh(-) 5.6%; A Rh(+) , 38.1%; A Rh(-), 6.2%; B Rh(+),10.5%; B Rh(-), 2.1%; AB Rh(+), 6.2%, and AB Rh(-), 1.3% . In our study blood typing results without considering Rh factor were detected in respective percentages of patients were as follows: A ,44.3%; 0, 35.7%; B, 12.5%, and AB, 7.5%. Rates of Rh (+) (84.9%), and Rh (-) (15.1%) were also calculated as indicated. |
| <b>Conclusion</b>           | Generally, in compliance with data in Turkey, in our study blood group A had a markedly higher while rates of blood groups B, and AB had the lowest incidence rates. We think that this study will contribute to the establishment of databank of Distribution of Blood Groups in Turkey.   |
| <b>Keywords</b>             | Blood; Blood Groups; Blood Donor; Blood Transfusion.  |

### Öz

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|--------------------------|--|
| <b>Amaç</b>              | Türkiye'de bir ilde yaşayan gönüllü kan bağışçılar tarafından bağışlanan kan ve kan ürünleri ile ABO ve Rh kan gruplarının dağılımını göstermek. ( <b>Sakarya Tıp Dergisi 2018, 8(4):753-758</b> ).  |
| <b>Gereç ve Yöntem</b>   | Ocak 2009 ve Eylül 2013 tarihleri arasında hastanemize başvuran 13116 gönüllü kan bağışçısı tarafından bağışlanan kan ve kan ürünleri verileri retrospektif olarak incelendi. Kan grupları, EDTA katkılı kan örnekleri ile tüp aglütinasyon yöntemi ve jel kart aglütinasyon teknikleri kullanılarak otomatik olarak gerçekleştirildi.   |
| <b>Bulgular</b>          | Sonuçlarımızın göre çalışma grubumuzdaki kan gruplarının dağılımı şu şekildedir: 0 Rh (+) % 30.2; 0 Rh (-) % 5.6; A Rh (+) % 38.1; A Rh (-) % 6.2; B Rh (+) % 10.5; B Rh (-) % 2.1; AB Rh (+) % 6.2 ve AB Rh (-) % 1.3. Çalışmamızda, Rh faktörü göz önüne alınmadan, kan faktörü sonuçları göz önüne alındığında hastaların aşağıdaki yüzdelerde olduğu tespit edilmiştir: A, % 44.3; 0, % 35.7; B, % 12.5 ve AB, % 7.5. Rh (+) (% 84.9) ve Rh (-) (% 15.1) oranları da belirtildiği gibi hesaplandı. |
| <b>Sonuç</b>             | Genel olarak, ülkemizdeki verilerle karşılaştırıldığında çalışmamızda A kan grubu belirgin olarak daha yüksek iken, B ve AB grupları en düşük insidans oranlarına sahipti. Bu çalışmanın Türkiye'de Kan Grupları Dağılımı Veritabanı'nın oluşturulmasına katkı sağlayacağını düşünüyoruz.  |
| <b>Anahtar Kelimeler</b> | Kan; Kan Grupları; Kan Donörü; Kan Transfüzyonu.   |

## Introduction

The preliminary studies concerning blood groups were started by Landois in the year 1875.<sup>1</sup> In the year 1937, Landsteiner and Wiener, experimented with serum of a rabbit immunized with erythrocytes of a *Macacus rhesus* monkey, and discovered Rh factor that agglutinated erythrocytes of 85% of Caucasian population.<sup>1</sup> Antigens of this system with carbohydrate structure are also found on the surface of vascular epithelial cells, intestinal, cervical, and mammary gland epithelial cells, apart from erythrocytes. Presently, a total of 30 blood group systems have been determined by International Society of Blood Transfusion.<sup>2</sup>

Clinically two important blood group systems namely ABO, and Rh systems are being used. According to ABO group system, blood groups are divided into A, B, AB, and 0 groups. In the transfusion practice, important blood group antigens other than ABO group are formed by Rh (Rhesus) system. The strongest antigen of Rh system having a protein structure is antigen D. Generally, rates of Rh D positivity changes between 85 and 90 %. Distribution of ABO and Rh demonstrates differences between countries, and regions.<sup>3</sup> Determination of blood groups among different groups of population is important in patient care, and blood transfusion.

Nowadays, every blood center, routinely analyzes ABO, and Rh systems before transfusion as a compatibility panel. In this study our aim was to demonstrate the distribution of ABO, and Rh blood groups in the blood, and blood products donated by volunteered blood donors living in Sakarya Province in Turkey. Besides, this study was performed with the thought of making contribution to the creation of a database for blood groups.

## Materials and Methods

**Study design:** The approval of the local institutional review board was provided before this descriptive study (050.01.04/55). Data of blood, and blood products donated by 13116 volunteered blood donors who presented to Sakarya University between January 2009, and September 2013 were retrospectively analyzed.

Blood typing was performed with EDTA-added blood samples using tube agglutination method, and gel card agglutination techniques in an automated blood grouping device.

The data for the study was presented using descriptive statistics

## Results

Distribution of blood, and blood products prepared in our center among blood groups within years is shown in Table 1. According to our results distribution of blood groups among our study participants was as follows: 0 Rh(+) 30.2%; 0 Rh(-) 5.6%; A Rh(+) , 38.1%; A Rh(-), 6.2%; B Rh(+),10.5%; B Rh(-), 2.1%; AB Rh(+), 6.2%, and AB Rh(-), 1.3% . In our study blood typing results without considering Rh factor were detected in respective percentages of patients were as follows: A ,44.3%; 0, 35.7%; B, 12.5%, and AB, 7.5%. Rates of Rh (+) (84.9%), and Rh (-) (15.1%) were also calculated as indicated.

The results of various relevant studies performed in our country, and in the world are shown in Table 2 and Table 3, respectively.<sup>3-32</sup>.

**Table 1. Distribution of blood, and blood products processed in our center according to blood groups between the years 2009, and 2012.**

|         | Years |      |      |      | Total        |                 |
|---------|-------|------|------|------|--------------|-----------------|
|         | 2009  | 2010 | 2011 | 2012 |              |                 |
| A Rh +  | 1484  | 2142 | 989  | 376  | 4991 (38.1%) | 5803<br>(44.3%) |
| A Rh -  | 240   | 328  | 138  | 106  | 812 (6.2%)   |                 |
| B Rh +  | 404   | 677  | 253  | 38   | 1372 (10.5%) | 1643<br>(12.5%) |
| B Rh -  | 72    | 85   | 85   | 29   | 271 (2.1%)   |                 |
| AB Rh + | 199   | 381  | 158  | 69   | 807 (6.2%)   | 974 (7.5%)      |
| AB Rh - | 51    | 53   | 43   | 20   | 167 (1.3%)   |                 |
| O Rh +  | 1254  | 1851 | 637  | 222  | 3964 (30.2%) | 4696<br>(35.7%) |
| O Rh -  | 211   | 264  | 160  | 97   | 732 (5.6%)   |                 |
| Total   | 3915  | 5781 | 2463 | 957  | 13116        |                 |

**Table 2. Distribution of blood groups O, A, B, AB and Rh in Turkey (%).**

|                                     | O     | A     | B     | AB   | Rh+   | Rh-   |
|-------------------------------------|-------|-------|-------|------|-------|-------|
| Ankara <sup>6</sup>                 | 32.24 | 44.62 | 15.45 | 7.69 | 88.13 | 11.87 |
| Denizli <sup>7</sup>                | 33.30 | 42.6  | 16.8  | 7.4  | 89.9  | 10.1  |
| Diyarbakır <sup>8</sup>             | 33.7  | 40.8  | 18.5  | 7    | 89.2  | 10.8  |
| Edirne <sup>9</sup>                 | 30.93 | 46.55 | 15.99 | 6.53 | 87.79 | 12.21 |
| Eskişehir <sup>10</sup>             | 31.1  | 41.91 | 16.85 | 8.5  | 86.65 | 13.31 |
| Gaziantep <sup>11</sup>             | 35.09 | 40.01 | 18.1  | 6.09 | 90.83 | 9.17  |
| Kayseri <sup>12</sup>               | 33.3  | 44    | 16.2  | 6.5  | 88.2  | 11.8  |
| Kırklareli <sup>5</sup>             | 33.05 | 44.99 | 15.04 | 6.92 | 87.6  | 12.4  |
| Konya <sup>13</sup>                 | 32.21 | 45.06 | 16.63 | 7.69 | 87.4  | 12.6  |
| İstanbul <sup>14</sup>              | 30.80 | 44.80 | 15.90 | 8.10 | 87.2  | 12.8  |
| Malatya <sup>15</sup>               | 37.23 | 41.21 | 14.99 | 6.56 | 89.3  | 10.7  |
| Şanlıurfa <sup>16</sup>             | 34.7  | 36.4  | 21.3  | 7.7  | 90.8  | 9.2   |
| Tekirdağ <sup>5</sup>               | 31.73 | 44.85 | 15.49 | 7.93 | 87.83 | 12.17 |
| Rize <sup>17</sup>                  | 44.07 | 44.07 | 9.26  | 2.6  | 83.7  | 16.3  |
| Van <sup>18</sup>                   | 30.65 | 45.05 | 16.14 | 8.16 | 90.4  | 8.6   |
| Anatolia <sup>4</sup>               | 33.01 | 43.31 | 15.90 | 7.54 |       |       |
| Eastern Anatolia <sup>19</sup>      | 32.25 | 42.25 | 17.23 | 7.97 | 88.36 | 11.64 |
| Southeastern Anatolia <sup>16</sup> | 35.08 | 38.42 | 18.30 | 8.2  | 91.97 | 8.21  |
| Turkey <sup>20</sup>                | 32.67 | 42.84 | 16.46 | 8.03 | 88.54 | 11.46 |

**Table 3. Distribution of blood groups O, A, B, AB and Rh in some countries (%).**

|                               | O     | A     | B     | AB   | Rh+ | Rh- |
|-------------------------------|-------|-------|-------|------|-----|-----|
| USA - caucasians <sup>3</sup> | 45.0  | 36.90 | 13,0  | 5.1  |     |     |
| USA - black race <sup>3</sup> | 49.30 | 37.2  | 20.0  | 3.5  |     |     |
| Germany <sup>21</sup>         | 41    | 41    | 11    | 5    | 85  | 15  |
| Bulgaria <sup>6</sup>         | 35.80 | 39.97 | 16.84 | 7.6  |     |     |
| India <sup>22</sup>           | 32.37 | 21.91 | 36.51 | 9.19 | 94  |     |
| England <sup>23</sup>         | 46.63 | 41.78 | 8.56  | 3.04 | 83  | 17  |
| Iran <sup>24</sup>            | 35    | 33    | 23    | 9    |     |     |
| Iraq <sup>3</sup>             | 36    | 30    | 26    | 8    |     |     |
| North Cyprus <sup>26</sup>    | 32.45 | 44.22 | 13.80 | 6.09 |     |     |
| South Cyprus <sup>21</sup>    | 35.36 | 46.36 | 12.25 | 6.05 |     |     |
| Nigeria <sup>28</sup>         | 53.3  | 25.3  | 16.7  | 2.7  | 94  | 6   |
| Pakistan <sup>29</sup>        | 35    | 23    | 33    | 8    |     |     |
| Sauid Arabia <sup>30</sup>    | 56.3  | 33.4  | 26    | 3.8  | 91  | 9   |
| Turkey <sup>19</sup>          | 32.67 | 42.84 | 16.46 | 8.03 |     |     |
| Yugoslavia <sup>3</sup>       | 33.48 | 42.81 | 17.07 | 6.63 |     |     |
| Greece <sup>31</sup>          | 35.80 | 39.97 | 16.84 | 7.6  |     |     |
| World <sup>32</sup>           | 47.0  | 41.0  | 9.0   | 3.0  |     |     |

### Discussion

In this study our aim was to demonstrate the distribution of AOB, and Rh group blood, and blood products donated by volunteered blood donors in Sakarya Province Turkey. According to our findings the most frequently encountered blood groups in order of decreasing frequency were as follows: A Rh(+), O Rh(+), B Rh(+), AB Rh(+), A Rh(-), O Rh(-), B Rh(-), and AB Rh(-) . In our study, groups A (44.3%), O (35.7%), B (12.5%), AB (7.5%) were detected in respective percentages of study participants.

Identification of ABO blood group antigens in the year 1901, is the most important advancement for safe blood transfusion procedures.<sup>1</sup> At the time being, hereditary transmission mechanism of ABO (on chromosome 9), and Rh (on chromosome 1) genes are best known among other human genes. Blood groups carry utmost importance both in clinical, and transfusion medicine Blood groups, and various blood factors in the population in question should be known so as to perform compatible blood transfusions, and tissue transplantations, and to demonstrate the relationships between blood groups, and various diseases. In our study, similar to the distribution of blood groups in Turkey, blood group A was the most prevalent blood group, followed by blood group O. Overall Turkey incidence rates of blood groups A, and O were reported as 36.02 - 45.06%, and 30.7 - 44.07%, respectively. For the Sakarya Province the corresponding rates are 44.3, and 35.7%, respectively. Blood group B is seen in 9.26 - 21.03 % of the Turkish population. For Sakarya Province the corresponding rate is 12.5%. The incidence of blood group AB for Turkey in general ranges between 6.09, and 8.5%, for Sakarya Province its incidence was determined as

7.5 percent. Rh+, and Rh- blood groups are seen in 83.7 - 91.97 %, and 8.21 - 13.31% of the Turkish population, respectively. The corresponding rates for Sakarya Province are 84.9, and 15.1%. Results of our study, and results of previous studies performed in various regions of our country were mostly comparable.

Overall our country distribution of blood groups of A, O, B, AB, and Rh+ were detected as 42.84, 32.67, 16.46, and 8.03, and 88.54 %, respectively.<sup>4</sup> Kızılay (Red Crescent) blood bank reported incidence rates of blood groups in the year 2012 based on blood, and blood products donated by donors as follows: A, 42%; O, 34%; B, 17%; AB, 7 %, Rh (+), 88%, and, Rh(-), 12%.<sup>5</sup>

Based on the analysis of regional distribution of blood groups all over Turkey, blood groups O, and A had the highest incidence in Rize, and their lowest incidence was seen in Tekirdağ, Edirne, and Istanbul. Distribution of blood group A in Sanliurfa region was much below the average rate determined for Turkey in general, while blood group B in Sanliurfa region was detected at a higher than the average incidence of Turkey.<sup>16</sup> In the regions of Western Turkey, blood group A is more frequently seen, while in the Southeast Anatolia its incidence decreases. According to these results regional differences in the distribution of blood groups in Turkey are seen. This condition may be due to immigrations, ethnic structure of these regions, and geographical characteristics.<sup>1-4</sup> Though distribution of blood groups vary slightly between regions of our country, ABO, and Rh blood group profiles demonstrate great differences due to ethnic, and racial diversities between countries. For example, blood group B is very prevalent in the population of India, and Lao, while blood groups O, and A are more widespread in Europe, America, and Southeast Asia.<sup>23-25</sup> Nearly 85%, and 15% of white people are Rh(+), and Rh(-), respectively. Rh (+) is seen in 95% of Indians, and Black population of USA, while it is observed in 100% of African black population.<sup>30,31</sup> Limitation of our study include the retrospective design and relatively small number of our series. Due to these restrictions, associations should be interpreted with caution.

### **Conclusion**

In conclusion, this study conveys importance in that any other study in the literature has not studied the distribution of ABO, and Rh blood groups in Sakarya Province of Turkey. Generally, in compliance with data in Turkey, in our study blood group A had a markedly higher while rates of blood groups B, and AB had the lowest incidence rates. We think that this study will contribute to the establishment of databank of Distribution of Blood Groups in Turkey.

1. Giblett ER: Genetic Markers in Human Blood, Black well Sci Publ, pp. 317-320, 1969.
2. International Society of Blood Transfusion (ISBT). "Table of blood group systems". Oct 2008, <http://ibgri.blood.co.uk/ibst>
3. Mourant AE, Kopec AC, Damaniewsta-Sobczak K. North-hermand central Europe. In: Distribution of human blood groups and other polymorphism. 2nd ed. Pp.62-9 Oxford University Press; 1976.
4. Büyükyüksel C. ABO and Rh (D) blood groups in the Turkish population. Rev Fr Transfus. 1973;16:403-10. [http://www.kanver.org/kan\\_2012.pdf](http://www.kanver.org/kan_2012.pdf)
5. Ergün A, Yardımcı S. Türkiye Genelinde ABO Kan Grupları ve Rh Faktörünün Dağılımı. Ankara Üniversitesi Tıp Fakültesi Mecmuası. 1993;527-533.
6. Balcı YI, Ovet G, Covut IE, Goncu F, Yılmaz F: ABO and Rh blood groups frequency in Denizli province. UHOD .2010;20:103-105.
7. Temiz H, Altıntaş A, Gül K: Distrubition of ABO and Rh blood groups in Diyarbakır. UHOD. 2008;4: 235-237.
8. Çobancı N. Trakya yöresinde ABO ve Rh kan gruplarının dağılımı ve genetik analizleri. Yüksek Lisans Tezi. Trakya Ün. Fen Bilimleri Enstitüsü, 1998;40-45.
9. Gezer S, Akgün N, Akın A, Işık A: Eskişehir bölgesinde ABO kan gruplarının sıklığı. Çocuk Sag Hast Derg. 1987;30:227-228.
10. Coşkun Y: Gaziantep bölgesinde ABO ve Rh Kan gruplarının dağılımı. Gaziantep Üni Tıp Fak Derg. 1990;1:13-15.
11. Torun AY, Kaynar LG, Karakükcü Ç, Yay M, Kurnaz F, Mutlu H, Çetin M, Eser B. ABO and Rh Blood Group distribution in Kayseri province. Turkey Turk J Hematol. 2012;29:97-98.
12. Çalışkan Ü, Yavuz H, Koç H, Odabaş D. Konya bölgesinde ABO ve Rh kan gruplarının sıklığı. Selçuk Ün Tıp Fak. Derg. 1989;5:128-129.
13. Gül M, Sucu Rİ, Uyar T. Şişli Etfal Eğitim ve Araştırma hastanesi kan merkezi kan donörlerinin ABO ve Rh kan gruplarına göre dağılımları. KSÜ Tıp Fak Derg. 2005;2:42-44.
14. Kuku İ, Kaya E, Erkurt MA, Dikilitaş M, Yıldız R, Orhan M, Görgel A, Aydoğdu İ. Malatya ve çevresi ABO ve Rh kan grubu dağılımı. İnönü Üniversitesi Tıp Fakültesi Dergisi. 2004;11:213-215.
15. Zerir M, Karakılıç AZ, Nazlıgül Y. Şanlıurfa bölgesinde ABO ve Rh kan gruplarının dağılımı. Harran Tıp Fak Der. 2004;1:15-17.
16. Özkasap S, Dereci S, Şahin K, Dilek RA, Kalyoncuoğlu E, Zengin T, Özata B. Analysis of ABO and Rh blood groups distribution in East Karadeniz region of Turkey. Dicle Med J. 2013;40:100-104.
17. Çiftçi İ. H, Önder E, Bozkurt H, Güdücüoğlu H, Körkoca H, M. Kurtoglu G. Van ilinde kan gruplarının dağılımı. Van Tıp Derg. 2004;11:22-24.
18. Yakıncı C, Durmaz Y, Şahin S, Karabiber H, Kayan Z, Turan F. Malatya yöresinde ABO ve Rh kan gruplarının dağılımı. Turgut Özal Tıp Merkezi Derg. 1995;2:277-279.
19. Akbay T, Demiröz P, Güney Ç, et al. Türkiye'de kan gruplarının coğrafi bölgelere göre dağılımı. GATA Bül. 1989;31:391-402.
20. Pelzer U, Klein F, Bahra M, Sinn M, Dörken B, Neuhaus P, Meyer O, Riess H. Blood group determinates incidence for pancreatic cancer in Germany. Front Physiol. 2013;24:118.
21. Agarwal N, Thapliyal RM, Chatterjee K. Blood group phenotype frequencies in blood donors from a tertiary care hospital in North India. Blood Res. 2013;48:51-54. <http://www.blood.co.uk/about-blood/blood-group-basics/>
22. Boskabady MH, Shademan A, Ghamami G, Mazloom R. Distribution of blood groups among population of the ty of Mashhad (North Eastof Iran). Pak J Med Sci Q. 2005;21:194-198.
23. Atun IH, Hacıbulgur M. Kıbrıs Türklerinde ve komşu ülkelerde kan grupları. Mikrobiyoloji Bülteni. 1979;210-214.
24. Adeyemo OA, Soboyejo OB. Frequency distribution Of ABO, RH blood groups and blood genotypes among the cell biology and genetics students of University of Lagos, Nigeria. Afr. J. Biotechnol. 2006;5:2062-2065.
25. Ali N, Anwar M, Bhalti FA, Nadeem M, Nadeem A, Ali M. Frequency of ABO and Rh blood groups in major ethnic groups and casts of Pakistan.Pakistan J. Med. Sci.2005;21:26-29.
26. Sarhan MA, Saleh KA, Bin-Dajem SM. Distribution of ABO blood groups and rhesus factor in South west Saudi Arabia. Saud iMed J. 2009;30:116-119.
27. Lialiaris T, Digkas E, Kareli D, Poulliliou S, Asimakopoulos B, Pagonopoulou O, Simopoulou M: Distribution of ABO and Rh blood groups in Greece: An update. Int J Immunogenet. 2011;38:1-5.
28. Garratty G, Glynn SA, Mc Entire R. ABO and Rh(D) phenotype frequencies of differentracial/ethnic groups in the United States. Transfusion. 2004;44:703-706.
29. Hamed CT, Bollahi MA, Abdelhamid I, MedMahmoud MA, Ba B, Ghaber S, Habti N, Houmeida A. Frequencies and ethnic distribution of ABO and Rh(D) blood groups in Mauritania: results of first nation wide study. Int J Immunogenet. 2012;39:151-154.
30. Guyton AC, Hall JE. Blood Types; Transfusion; Tissue and Organ Transplantation. In: Guyton AC, Hall JE. Textbook of Medical Physiology. ss. 452-3 Eleventh Edition, Philadelphia, 2006.