



# A Retrospective Study: ABO and Rh Phenotype Blood Group Distribution Amongst Different Types of Craniosynostosis Patients

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## Abstract

**Background:** Craniosynostosis refers to the premature fusion of cranial sutures. Premature closure can impair brain development and cognitive problems. Only available treatment of craniosynostosis is through surgical intervention which is associated with excessive blood loss.

**Objectives:** In this study, we investigate the prevalence of each ABO/Rh blood group amongst patients with different types of craniosynostosis.

**Methods:** We included 163 patients, under craniosynostosis treatment, in Imam Hossein children's hospital at Isfahan, Iran. A retrospective analysis was performed and the frequency of blood groups as well as types of craniosynostosis were reported. Moreover, the connection between ABO/Rh blood groups and the types of craniosynostosis was examined by chi-square test.

**Results:** Of 163 cases reviewed; The majority of participants had blood group A positive (32.5%), followed by O positive (31.3%). The rest of the blood groups were reported in order: B positive (22.1%), B negative (4.9%), AB positive (4.3%), O negative (2.5%), A negative (1.8%), AB negative (0.6%). Also, the most common type of craniosynostosis was metopic (27%) and the other types were pansynostosis (23.9%), sagittal (21.5%), coronal (16.6%), multisuture (10.4%) and lambdoid (0.6%) respectively. Due to connection between ABO/Rh blood groups and the types of craniosynostosis, no significant relationship was observed.

**Conclusion:** Based on the results of the present study, it was found that the frequency of ABO blood groups in children with craniosynostosis can be different from the population of the same area. Also, the ratio of different types of craniosynostosis was different from previous data.

**Keywords:** Craniosynostosis, Blood Groups, ABO/Rh

## 1. Background

Craniosynostosis is the premature fusion of calvarial bones in one or more cranial sutures, leading to an abnormal head shape.<sup>1,2</sup> Craniosynostosis is a common malformation that occurs in about 1 in 2000 to 2500 live births.<sup>2</sup> Premature closure of cranial sutures could happen anywhere; however, the most common site is the sagittal suture, which accounts for 56% of cases. In 13% of children with craniosynostosis, more than one suture is involved, causing an increased risk for the complications to happen.<sup>3,4</sup> The exact mechanism for premature closure of cranial sutures is unknown. However, mutations in specific genes have been identified in most of the patients. Mutations in fibroblast growth factor receptor, Twist-related protein 1, and ephrin-B1 (encoded by EFNB1) have been detected in patients with syndromic or non-syndromic craniosynostosis.<sup>5,6</sup> Many complications are associated with craniosynostosis, including increased intracranial pressure (ICP), inhibition of normal brain growth, and

impairments in cognitive and neurodevelopment function. Parents often complain of poor feeding, slow weight gain, and speech impairment.<sup>7-9</sup> A multidisciplinary team is needed to manage craniosynostosis patients. The only available treatment is surgical approach.

Craniosynostosis surgery improves the head shape, neurodevelopmental status and reduces ICP.<sup>10,11</sup> There are two surgical methods for craniosynostosis treatment: the open approach and the endoscopic approach. Yet, some forms of craniosynostosis can only be treated by the open approach. To obtain sufficient access to the cranial vault, a large incision is required. Endoscopic technique is done with a smaller incision and could be performed on younger patients.<sup>12-14</sup> Despite the benefits of open surgery, it may cause significant blood loss and may require a blood transfusion during the operation. The volume of blood loss during an operation can vary from 20% to 500% of total circulating volume; this depends on various factors such as age, duration of operation, and type of craniosynostosis.<sup>15,16</sup>

Therefore, it is critical to evaluate the blood group in patients with craniosynostosis. The blood storage in pediatric hospitals that perform craniosynostosis surgery should be commensurate with the variety of blood group distribution in each region. It is possible that differences in blood groups are associated with the prevalence of craniosynostosis. For instance, blood types are associated with an increased risk of congenital heart disease.<sup>17</sup>

## 2. Objectives

In this study, we investigate the prevalence of each ABO/Rh blood group among patients with different types of craniosynostosis.

## 3. Methods

### 3.1. Study Design

The present study is a cross-sectional study which was performed in Imam Hossein children's hospital, Isfahan, Iran from 2015 to 2019. The Research Center of Isfahan University of Medical Sciences approved the research protocol.

### 3.2. Study Population

Participants in the present study were children with a diagnosis of craniosynostosis who were referred to Imam Hossein Children's Hospital. A total of 176 participants were included in the study, 163 of whom had sufficient information.

### 3.3. Study Procedure

We used hospital records as the principal source of our study data. Records of patients diagnosed with craniosynostosis, who were referred to Imam Hossein Hospital between the years 2015-2019, were reviewed. We recorded patients' IDs, age, weight, ABO/Rh blood group, and type of involved suture. For data analysis, SPSS version 25 software was used. Chi-square test was our test of choice to examine the relationship between ABO/Rh blood groups and types of craniosynostosis.

## 4. Results

Of 176 cases reviewed, 163 patients were included in the study. The mean age of the participants was 7.94 months (SD=10.37), with the youngest patient being 11 days old and the oldest 95 months. The average weight of the participants was 6853 g. The majority of participants had blood group A positive (32.5%), followed by O positive (31.3%). The rest of the blood groups were reported in order: B positive (22.1%), B negative (4.9%), AB positive (4.3%), O negative (2.5%), A negative (1.8%), AB negative (0.6%). Also, the most common type of craniosynostosis was metopic (27%) and the other types were pansynostosis (23.9%), sagittal (21.5%), coronal (16.6%), multisuture (10.4%) and lambdoid (0.6%) respectively. The frequency of blood groups and types of craniosynostosis are shown in Table 1.

**Table 1.** Frequency of ABO/Rh blood groups and Types of Craniosynostosis

Variables	Frequency (n)	Percent	Cumulative Percent	
ABO/Rh	A/Rh positive	54	32.5	32.5
	A/Rh negative	3	1.8	34.4
	B/Rh positive	36	22.1	56.4
	B/Rh negative	8	4.9	61.3
	O/Rh positive	51	31.3	92.6
	O/Rh negative	4	2.5	95.1
	AB/Rh positive	7	4.3	99.4
	AB/Rh negative	1	0.6	100
Total	163			
Types of craniosynostosis	Sagittal	35	21.5	21.5
	Metopic	44	27.0	48.5
	Coronal	27	16.6	65.0
	Lambdoid	1	0.6	65.6
	Pansynostosis	39	23.9	89.6
	Multisuture	17	10.4	100
Total	163			

Moreover, the connection between ABO/Rh blood groups and the types of craniosynostosis was examined by chi-square test, yet no significant relationship was observed ( $P=0.81$ ).

## 5. Discussion

Craniosynostosis refers to the premature closure of the cranial sutures.<sup>18</sup> Premature closure can impair brain development, and cause skull and facial deformities, as well as cognitive problems.<sup>2</sup> It is also associated with many syndromes.<sup>2</sup> Managing children with craniosynostosis requires a multidisciplinary team, including plastic surgeons, neurosurgeons, dentists, medical geneticists, and ophthalmologists.<sup>19</sup> Treatment of craniosynostosis is through surgical intervention, which should usually be done in the first year of life. The major risk of craniosynostosis surgery is blood loss.<sup>20</sup> A 2011 study by Seruya et al on 212 children with a craniosynostosis, found that the average blood loss during surgery was 33.4% of estimated blood volume, which ranged from 2.3 to 201.6 percent.<sup>21</sup> This volume of blood loss indicates that the necessary equipment for blood transfusion should be available in the medical centers. The blood bank reserve of the medical centers and hospitals should be proportional to the distribution variety of blood groups in the area.

Based on our study, the frequency of blood groups in patients with craniosynostosis is different from the general population in the same area. According to the report of the Blood Transfusion Organization of Iran, the frequency of blood groups in Isfahan region is A (29.59%), B (25.32%), AB (7.88%), and O (37.21%).<sup>22</sup> However, according to our study, the frequency of blood groups A, B, AB, and O is 34.4%, 27%, 4.9%, and 33.7%, respectively. According to our findings, the

## Research Highlights

**What Is Already Known?**

Some of the demographic characteristics of patients with craniosynostosis were known, and the appropriate measures and solutions for its treatment are adopted according to the characteristics of the patients.

**What Does This Study Add?**

The frequency of blood groups in patients with craniosynostosis can help to find related genes involved in this disease.

frequency of different types of craniosynostosis in our study was different from the reported data. As stated by previous data, sagittal craniosynostosis was responsible for 40% to 58% of craniosynostosis,<sup>23</sup> however, in our study, it was estimated to be 21.5%. In our investigation, the most common single suture craniosynostosis was metopic suture (27%). According to previous reports, craniosynostosis of multiple sutures or pansynostosis accounts for approximately 5% of craniosynostosis<sup>19</sup>; but in this study, 34.4% of craniosynostosis were multisuture or pansynostosis. Besides, no significant association was found between blood groups and types of craniosynostosis.

Based on the results of this study and comparing it to previously reported information, it can be concluded that the frequency of ABO blood groups in patients with craniosynostosis, is different from previously collected data in the same area. This is important since the availability of each blood group should be as to meet the needs of medical centers. It was also found that the frequency of different types of craniosynostosis in Isfahan, Iran, is different from the information reported in other countries.

**6. Conclusion**

Based on the results of the present study, it was found that the frequency of ABO blood groups in children with craniosynostosis can be different from the population of the same area. Also, the ratio of different types of craniosynostosis was different from previous data so it is recommended that each country reviews data related to its region. This could help find more related genes involved in the disease.

**Author Contributions**

AR contributed as the main author with the concept of planning the study. AR and ML contributed in study design, patient selection and follow ups. AA and ML performed the statistical analysis and interpreted the data. ML and AA write the manuscript. All authors approved final revisions.

**Conflict of Interest Disclosures**

All authors declared that they have no conflict of interest.

**Ethical Approval**

This study was approved by Isfahan University of Medical Sciences Ethics Committee with code of IR.MUI.MED.REC.1398.150.

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