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RESEARCH

Association of ABO blood groups with risk factors of intracranial cerebral aneurysm formation

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ABSTRACT

Introduction: The association between ABO blood groups and intracranial aneurysms is not well-understood. Many co-morbid factors are associated with intracranial aneurysms. The prevalence of different blood groups and associations with the risk factors in patients with intracranial aneurysms are reviewed. **Methodology:** A retrospective analysis was conducted on patients presenting with intracranial aneurysms and undergoing active neurosurgical intervention at the Louisiana State University Health Sciences Center between 1st January 1993 and 31st December 2012. A total of 1248 patients were identified for the analysis. Data pertaining to demographics and clinical characteristics of these patients were extracted from the electronic patient records by two authors independently. A univariate and multivariate analysis was performed to investigate the association of ABO blood groups with risk factors in patients with intracranial aneurysms. **Results:** The most common ABO blood group in our study population was O (543 cases, 43.5%), followed by group A (525 cases, 42%). Blood group A (46% vs. 35.5% patients; $P = 0.01$) and blood group B (18% vs. 7% patients; $P = 0.000$) were significantly associated with the development of intracranial aneurysms in Caucasians and African Americans, respectively. We found smoking ($P = 0.01$) and hypercholesterolemia ($P = 0.006$) to be an independent risk factor for the development of intracranial aneurysms in blood group O and blood group A, respectively. **Conclusion:** Racial disparity in the distribution of blood groups and risk factor association with blood groups in the development of intracranial aneurysm needs to be considered. The findings from our study may be useful in identifying patients at increased risk of developing intracranial aneurysms.

Key words: ABO blood groups, intracranial aneurysms, risk factors association

Introduction

Intracranial aneurysms pose a potential risk of developing life threatening intracranial hemorrhage [1]. Although current treatment modalities have been successful in reducing the mortality rate from this fatal condition, there remains high morbidity as a result of postoperative complications [1,2]. Therefore, it is important to determine risk factors for cerebral aneurysm formation that help identify patients at increased risk, and also establish candidates for screening. Well-established risk factors implicated in the formation of cerebral aneurysms include female gender, congenital syndromes, smoking, high blood pressure, atherosclerosis, diabetes, high alcohol consumption, autosomal dominant polycystic kidney disease, infection, and trauma [1,3,4]. ABO blood groups have been identified as one of the major prognostic factors for several diseases including cancers and vascular diseases [5-7]. In addition, patients with blood group A have been found to be significantly associated with risk of gastric cancer [6], and patients with blood group B with long standing diabetes have a significant risk of pancreatic cancer [7]. Recent evidence suggested that abdominal aortic aneurysm patients with blood group A have a higher risk of complications and morality [8,9]. In 1967, a report revealed that patients with B, AB, O but not A blood group are at potential risk for intracranial arteriovenous malformation [10]. However, to our best knowledge, until date, there is no study that investigated the association of the ABO blood groups with risk of developing intracranial aneurysms. Therefore, in this study, we explored the burden of different ABO blood groups among patients presenting with intracranial aneurysms with major risk factors among these population in order to formulate screening and preventive strategies for intracranial aneurysms.

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Methodology

Study protocol and design

A retrospective cohort study aimed to determine the association between blood group type and Rh factor, with the risk factors of developing intracranial aneurysms was conducted at the Louisiana State University Health Sciences Center (LSUHSC), Shreveport. Electronic patient records for all patients presenting to the neurosurgical service with cerebral aneurysms and undergoing treatment through 1st January 1993 to 31st December 2012 were reviewed. The

Institutional Review Board at the LSUHSC provided approval for the study.

Patient population and data extraction

A total of 1248 patients having intracranial cerebral aneurysm were included in the study. To ensure reliability and accuracy of the data, demographic and clinical records for each of these patients were extracted independently from the electronic database by two authors (SCB and PB). Potential conflicts arising upon any clinical characteristic or variables were resolved by discussion and consensus.

Statistical analysis

Data were analyzed for descriptive and inferential statistics. Descriptive statistics included reporting mean ± standard deviation for continuous variables and proportions for categorical variables. Chi-square test was used to determine racial differences in patients with ABO blood types, and the relation between specific blood group and risk factors in patients with intracranial aneurysms. A multivariable logistic regression analysis was performed to determine the association of ABO blood groups with risk factors in patients with intracranial aneurysms. A $P \leq 0.05$ was considered statistically significant. Data were analyzed using SPSS version 21.0 (IBM Corp., Armonk, NY, USA).

Results

The demographic and clinical characteristics of patients presenting with intracranial aneurysms are presented in Table 1. The mean age of the patients was 52 ± 13 years and 31% were males. Aneurysms most commonly affected the anterior circulation (85.8%, 1071). In only 3% of the patients, both anterior and posterior cerebral circulations were affected. Blood group O (43.5%, 543) was the most prevalent blood group type observed in the patients' followed by group A (42%, 525), group B (11.5%, 142), and finally group AB (3%, 38), respectively. In addition, 81% of patients were Rh (+) ve while only 12% constituted Rh (−) ve type.

Blood group A (46% vs. 35.5% patients; $P = 0.01$) and blood group B (18% vs. 7% patients; $P < 0.0001$) were significantly associated with the development of intracranial aneurysms in Caucasians and African Americans, respectively [Table 2]. In addition, Rh (−) ve factor was significantly higher in Caucasians compared to that in African Americans ($P = 0.003$) [Table 2].

A comparison of aneurysms with different age groups and gender is depicted in Figure 1. Aneurysms were the most common between 3rd and 7th decades of life irrespective of gender, with a peak incidence in the 5th and 6th decades and had a female gender predisposition.

Literature-based evidence suggests the ethnicity, age, sex, smoking, hypertension, diabetes, alcoholism, hypercholesterolemia, history of CVA, and obesity to be related to intracranial aneurysms. Table 3 depicts the association of different risk factors with intracranial aneurysms in our cohort. A multivariable regression analysis demonstrated ethnicity and age had no significant effect on development of cerebral aneurysms in our study population; however female gender ($P < 0.0001$), smoking ($P < 0.0001$), hypertension ($P < 0.0001$), diabetes (0.031), alcoholism ($P < 0.0001$), hypercholesterolemia ($P = 0.033$), and obesity ($P = 0.023$) were significantly associated with the development of aneurysm [Table 4]. In relation to ABO blood group, the findings of univariate analysis showed a significant association of smoking ($P = 0.007$), age ($P = 0.031$), and ethnicity ($P = 0.05$) with ABO blood group on the formation of aneurysms; however, adjusted point estimates revealed only age ($P = 0.001$) and ethnicity ($P < 0.0001$) to be significantly associated with the risk of developing intracranial aneurysms [Table 4].

Table 1: Demographic and clinical characteristics of patients with intracranial aneurysms (*n*=1248)

Mean age±SD (years)	52±13
Gender, *n* (%)	
Male	383 (30.7)
Female	865 (69.3)
Ethnicity, *n* (%)	
Caucasians	759 (60.8)
African Americans	468 (37.5)
Asian	21 (1.7)
Location of aneurysms, *n* (%)	
Anterior cerebral circulation	1071 (85.8)
Posterior cerebral circulation	140 (11.2)
Both anterior and posterior circulation	37 (3.0)
Blood group type, *n* (%)	
A	525 (42.1)
B	142 (11.4)
AB	38 (3.0)
O	543 (43.5)
Rh factor, *n* (%)	
Positive	1099 (88.1)
Negative	149 (11.9)

SD: Standard deviation

Table 2: Disparity of distribution of blood group in different ethnicity

Parameters	OR	95% CI for OR	*P*
Blood group A: Caucasians versus African Americans	1.32	1.05-1.67	0.01
Blood group B: African Americans versus Caucasians	2.86	1.99-4.1	<0.0001
Rh (−) ve factor: Caucasians versus African Americans	1.79	1.2-2.6	0.003

CI: Confidence interval, OR: Odds ratio

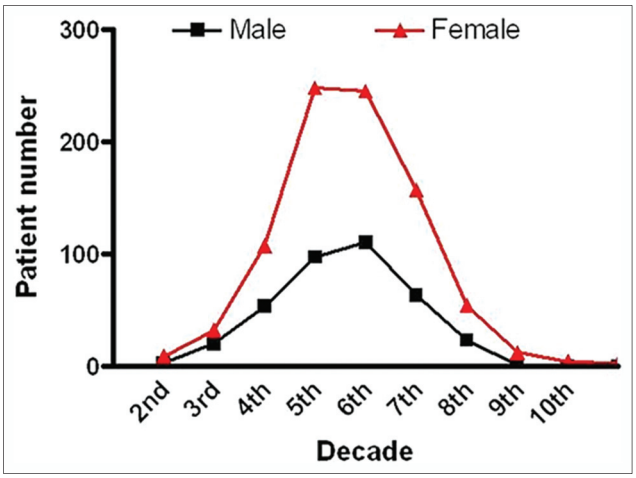

Figure 1 Age and sex distribution in study population with intracranial aneurysm showing peak distribution in 5th and 6th decades in both males and females. Females are having higher incidence rate compared to males

Table 3: Risk factors for intracranial aneurysms	
Risk factors	***P***
Ethnicity	0.836
Gender	<0.0001
Age	0.107
Hypertension	<0.0001
Diabetes	0.031
Alcoholism	<0.0001
Hypercholesterolemia	0.033
Smoking	<0.0001
Obesity	0.023

Table 4: Risk factors of intracranial aneurysm related to ABO blood group	
Risk factors	***P***
Univariate analysis	
Ethnicity	0.05
Age	0.031
Smoking	0.007
Multivariate analysis	
Ethnicity	<0.0001
Gender	0.521
Age	0.001
Hypertension	0.282
Diabetes	0.452
Alcoholism	0.442
Hypercholesterolemia	0.103
Smoking	0.07
Obesity	0.351

Incidence of smoking was significantly higher in aneurysm patients with O group compared to others [Table 5]. We found ethnicity and age to have a significant effect on aneurysm formation [Table 4]. In addition, we found smoking ($P = 0.01$) and hypercholesterolemia ($P = 0.006$) to be an independent risk factor for the development of intracranial aneurysm in blood group O and blood group A, respectively [Table 5].

Discussion

The association between ABO blood groups and prevalence of intracranial aneurysm are not well-understood. There is nil-to-limited information in the literature about a possible association of blood groups with risk factors of intracranial aneurysms. In the present study, we investigated the impact of ABO blood type in a large volume of patients with intracranial aneurysm. The findings of our study suggested blood group O to be the most common blood type in intracranial aneurysms followed by A, B, and AB. Interestingly, this finding reflects a similar pattern of distribution of blood group in the general population as well. Previous reports have shown association of non-O blood group is associated with the development of abdominal aortic aneurysm, peripheral arterial disease, angina, myocardial infarction, cerebral ischemia, and venous thromboembolism [5]. However, partially supporting our findings, a recent investigation carried out on a large volume of patients' demonstrated blood groups to have no impact on the development of coronary artery disease [11]. However, the results generated from our data revealed significant association of blood type A in Caucasians and blood type B in African American ethnic group to be associated with the development of intracranial aneurysms. Research-based evidence suggested that African Americans with non-O blood group have a higher risk of developing venous thromboembolism which partly supports our finding [12]. Therefore, racial disparity of blood group distribution in intracranial aneurysm could be a possibility. Rh factor is also a determinant of cardiovascular diseases including hemolytic diseases. Recent evidence has suggested that Rh negative children with intra-ventricular hemorrhage have higher mortality rate [13]. Our data suggest Caucasians with Rh negative blood group have higher rate of intracranial aneurysms than that African Americans ethnic group, implying racial disparity in ABO and Rh blood groups could play a vital role in screening patients with intracranial aneurysms in different ethnic groups.

Age and sex distribution has a significant impact in any disease population. Our finding is a partial agreement with the previous report showing the higher incidence of intracranial aneurysms in 5th or 6th decade in female patients [14]. Multiple risk factors including gender, hypertension, smoking, hypercholesterolemia, alcohol, and diabetes are involved in the formation of intracranial aneurysm [14,15]. Our finding relates partially to the previously published reports that showed a

Table 5: Risk factors of intracranial aneurysm related to ABO blood group

Risk factors	OR	95% CI for OR	*P*
Smoking: blood group O versus others	1.32	1.04-1.66	0.01
Hypercholesterolemia: blood group A versus others	1.54	1.1-2.1	0.006

CI: Confidence interval, OR: Odds ratio

positive association between gender, hypertension, alcoholism, hypercholesterolemia, smoking, obesity, and formation of intracranial aneurysm.

Till date, there has been no study investigating the association between ABO blood groups and major risk factors in respect to intracranial aneurysm formation. Multivariate and univariate analysis of our data indicate ethnicity, age, and smoking to have a positive association with ABO blood group in respect to aneurysm formation. Importantly, smoking is one of the most common risk factors for cardiovascular disorders [16]. We have found that smokers with O blood group have significantly higher chance of intracranial aneurysm formation. The findings of a recent study showed that the association of blood group O with smoking in the patients with chronic heart disease partially supports our finding [17]. Similarly, hypercholesterolemia, a common risk factor for intracranial aneurysm, when managed with statins can reduce the risk of intracranial aneurysm [18]. Our data indicate hypercholesterolemic patients with blood group A have significantly higher chance to develop intracranial aneurysm. Literature-based evidence also suggested that there is a positive association of A blood group and serum cholesterol in respect to coronary heart disease [19,20]. Therefore, current finding of the association between blood group O with smoking and blood group A with hypercholesterolemia may be used as predictive factors for intracranial aneurysm.

The major limitation of our study is its retrospective design, and subject to unmeasured confounding, and future studies should address these limitations.

Conclusion

To our knowledge, this is the first study evaluating the distribution of different blood groups in patients with intracranial aneurysms and its association with possible risk factors for developing aneurysms in these patients. Racial disparity in the distribution of ABO and Rh blood groups and association of risk factors with the blood groups need to be considered to understand the individual patient's risk. A prospective study and randomized trials looking into the association of ABO blood groups and its association with risk factors for developing aneurysms is warranted. In addition, future identification of genetic and environment factors among different ethnicity could provide deeper insight into our observed data and advance opportunities to better understand the control and development of intracranial aneurysms.

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Author's Contributions

SCB and PB conceptualized the research design, data acquisition, data analysis and interpretation of results. SCB and PK helped in drafting and revising the manuscript. SA and AN reviewed the manuscript and provided critical comments for improvisation. All authors have read and approved the final version of the manuscript.

Competing Interest

Nil

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