

## Original Research Article

# Hemorrhagic stroke in Saudi adult male population and the ABO blood group distribution: a comparative analysis

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## ABSTRACT

**Background:** Globally stroke is leading cause of death and disability. According to WHO every year 15 million people get stroke and one third of these subjects die and about 5 million become permanently disabled. In SA smoking, diabetes, and hypertension are highly prevalent and since these factors are among ten major risk factors for stroke it puts Saudi population at higher risk of stroke. In current study we studied prevalence of hemorrhagic (HS) stroke and analyzed if there is any correlation between incidences of HS and ABO blood groups in Saudi population.

**Methods:** Blood groups and other relevant data were collected for 2304 stroke patients registered at King Khaled hospital between 1/1/2008 to 1/6/2018. Statistical analysis was performed using Z calculator.

**Results:** We saw 5.4-fold increase in prevalence of diabetes type 2 and 8.7 fold increase in prevalence of hypertension among HS patients as compared to control subjects. Prevalence of smoking was higher in both control and HS patients. 21.7% of stroke patients were HS patients. Distribution of A blood group was significantly higher in male HS patients. AB blood group showed statistically significant reduction in HS patients as compared to control group. Results were statistically significant at ( $p < 0.01$ ). However, blood group B and O showed no significant differences between two groups.

**Conclusions:** Results of our studies show a correlation between ABO and the incidences of hemorrhagic stroke in Saudi adult male population. Larger studies are needed to confirm these results.

**Keywords:** ABO and Rh blood groups, Cardiovascular disease, Diabetes, Hypertension, Hemorrhagic stroke, Obesity

## INTRODUCTION

According to the “American stroke association’s estimates globally one in 4 people (25% of global population) will have a stroke at some point in life. Age is considered as one of the major determinants of the incidences of stroke. It has been suggested that the risk of stroke doubles every decade after the age of 55.<sup>1,2</sup> According to a recently published study ten major risk factors were identified which are responsible for the

majority (90%) of all the episodes of strokes: and they include lack of physical activity, a poor diet selection, obesity, diabetes, high cholesterol levels, hypertension, stress, current smoking status and the alcohol consumption.<sup>3</sup>

A stroke can be classified as a neurologic as well as a cardiovascular event. Three types of strokes have been identified: An ischemic stroke (IS), where the blood vessel supplying blood to the brain is blocked due to an emboli formation therefore restricting the normal flow of

oxygen and other important nutrients to the brain tissue. An IS accounts for 87% of all the incidences of stroke. Atherosclerosis is considered as the main cause of causing ischemic stroke. Hemorrhagic stroke (HS) occurs due to a ruptured blood vessel therefore the surrounding tissue gets less or no supply of oxygen and other nutrients. An uncontrolled or unregulated high blood pressure is considered to be the major cause of HS. We and others have previously reported a high prevalence of hypertension in Saudi adult male and female population.<sup>4-6</sup>

According to the American stroke association (ASA), two types of weakened blood vessels can be the main cause of hemorrhagic stroke; aneurism, and arteriovenous malformations (AVMs). Yet another kind of stroke called the “transient ischemic stroke (TIA) also known as “mini stroke “has also been identified in certain people. It’s a temporary clot and can represent a warning signs to the people. Occasionally, in few people the cause of stroke cannot be confirmed or identified. These cases of stroke without a known cause are termed as the “cryptogenic stroke”.

In recent past the old definition of stroke has recently been updated by the American stroke association.<sup>7</sup> According to the new definition: “Central nervous system infarction is defined as brain, spinal cord, or retinal cell death attributable to ischemia, based on neuropathological, neuro-imaging, and/or clinical evidence of permanent injury. Central nervous system infarction occurs over a clinical spectrum. Ischemic stroke specifically refers to central nervous system infarction accompanied by overt symptoms, while silent infarction by definition causes no known symptoms. Stroke also broadly includes intra-cerebral hemorrhage and subarachnoid hemorrhage”.<sup>7</sup>

Many studies have previously linked ABO and Rh blood groups with several non-communicable diseases such as diabetes, hypertension and myocardial infarctions.<sup>4,5,8-19</sup> Although several studies have linked incidences of stroke with the inheritance of ABO blood groups also however these results have not been consistent.<sup>20-22</sup> Therefore in the current study we decided to look at relationship between the occurrence of hemorrhagic stroke and the ABO blood groups in Saudi adult male population. Since there is high prevalence of smoking, obesity, diabetes and hypertension (major risk factors for stroke) in Saudi adult population, and since many of these risk factors have been associated with the inheritance of ABO blood groups, aim of the current study is to analyze if there was any possible association between the incidences of hemorrhagic stroke in Saudi adult male population with their inherited ABO blood groups.

## METHODS

This is a cross sectional study which was designed to investigate the possible association between the distribution of ABO and the Rh blood group antigens and the incidences of hemorrhagic stroke in Saudi adults’ male population of the Hail region. The data was collected for all adult stroke patients who had registered at the King Khaled hospital (KKH) between the years of January 2008 to June 2018.

### *Inclusion and exclusion criteria*

Data was collected for only male patents above 18 years of age. Patients data was not recorded unless complete ABO and Rh antigen information was included in their files. Data was collected only for adult male patients.

Before collecting any patient, data permission was requested and was promptly granted from the medical records office of KKH. Clinical data was collected by the fifth year medical students and the medical interns from the King Khaled hospital after getting permission from the appropriate hospital administrators. Data was collected for stroke patients who had registered at the King Khaled hospital from January 2008 to June 2018.

Authors also collected some random control data from the local shopping malls and from random student population. We collected information from subjects about their blood group type, tobacco use, and the past history family history of hypertension and diabetes. Patient’s ABO and Rh blood group distribution data was statistically analyzed using Z- test calculator for the two population proportions. Additionally, each participant in this study was asked to give their verbal consent and sign a written statement before using their data for the current research. This study was approved by the ethical committee of college of medicine at university of Hail.

## RESULTS

### *Total subjects who participated in this study*

For the current study, authors randomly selected a total of 2754 control subjects. Of them, 1540 (55.9%) were males and 1214 (44.01%) were females. Additionally, there were a total of 2304 stroke patients; among them 1292 (56.07%) were male patients and 1012 (43.92%) were female stroke patients (data not shown). Mean age of control male subjects was 30.2 years (Table 1). The mean age for male stroke patients was 71.3 years (Table 2).

**Table 1: Male controls.**

Number (n)	Age range (yrs)	Mean age (yrs)	Smokers (%)	Hypertension (%)	Type 2 DM (%)
1540	19-76	30.2	52	9.7	13.9

**Table 2: Male stroke patients.**

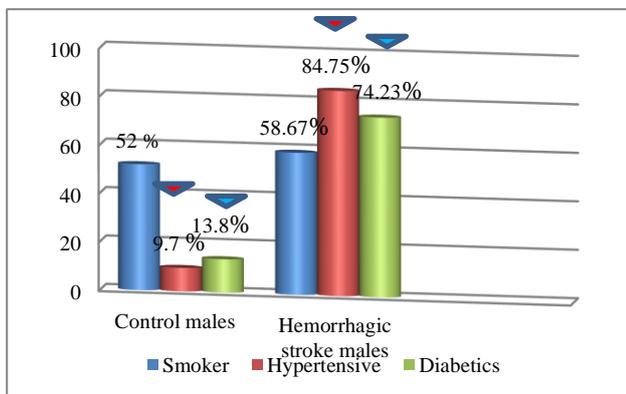
Number (n)	Age range (yrs)	Mean age (yrs)	Smokers (%)	Hypertension (%)	Type 2 DM (%)
1292	23-105	71.3	58.67	84.75	74.23

**High prevalence of hypertension and diabetes type 2 in stroke patients**

A high prevalence of smokers in Saudi male control subjects (52%) were found as well as among the male stroke patients (58.67%) (Table 1, 2). In contrast, a statistically high prevalence of hypertension and the incidences of diabetes type II were found only among male stroke patients (ischemic, hemorrhagic and transient ischemic stroke patients) as compared to the control subjects (Tables 1 and 2). Among the control males there were 9.7% subjects with hypertension as compared to 84.75% (8.7 fold increase) among the male stroke patients. These results suggest a significant increase in the prevalence of hypertension among male stroke patients as compared to the non-randomly selected control subjects. Likewise a significant increase (74.23%) in the cases of diabetes type 2 in male stroke patients were seen as compared to the control subjects (13.9%) These results show a 5.4 fold increase in cases of diabetes type 2 among all subtypes of male stroke patients (Figure 1). Statistical analysis using Z calculator showed these results were significant at  $p < 0.01$ . This study results confirm the current hypothesis and the previously published observations (O'Donnell et al) that diabetes and hypertension are among the major risk factors for stroke.<sup>3</sup>

**Table 3: Prevalence and types of strokes in Saudi adult male population.**

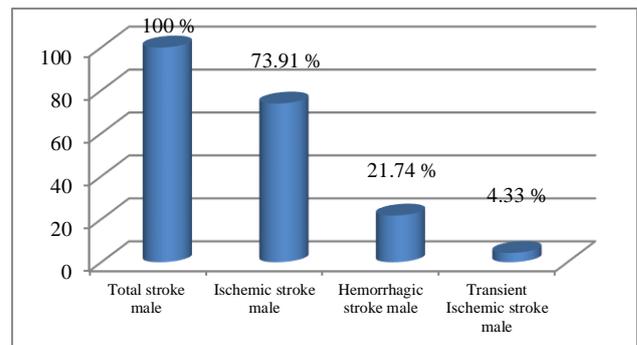
Type of stroke	Ischemic	Hemorrhagic	TIA
Number of male patients	955	281	56
Percent (%)	73.91	21.74	4.33



**Figure 1: About 8.7 fold increase in the prevalence of hypertension among stroke patients as compared to the control subjects (red arrow heads).**

**Types of stroke among male patients**

Next the types and percentage of strokes cases were calculated among the male stroke patients of Hail region. American stroke association has identified three types of strokes. The ischemic stroke (IS) in which the blood vessel that is supplying blood to the brain is blocked due to an emboli therefore hindering the regular flow of oxygen and other important nutrients to the brain tissue, the hemorrhagic stroke (HS) which occurs as a result of a ruptured blood vessel and the “transient ischemic stroke (TIA) which is also known as a “mini stroke” which has also been identified in a few people. Among our male patients we found majority of patients with IS (73.91%), while 21.74% patients had hemorrhagic stroke and only 4.33% had an episode of TIA (Table 3).



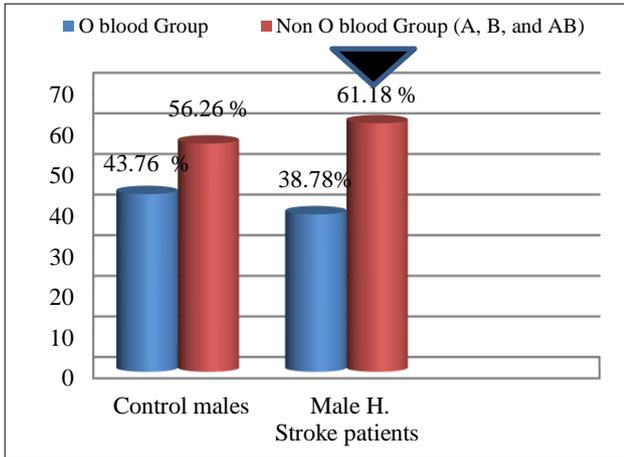
**Figure 2: Prevalence and types of strokes in Saudi adult male population.**

Out of total of 955 male stroke patients (100 %), Ischemic stroke was the most prevalent type of stroke among Saudi male population (73.91%), followed by cases of hemorrhagic stroke (21.74%). Among all stroke cases transient ischemic stroke was the least prevalent at 4.33% (Figure 2).

**Distribution of O versus non-O blood groups in control and the hemorrhagic stroke male patients**

Since many studies have recently linked incidences of stroke with ABO blood groups and since these results have not been consistent, therefore next we analyzed our randomly selected control and hemorrhagic stroke patient ABO data to see if there was any association. First comparisons were made between O blood groups versus non O blood group (A, B and AB) distribution among HS patients. a statistically significant increase in the distribution of non O blood groups (61.18%) was found as compared to the O blood groups (38.78%) in male hemorrhagic stroke patients (Figure 3). Likewise a similar

increase in non-O blood group distribution was also seen (56.76%) among control group as compared to their respective O blood group (43.76%) distribution. In summary these results show that when compared with their respective O blood group distributions, the non-O blood groups showed no significant increase among HS patients (157.8%) versus in control groups (128.6%). The p value is 0.121 and the results are not significant at  $p < 0.05$ .



**Figure 3: Distribution of O versus non-O blood groups in control and male hemorrhagic stroke.**

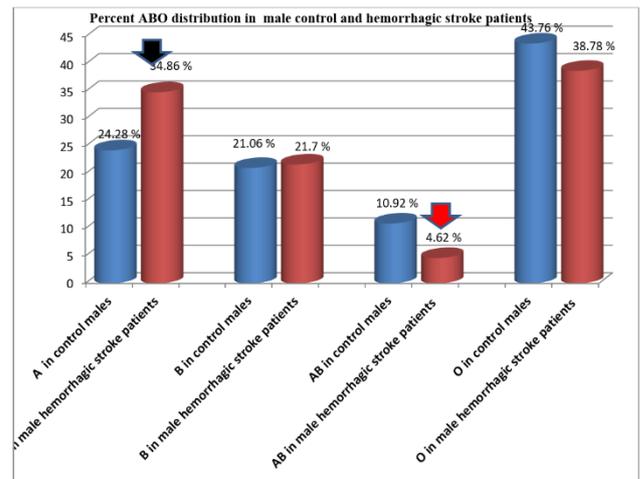
**Distribution of ABO blood groups in control and the hemorrhagic stroke male patients**

Since the non-O blood groups showed an increase in their distribution among male HS patients (157.8%) as well as in control group (128.6%), next we wanted to investigate, if all or some of the non-O blood groups (A, B and AB) show any significant differences in their distribution as compared to the control blood groups. Further analysis of our results showed that the distribution of A, blood group was statistically significantly higher (red bar, black arrow) in male hemorrhagic stroke patients as compared to the controls (Figure 4). The results were statistically significant at ( $p < 0.01$ ). On the other hand, blood group B and blood group O distributions do not show any significant difference as compared to the control groups. The results were statistically insignificant at ( $p < 0.5$ ). In contrast the blood groups AB showed a statistically significant reduction in their distribution in HS patients ( $p < 0.01$ ) as compared to the control group (red arrow and red bars) (Figure 4). These results suggested that AB blood group may provide resistance against hemorrhagic stroke in male patients, although larger studies need to be done to confirm our results.

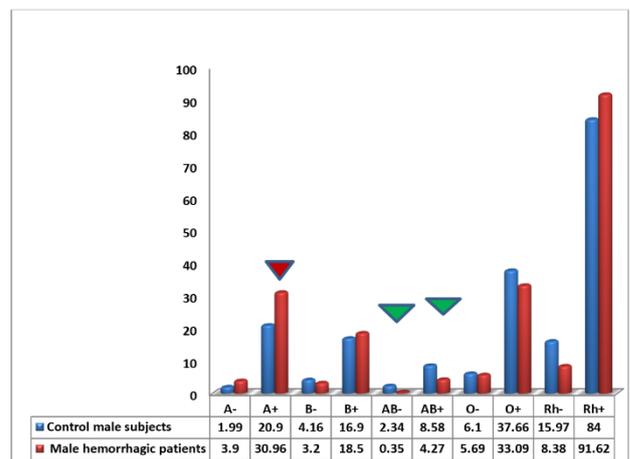
**Distribution of ABO and Rh blood groups in control and the hemorrhagic stroke male patients**

Next we wanted to further investigate and compare if ABO-Rh antigens show any difference in their expression between the control and the stroke patients. The results

still show the similar pattern as in Figure 4. The distribution of A+ blood group is significantly higher when compared with the distribution of A+ in control group (Figure 5 red arrow heads). The results were statistically significant at  $p < 0.01$ . However, the blood groups B+ and O+ distributions did not show any statistically significant difference between the controls and the hemorrhagic stroke patients. The results were statistically insignificant at ( $p < 0.05$ ). On the other hand AB+ and the AB- blood group showed a statistically significant reduction in their distribution in HS patients ( $p < 0.01$ ) as compared to the control group (Figure 5 green triangles, red bars).



**Figure 4: Distribution of ABO blood groups in randomly selected control (blue bars) and the male hemorrhagic stroke patients (red bars).**



**Figure 5: Distribution of ABO and Rh antigens in male control and hemorrhagic stroke patients.**

**DISCUSSION**

Globally, stroke is a major cause of death and causing disability. WHO estimates 15 million incidences of stroke every year, about one third die and about five million of them become permanently disabled. In the past many

studies have shown an association between ABO blood groups and several non-communicable diseases.<sup>4,5,8-19</sup> Likewise many studies have also shown an association between the incidences of stroke and the ABO blood groups.<sup>20-23</sup> however the results of these and other studies have hardly been consistent. For example some studies found no association between the ABO blood groups and ischemic stroke, while some researchers found patients with AB blood type with increased risk of stroke.<sup>22,23</sup> while some researchers found B allele to be associated with increased risk of ischemic stroke.<sup>21</sup>

In the current study high prevalence of HS was found in male Saudi adults with blood type A and dramatic reduction in incidences of stroke in patients with blood group AB. Like us other researchers from other countries also came to same conclusion that AB blood group reduces risk of coronary heart disease (CHD) due to the higher concentration of HDLc and O blood group increases the risk of CHD as a result of lower HDLc in Bengali population of eastern India.<sup>17</sup> Our results are also strengthened by some studies that have suggested that people with A blood group have high total cholesterol (TC) and low density lipoprotein cholesterol (LDLc) levels than the other blood types.<sup>24</sup>

Our results are also supported by previously published studies in which the non-O blood group members have been shown to have greater concentrations of Von Will brand clotting factors.<sup>25,26</sup> Since high cholesterol and high concentration of Von will brand factors in blood type A population (a non-O blood group) puts a person at higher risk of stroke and it is reasonable to assume that the patients of A blood group in Saudi adult population are at higher risk of stroke as suggested by our results in this study. In the current study as expected, we also found a high prevalence of smoking however we found high prevalence of smoking not only in control subjects but also in male stroke patients (Tables 1 and 2). According to a recent study on stroke in young adults and children, there were less cases of diabetes and alcohol abuse was the major risk factor for stroke however in our study except diabetes, hypertension and smoking we could not find any data on alcohol abuse in our HS SA male patients.<sup>27</sup>

In addition to smoking as we reported earlier we also found high prevalence of diabetes and hypertension in Saudi adult male stroke patients (Tables 1 and 2). According to American Heart Association people who have diabetes are 1.5 times are more likely to have stroke than those who are non-diabetics. According to WHO diabetes is highly prevalent in Middle East and if not controlled it can lead to stroke which is considered as the second leading cause of death and the third leading cause of disability worldwide.<sup>28,29</sup>

Due to the cultural restrictions and limitations in the Middle Eastern culture it is very difficult to find female volunteers for the current study. The data was collected

from patient's files who had previously registered at the hospital.

## CONCLUSION

Statistically no differences was found in the distributions of B or O blood groups in control versus HS adult male patients, however the blood group A shows a statistically significant increase and the blood group AB show a significant reduction in their distributions as compared to the randomly selected controls. These results suggest a possible association between ABO blood groups and the incidences of HS in Saudi adult male population.

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