

FREQUENCY OF ABO BLOOD GROUPS AMONG PATIENTS WITH ISCHEMIC STROKE

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ABSTRACT

Objective: The objective of this study was to find out the blood groups among the patients presenting with ischemic stroke either AB blood group or O blood group is more common (frequent) among these patients irrespective of other known factors responsible for stroke.

Materials & Methods:

We included total 292 patients (40-70 years of age), with ischemic stroke documented on CT scan brain of both gender (male and female).Blood sample of these patients were sent to the central laboratory of hospital for blood group determination using standard techniques.

Results:

Mean age was 56.26 ± 8.28 years. Out of the 292 patients, 163 (55.82%) were male and 129 (44.18%) were females with male to female ratio of 1.3:1. Frequency of blood group A, B, AB and O was found to be 114patients blood group A (39.04%), 53patients blood group B (18.15%), 26patients blood group AB (8.90%) and 99patients blood group O (33.90%) respectively.

Conclusion:

Our study results concluded *that there is an* association between ABO blood groups and ischemic stroke, irrespective of other risk factors. Our study results have observed that individuals belonging to non-O blood groups (A, B, or AB) are at an increased risk of ischemic stroke as compared to O blood group carriers however we did not control possible impact of confounders such as diabetes, hypertension and dyslipidemia etc .Many studies proved that persons with AB blood groups are at increased of atherosclerosis but no study showed that these persons have increased risk of ischemic stroke or not.

Keywords: Ischemic stroke, ABO blood groups

INTRODUCTION

Stroke is defined as any rapidly developing deficit of a part or whole side of body that persists more



than 24 hours.1 It is either Hemorrhagic or Ischemic that leads to decreased supply of blood and nutrients to that part of brain.² It is estimated that more than 15 million people have stroke, worldwide each year. Among two thirds of these 15 million people, One-third die and one-third develop disability. In developing countries, stroke is the third most common cause of death preceded by coronary heart disease and cancers respectively.³ Ischemic stroke is the most common type which is responsible for 85% of all strokes.⁴Study in United States showed that about 800,000 people have stroke each year in America and 82-92% among them were have ischemic stroke.⁵ Atherosclerosis and embolism are the two main causes of ischemic stroke, however vasculitis, endocarditis and venous infarcts are the other causes of ischemic stroke.^{7,8}Recognition of underlying cause is important because the subsequent management of each patient is quite different. Neuroimaging (CT-Scan brain) is the most important investigation not only in the early diagnosis of stroke type but also in the further management and treatment of the patient.⁹ In ischemic stroke tissue plasminogen activator is the treatment of choice if patient presents within 3 hours of symptoms.¹⁰

^{Carl} Landsteiner discovered ABO blood group system in human beings in early nineteenth century based on the presence or absence of two genes, A and B which are producing antigens A&B respectively while blood group O does not have such alleles so don't have such antigens, producing four types of blood groups(A43%, B4%, AB19% and O44%). Early recognition of ABO blood group was concerned with blood transfusion only to avoid cross reactions while transfusing the blood but now a days it has been proved that this system has a role in different diseases like atherosclerosis, MI, stroke, diabetes, peptic ulcer and even cancers. Gong P1et all and others also noted that persons with non o blood group are at increased risk of atherosclerosis. ^{12,13,33,34}

Sabino AP et al showed that different blood groups behave differently for ischemic stroke and peripheral arterial disease rendering non-O blood groups (A, B, or AB) more prevalent to have increased chance of above mentioned conditions. ¹⁴Hanson E et al¹⁵ in his study has shown that ischemic stroke is present in following frequencies in blood groups A47%, B14%, AB6% (66%) and O34%.

Our purpose of study was to see the risk (frequency) of ABO blood groups present among our patients presenting with ischemic strokes independent of other known risk factors.

MATERIALS & METHODS

This was a descriptive, Cross-sectional study, conducted in the department of medicine, DHQ teaching Hospital Sahiwal from May 2017 to May 2018 with consent of patients having ischemic stroke of both genders and 40-70 years of age. Those who were having head trauma or hemorrhage on neuro imaging were excluded. Non-probability, Consecutive sampling used by taking following values. p=Frequency of ABO blood groups among patients with ischemic stroke =5%. ¹⁵ e=margin of error=2.5%. Of these 292 patients with ischemic stroke admitted to, DHQ teaching Hospital Sahiwal, fulfilling the inclusion/exclusion criteria were selected. After taking consent, blood samples taken from peripheral vein for blood grouping were sent to the Central Laboratory of the DHQ teaching Hospital. Laboratory technician determined blood group using standard techniques. All this information was collected through a Performa.

All data were processed and analyzed using computer based software program SPSS version 22.0 for windows. Numerical variables like age have been presented by calculating as mean and standard deviation. Qualitative data like gender, ABO blood group have been presented by calculating frequency and percentage. Effect modifiers like age, gender and family history of ischemic stroke (yes/no) have been controlled after making stratification tables and post-stratification chi square was applied to see their effect on outcome and P-value ≤0.05 has been taken as significant.

RESULTS

Age range in this study was from 40 to 70 years with mean age of 56.26 ± 8.28 years. Majority of the patients 123 (42.12%) were between 51 to 60 years of age as shown in Table I. Out of the 292 patients, 163 (55.82%) were male and 129 (44.18%) were females with male to female ratio of 1.3:1 (Figure I).

Frequency of blood group A, B, AB and O was found to be 114 patients having blood group A (39.04%), 53 patients having blood group B (18.15%), 26 patients having blood group AB (8.90%) and 99 patients having blood group O (33.90%) respectively (Figure II). When Stratification of blood groups was done on age groups, significant difference was found between different age groups as shown in Table II which showed no significant



difference between male and female. Table IV has shown the stratification of blood groups with respect to family history of ischemic stroke.

Table-I: Age distribution of patients (n=292).

Age (in years)	No. of Patients	%age
40-50	74	25.34
51-60	123	42.12
61-70	95	32.53

• Mean \pm SD = 56.26 \pm 8.28 years

Figure-I: %age of patients according to gender (n=292).

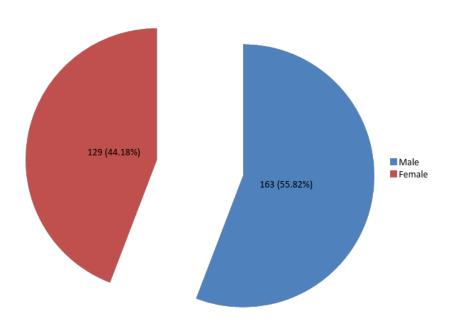




Figure II: %age of patients according to ABO blood group (n=292)

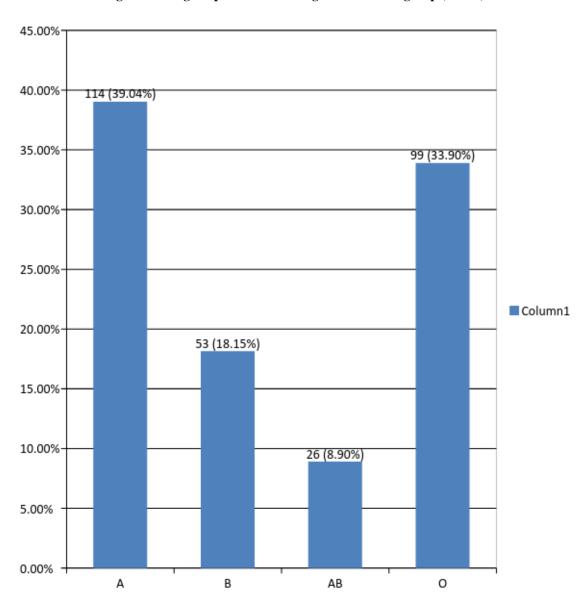


Table II: Stratification of Blood groups with respect to age groups.

	Blood group				p-value
Age (years)	A	В	AB	0	
40-50	27 (36.49%)	18 (24.32%)	10 (13.51%)	19 (25.68%)	
51-60	50 (40.65%)	43 (34.96%)	06 (4.88%)	24 (19.51%)	0.000
61-70	37 (38.95%)	10 (10.53%)	10 (10.53%)	38 (40.0%)	



Table III: Stratification of Blood groups with respect to age gender.

	Blood group				p-value
Gender	A	В	AB	0	
Male	54 (33.13%)	59 (36.20%)	18 (11.04%)	32 (19.63%)	
Female	60 (46.51%)	40 (31.01%)	08 (6.20%)	21 (16.28%)	0.102

Table IV: Stratification of Blood groups with respect to family history of stroke.

	Blood group			p-value	
Family history	A	В	AB	0	
Yes	74 (38.95%)	63 (33.16%)	19 (10.0%)	34 (17.89%)	
No	50 (49.02%)	36 (35.29%)	07 (6.86%)	19 (18.63%)	0.623

Discussion

Various studies have shown that thrombosis is not a simple process for blood coagulation, rather it is genetically determined and certain genetic variants are responsible for thrombosis. ^{16, 17} Not only the structure but also the function of thrombosis is based on genetics depending on fibrin and others factors for formation and lysis of thrombosis ^{18,19} when this thrombosis occurs in brain this becomes the leading cause for deaths and morbidities in developed nations. ¹⁶ ABO blood group system consists of different antigens present on red blood cells and vascular endothelium, and have some association with procoagulant proteins like factor ⁸ and won villibrand factors and others present on endothelium surfaces thus playing role for thrombus formation ²⁰⁻²². This blood grouping system thus playing role not only for Blood transfusions or organ transplantation but also put the people at increased chances of cerebrovascular events like MI, ischemic stroke. ²⁰

Out of the 292 patients, 163 (55.82%) were male and 129 (44.18%) were females with male to female ratio of 1.3:1 showing male gender preponderance. In literature, different studies have already documented male gender predominance in ischemic stroke patients. A study conducted by Luo et al ²³ from China has also reported male gender outnumbering female gender. These findings of Luo et al ²³ are in compliance with that of our study. Another study from Karachi by Sheikh et al ²⁴ has also reported 61 % male patients were having ischemic stroke which is in compliance with our finding.

Age range in this study was from 40 to 70 years with mean age of 56.26 ± 8.28 years. Majority of the patients 123 (42.12%) were between 51 to 60 years of age. Khan et al 25 reported 58.11 ± 15.29 years mean age which is close to our study results. Abid et al 26 reported 55.96 ± 13.75 years mean age of the patients presenting with ischemic stroke which is similar to that of our study results. He M et al showed that ABO blood type is associated with venous thromboembolism (VTE) and inconsistently with myocardial infarction 27 . In a genetic study Wiggins KL have identified the alleles for A and B Blood groups that increased myocardial infarction, stroke, and VTE risk in those with hypertension or in postmenopausal women. In our study, frequency of blood group A, B, AB and O was found to be 114 (39.04%), 53 (18.15%), 26 (8.90%) and 99 (33.90%) respectively.

Hanson E et al¹⁵ in his study has shown the frequency of blood group A, B, AB and O as 47%, 14%, 5% and



34% respectively in patients of ischemic stroke ,results are closer to our study results.

Sabino AP et al 14 observed significant difference for O1 alleles among Ischemic Stroke patients while significant differences were observed for B phenotype (26.3 vs 9.5%, OR 3.42, 95% CI 1.32-8.76, p = 0.01, patients vs controls, respectively) and alleles A1, O2 and B alleles for PAD patients. O1 allele was an independent variable for IS patients. This data is clearly showing that non-O blood groups has genetic predisposition for thrombosis events and vice versa for O blood group.

Zakai NAet al¹³ again showed that AB blood group is associated with increased risk of ischemic stroke. The percentages of blood groups among participant were 43.0% for blood group A, 13.5% for blood group B, 3.9% for blood group AB, and 39.6% for blood group O. Wiggins KL1 in his study tried to find which allele whether A or B is associated with venous thrombosis and ischemic stroke. He found that in comparison with O group, the A and B allele were associated with increased risk of VT and IS, and blood type B was associated with ischemic stroke more but not blood type AB.²⁸ Williams FM and colleagues in ABO gene variant study described interesting fact that such events of IS are associated with large vessels and cardioembolic phenomena but not in small vessel disease, including 1544 stroke patients and 19 602 controls. However in advanced stage of study, they also showed that genes for coagulation factors and fibrin structure/function, a single nucleotide polymorphism in the ABO locus was responsible for ischemic stroke.²⁹ Moreover, a meta-analysis also observed that there was low but significantly enhanced risk of stroke for the patients having non-O phenotypes as compared with those of having O phenotype ³⁰. This study was based on seven studies using different criteria for stroke definition and including different types of stroke definitions of stroke in all age groups, while we included only patients with ischemic stroke(on imaging) before the age of 70 years. Zhou S et al 31 in his study has found that locus on ABO blood group for vWF and FVIII determines their quality and levels which in turn put the person at increased risk of VTE as compared to O blood groups, group O to be at lower risk for such events.

A study conducted in Croatia also confirmed that there was association between non-OO blood group genotypes with increased risk of thrombosis. This association of increased thrombotic risk was documented to be A1 B/A2 B blood group genotypes, followed by BB/O1 B/O2 B.

More recently a Chinese study showed the evidence of increased atherosclerosis in large arteries in AB blood group patients. *On the whole, it is concluded that there is an* association between ABO blood groups and ischemic stroke, indicating that individuals belonging to non-O blood groups (A, B, or AB) present an increased risk of ischemic stroke as compared to O blood group carriers.

CONCLUSION

Our study results concluded *that there is an* association between ABO blood groups and ischemic stroke. Our study results have observed that individuals belonging to non-O blood groups (A, B, or AB) are at an increased risk of ischemic stroke as compared to O blood group carriers however we did not control possible impact of confounders such as diabetes, hypertension and dyslipidemia. Further studies are required to see this observation and to prove this as independent risk factor for ischemic stroke.

REFERENCES

- 1. Fonarow GC, Saver JL, Smith EE, Broderick JP, Kleindorfer DO, Sacco RL, et al. Relationship of national institutes of health stroke scale to 30-day mortality in medicare beneficiaries with acute ischemic stroke. J Am Heart Assoc. 2012;1(1):42-50.
- 2. Arshi S, Naheed F, Badshah M, Naz F, Nisa F. Hemorrhagic and ischemic stroke; frequency in hypertensive patients presenting with stroke at Pakistan Institute of Medical Sciences, Islamabad. Professional Med J. 2012;19(3):1-5.
- 3. Go AS, Mozaffarian D, Roger VL, Benjamin EJ, Berry JD, Borden WB. Heart disease and stroke statistics—2013 update: a report from the American Heart Association. Circulation. 2012:e2–241.
- 4. Bushnell C, McCullough LD, Awad IA, Chireau MV, Fedder WN, Furie KL, et al. Guidelines for the prevention of stroke in women: a statement for healthcare professionals from the American Heart Association/American Stroke Association. Stroke. 2014;45(5):1545-88.



- 5. Roger VL, Go AS, Lloyd-Jones DM, Benjamin EJ, Berry JD, Borden WB, et al. Heart disease and stroke statistics--2012 update: a report from the American Heart Association. Circulation. 2012;125(1):e2-e220.
- 6. Arshi S, Naheed F, Badshah M, Naz F, Nisa F. Hemorrhagic and ischemic stroke; frequency in hypertensive patients presenting with stroke at Pakistan Institute of Medical Sciences, Islamabad. Professional Med J. 2012;19(3):1-5.
- 7. Mullins ME, Lev MH, Schellingerhout D, Gonzalez RG, Schaefer PW. Intracranial hemorrhage complicating acute stroke: how common is hemorrhagic stroke on initial head CT scan and how often is initial clinical diagnosis of acute stroke eventually confirmed? AJNR Am J Neuroradiol. Oct 2005;26(9):2207-12.
- 8. Nighoghossian N, Hermier M, Adeleine P, Blanc-Lasserre K, Derex L, Honnorat J. Old microbleeds are a potential risk factor for cerebral bleeding after ischemic stroke: a gradient-echo T2-weighted brain MRI study. Stroke. Mar 2002;33(3):735-42.
- 9. Dirnagl U, Iadecola C, Moskowitz MA. Pathobiology of ischaemic stroke: an integrated view. Trends Neurosci. Sep 1999;22(9):391-7.
- 10. Tissue plasminogen activator for acute ischemic stroke. The National Institute of Neurological Disorders and Stroke rt-PA Stroke Study Group. N Engl J Med. Dec 14 1995;333(24):1581-7.
- 11. Liumbruno GM, Franchini M. Hemostasis, cancer, and ABO blood group: the most recent evidence of association. J ThrombHaemost. 2013;38(2):160-66.
- 12. Yang N, Zhang B, Xie L, Yin J, He Y, Yang X, et al. The association baseline NIH Stroke Scale score with ABO blood-subtypes in young patients with acute ischemic stroke. Atherosclerosis. 2014; 236(1):144-9.
- 13. Zakai NA, Judd SE, Alexander K, McClure LA, Kissela BM, Howard G, et al. ABO blood type and stroke risk: the Reasons for Geographic and Racial Differences in Stroke Study.J ThrombHaemost. 2014;12(4):564-70.
- 14. Sabino AP, Ribeiro DD, Domingheti CP, Rios DR, Dusse LM, CarvalhoMd, et al. ABO blood group polymorphisms and risk for ischemic stroke and peripheral arterial disease. MolBiol Rep. 2014;41(3):1771-77.
- 15. Hanson E, Karlsson S, Jood K, Nilsson S, Blomstrand C, Jern C. No evidence for an association between ABO blood group and overall ischemic stroke or any of the major etiologic subtypes. Thromb Res. 2012;130(3):339-42.
- 16. Lopez AD, Mathers CD, Ezzati M. Global and regional burden of disease and risk factors, 2001: systematic analysis of population health data. Lancet 2006;367:1747–1757.
- 17. Souto JC, Almasy L, Borrell M, et al. Genetic susceptibility to thrombosis and its relationship to physiological risk factors: the GAIT study. Genetic Analysis of Idiopathic Thrombophilia. Am J Hum Genet 2000;67:1452–1459.
- 18. Carter AM, Cymbalista CM, Spector TD, Grant PJ. Heritability of clot formation, morphology, and lysis. The EuroCLOT study. ArteriosclerThrombVascBiol 2007;27:2783–2789.
- 19. Williams FM, Carter AM, Kato B, et al. Identification of quantitative trait loci for fibrin clot phenotypes: the EuroCLOT study. ArteriosclerThrombVascBiol 2009;29:600–605.
- 20. Zhang H, Mooney CJ, Reilly MP. ABO blood groups and cardiovascular diseases. Int J Vasc Med 2012; 2012: 641917.
- 21. Ohira T, Cushman M, Tsai MY, Zhang Y, Heckbert SR, Zakai NA, Rosamond WD, Folsom AR. ABO blood group, other risk factors and incidence of venous thromboembolism: the longitudinal investigation of thromboembolism etiology (LITE). J ThrombHaemost 2007; 5: 1455–61.
- 22. Barbalic M, Dupuis J, Dehghan A, Bis JC, Hoogeveen RC, Schnabel RB, et al. Large-scale genomic studies reveal central role of ABO in sP-selectin and sICAM-1 levels. Hum Mol Genet 2010;19:1863–72.
- 23. "Luo Y, Li J, Zhang J¹, Xu Y. Low HDL cholesterol is correlated to the acute ischemic stroke with diabetes mellitus. Lipids Health Dis. 2014 Nov 14;13:171. doi: 10.1186/1476-511X-13-171.
- 24. Shaikh NA, Bhatty S, Irfan M, Khatri G, Vaswani AS, Jakhrani S. Frequency, characteristics and risk factors of carotid artery stenosis in ischaemic stroke patients. J Pak Med Assoc. 2010;60(1):8-12".
- 25. Khan MN, Khan HD, Ahmad M, Umair M. Serum total and HDL-cholesterol in ischemic and hemorrhagic stroke. Ann Pak Inst Med Sci 2014;10(1)22-26.
- 26. Abid N, Khan SA, Taseer IH. Frequency of hyperlipidemia in patients presenting with ischemic stroke. Pak J Med Health Sci. 2012;6(2):423-28."
- 27. He M, Wolpin B, Rexrode K, Manson JE, Rimm E, Hu FB, Qi L. ABO blood group and risk of



- coronary heart disease in two prospective cohort studies. ArteriosclerThrombVascBiol 2012; 32: 2314-20
- 28. Wiggins KL, Smith NL, Glazer NL, Rosendaal FR, Heckbert SR, Psaty BM, Rice KM, Lumley T. ABO genotype and risk of thrombotic events and hemorrhagic stroke. J ThrombHaemost 2009; 7: 263–9.
- 29. Williams FM, Carter AM, Hysi PG, Surdulescu G, Hodgkiss D, Soranzo N, et al. Ischemic stroke is associated with the ABO locus: the EuroCLOT study. Ann Neurol 2013;73:16–31.
- 30. Ionescu DA, Marcu I, Bicescu E. Cerebral thrombosis, cerebral haemorrhage, and ABO blood-groups. Lancet. 1976;1:278–80.
- 31. Ling X, Zheng Y, Tao J, Zheng Z, Chen L. Association study of polymorphisms in the ABO gene with ischemic stroke in the Chinese population. BMC Neurol. 2016 Aug 19;16(1):146.doi: 10.1186/s12883-016-0671-