Association of ABO Blood Group Antigen and Neurological Tumors

Gopal K. Patidar[1] Yashaswi Dhiman[2] Anjali Hazarika[1]

[1] Department of Transfusion Medicine, All India Institute of Medical Sciences, New Delhi, India
[2] Department of Immunohematology and Blood Transfusion, Himalayan Institute of Medical Sciences, Swami Rama Himalayan University, Dehradun, Uttarakhand, India

Address for correspondence Gopal K. Patidar, MD, Department of Transfusion Medicine, All India Institute of Medical Sciences, New Delhi 110029, India (e-mail: drgpatidar@gmail.com).

J Neuroanaesthesiol Crit Care 2022;9:93–98.

Abstract

Background Various risk factors for tumors such as smoking, alcohol consumption, diet, and radiation, etc., were already identified. ABO blood group antigens are also present on epithelia, endothelia, and neurons. Recent evidence suggested the role of ABO antigens in the pathogenesis of certain malignancies.

Materials and Methods A retrospective observational study was conducted in a tertiary care neurosurgical center in North India from January 2016 to December 2018. The hospital information system was used to obtain patient information while the blood center information system was used to collect blood group information. Brain tumors were majorly divided into cavernoma, glioma, meningioma, neuroma, pituitary adenoma, schwannoma, and others.

Results We found a total of 1,970 patients with brain tumors admitted during our study period. Most patients had glioma (33.55%), followed by pituitary adenoma (20.05%) and neuroma (2.23%). B blood group individuals had more prevalence of cavernoma, glioma, meningioma, pituitary adenoma, schwannoma, and others followed by O, A, and AB. Only association of O blood group with neuroma tumor was found statistically significant.

Conclusions Our patient population had blood group distribution similar to our general population and no significant association was observed by blood group antigens and brain tumors. Although neuroma was significantly associated with blood group O but the prevalence of neuroma in our patient population is very low hence large sample study is required to draw a firm conclusion regarding this association.

Keywords
- blood groups
- neurological tumors
- association
- neuroma

Introduction

Tumors accounts for one of the leading causes of death worldwide.[1] A considerable proportion of research is dedicated to revealing risk factors for these tumors such as smoking, alcohol consumption, diet, obesity, infections, environmental pollution, and radiation since centuries.[2] Genetic factors such as gene mutations and ABO blood types were also identified, with increased tumor risk.[3–5]

published online
July 20, 2022

DOI https://doi.org/10.1055/s-0042-1749656.
ISSN 2348-0548.

Thieme Medical and Scientific Publishers Pvt. Ltd., A-12, 2nd Floor, Sector 2, Noida-201301 UP, India

In 1900, Karl Landsteiner discovered the ABO blood group system based on the presence or absence of A and B antigens on the surface of red cells. These ABO antigens are complex carbohydrate molecules on the red blood cell membranes' extracellular surface.[6] ABO blood group antigens are also present on a wide range of human cells and tissues including epithelia, platelets, vascular endothelia, and neurons.[7] Since long, researchers have been attempting to shed light on the clinical implication of biological characteristic of the ABO blood system beyond transfusion medicine and transplantation. Recent evidence on the role of ABO antigens in the pathogenesis of certain malignancies like pancreatic, hepatocellular, and gastric, infectious disorders, and cardiovascular are established.[8–10] This ABO blood groups, and disease association can be utilized as screening biomarkers of the disease. A meta-analysis concluded that individuals with blood group A are more likely to develop pancreatic, gastric, breast, ovarian, and nasopharyngeal cancers while blood group O individuals have lesser risk.[5] Several possible mechanisms such as immune surveillance for malignant cells, intercellular adhesion, and inflammation, have been proposed to explain such associations.[11–13]

Recently, the incidence of brain tumors is increasing worldwide with glioma, meningioma, and pituitary adenoma, being the three main types of primary brain tumor. However, the cause remains largely unknown but the potential risk factors, such as smoking, alcohol abuse, and caffeine intake, could provide limited insight and restricted scope to take anticipatory action.

Previous literature regarding the association of ABO blood group antigens and brain tumors showed contradictory results. Diamond et al[14] found a nonsignificant positive correlation between pituitary adenomas and blood group O. However, Selverstone and Cooper[15] reported that individuals with blood groups O and B had a significantly lesser number of astrocytic tumors while higher incidence in blood group A individuals. Sowbhagya et al[16] found a significantly higher frequency of medulloblastoma patients in the group B population. In contrast, others[17,18] did not find any significant association in the frequency of blood types with astrocytoma or other brain tumors.

The study was designed with notion in mind that ABO blood groups can be utilized as a biomarker for screening of the neurological tumors in Indian population. Although there are many previous studies which attempted to know the association of ABO blood group antigens and neurological tumors, but in best of our knowledge no study was from India. Therefore, in order to contribute our view, this observational study was performed on the patients admitted to a tertiary care hospital of North India.

Materials and Methods

Study Setting

This retrospective observational study was conducted in a tertiary care neurosurgical center in North India from January 2016 to December 2018. The study was approved by the institutional ethics committee and patient's informed consent was waived off.

Study Plan

Patientsof all ages with neurological tumors who were admitted to our institute for surgical intervention were included in the study. The hospital information system was used to obtain patient demographic information such as age, gender, and diagnosis, while the blood center information system was used to collect blood group information. Brain tumors were majorly divided into seven groups, that is, cavernoma, glioma, meningioma, neuroma, pituitary adenoma, schwannoma, and others. The cavernoma group includes cavernoma and cavernous hemangioma tumors. Glioma includes gliomas, astrocytoma, ependymoma, granuloma, and fronto-basal tumors. Neuroma includes neurofibroma and neuroblastoma. Pituitary adenoma includes pituitary adenoma and craniopharyngioma. Meningioma and schwannoma do not include any other type of tumors. The other group of tumors included space-occupying lesions which cannot be categorized into the above-mentioned tumors. The collected data were plotted in Microsoft Excel software (Office 365, Microsoft Corp. USA). Tumor frequency was analyzed against blood group antigens, age, and gender of the patients. Inter- and intragroup comparisons were also carried out. Chi-square test was used for statistical analysis using online calculator SPSS software and significant results were considered with a p-value of < 0.05.

Results

During the study period, we found a total of 1,970 patients with brain tumors admitted to the neurosurgical department. There were 1,111 male patients and 859 female patients. Most patients had glioma (33.55%), followed by pituitary adenoma (20.05%), and the least number had neuroma (2.23%) (►**Table 1**). Based on blood group frequency analysis, we found that blood group B patients had a higher prevalence of neurological tumors, led by O, A, and AB (►**Table 2**). Glioma and meningioma were more in the B blood group as compared to O blood group patients, while pituitary adenoma was more prevalent in O blood group patients as compared to B and these findings were statistically insignificant. In comparison to blood groups A, B, and

Table 1 Frequency of neurological tumors in our study

Tumor	Frequency	%
Cavernoma	50	2.54
Glioma	661	33.55
Meningioma	366	18.58
Neuroma	44	2.23
Pituitary adenoma	395	20.05
Schwannoma	177	8.98
Others	277	14.06
Total	1,970	100.00

Table 2 ABO blood group frequency

Blood group	A	B	O	AB	Rh positive	Rh negative
$N = 1,970$ (100%)	412 (20.91%)	739 (37.51%)	645 (32.74%)	174 (8.83%)	1,876 (95.23%)	94 (4.77%)

Table 3 Association of neurological tumors with ABO blood group antigens

Blood group	Cavernoma ($n = 50$)	Glioma ($n = 661$)	Meningioma ($n = 366$)	Neuroma ($n = 44$)	Pituitary adenoma ($n = 395$)	Schwannoma ($n = 177$)	Others ($n = 277$)	Total ($n = 1,970$)
A	8 (16%)	136 (20.57%)	72 (19.67%)	9 (20.45%)	88 (22.28%)	37 (20.90%)	62 (22.38%)	412
B	22 (44%)	235 (35.5%)	140 (38.25%)	11 (25.0%)	152 (38.84%)	70 (39.55%)	109 (39.35%)	739
O	14 (28%)	225 (34.04%)	120 (32.79%)	21 (47.73%)[a]	120 (30.38%)	59 (33.33%)	86 (31.05%)	645
AB	6 (12%)	65 (9.83%)	34 (9.29%)	3 (6.82%)	35 (8.86%)	11 (6.21%)	20 (7.22%)	174
p-Value (O versus non-O blood group)	0.567	0.37	0.983	0.02	0.542	0.86	0.265	1,970

[a] $p < 0.05$ significant.

Table 4 Gender distribution frequency of neurological tumors

Gender	Cavernoma ($n = 50$)	Glioma ($n = 661$)	Meningioma ($n = 366$)	Neuroma ($n = 44$)	Pituitary adenoma ($n = 395$)	Schwannoma ($n = 177$)	Others ($n = 277$)
Male (56.39%) ($n = 1,111$)	22	431	156	28	223	92	159
Female (43.61%) ($n = 859$)	28	230	210	16	172	85	118

AB, blood group O was statistically significantly associated with neuroma tumors (►**Table 3**).

Gender Distribution Analysis

We found that the overall prevalence of brain tumors was higher in male patients (56.39%) as compared to female (43.61%), but cavernoma and meningioma were slightly higher in female patients (►**Table 4**).

In male patients, glioma was more prevalent in O blood group individuals (35.49% [153/431]) as compared to B blood group individuals (34.8% [150/431]), while in the female it was vice versa (B blood group [36.95% [85/230]] > O blood group [31.3% [72/230]]) although this difference was statistically nonsignificant in both male and females. Meningioma was more prevalent in females with O and AB blood group and the association was statistically significant ($p > 0.05$), other group tumors were also higher in O blood group male patients and in B blood group female patients (►**Table 4**, ►**Fig. 1**).

Age Distribution Analysis

We found that glioma was more prevalent in patients less than 50 years of age while meningioma was more in patients more than 50 years (►**Table 5**). Cavernoma and neuroma were more prevalent in the middle age group (11–40 years) while rare in extremes of age ($\leq$ 10 and > 60 years). In patients of 11 to 30 years of age, the prevalence of cavernoma, meningioma, pituitary adenoma, and others were higher in the B blood group as compared to the O blood group while glioma and neuroma showed the opposite results (O > B).

Whereas in patients of 31 to 50 years of age, glioma, meningioma, pituitary adenoma, schwannoma, and others showed statistically nonsignificant higher prevalence in the B blood group as compared to the O blood group.

In patients of 51 to 60 years prevalence of meningioma, glioma, and pituitary adenoma was higher in blood group O patients as compared to blood group B similar to the prevalence of meningioma in patients > 60years of age.

Discussion

In India, the prevalence of brain tumors varies from 5 to 10 per million people, accounting for 2% of all malignancies.[19,20] The distribution of blood groups ABO, and Rh (D) among

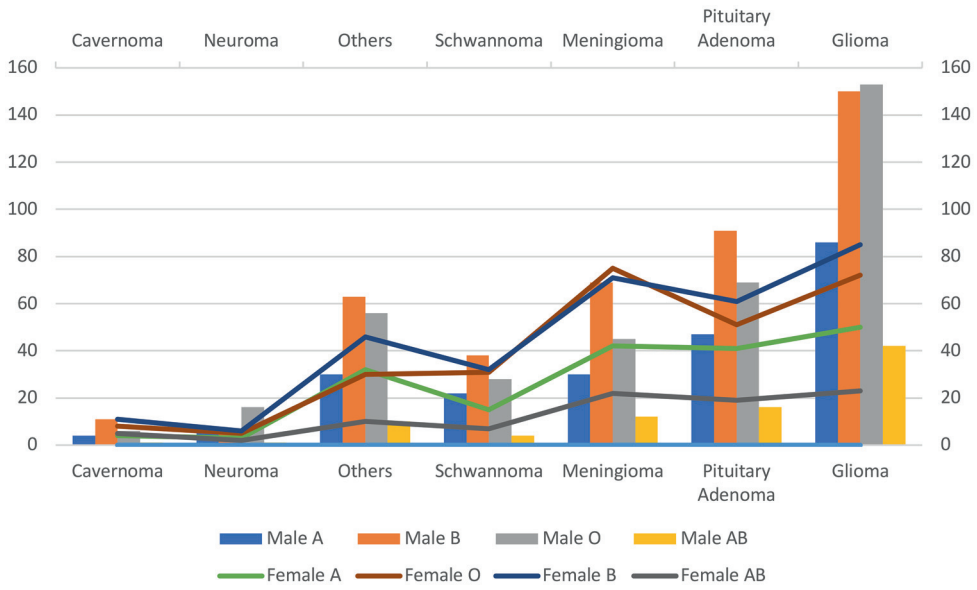

Fig. 1 The association of gender, blood group, and neurological tumors.

Table 5 Frequency of neurological tumors according to age of the patients

Age	Cavernoma ($n = 50$)	Glioma ($n = 661$)	Meningioma ($n = 366$)	Neuroma ($n = 44$)	Pituitary adenoma ($n = 395$)	Schwannoma ($n = 177$)	Others ($n = 277$)	Total ($n = 1,970$)
≤ 10	2 (1.18%)	74 (43.79%)	11 (6.51%)	4 (2.37%)	29 (17.16%)	3 (1.78%)	46 (27.22%)	169 (100%)
11–20	14 (5.45%)	100 (38.91%)	19 (7.39%)	8 (3.11%)	48 (18.68%)	21 (8.17%)	47 (18.29%)	257 (100%)
21–30	12 (2.91%)	147 (35.59%)	55 (13.32%)	13 (3.15%)	80 (19.37%)	43 (10.41%)	63 (15.25%)	413 (100%)
31–40	7 (1.71%)	137 (33.41%)	80 (19.51%)	7 (1.71%)	91 (22.20%)	44 (10.73%)	44 (10.73%)	410 (100%)
41–50	9 (2.61%)	104 (30.14%)	96 (27.83%)	6 (1.74%)	62 (17.97%)	33 (9.57%)	35 (10.14%)	345 (100%)
51–60	6 (2.60%)	61 (26.41%)	62 (26.84%)	5 (2.16%)	49 (21.21%)	21 (9.09%)	27 (11.69%)	231 (100%)
> 60	–	38 (30.65%)	43 (34.68%)	1 (0.81%)	36 (29.03%)	12 (9.68%)	15 (12.10%)	145 (100%)

patients in our study was nearly identical to that of Northern Indian populations.[21]

The relationship between blood group antigens and tumor incidence has been studied for a long time, and researchers have discovered significant association between these antigens and several tumors such as pancreatic, gastrointestinal, and ovarian tumors. The aim of this study was to determine the risk relationship between blood group antigen and neurological tumors in our country.

Genetic changes in the chromosomal region 9q34 are often reported as a risk factor for neurological tumors such as giant cell tumors, medulloblastoma, and schwannomas which is proximal to the chromosomal site of the ABO blood group gene.[22–24] Dysregulation of the ABO glycosyltransferases enzymes activity due to ABO locus genetic variation may influence the cellular membrane signaling and intracellular adhesion. In view of the same, previous researchers investigated the association of ABO blood group antigen with risk factors for neurological tumors but there findings were contradictory. It has been postulated earlier that the epidermal growth factor receptor (EGF-r) of A431 cells (a cell line originating from human epidermoid carcinoma) has antigens on glioma's vascular endothelial cells. Because of the variation in carbohydrate chains of EGF-r, this was found to be present only in people of blood group A and not in the others. This was important in the research of monoclonal antibodies for these receptors since A antigens were targeted by these antibodies.[25] This emphasizes the role of ABO antigens in brain tumors as glioma tumors are more prevalent in A blood group individuals due to abundance of EGF-r.

In a broader view, we found that glioma and neuroma were the most and least frequent types of neurological tumors, respectively, in our study population, which is almost identical to the overall prevalence of neurological

tumors in India.[26] Glioma tumors were most frequently found in patients aged 21 to 40 years, with the fewest at the extremes of age (> 60 years) in our study, which was consistent with the results of Lin et al.[27] In our study, the blood group and association with glioma was maximum in the B blood group, followed by O, A, and AB. Few previous studies have shown a higher incidence of glioma in the O blood group relative to B blood group,[28,29] whereas others have found a higher incidence in blood group A individuals.[30] Some studies concluded that blood group O has a lesser risk for malignant gliomas[31,32] while others found vice versa results.[33] In concurrence with our findings a large prospective cohort studies also concluded that no association exists between the ABO antigens and gliomas.[34] Concerning age and blood group, glioma was in higher prevalence in the O blood group of patients with less than 40 years of age while it was in higher prevalence in B blood group patients with more than 40 years of age. In our study, the gender distribution of glioma was higher in male patients than female patients, and it was almost equal in O and B blood group male patients though higher in B blood group female patients.

Pituitary adenoma and meningioma were observed in about 20% of the patient population in our study, which was close to Mehrazin's finding in more than 15% of the population.[35] On blood group-wise distribution pituitary adenoma was almost similar in all blood group patients, our findings supported the previous studies by Mehrazin[35] and Aird et al[36] while in contrast to Mayr and colleagues[14] who found a higher number of pituitary adenoma in blood group O individuals and with Chang et al[28] who found significant lower incidence in B and AB groups of patients. There was no difference in the prevalence of pituitary adenoma in both genders in all blood group patients in our study. On age and blood group-wise distribution, pituitary adenoma was found in a higher number in B blood group patients with 21 to 40 years of age. Association of the prevalence of meningioma with ABO blood groups also varies in previous studies like Sowbhagya et al,[16] which found more meningioma in O blood groups individuals, while Pearce and Yates[37] found more in A blood group and Mayr and colleagues[14] found more in B blood group individuals. In our study, it was found almost equal in all blood group individuals. Meningioma was shown to be statistically more common in females with the O and AB blood groups.

In our study, neuromas were observed in about 2.23% of the patients. On a group-wise basis, neuroma was found to be more common in group O patients than in non-O group patients, with a statistically significant difference. To the best of our knowledge, no previous study reported the association of neuroma tumors with the ABO blood group. It was highest in the middle of the age range, 21 to 40 years of age, relative to the extremes of age, 0 to 10 years and more than 60 years.

Conclusions

Our patient population had blood group distribution similar to our general population and no significant association was observed by blood group antigens and brain tumors. Although neuroma was significantly associated with blood group O but the prevalence of neuroma in our patient population is very low hence large sample study is required to draw a firm conclusion regarding this association. This study, however, paves a way for further analysis of these associations with large sample size and a meta-analysis to determine certain associations of brain tumors and ABO blood group antigens.

Conflict of Interest
None declared.

References

1 Torre LA, Bray F, Siegel RL, Ferlay J, Lortet-Tieulent J, Jemal A. Global cancer statistics, 2012. CA Cancer J Clin 2015;65(02): 87–108
2 Anand P, Kunnumakkara AB, Sundaram C, et al. Cancer is a preventable disease that requires major lifestyle changes. Pharm Res 2008;25(09):2097–2116
3 Garber JE, Offit K. Hereditary cancer predisposition syndromes. J Clin Oncol 2005;23(02):276–292
4 Franchini M, Liumbruno GM. ABO blood group and neurodegenerative disorders: more than a casual association. Blood Transfus 2016;14(02):158–159
5 Zhang BL, He N, Huang YB, Song FJ, Chen KX. ABO blood groups and risk of cancer: a systematic review and meta-analysis. Asian Pac J Cancer Prev 2014;15(11):4643–4650
6 Storry JR, Olsson ML. The ABO blood group system revisited: a review and update. Immunohematology 2009;25(02):48–59
7 Eastlund T. The histo-blood group ABO system and tissue transplantation. Transfusion 1998;38(10):975–988
8 Li Q, Yu CH, Yu JH, et al. ABO blood group and the risk of hepatocellular carcinoma: a case-control study in patients with chronic hepatitis B. PLoS One 2012;7(01):e29928
9 Song HR, Shin MH, Kim HN, et al. Sex-specific differences in the association between ABO genotype and gastric cancer risk in a Korean population. Gastric Cancer 2013;16(02):254–260
10 Rizzato C, Campa D, Pezzilli R, et al. ABO blood groups and pancreatic cancer risk and survival: results from the PANcreatic Disease ReseArch (PANDoRA) consortium. Oncol Rep 2013;29 (04):1637–1644
11 Wang Z, Liu L, Ji J, et al. ABO blood group system and gastric cancer: a case-control study and meta-analysis. Int J Mol Sci 2012; 13(10):13308–13321
12 Poole EM, Gates MA, High BA, et al. ABO blood group and risk of epithelial ovarian cancer within the Ovarian Cancer Association Consortium. Cancer Causes Control 2012;23(11):1805–1810
13 Nakao M, Matsuo K, Ito H, et al. ABO genotype and the risk of gastric cancer, atrophic gastritis, and Helicobacter pylori infection. Cancer Epidemiol Biomarkers Prev 2011;20(08):1665–1672
14 Diamond LK, Levine RP, Mayr E, Mayr M. Suspected correlation between blood-group frequency and pituitary adenomas. Science 1956;124(3228):932–934
15 Selverstone B, Cooper DR. Astrocytomas and ABO blood groups. J Neurosurg 1961;18:602–604
16 Sowbhagya P, Kolluri VRS, Krishna DKS, Das S, Das BS, Reddy GN. Intracranial tumours and blood groups. Eur J Cancer 1991;27(02): 221–222
17 Carter RL, Hitchocock ER, Sato F. Malignant glioma and ABO blood group. BMJ 1964;1:122
18 Garcia JH, Okazaki H, Aronson SM. Blood-group frequencies and astrocytomata. J Neurosurg 1963;20:397–399
19 Nair MK, Varghese C, Swaminathan R. Cancer: Current scenario, intervention strategies and projections for 2015. NCHM Background papers-Burden of Disease in India 2005:219–225

20 Yeole BB. Trends in the brain cancer incidence in India. Asian Pac J Cancer Prev 2008;9(02):267–270
21 Patidar GK, Dhiman Y. Distribution of ABO and Rh (D) Blood groups in India: a systematic review. ISBT Sci Ser 2020;16:37–48
22 Biegel JA. Cytogenetics and molecular genetics of childhood brain tumors. Neuro-oncol 1999;1(02):139–151
23 Warren C, James LA, Ramsden RT, et al. Identification of recurrent regions of chromosome loss and gain in vestibular schwannomas using comparative genomic hybridisation. J Med Genet 2003;40 (11):802–806
24 Bayani J, Pandita A, Squire JA. Molecular cytogenetic analysis in the study of brain tumors: findings and applications. Neurosurg Focus 2005;19(05):E1
25 Jones NR, Rossi ML, Gregoriou M, Hughes JT. Investigation of the expression of epidermal growth factor receptor and blood group A antigen in 110 human gliomas. Neuropathol Appl Neurobiol 1990;16(03):185–192
26 Dasgupta A, Gupta T, Jalali R. Indian data on central nervous tumors: a summary of published work. South Asian J Cancer 2016;5(03):147–153
27 Lin Z, Yang R, Li K, et al. Establishment of age group classification for risk stratification in glioma patients. BMC Neurol 2020;20 (01):310
28 Chang L, Zhao S, Dan Z, et al. ABO blood group system and risk of brain tumors: a retrospective case–control study in Northeast of China. Translational Surgery. 2018;3:49
29 Campbell AC, Gaisford W, Paterson E, Steward JK. Tumours in children. A survey carried out in the Manchester region. BMJ 1961;1(5224):448–452
30 Zampieri P, Meneghini F, Grigoletto F, et al. Risk factors for cerebral glioma in adults: a case-control study in an Italian population. J Neurooncol 1994;19(01):61–67
31 Allouh MZ, Al Barbarawi MM, Hiasat MY, Al-Qaralleh MA, Ababneh EI. Glioblastoma and ABO blood groups: further evidence of an association between the distribution of blood group antigens and brain tumours. Blood Transfus 2017;15(06):543–547
32 Turowski K, Czochra M. ABO blood groups in glioblastoma multiforme [in Polish]. Neurol Neurochir Pol 1979;13(02): 173–176
33 Kumarguru BN, Pallavi PSunila Manjunath GV, Vasan TS, Rajalakshmi BR. Histopathological study of central nervous system lesions: emphasizing association of neoplasms with ABO blood groups. J Clin Diagn Res 2017;11(04):EC15–EC20
34 Cote DJ, Downer MK, Zoltick ES, Smith TR, Stampfer MJ. ABO blood group and risk of glioma. Neuro-oncol 2017;19(06):871–873
35 Mehrazin M. ABO blood group frequency and brain tumors. Asian Pac J Cancer Prev 2006;7(04):582–584
36 Aird I, Lee DR, Roberts JA. ABO blood groups and cancer of oesophagus, cancer of pancreas, and pituitary adenoma. BMJ 1960;1(5180):1163–1166
37 Pearce KM, Yates PO. Blood groups and brain tumours. J Neurol Sci 1965;2(05):434–441

