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Study of Arteriovenous Crossings of Retinal Vasculature in Relation with Abo Blood Grouping in 500 Normal Subjects

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Abstract: ***In an attempt to find out whether any relation exists in between the arteriovenous crossings of retinal vasculature and the blood group of a person, we compared the database of vein posterior to artery (VPA) and vein anterior to artery (VAA) with the person's blood group in 500 normal subjects. Fundi of both the eyes were dilated in normal subjects and retinal photographs were taken with the fundus camera. Each eye was divided into four Quadrants- the Superotemporal, Inferotemporal, Superonasal and Inferonasal. Vessels were distinguished on the basis of colour, central reflux, and diameter. Subjects having any systemic disease like hypertension, diabetes, and with any anomaly of the eye or face were excluded from the study. We did not include subjects below 18 years and above 40 years of age. We compared the database (percentage, frequency) of arterial overcrossings (VPA) and venous overcrossings (VAA) with the blood group of subjects in all the four quadrants of both the eyes. Based on our study we found p=0.027 in the Superonasal quadrant of left eye for arterial overcrossings. In rest all the quadrants of both eyes, p value was non significant. Statistically, the Superonasal quadrant of left eye was found to have more frequency of two Arterial Overcrossings (n_1=2) in the AB+ blood group than any other blood group studied. A more reliable data can possibly be obtained by increasing the number of subjects.***

Keywords: Arteriovenous Crossings of Retina, Obstructions, Blood Group.

1. Aims and Objectives

- To form data base for Arteriovenous Crossings of Retinal Vasculature in study population.
- To compare types of Arteriovenous Crossings of Retinal Vasculature with ABO Blood Group.

2. Introduction

The retina is a light sensitive layer that lines the inner wall of the eye ball. The retinal blood vessels enter the eye ball at the optic disc and branch in a complex pattern to serve the metabolic needs of the inner retina. Small veins, within the retina (branch veins) drain blood from the retina to a large central vein which drains blood out of the eye. Sometimes an artery compresses the underlying vein making it difficult for blood to exit the eye. This blockage called retinal vein occlusion (RVO) causes the vein to dilate and leak fluid and blood.[01]

The vasculature of retina allows direct noninvasive visualization of the body's mircrovasculature. We know the retina and other end organs (like kidney and brain) have similar features anatomically and physiologically, the retinal vessels gives a unique and easily accessible window to study the health and disease of the human microcirculation.[02]

The retinal vasculature has been an object of intense interest because of its central role in the pathogenesis of several common human diseases, including diabetic retinopathy, age related macular degeneration, and retinopathy of degeneration.[03]

The retinal arterioles share similar anatomic, physiologic, and embryologic characteristics with cerebral arterioles. Therefore, pathologic changes seen in the retinal circulation, such as microaneurysms, retinal haemorrhages, arteriovenous (AV) nicking, and arteriolar narrowing, may be risk markers for concomitant or subsequent cerebrovascular disease. These signs are sometimes referred to as *hypertensive retinopathy*.[04]

BRVO occurs at arteriovenous crossing site. This observation is according to Leber, a German ophthalmologist about 100 years ago, who first time suggested the vulnerability of arteriovenous crossing and the importance of arteriosclerosis in the pathogenesis of BRVO. This observation has been reaffirmed many times since. The blocked venous branch can almost always be localized to a nearby arteriovenous crossing. In the majority of retinal arteriovenous crossings, the artery is situated anterior to the vein towards the vitreous cavity. It was seen that venous over crossings occur at 30% of all crossings in the retinas of normal eyes. Artery lies over the vein in 97% of arteriovenous crossings where BRVOs occur. Both types of crossings have been demonstrated histologically. About in 60% of normal arteriovenous crossings, artery found anterior to vein and some crossings are affected by branch retinal vein occlusion. Arterial over crossings are at comparatively higher risk of BRVO than venous over crossings, and that the risk of BRVO in an eye is

proportional to the number of arterial over crossings in the eye.[05]

The second commonest sight threatening vascular disorder are retinal vein occlusions (RVO). Central retinal vein occlusion (CRVO) and Branch retinal vein occlusion (BRVO) are its two basic types of vein occlusion. Leber in 1877 first described BRVO.[05]

In1855, Liebreich first described the clinical picture of retinal vein occlusion and called it "retinal apoplexy." Von Michel established it as a clinical entity resulting from thrombosis in 1878. [06]

Branch retinal vein occlusion can be defined as a focal occlusion of a retinal vein at an arteriovenous crossing site. Together with central retinal vein occlusion and hemicentral retinal vein occlusion, BRVO is the second most common cause of retinal vascular disease, exceeded only by diabetic retinopathy. In all but a few rare cases, the BRVO occurs at crossing sites where the artery is passing anteriorly (superficially) to the vein.[07]

The association between ABO blood group and the risk of venous thrombosis has been known since the late 1960s, with a higher risk in those with non-O blood groups than those with blood group O (2- to 4-fold increased risk). These individuals also have higher von wille brand factor levels and higher factor VIII levels, and in all likelihood this is the mechanism by which blood group is related to thrombotic risk. In the leiden thrombophilia study, it was observed that, with OO-genotypes as a reference group, the risk was almost 2-fold increased for all non-OO genotypes. Carriers of non-OO blood group genotypes and factor V Leiden had a 23-fold increased thrombosis risk compared to subjects with OO genotypes without factor V Leiden.[08]

The association between thrombosis and ABO(H) blood groups has a long history suggesting that non –O blood groups confer a higher risk of myocardial infarction, angina, peripheral vascular disease, cerebral ischaemia of arterial origin, and venous thromboembolism than group O. However, no consensus exists regarding whether these associations are real, what its magnitude is, whether such associations affect all vascular diseases equally, whether they result from a protection by O(H)(or a deleterious effect of group A), whether the association is causal and what utility there is in including ABO(H) as part of testing to identify those at risk.[09]

In a normal fundus photograph taken after fundus dilation, there are two types of vessels, arteries and veins seen. Arteries are brighter, because they transport blood rich in oxygen to the organs of the body. The veins than transport the blood, which is in low oxygen level and thus darker, to the lungs and the liver. In medical applications it would be of great help, if the vessels could be distinguished into arteries and veins, because there are many diseases with one symptom being an abnormal ratio of the size of arteries verses veins. Like in diabetes, the veins are abnormally wide, whereas diseases of the pancreas lead to narrowed arteries and high blood pressure results in thickened arteries. For detection of these diseases the retina is routinely examined. Since a basis for classification a good segmentation of blood vessels is of course needed. There are main four different features that can be used to distinguish arteries from veins in general:

- Arteries are brighter in color than veins
- Arteries are thinner than neighboring veins
- The central reflex (the light reflex of the inner parts of the vessels) is wider in arteries and smaller in veins.
- Arteries and veins generally alternate near the optic disk before branching out; that means near the optic disk, one artery is usually next to two veins and the other way round.

It is One of the most important features for the discrimination of arteries and veins is the central reflex in the red channel. Arteries and veins can be discriminated by color, size, central reflex size and topological properties. These features often provide enough information to successfully classify a vessel as artery or vein.

However, in many cases they do not suffice for the following reasons:

- When the quality of image is not good enough - which is especially the case in the outer regions of the image - the central reflex often vanishes.
- The Vessels in the outer regions of the image are generally very dark due to the shading effect (inhomogeneous lighting of the image). Arteries and veins in this region look very much alike, which necessarily leads to the misclassification of some vessels.
- Also the width of the vessel is not very useful for classification, as it changes being largest near the optic disk and smallest on the outer parts of the image.
- The alternation of veins and arteries only holds true for the vessels very near to the optic disk. When they start branching out, it is common that two branches of the same vessel lie next to each other.

So none of the typical features of arteries and veins is globally valid.[10]

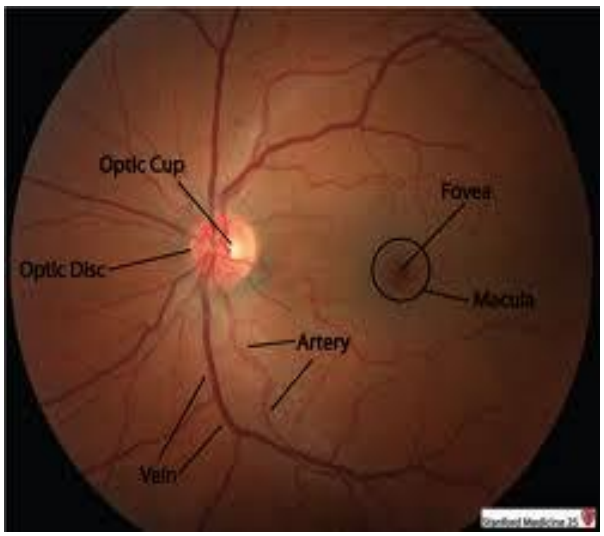

Figure 1: Normal Fundus Photograph of Left Eye Taken from A Fundus Camera after Fundus Dilation

3. Review of Literature

According to White LE (1978), the distribution of ABO blood groups in 79 patients with a retinal venous occlusion was not significantly different from that of local blood donors. In 67 of these patients it was found that the visual outcome six months after the retinal venous occlusion was significantly associated with the patients' ABO blood groups. For central and branched retinal vein occlusions taken together, 18 % of patients with blood group A had a vision of 6/9 or better in the affected eye, whereas 46 % of patients with blood group O and 49% of patients with blood groups, O, B or AB achieved this vision.[11]

An evaluation retrospectively done by Duker JS et al (1989) for the cases of 25 patients (26 eyes) with a recent, temporal, branch retinal vein obstruction to determine the relative anatomic position of the obstructed vein in relation to its crossing artery. In all the cases, the artery lay anterior to the vein, toward the vitreous cavity. They concluded that the likelihood that the artery would lie anterior to the obstructed vein at the site of blockage in a branch retinal vein obstruction was substantially greater than what would be expected by chance alone. This kind of anatomic relationship between artery and vein seems to be playing a role in the cause of a branch retinal vein obstruction and might be having therapeutic significance in light of a recent report concerning surgical treatment of such obstructions.[12]

To find out anatomy of arteriovenous crossings in branch retinal vein occlusion, Weinberg D et al (1990) studied the photographic records of 292 eyes, which includes 103 eyes with branch retinal vein occlusion, 90 fellow eyes, and 99 control eyes without any branch retinal vein occlusion. The data shown that arterial overcrossings were at relatively higher risk of branch retinal vein occlusion than the venous overcrossings, and that the risk of branch vein occlusion in an eye was proportional to the number of arterial overcrossings in the eye.[13]

Weinberg DV et al (1993) studied standard fundus photographs of 51 subjects without retinal disease. They found that in the superotemporal quadrant, crossings were distributed closer to the optic disc ($P < 0.001$), and a greater proportion of crossings were vein-posterior ($P = 0.01$) than in the inferotemporal quadrant. As a result, within a 3-disc diameter (DD) radius of the optic disc, there were significantly more vein-posterior crossings in the superotemporal than in the inferotemporal quadrant ($P < 0.001$). These findings further defined normal retinal vascular anatomy and explained the predilection for branch retinal vein occlusions to occur in the superotemporal quadrant.[14]

Peter Jefferies et al (1993) did a anatomical study of retinal arteriovenous crossings and their role in the pathogenesis of retinal branched vein occlusion and they found that branch vein occlusion occured more frequently in the superior retinal quadrant than the other three because it had more AV crossings..[15]

Ronald Klein et al (2008) did a study to describe the 15 year incidence of retinal vein occlusion and associated risk factors. They found the higher frequency of BRVO in the superotemporal quadrant compared with other Quadrants and the high frequency of the retinal arteriole found lying anterior to the vein toward the vitreous cavity. The higher frequency in the superotemporal quadrant had been attributed to a larger number of arteriovenous crossings in that quadrant or possibly to relative quadrantic differences in the type of direct contacts of the arterioles to the venules.[16]

Muraoka Y. (2013) did a study on 25 patients (25eyes) to find out morphological and functional changes in retinal vessels associated with branch retinal vein occlusion and found that at the affected A/V crossing, arterial overcrossings were found in 17 eyes and venous overcrossings were seen in 8 eyes. Where arterial overcrossing, the retinal vein was running deep under the artery at the arteriovenous crossings, and the venous lumen appeared to be preserved even at the A/V crossing. Where arterial overcrossing, the retinal vein looking to be choked and compressed between the internal limiting membrane and the arterial wall at the arteriovenous crossings. [17]

4. Material and Methods

500 subjects with known Blood Groups will be taken from MMIMSR, MULLANA. The fundi of both the eyes will be photographed and digital photographs will be taken. The Arteriovenous Crossings of Retinal Vasculature will be studied and analysed.

ABO blood grouping of each subject will be noted down in the proforma. In each quadrant total number of Arteriovenous Crossings (n) will be counted. Number of Arteriovenous Crossings where an artery crosses a vein (n_1) will be noted down and number of Arteriovenous Crossings where vein crosses an artery (n_2) will be noted. The data so obtained will be compiled and percentage of n_1 and n_2 will be calculated. These findings will be compared with the subjects having A, B, O and AB Blood Group. The data so collected will be compiled, tabulated, analysed and result will be presented.

Exclusion Criteria

- Any anomaly of face or eye will be excluded.
- Subjects below 18 and above 40 years of age.
- Person having any systemic disease like Hypertension, Diabetes.

Retinal photographs are being taken by Fundus Camera

5. Observations

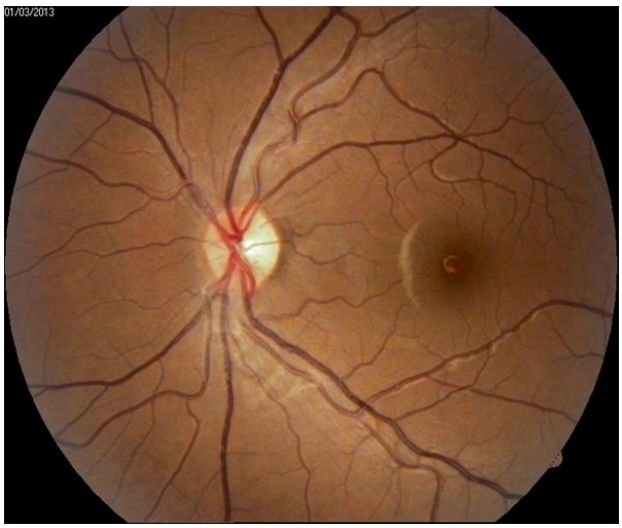

Figure 2: Left Eye with two Arterial Overcrossings in Superonasal Quadrant. (AB+ Blood Group).

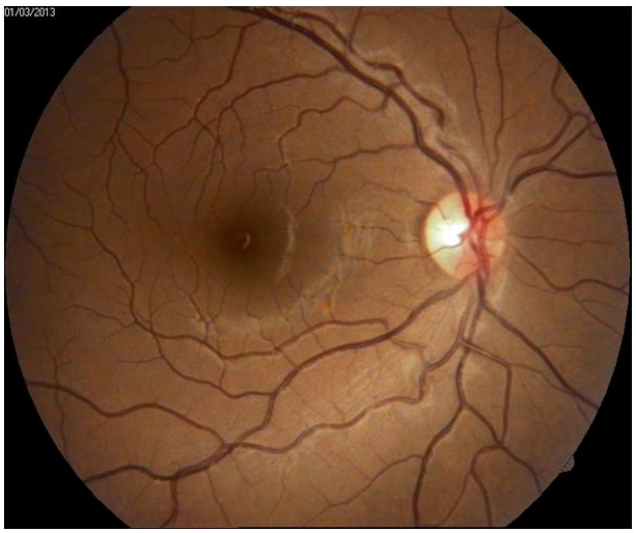

Figure 3: Right Eye with AB+ Blood Group

Table 1: Frequencies of Blood Group included in the study

Blood Groups					
		Frequency	Percent	Valid Percent	Cumulative Percent
Valid	A-	36	7.2	7.2	7.2
	A+	89	17.8	17.8	25
	AB-	8	1.6	1.6	26.6
	AB+	44	8.8	8.8	35.4
	B-	30	6	6	41.4
	B+	138	27.6	27.6	69
	O-	39	7.8	7.8	76.8
	O+	116	23.2	23.2	100
	Total	500	100	100	

Out of 500 subjects included in our study 36 subjects were having A- blood group, 89 subjects were of A+ blood group, 8 subjects were of AB- blood group, 44 subjects were of AB+ blood group, 30 subjects were of blood group B-, 138 subjects were of B+ blood group, 39 subjects were of O- blood group, and 116 subjects were of O+ blood group.

Table 2: Left Eye Superonasal Quadrant Arterial Overcrossings. (P=0.027, Significant).

			BLOOD GROUP								Total
			A-	A+	AB-	AB+	B-	B+	O-	O+	
	0	Count	1	5	1	1	0	10	1	8	27
		% within Blood Group	2.80%	5.60%	12.50%	2.30%	0.00%	7.20%	2.60%	6.90%	5.40%
	1	Count	7	22	0	4	7	31	8	33	112
		% within Blood Group	19.40%	24.70%	0.00%	9.10%	23.30%	22.50%	20.50%	28.40%	22.40%
	2	Count	9	18	2	19	8	44	11	26	137
		% within Blood Group	25.00%	20.20%	25.00%	43.20%	26.70%	31.90%	28.20%	22.40%	27.40%
	3	Count	11	23	1	7	5	18	8	25	98
		% within Blood Group	30.60%	25.80%	12.50%	15.90%	16.70%	13.00%	20.50%	21.60%	19.60%
	4	Count	4	8	1	9	4	17	6	14	63
		% within Blood Group	11.10%	9.00%	12.50%	20.50%	13.30%	12.30%	15.40%	12.10%	12.60%
	5	Count	3	7	2	1	2	11	1	5	32
		% within Blood Group	8.30%	7.90%	25.00%	2.30%	6.70%	8.00%	2.60%	4.30%	6.40%
	6	Count	1	1	0	3	2	5	2	4	18
		% within Blood Group	2.80%	1.10%	0.00%	6.80%	6.70%	3.60%	5.10%	3.40%	3.60%
	7	Count	0	4	0	0	2	2	2	0	10
		% within Blood Group	0.00%	4.50%	0.00%	0.00%	6.70%	1.40%	5.10%	0.00%	2.00%
	8	Count	0	1	1	0	0	0	0	1	3
% within Blood Group		0.00%	1.10%	12.50%	0.00%	0.00%	0.00%	0.90%	0.60%		
Total		Count	36	89	8	44	30	138	39	116	500
		% within Blood Group	100.00%	100.00%	100.00%	100.00%	100.00%	100.00%	100.00%	100.00%	100.00%

AB+ blood group has more frequency of two number of n_1 than other blood groups.

Chi-Square Tests			
	Value	df	Asymp. Sig. (2-sided)
Pearson Chi-Square	78.100(a)	56	0.027
Likelihood Ratio	69.508	56	0.106
Linear-by-Linear Association	2.344	1	0.126
N of Valid Cases	500		
a 42 cells (58.3%) have expected count less than 5. The minimum expected count is .05.			

Only this is significant. Rest all quadrants of both the eyes the value we found is insignificant.

6. Discussion

This study was conducted in Maharishi Markandeshwar Institute of Medical Science and research, Mullana, Ambala on 500 subjects. The aim of the study was to form database of Arteriovenous Crossings of Retinal Vasculature and to compare the blood groups of subjects with the database of Arteriovenous Crossings. Subjects below 18 years or above 40 years of age were not included in the study. Subjects with any anomaly of eye or face were excluded. Subjects having any systemic disease like diabetes, hypertension were also excluded. The subjects after dilation were made to sit in front of fundus camera and retinal photographs were taken of both eyes of each subject. Then these photographs were divided into four quadrants namely Superotemporal quadrant, Inferotemporal quadrant, Superonasal quadrant, and Inferonasal quadrant. Further these quadrants were analysed for arterial overcrossing (n_1) and venous overcrossings (n_2) in each quadrant of each eye. The data so obtained were tabulated, analysed and compared with the blood group of the subjects.

We found that out of 500 subjects included in the study 36 subjects were having A- blood group, 89 subjects were of A+ blood group, 8 subjects were of AB- blood group, 44 subjects were of AB+ blood group, 30 subjects were of B- blood group , 138 subjects were of B+ blood group, 39 subjects were of O- blood group, and 116 subjects were of O+ blood group.

From our study we found that in the Superonasal quadrant of the left eye the p value was significant (p=0.027). In rest all the quadrant the p value was non significant. The p values were calculated by chi-square test.

Furthermore we also found that in the Superonasal quadrant of the left eye there was more frequency of two arterial overcrossings (n1=2) in the AB+ blood group than any other blood group studied.

We could not find any other study of similar type in India or Abroad for comparison. This study aims at providing a baseline data and to find out relationship between blood groups and Arteriovenous Crossings of retinal vasculature.

7. Summary and Conclusion

In the present study conducted on 500 subjects, all four quadrants of each eye were studied. Number of Arteriovenous Crossings were noted. An attempt was made to find a co-relation between Arteriovenous Crossings and ABO blood group. It was found that in the Superonasal quadrant of the left eye the p value was significant for Arterial Overcrossings (p=0.027). In rest all the quadrants the p value was non significant.

It was observed that in the Superonasal Quadrant of the left eye there was more frequency of two arterial overcrossings (n_1=2) in the AB+ blood group than any other blood group studied.

A more reliable data can possibly be obtained by increasing the number of subjects.

Relationship between Arteriovenous Crossings and ABO blood group may provide more information in patients with known familial and genetically predetermined diseases like Insulin Dependent Diabetes Mellitus, Essential Hypertension, Thalassemia etc.

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