A CASE CONTROL STUDY OF RETINAL VESSEL DIAMETER IN PATIENTS OF RETINAL ISCHAEMIA AND PATIENTS WITHOUT RETINAL ISCHAEMIA

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INTRODUCTION:
Retinal ischaemic disorders have got a large impact on the quality of vision and quality of life of the patients as they have blinding complications like neovascular glaucoma if left untreated and they also have a predictive value for cardiovascular and cerebrovascular events[4]. Amongst retinal ischaemic disorders diabetic retinopathy is the most common[1,2], and widely studied disease. Other common ischaemic diseases include retinal arterial and venous occlusions, ocular ischaemic syndrome etc.

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This study was aimed to evaluate difference between retinal vessel diameter including retinal arteriolar and venular width and arterio-venous ratio in patients with retinal ischaemia versus patients without retinal ischaemia and also to study the risk factors associated with retinal ischaemic disorders.

MATERIAL AND METHODS:
The study was conducted in the Department of Ophthalmology, SSG Hospital, Vadodara, during November 2012 to September 2013. Approval was obtained from the ‘Institutional research and ethics committee’. Written and informed consents from all the participants of our study were obtained. The recruited subjects were male and female aged 25-65 years. In the case group 37 patients taking their treatment for retinal ischaemia at SSG Hospital were included whereas in control group 71 normal subjects either patient’s relatives or patients visiting outpatient department of SSG Hospital were included. All participants underwent history taking, blood pressure, heart rate, random blood glucose and body mass index measurement followed by which all subjects underwent mydriatic digital retinal photography for each eye.

RESULTS:
65% of the cases occurred in the age group between 46 and 65 years. 65% cases of retinal ischaemia were male and 35% were female. 54% of cases were of retinal venous occlusion including CRVO, BRVO and HRVO. 24% of cases were of PDR. 35% of cases had raised homocysteine levels. The average arteriolar and venular diameter was 75.81 microns and 162.21 microns in cases whereas the average retinal arteriolar and venular diameter in controls was 98.5 microns and 141.7 microns respectively. The mean A/V ratio value was found to be 0.47 and 0.70 amongst cases and controls respectively.

CONCLUSION:
In this study patients of retinal ischaemia were found to have increased retinal venular diameter whereas retinal arteriolar diameter and the arterio-venous ratio was found to be decreased compared to those without retinal ischaemia.

KEY WORDS: Retina vessel diameter, Retinal ischaemia, Diabetic retinopathy

ABSTRACT:
BACKGROUND AND OBJECTIVES: This study was aimed to evaluate difference between retinal vessel diameter including retinal arteriolar and venular width and arterio-venous ratio in patients with retinal ischaemia versus patients without retinal ischaemia and also to study the risk factors associated with retinal ischaemic disorders.

MATERIAL AND METHODS: In this case control study 37 patients having retinal ischaemic diseases with ongoing treatment and 71 normal age and sex matched controls subjects visiting outpatient department of SSG Hospital were included. All participants underwent history taking, blood pressure, heart rate, random blood glucose and body mass index measurement followed by which all subjects underwent mydriatic digital retinal photography for each eye.

RESULTS: 65% of the cases occurred in the age group between 46 and 65 years. 65% cases of retinal ischaemia were male and 35% were female. 54% of cases were of retinal venous occlusion including CRVO, BRVO and HRVO. 24% of cases were of PDR. 35% of cases had raised homocysteine levels. The average arteriolar and venular diameter was 75.81 microns and 162.21 microns in cases whereas the average retinal arteriolar and venular diameter in controls was 98.5 microns and 141.7 microns respectively. The mean A/V ratio value was found to be 0.47 and 0.70 amongst cases and controls respectively.

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patients without retinal ischaemia. Patients who had previous pan retinal photocoagulation or extensive focal laser treatment or anti VEGF intravitreal injections, refractive error beyond sphere equivalent of +/- 3 in either eye, concurrent ocular pathology like cataract, glaucoma, corneal/vitreous opacities, small pupil, other retinal or optic nerve head pathology, uncontrolled systemic hypertension (>140/90)[12]were excluded from the study. Patients who underwent angioplasty or have had stroke or myocardial ischaemia in past were also excluded. All participants were invited for a single visit during which detailed ocular and systemic history was taken and their blood pressure, heart rate, random blood glucose and body mass index were recorded followed by which all subjects underwent mydriatic retinal photography with 50 degree nasal and temporal retinal images for each eye[10]. Three set of retinal images were captured for each subject ten minutes apart. Each set consisted of nasal and temporal field images for each eye. Then all subjects underwent fundus fluorescein angiography, the images of which were used to calculate the vessel diameter[9] and correlated with the colour fundus photograph. Two values were taken and an average was taken.

RESULTS: All subjects of retinal ischaemia were between the ages of 25 to 65. Among the cases the incidence of retinal ischaemia was found to be higher among patients aged 46 to 65 years whereas it was least between ages of 25 to 35 years. Among controls, maximum number of patients were between 46 to 55 years and lesser between ages of 56 to 65 years. Retinal ischaemia was found to be more in males (65%) than females (35%) among cases whereas among controls nearly equal males and females were recruited, 51% and 49% respectively. Amongst the 37 cases of retinal ischaemia, CRVO was found to be the most frequent cause with 12 of 37(33%) patients having it. PDR and BRVO came in close second with 9(24%) patients each having the aforementioned disorders. Only 2(5%) patients presented with CRAO and OIS whereas there was only one (3%) patient each of HRVO, pre-eclampsia and ischaemic retinopathy in our study. No patient presented with sickle-cell retinopathy or Eales’ disease which were also part of our study (Figure 3).

FIGURES

- Figure 1: showing the annotated image of a patient with CRVO with vessel diameter noted in millimetres (1: 0.112 mm, 2: 0.187 mm)

- Figure 2: A fundus fluorescein angiographic image which was used to calculate the vessel diameter and correlated with the colour photograph. Two values were taken and the average was taken.
Of cases, 27% of patients gave an affirmative on having smoked. Amongst controls, 5% had history of smoking. The left eye was involved in 62% of the patients and the right eye was involved in 35% patients; in 3% there was bilateral involvement. In approximately half the number of controls right eye was taken and in rest half the left eye was taken in a random manner. The visual acuity varied between hand movements to perception of light in OIS to 6/36 in patients with BRVO. Lipid levels were found to be elevated in 68% patients of case group. In none of the controls any abnormality in the lipid levels was detected. Carotid doppler angiogram was done in 37 cases out of which 8% had narrowing of lumen (> 80% narrowing) whereas in 92% it was found to be normal. 35% of cases had raised homocysteine levels and were between 37 and 64 years of age. Amongst case group, 72% males and 60% females had abnormal body mass index (either overweight or obese) whereas amongst control group 68% males and 52% females had abnormal body mass index. Student z test was performed (t-test in samples greater than 30). The arteriolar vessel width in cases was found to be 75.81 microns with standard deviation of 28.4 and in controls it was 98.50 microns with standard deviation of 17.25. The standard error of means was -4.398 with a 95% confidence interval from 31.4 to -13.9. The P value was <0.0001 in the t-test. (Table: 1) The venular diameter was 162.21 microns in cases with a standard deviation of 45.42 and 141.74 microns in controls with standard deviation of 19.56. The standard error of means was 5.869 with a 95% confidence interval from 8.8 to 32.0. The P value was 0.0007. (Table: 1)

### Table 1: Arteriolar and venular diameter

<table>
<thead>
<tr>
<th></th>
<th>Arteriolar</th>
<th>Venular</th>
</tr>
</thead>
<tbody>
<tr>
<td>Diameter (microns)</td>
<td>Standard Deviation (microns)</td>
<td>Standard Error</td>
</tr>
<tr>
<td>Cases</td>
<td>75.81</td>
<td>28.40</td>
</tr>
<tr>
<td>Controls</td>
<td>98.50</td>
<td>17.25</td>
</tr>
<tr>
<td>Venular</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cases</td>
<td>162.21</td>
<td>45.42</td>
</tr>
<tr>
<td>Controls</td>
<td>141.74</td>
<td>19.56</td>
</tr>
</tbody>
</table>

P<0.05 considered significant

The t-test was applied to the arteriolar–venular ratio. The A/V ratio was found to be 0.47 in the cases and 0.70 in the controls. The standard deviation in the cases was 0.13 and was 0.09 in the controls. The standard error of means was 0.0214 with a 95% confidence interval from -0.27 to -0.18. The P value was <0.0001 and was highly significant. (Table: 2)
Table 2: Arteriolar/Venular width ratio

<table>
<thead>
<tr>
<th>A/V RATIO</th>
<th>Diameter (microns)</th>
<th>Standard Deviation (microns)</th>
<th>Standard Error</th>
<th>95% Confidence Interval</th>
<th>Significance level</th>
</tr>
</thead>
<tbody>
<tr>
<td>cases</td>
<td>0.47</td>
<td>0.13</td>
<td>0.0214</td>
<td>-0.27 to -0.18</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>controls</td>
<td>0.70</td>
<td>0.09</td>
<td></td>
<td></td>
<td></td>
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</tbody>
</table>

P<0.05 considered significant

The odds ratio cross product test was performed. The ratio was calculated as 34x61/3x10. (Table: 3)

Table 3: Odds ratio- cross product of A/V ratio in cases and controls

<table>
<thead>
<tr>
<th>A/V RATIO</th>
<th>CASES</th>
<th>CONTROLS</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;0.60</td>
<td>34</td>
<td>10</td>
</tr>
<tr>
<td>&gt;0.60</td>
<td>3</td>
<td>61</td>
</tr>
</tbody>
</table>

The odds ratio was 69.1. The likelihood of retinal ischaemia is 69.1 times higher in person having an A/V ratio of less than 0.6. The minimum arteriolar diameter in cases was found to be 31 microns and maximum diameter was 134 microns. In controls, the minimum arteriolar diameter was 69 microns and the maximum diameter was 135 microns. The minimum venular diameter in cases was found to be 80 microns and maximum diameter was 268 microns. In controls, the minimum venular diameter was 111 microns and the maximum diameter was 207 microns. (Figure: 4)

Venular diameter was significantly higher among the cases, which was consistent with the pathology of certain ischaemic conditions such as central retinal vein occlusion and proliferative diabetic retinopathy.

**DISCUSSION:** Numerous studies have been published over the last 40 years on the importance of retinal arteriolar and venular diameter in systemic and ocular disorders. The retinal vessels are the only vessel of the body which can be directly visualized. Normal retinal arterial diameter ranges between 40-160 microns. [3] In this study we compared the retinal arteriolar and venular diameter and the arterio-venous ratio in 2 groups which included 37 cases and 71 controls. 65% of the cases occurred in the age group between 46 and 65. In the younger age group, it is imperative not to miss a condition like pre-eclampsia and Eales’ which present with feature of ischaemia and if caught in their prime, may not cause severe loss of vision. In our study 65% of the cases of retinal ischaemia were males and 35% were females, the reason of which are manifold including greater susceptibility of male for atherosclerosis, hypertension and history of smoking. 54% of cases were of retinal venous occlusion including CRVO, BRVO and 1 case of HRVO. 24% of cases were of PDR. The visual acuity varied between hand movements to perception of light in OIS to 6/36 in patients with BRVO. 27% of the cases had a history of smoking and 32% had raised lipid level. Lipid and cholesterol
levels do contribute towards occurrence of retinal ischaemia and form a part of vicious cycle by which they lead to atherosclerosis, stroke and hypertension which can all predispose to retinal ischaemia. 35% of cases had raised homocysteine levels and were between 37 and 64 years of age. In the study conducted by Gao W. Et al[5], hyperhomocysteinemia and low folate levels were found to be risk factors for central retinal vein occlusion. The CRVO patients had a significantly higher homocysteine level than normal controls. Thus, our study had also shown that the raised homocysteine levels is a significant risk factor in the occurrence of the retinal ischaemia in middle aged individuals. The mean arteriolar and venular diameter was 75.81 microns and 162.21 microns in cases whereas the average retinal arteriolar and venular diameter in controls was found to be 98.5 microns and 141.7 microns respectively taking into fact that according to the T test, a p<0.05 is significant, our findings proved to be highly significant and the arteriolar width of controls was also comparable with the study done by J.Jost B. et al[6]. The study conducted by Monique et al[7] was specifically designed for proliferative diabetic retinopathy. The study concluded that even sole venular dilatation is independent and early indicator of progression of NPDR to PDR in African American population with diabetes mellitus. In our study, the average venular diameter in PDR patients was 143 microns but with significant amount of arteriolar attenuation which was concurrently seen. The difference in the values between our study and the Monique et al study were manifold. Firstly, Monique et al included type 1 diabetic mellitus patients whereas in our study all diabetics were of type 2 diabetes mellitus. Secondly, the age of patients in Monique was less than 30 years and in our study it was between 40 to 65 years. Thirdly, the technique used for calculation was different in the study by Monique, they used seven stereo photographic methods and lastly they included only African American patients whereas our study was conducted on Indian patients. The A/V ratio was calculated in the study conducted by Mitchelle et al[8]. This was calculated for Asian Regional Integration Centre (ARIC) and the mean value was found to be 0.84. In our study, the mean value was found to be 0.70 amongst controls. The A/V ratio was significantly smaller in patients with retinal ischaemia (0.47 compared to 0.70 in controls) and this may be either due to venular dilatation or due to arteriolar constriction or both these factors being important. Carotid Doppler angiography showed >80% narrowing in 8% of cases – 2 were of OIS and one was of CRAO. It could be a useful tool and help in the clear cut diagnosis and the management of OIS. Arteriolar and venular vessel diameter can be estimated by retinal fundus photographs, albeit in a little crude manner even without any supplementary and expensive equipment or software. They can be a useful tool in the study of retinal ischaemic disorders. CONCLUSION: From our study, we derived that in patients of retinal ischaemia, the retinal venular diameter was found to be increased and the retinal arteriolar diameter as well as the arterio-venous ratio was found to be decreased compared to those without retinal ischaemia. In our study, hyperhomocysteinaemia was found to be a risk factor for retinal ischaemic disorders. The limitation of this study is the lack of large sample size and advanced equipments for retinal vascular widths measurement. A multicentric study with large sample size would throw light on future course.

REFERENCES:


