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Original Research Article

Retinal vein occlusion in patients with diabetes mellitus in a tertiary care teaching hospital

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ABSTRACT

Background: Retinal vein occlusion is an important cause of vision loss. Diabetes mellitus, hypertension and dyslipidemia increase the risk for endothelial damage or abnormal blood flow and thus associated with retinal vein occlusion. To access the prevalence of retinal vein occlusion in diabetic patients and its association with systemic illness in a tertiary care teaching hospital, Gorakhpur.

Materials and Methods: A descriptive, observational study was done on diabetic patients attending the eye OPD. Consent was taken and patient underwent direct and indirect ophthalmoscopy, optical coherence tomography and fundus fluorescein angiography. Medical history regarding duration of diabetes, hypertension, hyperlipidemia, cerebro-vascular accidents were obtained.

Result: The study included 846 patients with type II diabetes mellitus. In this study 6.6% (n=56) patients detected with RVO in which 34(61%) were male and 22 (39%) were female. The mean age was 58 years. 78.5% (n=44) of them had BRVO and 21% (n=12) had CRVO. The frequency of unilateral BRVO (n=34, 81%) was more common than bilateral BRVO (n=10, 71%). The frequency of unilateral CRVO was 19% (n=8) and bilateral CRVO was 28.5% (n=4). The duration of diabetes and uncontrolled diabetes affects the occurrence of RVO.

Macula involving BRVO was found in 59% (n=26) of patients, suggesting that diabetic patients with RVO has greater risk of severe vision loss due to macular involvement in BRVO.

Diabetic patients with history of hypertension, hyperlipidemia, CVA were significantly associated with RVO ($p < 0.0001$).

Conclusion: Patients with type II diabetes mellitus carries risk for development of RVO.

1. Introduction

Diabetic retinopathy is a leading cause of blindness among the working age adults worldwide and in the elderly age group.[1,2] Retinal vein occlusion (RVO) is the second most common cause of retinal vascular disease after diabetic retinopathy and a significant cause of painless loss of vision.[3–5] Global estimation of retinal vein occlusion in adults are 16.4 million in which 13.9 million affected with BRVO and 2.5 million by CRVO.[6] In current scenario, changes in the life style towards sedentary life may lead to increase in systemic diseases such as diabetes mellitus, hypertension, hyperlipidemia and cardiovascular diseases predispose to retinal problems.[7] Late detection and delayed treatment may result in irreversible visual impairment and blindness from vision threatening complications.[8] The Blue Mountain Eye study found that a 10-year risk of RVO in the United States to be 1.6% with no predilection for gender or race. The Beaver Dam Eye Study found that a 15-year risk of BRVO to be 1.8%, which is three times more common than CRVO at 0.5%.[9] A study from United States found that higher prevalence in Asians and Hispanics compared

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to Caucasians, but this was not statistically significant.[6]

On the basis of location of venous occlusion, retinal vein occlusion is classified into Branch retinal vein occlusion (BRVO) and Central retinal vein occlusion (CRVO).[10,11] BRVO is further classified into macula involving and macula not involving. CRVO is also classified into ischemic and non-ischemic.

BRVO is more common than CRVO.[12]

The main pathogenesis for development of BRVO is arterial stiffening, which may cause venous compression at the arterio-venous crossing site where it shares a common adventitial sheath. This compression of the vein causes turbulent blood flow that leads to thrombus formation in the lumen of the vein.[9] Most commonly affected quadrant in BRVO is superotemporal in 63% to 66% of eyes affected with BRVO. Inferotemporal retina involvement in 22% to 43% of eyes affected with BRVO. Similarly, the central retinal vein and artery posses a common sheath at crossing points posterior to the lamina cribrosa so that atherosclerotic changes of the artery may cause CRVO.[13] The fundus findings in case of retinal vascular damage associated with diabetic retinopathy or retinal vascular occlusion are presence of retinal haemorrhages, exudates, cotton wool spots and signs of development of retinal complications such as neovascularization or macular edema.[14] The extent of retinal ischemia because of vein occlusion is detected with the help of fundus fluorescein angiography.

Increasing age, diabetes, hypertension, smoking, hyperlipidemia, are the major risk factors for development of BRVO.[15] Risk of BRVO in the fellow eye increases 7% to 10%, when one eye has already developing BRVO.[16]

2. Materials and Methods

The present study is a descriptive observational study conducted from January 2021 to December 2021. All patients with type II diabetes, attending OPD of Department of Ophthalmology at BRD Medical College, Gorakhpur, Uttar Pradesh have been included in this study.

Written consent were taken and patient underwent for visual acuity assessment with snellen's chart, intra ocular pressure (IOP) measurement, slit lamp examination, direct and indirect ophthalmoscopy, OCT and FFA where needed. A detailed history was obtained using a standardized questionnaire. All subjects underwent blood examination for fasting blood sugar levels, 2 hour postprandial blood sugar, random blood sugar level and percentage of HbA1c. Blood examination was done for serum lipid profile also. Measurement of blood pressure was recorded using standard technique.

ICMR (Indian Council of Medical Research) guidelines were used for documentation of status of Diabetes.[17] We defined a good control of diabetes when fasting plasma glucose <110 mg/dl, 2 hour postprandial glucose <140 mg/dl and HbA1c <5.7%. We defined a person as diabetic when fasting plasma glucose level was >126 mg/dl, 2 hour postprandial glucose >200 mg/dl, random blood glucose >200 mg/dl and HbA1c >6.5%. As per Indian standards, hypertension was defined as normal when the blood pressure was <130/86 mmHg and hypertensive when the blood pressure was >140/90 mmHg.[18]

The classification for hyperlipidemia are based on the national cholesterol education panel"s (NCEP) adult treatment programme 3 guidelines.[19] Lipid profile was considered normal when triglyceride level was <150 mg/dl and abnormal when >150 mg/dl and total cholesterol level was considered as normal when <200 mg/dl and abnormal when >200 mg/dl. High density lipoprotein (HDL) was considered as normal when >40 mg/dl and abnormal when <40 mg/dl. Low density lipoprotein (LDL) was taken as normal when <130 mg/dl and abnormal when >130 mg/dl.

The definition of stroke was considered as per World Health Organization (WHO) criteria:[20] (1) in which an area of brain is transiently or permanently affected by ischemia or bleeding or (2) in which one or more brain blood vessels are primarily involved in a pathological process, or (3) a combination of these conditions. Visual impairment was determined on the basis of International Classification of Disease 10^{th} edition.[21] We defined as visual impairment when best corrected visual acuity (BCVA) was <6/18, low vision was defined as a BCVA <6/18 but not less than 3/60. Blindness was considered when BCVA was <3/60.

2.1. Inclusion criteria

All patients with type II diabetes mellitus with RVO, age more than 45 years, both male and female gender.

2.2. Exclusion criteria

Patients with type II diabetes mellitus but with no confirmation of RVO tested by ocular examination and expert opinions, age less than 45 years, any associated ocular diseases causing visual impairment, immuno-compromised patients or patients on immuno-suppressive drugs, pregnant ladies and patient unwilling for long term follow up.

2.3. Statistical analysis

Chi-square test was used to analyze the data. P value <0.05 was considered statistically significant.

3. Results

The study was conducted among all patients with type II diabetes mellitus attended the OPD of Ophthalmology department of BRD Medical College, Gorakhpur, Uttar Pradesh, between the time period from January 2021–December 2021. The study included 846 diabetic patients. The mean age was 58 years. In this study, 6.6%

Table 1: Gender distribution

Gender	No.ofpatients (n=56)	Percentage
Male	34	61%
Female	22	39%

Table 2: Clinical profile of RVO in diabetic patients

Category	No. of subjects (n, %)	No. of eyes	No. of subjects Both eyes involvement (n, %)	No. of subjects One eye involvement (n, %)	Right eye (n, %)	Left eye (n, %)
BRVO	44(78.5%)	68	10(71%)	34(81%)	24(80%)	10(83%)
CRVO	12(21%)	20	4(28.5%)	8(19%)	6(20%)	2(16.6%)
Total	56	88	14	42	30	12

Table 3: Vision threatening RVO in diabetic population

BRVO, No. of eyes (n,%)			CRVO, No. of eyes (n,%)		
Macula involved	Macula not involved	Total	Non-Ischemic	Ischemic	Total
26(59%)	18(41%)	44	9(75%)	3(25%)	12

Table 4: BCVA among the subjects with RVO

Visual acuity	Total RVO		BRVO		CRVO	
	No. of subject	%	No. of subject	%	No. of subject	%
Normal vision	35	62.5	26	59	9	75
Low vision	21	37.5	18	41	3	25
Total	56		44		12	

Table 5: Duration of diabetes in people with RVO

Diabetes duration	Right Eye Patients	%	Left Eye Patients	%	Both Eyes Patients	%
≤5 years	8	36.3%	6	30%	4	28.5%
6-10 years	6	27.2%	6	30%	2	14.2%
11-15 years	4	18%	4	20%	4	28.5%
>16 years	4	18%	4	20%	4	28.5%
Total	22		20			14

Table 6: Status of diabetes control at presentation in people with retinal vascular occlusion

Control of diabetes	Right eye Patients	%	Left eye Patients	%	Both eye Patients	%
Well controlled	2	9	4	20	2	14
Not controlled	16	72	14	70	11	78
No data	4	18	2	10	1	7
Total	22		20		14	

Table 7: Association between RVO and its risk factors

Risk factors		Retinal vein occlusion				
		Yes	No	Total	SD	P value
Hypertension	No	16	379	395	15.64	
	Yes	26	425	451	16.98	P<0.0001
	Total	42	804	846		
CVD	No	38	770	808	14.86	
	Yes	4	34	38	13.88	P<0.0001
	Total	42	804	846		
Hyperlipidemia	No	20	442	462	15.42	
	Yes	22	362	384	14.87	P<0.0001
	Total	42	804	846		

(n=56) patients were detected with RVO with 34 (61%) male and 22 (39%) female.

BRVO was found in 78.5% (n=44) of patients among them 34 patients (81%) had unilateral BRVO and 10 patients (71%) had bilateral involvement. CRVO was found in 21% (n=12) of patients among them 8 (19%) patients had unilateral involvement and 4 patients (28.5%) had bilateral CRVO.

The frequency of BRVO was greater than CRVO. BRVO was found 3.7 times more common than CRVO. Frequency of unilateral BRVO was greater than bilateral BRVO. Macula involving BRVO was found in 59% (n=26) of patients, suggesting that it is more common than non-macula involving BRVO (n=18, 41%). Non-Ischemic CRVO (n=9, 75%) was found more than the ischemic CRVO (n=3, 25%).

37.5% (n=21) of total RVO subjects had low vision in better eyes after best correction. Among the subjects with BRVO and CRVO, low vision was 41% (n=18) and 25% (n=3) respectively. Frequency of low vision was seen more in patients with BRVO as occurrence of BRVO is more common than CRVO.

The duration of diabetes varied from >5 years to >16 years. The frequency of RVO in this study was maximum within 5 years of detection of diabetes mellitus (n=8, 36%).

Diabetic patients along with history of hypertension, hyperlipidemia, CVA were significantly associated with occurrence of RVO ($p<0.0001$) in this study.

4. Discussion

RVO is the second most common retinal vascular disorder and cause of vision loss due to macular edema and retinal ischemia. The prevalence of RVO in this study was 6.6%. In our study there was significant association found between RVO, Diabetes mellitus and Hypertension which is similar to Beaver Dam study.[22]

P M Dodson et al.[23] reported that Asian population are at higher risk for occurrence of RVO than Caucasians in the diabetic population and concluded that the main underlying medical conditions for RVO in diabetics are hypertension and hyperlipidemia. They reported that 80% of diabetics with BRVO, were hypertensive.

A study conducted by Harsha Bhattacharjee et al.[24] in India concluded that RVO is a frequent finding in people with type II diabetes mellitus. Medical history of hypertension and stroke carries the risk for occurrence of RVO. Our study also showed similar results of association and risk factors for development of RVO in diabetic patients.

An another study by Yun Wang et al.[25] suggested that diabetes is an important risk factor for RVO.

Kassiani Giannaki et al.[26] established the role of diabetes, hypertension and hyperlipidemia in the majority of patients.

Hayreh et al.[27] found that uncontrolled diabetes in the elderly age group and male gender increases the risk of RVO. It is very similar with our study in which 78% of subjects had uncontrolled diabetes who developed RVO.

A study conducted by Cugati et al.[28] documented that in the diabetic patients of 43-69 years of age group, RVO is a risk factor for cardio vascular mortality. Another study showed that patients with RVO have a higher prevalence of stroke[5] and a greater risk of cardiovascular disease[29] than similarly aged individuals without RVO. The present study also shows the significant association of RVO and cardio vascular mortality.

E Z Rath et al.[30] established the important risk factors for the development of RVO are male gender, open angle glaucoma and hypertension. Their result showed that the presence of diabetes, coronary artery disease or shock were not significant risk factors in their studied population.

According to the result of Raba Thapa et al.[31] the risk of RVO increased with aging and among those with hypertension and with diabetes and hypertension.

Another similar study by A P Appiah et al.[32] showed that hypertension is most commonly associated with RVO. Other risk factors like diabetes, atherosclerotic heart disease may also responsible for RVO but found that these factors were not statistically significant ($p>0.05$).

In our study about 6.6% of patients with diabetes mellitus had RVO. This prevalence is higher than the Blue Mountain Eye Study, the Framingham Eye Study[33] and Beaver Dam Eye Study[22] where the prevalence of RVO was 1.6%, 0.15% and 0.8% respectively. The reason of high prevalence in our study is that this tertiary care centre covers several neighbouring districts and most of the patients attended the tertiary care centre very late with severe vision loss due to already developed RVO along with it's complications.

A similar study in India by Harsha Bhattacharjee et al.[24] reported 3.4% prevalence of RVO in diabetic subjects which again shows less prevalence than our study result. A study conducted by Jonas et al.[34] on prevalence and associations of retinal vein occlusions in rural central Indian population, included 4,711 subjects with 30 years and older age group, found retinal vein occlusion in 38 eyes. They concluded that presence of RVO was associated with higher age ($p=0.007$), systolic blood pressure ($p<0.001$), blood concentration of urea ($p=0.02$) and narrow angle of anterior chamber ($p<0.03$). They found no significant association with blood concentrations of glucose, cholesterol and high density lipoproteins. They reported 0.8% prevalence of RVO. In the present study 78.5% of subjects had BRVO while 21% of subjects had CRVO that means BRVO is approximately 3.7 times more common than CRVO. This result shows similarity with a paper published by International Eye disease Consortium by S. Rogers et al.,[6] reported the prevalence of RVO in the USA, Australia, Europe and Asia. This combined pooled data analyze that

BRVO is 4 times more common than CRVO. Also, the Beaver Dam Eye Study found that BRVO was 3 times more common than CRVO. An another report by Jonas et al. showed in their study that branch retinal vein occlusions being approximately seven times more common than central retinal vein occlusions.

The present study was done in a tertiary care centre that covers 300 km^2 area around Gorakhpur, serving patients from 15 surrounding districts and catering to a population of about 5 crores. So it is the backbone of health care in the eastern Uttar Pradesh. That's why the importance of this study is that it reflects the prevalence of RVO in diabetic patients of eastern Uttar Pradesh population, not only the prevalence of this region.

The major limitation of the study was that it was an opportunistic hospital-based screening of that patients who attended the Ophthalmology OPD in the same tertiary care centre, so we did not estimate the prevalence of RVO in the general population and another limitation was that we are unable to determine the prevalence and risk factors of RVO in young age diabetic population, also the sample size is restricted in terms of age because the study includes only type II diabetic patients with already developed RVO attending this tertiary care centre.

5. Conclusion

Sudden onset diminution of vision is the predominant presentation in RVO. Some patients may also present with gradual diminution of vision. Visual acuity is decreased mainly due to macular edema and retinal ischemia.

Retinal vein occlusion is a multifactorial disease. Increasing age, hypertension, hyperlipidemia, CVA are some of the predisposing factors associated with RVO in poorly controlled diabetic population. So, it is very important to timely assess the high blood pressure, lipid profile derangement and other associated risk factors in diabetic patients with RVO, if recurrence and further visual loss is to be prevented. Patients should be encouraged for healthy life style, low fat diet, less salt intake, weight control, exercise and keep the blood glucose levels under control. With the help of modern technology and instruments, retinal vein occlusion can be easily diagnosed and treated.

6. Source of Funding

None.

7. Conflict of Interest

None.

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