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Original Article

CLINICAL SUBTYPES OF BRANCH RETINAL VEIN OCCLUSION

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Abstract

Aims: *To investigate the subtypes of branch retinal vein occlusion (BRVO) and study the prevalence of systemic disorders associated with each subtype.* ***Settings and design:*** *An observational retrospective study conducted from 2017 to 2019.* ***Methods and material:*** *The study included patients with BRVO of different subtypes (superotemporal, inferotemporal, macular, and nasal BRVO). Data collected from the patients included age, sex, laterality of the affected eye, and history of medical diseases. The patients were thoroughly examined, and fundus fluorescein angiography and spectral domain optical coherence tomography were performed. All data were statistically analysed using SPSS software.* ***Results:*** *Eighty-one eyes of 78 patients were included in this study. Superotemporal BRVO was observed in 28 eyes (34.6%), inferotemporal BRVO was observed in 27 eyes (33.31%), and macular BRVO was observed in the remaining 25 eyes (30.9%). There were 13 (46.4%), 14 (51.9%), and 11 (44%) men in the superotemporal, inferotemporal, and macular BRVO groups, respectively (P= 0.843). Overall, 10 (35.7%), 15 (55.6 %), and 11 (44%) right eyes were affected in the superotemporal, inferotemporal, and macular BRVO groups, respectively (P= 0.569). Macular edema occurred in 23 (82.1%), 23 (85.2%), and 22 (88%) patients in the superotemporal, inferotemporal, and macular BRVO groups, respectively (P= 0.837).* ***Conclusions:*** *Superotemporal, inferotemporal, and macular BRVO are common subtypes of BRVO, and all have similar risk factors, regardless of sex or eye preference.*

Keywords: *Branch retinal vein occlusion, Anatomical subtypes, Macular edema, Retinal ischemia.*

1. Introduction

Branch retinal vein occlusion (BRVO) is a common disease affecting vision. Its significance is being a category of retinal vein occlusion (RVO) disorders, which are the second most common type of retinal vascular disorder, after diabetic retinopathy, and one of the most common causes of the sudden painless unilateral diminution of vision [1]. RVO is divided into two main types: central retina vein occlusion (CRVO) and BRVO. BRVO is further subdivided into two different types: major BRVO, which involves an occluded major branch retinal vein, and macular BRVO, which is when one of the macular venules is occluded [2]. The reported prevalence of retinal vein occlusion is 5.20 per 1000 for any RVO, 4.42 per 1000 for BRVO, and 0.80 per 1000

for CRVO. It has also been reported that BRVO is approximately 3 or 4 times more common [3,4], with an overall prevalence of 0.6% [4]. Generally, BRVO has a better prognosis than CRVO, because visual acuity can still improve in eyes with BRVO even without treatment, but significant improvement beyond 20/40 was uncommon [5]. Although most relevant studies have compared the clinical characteristics among different types of RVO [6-10], to our knowledge, few studies have discussed the clinical characteristics of different subtypes of BRVO [11,12]. The current study aimed to investigate the subtypes of branch retinal vein occlusion (BRVO) and study the prevalence of systemic disorders associated with each subtype.

2. Subjects and Methods

This observational retrospective study was conducted at a university hospital-based referral investigation unit from 2017 until 2019. It was conducted in the investigation unit of the Department of Ophthalmology, South Valley University Hospital, Qena, Egypt. The study included 81 eyes of 78 patients with BRVO of different subtypes (superotemporal, inferotemporal, macular, and even nasal BRVO). From patientnotes, we collected data including age, sex, laterality of the affected eye, and history of medical diseases such as hypertension, diabetes, hypercoagulability disorders and vascular collagen disease. Each patient record was revised regarding best corrected visual acuity using a Landolt chart, intraocular pressure using a Goldmann applanation tonometer, slit lamp examination of the anterior segment, and careful fundus examination by both direct and indirect ophthalmoscopy. Macular edema was examined by contact lens biomicroscopy. The patient was requested to undergo fundus photography to document the subtype of BRVO. Fundus fluorescein angiography was performed (in the involved eye only except in cases of bilateral BRVO) to detect the presence of macular ischemia (areas of nonperfusion) and macular edema. The presence of macular edema was confirmed and quantitatively evaluated using a spectral domain optical coherence tomography device (RTVue; Optovue, Inc., Fremont, CA), and the foveal thickness within 1 mm (ETDRS determined) was used for comparison between different cases.

2.1. *Inclusion criteria*

This study included only patients who were diagnosed as having BRVO of different subtypes (superotemporal, inferotemporal, macular, and even nasal BRVO).

2.2. *Exclusion criteria*

Patients were excluded if they had any concurrent eye disease affecting vision, such as cataract, glaucoma, CRVO, optic neuropathy, or diabetic retinopathy, except mild nonproliferative diabetic retinopathy. In addition, patients with previous retinal argon laser sessions were excluded. Cases with incomplete data were also excluded. The clinical parameters were compared among the four main subgroups of BRVO. Considering the low number of cases (only one eye in a patient with bilateral BRVO that was discovered accidentally during examination), the nasal BRVO group was excluded from the comparative statistical analysis. Informed consent was obtained from all the participants after the nature of the study had been explained to them. The study obtained ethics approval from the ethics committee of Qena Faculty of

Medicine at South Valley University. The study was conducted in accordance with the tenets of the Declaration of Helsinki.

2.3. *Statistical analysis*

Data were verified, coded by the researcher, and analyzed using IBM-SPSS 23 (Statistical Package for Social Science, version 23; SPSS Inc., Armonk, NY) Descriptive statistics, including means, standard deviations, medians, ranges, and percentages, were calculated. The Chi-square test was used to compare the difference in distribution of frequencies among the different groups. For continuous variables, analysis of variance was calculated to test the mean differences of the data that followed a normal distribution and independent samples. The Kruskal-Wallis test was used to compare the median difference between groups that did not follow the normal distribution. The post-hoc test was calculated using Bonferroni corrections. A *P* value less than 0.05 was considered significant.

3. Results

Eighty-one eyes of 78 patients were included in this study. Three (3.8%) patients had bilateral BRVO and 75 (96.2%) had unilateral BRVO. One of the three bilateral cases had right macular and left asymptomatic nasal BRVO, fig. (1). This eye (1.2%) was excluded from the final statistical analysis. Superotemporal BVRO was observed in 28 eyes (34.6%), whereas inferotemporal BRVO was observed in 27 eyes (33. 31%). The 25 remaining eyes (30.9%) had macular BRVO. Table (1) summarizes the number of eyes for each group in the study. Regarding demographic data analysis comparing the three groups, the mean patient age was 53.86±9.99, 52.93±7.63, and 54.20 ± 7.15 years in the superotemporal, inferotemporal, and macular BRVO groups, respectively (*P*= 0.850). There were 13 (46.4%), 14 (51.9%), and 11 (44%) men in the superotemporal, inferotemporal, and macular BRVO groups, respectively (*P*= 0.843). The right eye was affected in 10 eyes (35.7%), 15 eyes (55.6%), and 11 eyes (44%), whereas the left eye was affected in 16 (57.14%), 12 (44.4%), and 13 eyes (52%) in the superotemporal, inferotemporal, and macular BRVO groups, respectively (*P* = 0.569). Bilateral affections occurred twice (7.14%) in the superotemporal group and once (4%) in the macular group. With regard to association with systemic diseases, systemic hypertension was found in 20 (71.4%), 19 (70.4%), and 18 (72%) in the superotemporal, inferotemporal, and macular BRVO groups, respectively (*P*= 0.991); diabetes mellitus was found in 17 (60.7%), 13 (48.1%), and 9 (36%) in the superotemporal, inferotemporal, and macular BRVO groups, respectively (*P*= 0.198); and collagen vascular disease was found in 1 (3.6%), 1 (3.7%), and 2 (8%) in the superotemporal, inferotemporal, and macular BRVO groups, respectively (*P*= 0.708) and the detected disase was systemic lupus erthrymatosus. No hypercoagulability disorder was detected in the study sample. Best corrected visual acuity was 0.71 ± 0.19, 0.61 ± 0.17, and 0.83 ±0.18 in the superotemporal, inferotemporal, and macular BRVO groups, respectively (*P*< 0.001). Table (2) shows the demographic and clinical characteristics of the different BRVO subtypes. Of the superotemporal BRVO group, 12 (42.9%) eyes had retinal ischemia and 23 (82.1%) had macular edema with a mean central foveal thickness of 360 ± 70 μm. Of the inferotemporal BRVO group, 14 (51.9%) eyes had had retinal ischemia and 23 (85.2%) had macular edema with a mean central foveal thickness of 384±97 μm. Of the macular subtype, 13 (52%) had retinal ischemia and 22 (88%) had macular edema with a mean central foveal thickness of 421± 13 μm. There was no statistically significant difference between the three groups regarding retinal ischemia and the presence of

macular edema, but there was a significant difference regarding the central foveal thickness (P= 0.094) and it was more in macular BRVO. Table (3) shows the results of retinal ischemia and macular edema among the different BRVO subtypes.

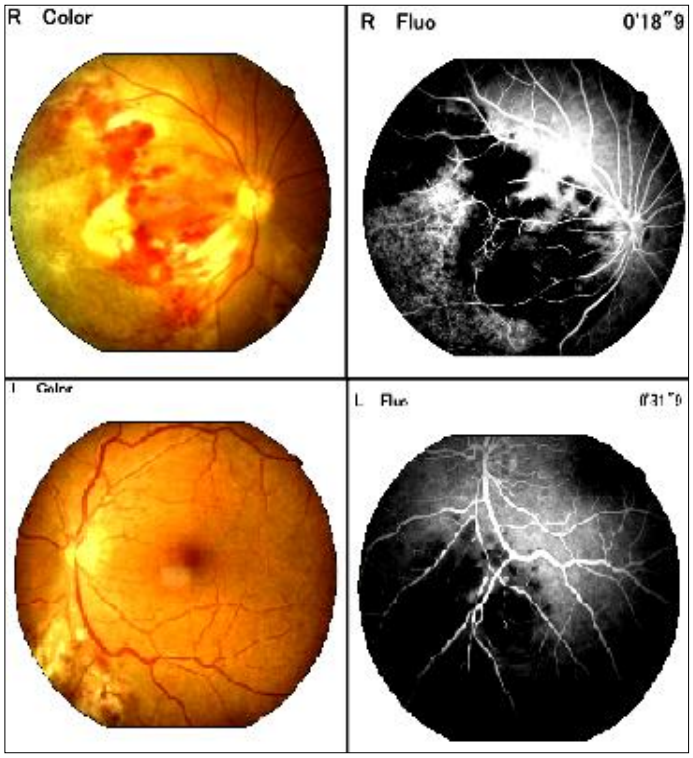

Figure 1. A case of bilateral BRVO. Right ischemic macular BRVO (top images) and left inferonasal BRVO (bottom images) that discovered accidentally. This patient had the diagnostic criteria of systemic lupus erythematosus.

Table 1. Total number of eyes of different BRVO subtypes

BRVO subtype	Number of eyes	Percentage
Superotemporal	28	34.6
Inferotemporal	27	33.3
Macular	25	30.9
Nasal	1	1.2
Total	**81**	**100**

One eye had nasal BRVO and was excluded from the final statistical analysis.

Table 2. Demographic and clinical characteristics of different BRVO subtypes

Variable	No. (%)			P value
	Superotemporal	***Inferotemporal***	***Macular***	
Age, mean ± SD	53.86 ± 9.99	52.93 ± 7.63	54.20 ± 7.15	0.850
Male (%) **Female (%)**	13 (46.4%) 15 (53.6%)	14 (51.9%) 13 (48.1%)	11 (44%) 14 (56%)	0.843
BCVA, log Mar	0.71 ± 0.19	0.61 ± 0.17	0.83 ±0.18	<0.001
Laterality				
- OD	10 (35.7%)	15 (55.6 %)	11 (44%)	0.569
- OS	16 (57.14%)	12 (44.4%)	13 (52%)	
- OU	2 (7.14%)	0 (0)	1(4%)	
Systemic diseases				
Hypertension (%)	20 (71.4%)	19 (70.4%)	18 (72%)	0.991
Diabetes mellitus (%)	17 (60.7%)	13 (48.1%)	9 (36%)	0.198
Collagen vascular disease (%)	1 (3.6%)	1 (3.7%)	2 (8%)	0.708

***BCVA**, best corrected visual acuity; OD, right eye; OS, left eye; OU, bilateral.*

Table 3. Results of retinal ischemia and macular edema in different BRVO subtypes

Variable	No. (%)			*P* value
	Superotemporal	*Inferotemporal*	*Macular*	
Ischemic BRVO	12 (42.9%)	14 (51.9%)	13 (52%)	0.741
Non-ischemic	16 (57.1%)	13 (48.1%)	12 (48%)	0.837
Presence of macular edema*	23 (82.1 %)	23 (85.2%)	22 (88%)	0.837
CRT, mean ± SD	360 ± 70 µm	384 ± 97 µm	421 ± 13 µm	0.094

** The presence of macular edema was defined here according to spectral domain optical coherence tomography, **CRT**, central retinal thickness.*

4. Discussion

BRVO is an important vascular disease affecting the retina and subsequently the vision; therefore, it is important to study its prevalence and the associated systemic risk factors of each subtype. Our study showed that the unilateral occurrence of BRVO is much more common (96.2%) than bilateral occurrence (3.8%). Bilateral BRVO was reported in 1.6% of patients in a long-term study [13] that included only 1 patient with bilateral BRVO among 64 patients with BRVO. The prevalence of the other three BRVO subtypes is similar at 34.6%, 33.31%, and 30.9% for the superotemporal, inferotemporal, and macular subtypes. Some studies [14,15] have suggested a more frequent occurrence of superotemporal BRVO, whereas others [1,16] have reported equal occurrence of inferotemporal and superotemporal BRVO and assumed that presentation bias was the cause of the difference, given that inferotemporal BRVO may be asymptomatic. For the current study, this presentation bias may be the reason for the low incidence of nasal BRVO (1.2%), which was accidentally discovered on examination of the contralateral eye in a patient with right macular BRVO. Other studies have reported a higher incidence of nasal BRVO (e.g., 9.2 % [13], 18.2% [4], and 15.4% [1]. The mean patient age for each subtype was similar. For superotemporal, inferotemporal, and macular BRVO, the mean patient age was 53.86 ± 9.99, 52.93 ± 7.63, and 54.20 ± 7.15 years, respectively, with no statistically significant differences. Hayreh reported that most patients with RVO were older than 65 years and that 5% of patients with BRVO were younger than 45 years [17]. There was no statistically significant difference in the occurrence of any of the BRVO subtypes between male and female patients. Thus, BRVO did not differ by sex, a finding that matches that found in other studies [13,16]. The affection of right and left eyes was also similar between the different BRVO subtypes in this study, with no statistically significant difference. These results coincide with the results of the long-term study [13]. However, an older study [17] reported that the right eye was more frequently affected. In this study, systemic hypertension was an important risk factor and association in all BRVO subtypes and was found in more than 70% of cases in all groups. It was more common than diabetes mellitus. However, neither showed a significant difference when comparing the three groups with each other. Other studies have reported a significant association between BRVO and hypertension and diabetes mellitus but no association with blood glycemic level [1,16,18]. To our knowledge, no studies have differentiated the association of these factors with each BRVO subtype other than Maurizio et al [19], who reported that macular BRVO has similar risk factors as major BRVO, particularly regarding systemic hypertension. Collagen vascular disease was found in 4 patients in the study (5.1%), 2 of whom had a diagnosis of systemic lupus erythematosus, fig. (1). However, there was no preference of a certain BRVO subtype to occur with SLE. Both eyes affection in this study occurred in 3 patients, 2 of whom had systemic lupus

erythematosus. This bilateral affection was reported with lupus retinopathy [20]. In our study, there was a similar incidence of ischemic and non-ischemic retinopathy with BRVO, with no statistical difference between BRVO subtypes. A 1983 study [21] reported that non-ischemic major BRVO occurred in one third of cases. In this study, macular edema occurred in nearly 80% of the cases. No significant difference was found in its occurrence between the BRVO subtypes, but quantitatively, macular edema was more prevalent in macular BRVO with a mean central foveal thickness of 421 ± 13 μm, which differed significantly from other subtypes. The reported incidence of macular edema with overall BRVO ranged from 48% to 67% [19]. Our higher incidence may be attributed to the tertiary hospital-based study where mainly symptomatic and visually affected patients are refereed. Our study had some limitations. The main limitation was that it was conducted in an investigation unit as a tertiary hospital-based sampling study, rather than a primary care or population-based study to investigate different anatomical subtypes of BRVO. As most patients at such a tertiary level are visually disabled, we may have missed cases of subtle BRVO and cases of asymptomatic or minimally symptomatic BRVO.

5. Conclusion

Superotemporal, inferotemporal, and macular BRVO are common subtypes of BRVO and all have similar risk factors, with no sex or eye preference. Further population-based studies are recommended to prove or negate the results of this study.

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