



Original Research Article

Role of thrombophilia testing in retinal vein occlusion: single centre experience from Oman

Khalid N Al Hashmi^{1,*}, Fahad Al-Ghafri¹, Anil Pathare²

¹Dept. of Hematology, Armed Forces Hospital, Seeb, Muscat, Oman

²Sultan Qaboos University Hospital, Al Khoud, Muscat, Oman



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ABSTRACT

Background: Thrombophilia is a known predisposition to venous thromboembolism however there was no significant relationship with retinal vein occlusion (RVO). Herein, we aimed to study the prevalence of thrombophilia among Omani patients presented with RVO.

Material and Methods: In a retrospective study, 11 consecutive patients diagnosed by the ophthalmologists at Armed Forces Hospital with RVO (central RVO, n=7; branch RVO, n=4) were included. Thrombophilia testing including factor V Leiden, Prothrombin gene mutation (G20210A) and Janus Kinase-2 (JAK2 V617F) mutation analysis; presence of autoantibodies including Anti-nuclear antibody (ANA), Anti-neutrophil cytoplasmic antibody (ANCA), Lupus anticoagulant (LA), Anti-cardiolipin antibody (ACA), Anti-B2 glycoprotein positivity; abnormal coagulation protein levels including protein S, Protein C, Anti-thrombin and Factor VIII as well as biochemical parameters like elevated serum lipoprotein 1a, triglycerides, total cholesterol and homocysteine levels were performed.

Results: Patient's ages ranged between 25 to 75 years (mean + SD; 48.8 + 13.6) with a mild male preponderance (54.5%). None of them gave history of smoking. However, 27.3% and 45.5% had history of diabetes and hypertension, respectively. Amongst the thrombophilia tests evaluated, only one patient was positive for an underlying Prothrombin gene (G20210A) heterozygosity, another patient was positive for Anti-beta2 glycoprotein antibody and one patient with high serum homocysteine.

Conclusion: Our study demonstrated that thrombophilia is not prevalent in omani patients diagnosed with RVO in the armed forces hospital. Furthermore, 27.3% and 45.5% of those patients were suffering from diabetes and hypertension, respectively which are known risk factors for RVO.

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1. Introduction

Retinal vein occlusion (RVO) is a serious retinal vascular disorder second only to diabetic retinopathy and is an imperative cause of blindness and visual indisposition.^{1,2} It is classified into two types, depending whether the central retinal vein (CRVO) or a branch of retinal vein (BRVO) is occluded.^{3,4} Hayreh in 2005, further divided RVO into three types: BRVO which is classified into major and macular; CRVO which is divided into ischemic and non-ischemic types; and hemi-RVO with involvement of only one half of the retina surface which is divided into ischemic and non-

ischemic types.⁵

The prevalence of RVO is about 0.7% with the 5 years incidence of new cases being 0.8%. It is more prevalent in men than women and is more frequent in older patients over the age of 65 years.^{2,6} It is believed that BRVO is 4 times more common than CRVO and the recurrence of RVO within the same eye, within 4 years is estimated at 10%.^{2,6}

Although the pathogenesis is still not completely understood, several studies have shown that systemic risk factors such as hypertension, diabetes and hypercholesterolaemia are associated with RVO, however, the symptoms, risk factors and the treatment options are different between CRVO and BRVO.^{3,7,8}

* Corresponding author.

E-mail address: khalidnalhashmi@gmail.com (K. N. A. Hashmi).

Several publications have reported weak relationship between RVO and disorders of haemostasis^{9,10} or among RVO and thrombophilia.^{11–14}

Thrombophilia is a known predisposition to vascular thrombosis and RVO is a major cause of visual loss hence we aimed to study the prevalence of thrombophilia among those patients with RVO.

2. Materials and Methods

A total of 11 patients referred by the ophthalmologists with RVO (central RVO, n=7; branch RVO, n=4) were retrospectively enrolled in this single institution study after an informed consent.

All patients underwent a routine physical examination and submitted a sample of blood for routine and thrombophilia testing. Blood was obtained by venipuncture into Vacutainer tubes with EDTA anticoagulant and plain tubes. Complete blood counts were obtained with an automated cell counter (Sysmex XT-4000i, Sysmex corporation). Several routine biochemical parameters of renal and liver function were measured by Cobas 6000 analyzer including serum triglycerides (mmol/L), Lipoprotein 1a (g/L) total cholesterol (mmol/L) and homocysteine ($\mu\text{mol/L}$). Thrombophilia tests included Factor V Leiden, Prothrombin gene mutation (G20210A) and JAK2 (V617F) mutation analysis; autoantibody assays like ANA, ANCA, LA, ACA, Anti-beta2 glycoprotein activity and coagulation proteins estimations including Protein S, Protein C, Anti-thrombin III and Factor VIII levels were also performed.

2.1. Statistics

Continuous variables were assessed for normality using the Kolmogorov-Smirnov test and the data presented as mean + standard deviation. Categorical variables are presented as number (%).

3. Results

The study enrolled a total of 11 consecutive patients diagnosed with RVO. Patient's ages ranged between 25 to 75 years (mean + SD; 48.8 + 13.6) with a mild male preponderance (54.5%). Majority of patients developed CRVO (64%), with the remaining developing BRVO (36%). There was also a significantly higher incidence with right sided involvement (64%). None of them was smoker, but 27.3% and 45.5% had history of diabetes and hypertension, respectively.

Amongst the thrombophilic risk factors evaluated, only one patient each, showed positivity for anti-B2 glycoprotein antibody (11.1%), Prothrombin gene mutation (G20210A) heterozygosity (14.3%) and elevated serum homocysteine level ($23.3\mu\text{mol/L}$). None of the other thrombophilic factors including factor V Leiden and JAK2 (V617F) mutations;

autoantibodies to ANA, ANCA, LA, ACA and coagulation proteins including protein S, protein C, antithrombin III and factor VIII levels were abnormal.[Table 1] Biochemical studies showed that S. lipoprotein 1a levels were normal and ranged between 0.1-0.5 (g/L), S.triglycerides ranged between 0.8-2 (mmol/L) with mean of 1.34., Stotal cholesterol ranged between 2.4-6.6 (mmol/L) with mean of 4.8 and S.homocysteine ranged between 7.2-23.3 ($\mu\text{mol/L}$) with mean of 9.3.

All patients received an initial treatment with Ranibizumab (Lucentis[®]) which is anti-angiogenic monoclonal antibody). Furthermore, almost a quarter of the patients in this small cohort showed recurrence in RVO involving the same eye (27.3%). Amongst these, one patient had a primary open angle glaucoma and one patient with recurrence needed treatment with anti-coagulant therapy using low molecular weight heparin Tinzaparin (initially) followed by oral anti-coagulant Rivaroxaban with satisfactory improvement.

4. Discussion

It is believed that RVO has local and systemic risk factors with especially Virchow's triad playing an important role.^{2,6} In our study, 8 out of the 11 patients could be identified with an underlying well-defined risk factor. Furthermore, although RVO is more prevalent over the age of 65 years,^{6,15} in this cohort only one patient was above that age with the rest (91%) were below 60 years of age with the median age in this cohort being 50 years. Rogers S et al.,¹⁶ reported that BRVO was 4 times more common than CRVO with a prevalence of 4.42 per1000 for BRVO, and 0.80 per 1000. However, in our study, CRVO (64%) was apparently more prevalent than BRVO (36%).

Several studies have shown that systemic diseases such as hypertension, hypercholesterolaemia and diabetes are associated with the development of RVO [2, 6, 17, and 18]. In a small study on 14 patients, Schmidt reported that 11 of the 14 patients studied had one of these factors.¹⁷ Those findings are similar to our study.

RVO is more prevalent in men than women.⁶ Although Maurya et al. reported RVO in 16.36% pregnant women's.¹⁸ Pregnancy itself a hypercoagulable state and management of thrombophilia during pregnancy is quite challenging.

The role for thrombophilia testing in RVO remains controversial as several studies have shown conflicting results.^{9–14} Nevertheless, plasma homocysteine has been identified as an independent risk factor for RVO,¹⁹ and was observed in one of our patients. We also identified one patient with Prothrombin gene mutation (G20210A) heterozygosity aged 36years and Anti-beta2 glycoprotein antibody positivity in another patient. In a case control study, Glueck et al identified elevated homocysteine and Factor V Leiden as weak risk factors but found no association of Anti-cardiolipin antibodies or lupus

Table 1: Characteristics of RVO patients in the study cohort [n=11]

Characteristic		Value
Site of Involvement — no. (%)		
Rt CR		4(36.4)
Lt CR		3(27.3)
Rt BR		3(27.3)
Lt BR		1(9.0)
Age — yrs.		
Female sex — no. (%)		5 (45.5)
History of Diabetes — no. (%)		3 (27.3)
History of Hypertension — no. (%)		5 (45.5)
History of smoking – no (%)		0 (0)
Risk Factors		
FV Leiden mutation, n/n (%)	Negative	7/7 (100)
Prothrombin Gene mutation, n/n (%)	Positive	1/7 (14.3)
JAK2V612F mutation, n/n (%)	Negative	4/4 (100)
ANA, n/n (%)	Negative	8/8 (100)
ANCA, n/n (%)	Negative	5/5 (100)
LA, n/n (%)	Negative	9/9 (100)
ACA, n/n (%)	Negative	9/9 (100)
Anti-Beta2, n/n (%)	Positive	1/9 (11.1)
PS, n/n (%)	Normal	5/5 (100)
PC, n/n (%)	Normal	7/7 (100)
AT, n/n (%)	Normal	7/7 (100)
F VIII, n/n (%)	Normal	5/5 (100)
S. Lipoprotien 1a—g/L, n/n (%)	Normal	3/3 (100)
S. Triglycerides — (□mol/L, Mean + SD (Range)		1.34±0.36 (0.8-2)
S. Total Cholesterol — (□mol/L, Mean + SD (Range)		4.8±1.3 (2.4-6.6)
S. Homocystine— (□mol/L, Mean + SD (Range)		9.3±2.6 (7.2-23.3)
Recurrence, n (%)		3/11 (27.3)
Treatment received		
anti-VEGFRanibizumab (Lucentis®)	n/n(%)	11/11 (100)
Aspirin, n/n (%)		11/11 (100)
Statin (Atorvastatin), n/n (%)		9/11 (81)
LMWH (Tinzaparin), n/n (%)		1/11 (9)

anticoagulant with CRVO.²⁰ Thus, there is no evidence for thrombophilia testing in the RVO.

Our study has several limitations especially given the small number of patients and some incomplete data. But this is also a reflection of the real-world evidence that one comes across in daily practice. Nevertheless, all these patients were evaluated to the best of our ability and feasibility and we still feel that thrombophilia testing is controversial. It is also imperative that the study can be expanded to help validate and assess the need for thrombophilia testing in this setting.

5. Source of Funding

None.

6. Conflict of Interest

The authors declare no conflict of interest.

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Author biography

Khalid N Al Hashmi, Senior Consultant Internist

Fahad Al-Ghafri, Senior Specialist Haematologist

Anil Pathare, Senior Consultant Haematologist

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