Original research article

A Comparative Study between the Retinal Vein Occlusion with Serum Lipid Levels in Adults in Banaskantha District and Adjoining Area of Gujarat and Rajasthan(India)

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Abstract

Purpose: To study the serum lipid levels of patients with retinal vein occlusion and compare the lipid levels with age matched control group, also correlate with RVO induced macular edema.

Study Design: A comparative study.

Methods: This was a comparative study. Total 172 patients were included. Among them there were around 86 patients /cases in group1, (26 CRVO, 55 BRVO, 5 HRVO) diagnosed and 86 controls (selective age matched) in group 2 enrolled into the study. Group 1 cases were those who meet our inclusion and exclusion criteria. After taking informed consent, detailed history taken and thorough ophthalmological examination was done, All patients with retinal vein occlusion in group 1 underwent optical coherence tomography scan to assess macular edema to detect central retinal thickness. Later they were advised for fasting serum lipid levels in an advanced biochemistry laboratory.

Results: Total cholestrol, triglycerides , HDL, LDL levels were elevated significantly in cases with RVO group 1 as compared to age matched controls group 2.

Conclusion: Hyperlipidemia is a common independent risk factor for occurrence RVO in adults. Total cholesterol, Triglycerides, LDL levels were raised (p-value <0.001) and HDL levels were reduced (p value <0.001) in patients with retinal vein occlusion as opposed to age matched comparison control group which was statistically significant. Hyperlipidemia are common risk factors for RVO in adults. It remains to be determined that serum lipid levels can improve visual acuity or the complications of RVO

Introduction

Retinal vein occlusion (RVO) is the second commonest sight threatening retinal vascular disorder after diabetic retinopathy that is related to visual morbidity (1). RVO is an obstruction of the retinal blood vessel system, and will involve the central retinal vein or a branch retinal vein. Attainable causes are external compression or diseases of the vein wall like vasculitis. RVO are often divided into two primary classes, branch RVO (BRVO) and central RVO (CRVO), depending on the positioning of occlusion, with BRVO occurring more usually than CRVO. CRVO is again classified as ishaemic, if there's not enough pressure in the capillary system that can lead to areas without blood flow. If there are no areas of capillary non-perfusion, CRVO is taken into account to be non-ischaemic (2). Retinal vein occlusion have a characteristic, though some variable features like Intra retinal hemorrhages, tortuous expanded retinal veins, cotton wool spots, macular, retinal edema and disc edema.

Baseline visual acuity was moderately poor, starting from 6/9 to 6/60 in each BRVO and CRVO eyes. Though the visual acuity in untreated BRVO usually improves over time, it seldom improves beyond 6/9(1). The vision in CRVO eyes generally decreases over time if not treated (3). About 5–15% of eyes with BRVO develop macular edema over one year and also the majority of patients with CRVO have signs of macular edema at presentation. (1, 3) .The global burden of people affected with RVO is calculated to be around 16.4 million adults worldwide. The prevalence of BRVO and CRVO is 4.42 and 0.8 per one thousand persons and it increased with age however doesn't differ with gender.(4) The presence of open angle glaucoma is a risk factor for the development of both BRVO and CRVO. Bilaterality isn't common in each BRVO and CRVO.

Central retinal vein occlusion and Hemi retinal vein occlusion were believed to be results of a blood clot within the central retinal vein at or posterior to the lamina cribrosa. Arterio sclerosis of the neighboring central retinal artery that causes turbulent venous blood flow and leading to endothelial tissue injury. Other theory was thrombosis of central retinal vein as final stage phenamenon. Branch retinal vein occlusion occurs at an arteriovenous crossing, wherever the artery and vein share a typical membrane sheath called common adventitial sheath. The artery is often anterior to the vein. Rigid induration due to arteriosclerosis, artery compresses the retinal vein, leading to turbulent blood flow thrombosis and occlusion(5). Many systemic risk factors were related to retinal vein occlusion with most typical association being older age, other common risk factors Hypertension, Diabetes mellitus, hyperlipidemia, atherosclerotic cardiovascular diseases, oral contraceptive pills use among young patients, smoking and uncommon conditions like hyperviscosity syndrome, hyperhomocystinemia, dehydration, antiphospholipid antibody syndrome, inflammatory disorders related to occlusive periphlebitis, orbital diseases, chronic kidney failure and ocular risk factors like hypermetropia and glaucoma. (5) As retinal vein occlusion has been related to several systemic diseases. Detection of these diseases has been aimed toward preventing future occurrence of vascular occlusive events each ocular and systemic. Routine investigations are recommended to diagnose systemic end organ damage related to cardiovascular risk factors commonly found in association with retinal vein occlusion. These investigations facilitate in interference of further non ocular injury from occurring and additionally helps in systemic management of associated conditions to reduce the chance of continuous recurrence of retinal vein occlusion.(6)

MATERIAL AND METHODS

Study Site: Department of ophthalmology, Banas Medical College and research institute Palanpur ,Gujarat

Study Population: Banaskantha district of Gujarat and adjoining area of Gujarat and Rajasthan.

Study Design: "A comparative study."

Sample size with Justification: A sample size of 172, of which 86 subjects per group is needed to detect a difference in prevalence of hyperlipidemia between study (on retinal vein occlusion cases) group and the age matched controls (no evidence of retinal vein occlusion) group determined.

Formula for estimation of sample size with substitution of values used.

To estimate proportion p in the study population, sample size required is (6, 7)
$n_B=[p_A(1-p_A)\kappa+p_B(1-p_B)][(z_\alpha+z_{1-\beta}(p_A-p_B)]^2$

- *nB* = Sample size in the case group k =ratio of subjects between 2 groups ($n_A=kn_B$; k=1 for equal number of subjects in the 2 groups),
- Proportion in group A(controls), p_A= 0.15 (15%) & proportion in group B (RVO cases), p_B=0.32(32% prevalence of Hyperlipidemia)
- α is Type I error =5%; z_α=1.96 two sided , z_α =1.64 one sided
- β is Type II error, 1−β is power; $z_{1-\beta}$=0.84 for 1−β=80%

Inclusion criteria:
1. All patients with recently diagnosed Retinal vein occlusion.
2. Age more than 25years.
3. Both gender.

Exclusion criteria:
1. Age >85years, <25years
2. All causes of vasculitis causing retinal vein occlusion were excluded.
3. Associated ocular diseases causing significant visual impairments
4. Imunocompromised, pregnant patients,
5. Patients on antilipidemic drugs, oral contraceptive drugs, glucocorticoid drugs, thiazide diuretics as they all known to cause dyslipidemia.
6. Uncooperative patient not willing to adhere to follow up.

METHODOLOGY:

Method of investigation:

Method of measurement of outcome of interest:
This is a comparative study, around 172 eyes were studied that is 86 cases and 86 control group were enrolled into the study after taking informed and written consent. After detailed history taking and ocular examination was carried, Investigations were carried out as per the predesigned proforma
External ocular examination: Visual acuity testing for distance and near:

- Evaluation of Best Corrected Visual Acuity - distant and near . It was done by using Snellen's visual acuity charts.

Slit lamp examination: Detailed slit-lamp bio microscopy,
1. Detailed Slit-lamp Examination
2. Application Tonometry

➢ Done using Goldman Application Tonometry
➢ To record IOP.

- Dilated pupil examination with tropicamide and phenylephrine eye drops.
- Fundus Examination :
- It was done using a volk 90/78 D lens slit-lamp biomicroscopy & indirect ophthalmoscopy.
- Stereoscopic fundus photographs were taken for documentation
- Retinal evaluation to rule out any other retinal disease.

each individual subjected for systemic examination for the evaluation of blood pressure and fasting sugar levels and mainly hyperlipidemia.

A complete fasting lipid profile was done in all patients which included total cholesterol, Triglycerides, LDL, HDL. Increase in blood lipid levels are well documented risk factors for cardiovascular disorders.

The current classification schemes for hyperlipidemia are based on the national cholesterol education panel"s (NCEP) adult treatment programme 3 guidelines (8)

Results: The mean age of RVO cases in group 1 and controls in group 2 was 58.43 years and 56.34 years respectively. Of 86 cases there were 26 cases with CRVO, 55 cases with BRVO, 5 cases with HRVO.

Total cholesterol (mean, 220.31 mg/dl with SD 54.58) levels were elevated significantly in cases with RVO group 1 as opposed to control subjects group 2(mean 171.24 mg/dl with SD 35.04) ($p<0.001$).

Triglycerides (mean, 180.97 mg/dl with SD 62.44) levels were elevated in group 1 as opposed to control subjects in group 2 (mean 116.83 mg/dl with SD 49.83) ($P<0.001$).

HDL(mean 36.48 mg/dl with SD 4.89) levels were reduced significantly in RVO cases in group 1 as opposed to control subjects in group 2(mean 42.74 mg/dl with SD 8.83)($p <0.001$).

LDL (mean 149.75 mg/dl with SD 38.26)levels were raised significantly in RVO cases in group 1 as opposed to control subjects in group 2(mean 112.72 mg/dl with SD 32.20)($p<0.001$). Systemic illnesses in both groups were comparable

Table 1: Reference values of serum lipid levels are taken from NCEP ATP 3 guidelines.

	Normal	Abnormal
Total cholesterol	<200 mg/dl	>200 mg/dl
Triglycerides	<150 mg /dl	>150 mg/dl
HDL	>40 mg/dl	<40 mg/dl
LDL	<130 mg /dl	>130mg/dl

Table 2: Mean serum lipid levels in group 1

Group 1	**Type of occlusion**	**N**	**Mean**	**SD**
Cholesterol	CRVO	26	202.08	50.88
	BRVO	55	227.81	55.19
	HRVO	5	232.60	53.62
Triglycerides	CRVO	26	174.14	61.59
	BRVO	55	183.72	62.91
	HRVO	5	186.20	72.49
HDL	CRVO	26	36.73	4.67
	BRVO	55	36.19	4.67
	HRVO	5	38.40	4.28
LDL	CRVO	26	155.24	43.51
	BRVO	55	147.16	37.28
	HRVO	5	149.80	14.79

Table 3: Mean lipid levels among group 1 and group 2

		n	**Mean**	**SD**	**p-value**

Cholesterol	**Group1**	**86**	**220.31**	**54.58**	**<0.001**
	Group2	**86**	**171.24**	**35.04**	
Triglycerides	**Group1**	**86**	**180.97**	**62.44**	**<0.001**
	Group2	**86**	**116.83**	**49.83**	
HDL	**Group1**	**86**	**36.48**	**4.89**	**<0.001**
	Group2	**86**	**42.74**	**8.83**	
LDL	**Group1**	**86**	**149.75**	**38.26**	**<0.001**
	Group2	**86**	**112.72**	**32.20**	

Table 4: Comparison of cholesterol levels with respect to type of occlusion in group1

Cholesterol	**Type of occlusion**			**Total**	**p-value**
	CRVO	**BRVO**	**HRVO**		
Abnormal	**7**	**17**	**1**	**25**	**0.924**
Normal	**19**	**38**	**4**	**61**	
Total	**26**	**55**	**5**	**86**	

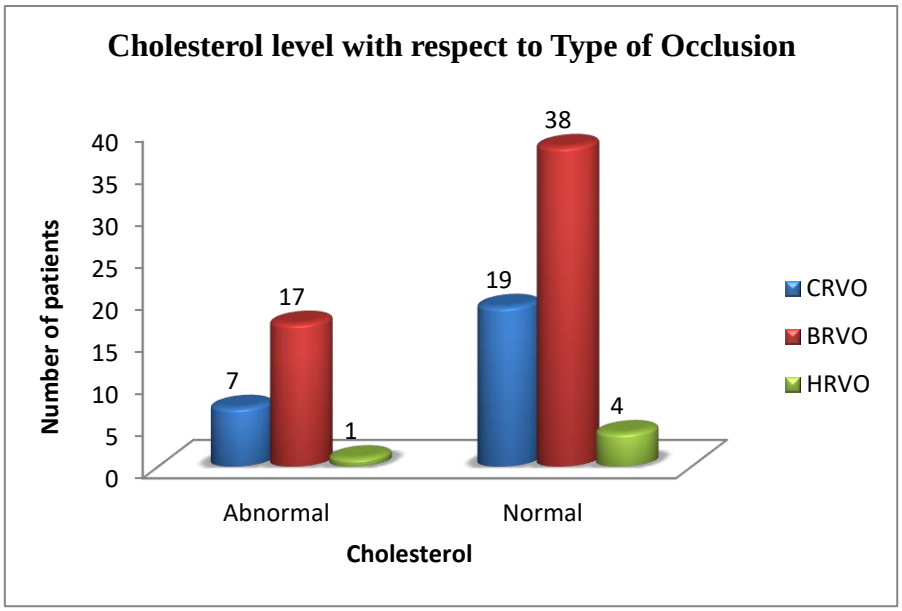

Figure 1: Comparison of cholesterol levels with respect to type of occlusion in group1 cases

Conclusion:- By using Chi-square test p-value > 0.05 therefore there is no significant association between cholesterol level with type of retinal occlusion.

Table 5: Comparison of cholesterol levels between group 1 and group 2

Cholesterol	**Group**		**Total**	**p-value**
	Group 1	**Group 2**		
Abnormal	**25**	**6**	**31**	**< 0.001**
Normal	**61**	**80**	**141**	
Total	**86**	**86**	**172**	

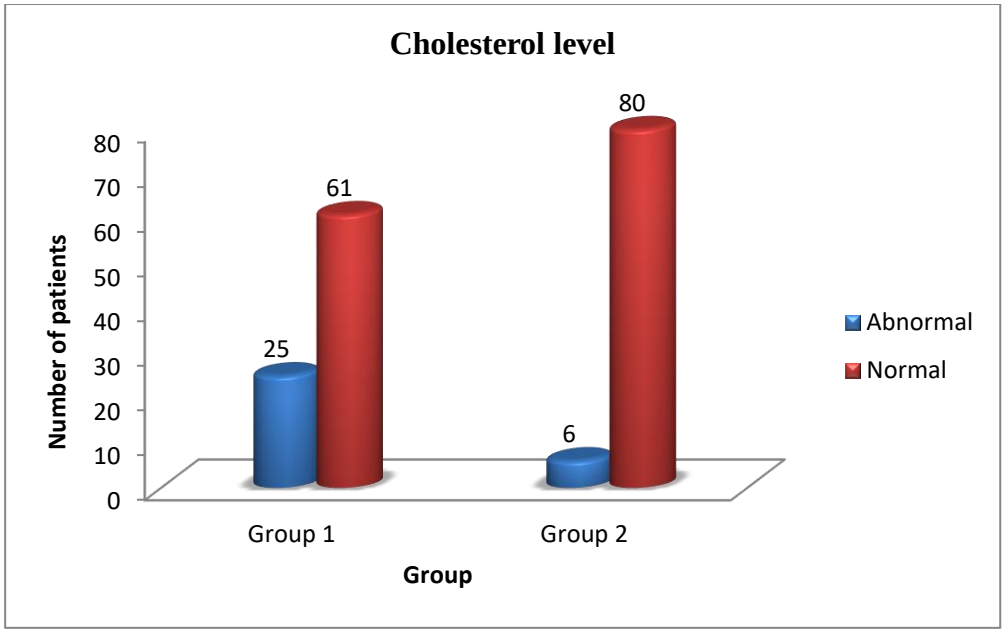

Figure 2: Comparison of cholesterol levels between group 1 and group 2

Conclusion: - By using Chi-square test p-value < 0.001 therefore there is significant association between total cholestrol level in group 1 and group 2.

Table 6: Comparison of triglycerides levels with respect to type of occlusion in group 1

Triglycerides	Type of occlusion			Total	p-value
	CRVO	BRVO	HRVO		
Abnormal	17	38	4	59	0.930
Normal	9	17	1	27	
Total	26	55	5	86	

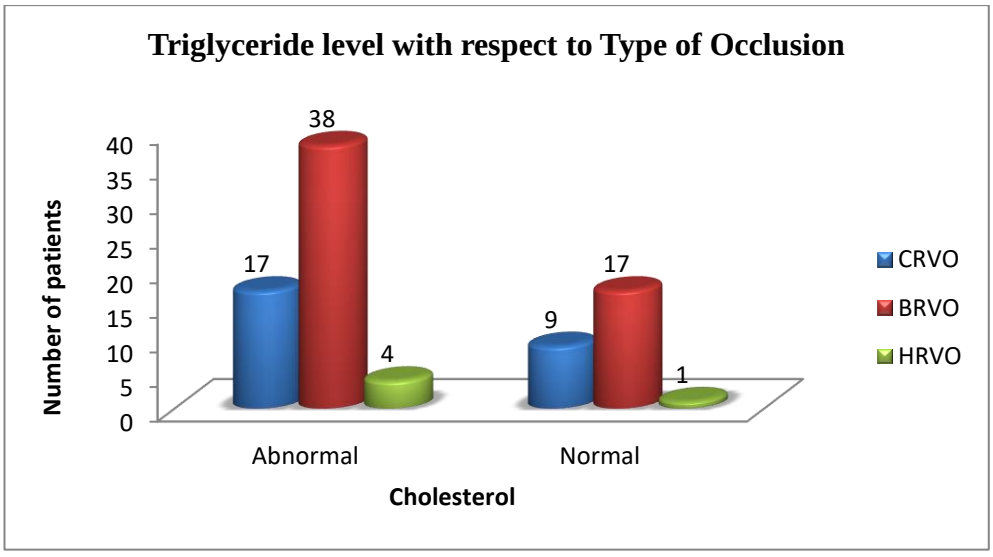

Figure 3: shows comparison of triglyceride levels with respect to type of occlusion

Conclusion: - By using Chi-square test p-value > 0.05 therefore there is no significant association between triglycerides levels with respect type of retinal occlusion.

Table 7: Comparison of triglycerides levels between group 1 and group2

Triglycerides	Group		Total	p-value
	Group 1	Group 2		
Abnormal	59	18	77	< 0.001
Normal	27	68	95	
Total	86	86	172	

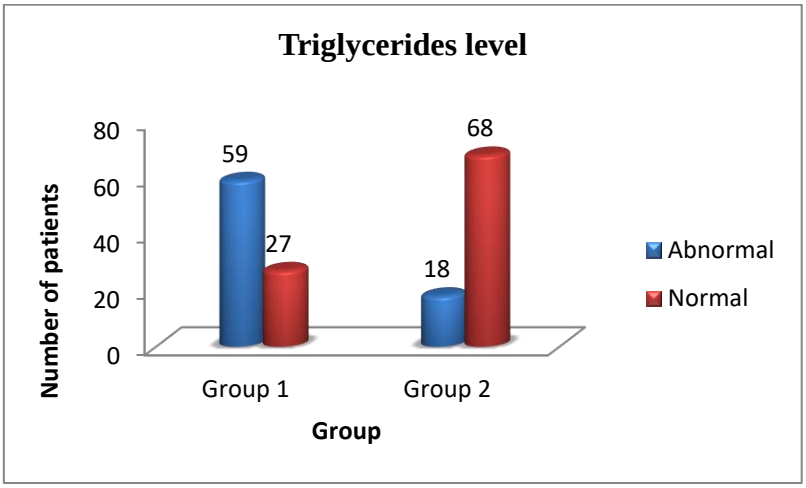

Figure 4: comparison of triglycerides levels between group 1 and group 2

Conclusion: By using Chi-square test p-value < 0.001 therefore there is significant association between groups

Table 8: Comparison of HDL levels with respect to type of occlusion in group 1

HDL	Type of occlusion			Total	p-value
	CRVO	BRVO	HRVO		
Abnormal	20	41	4	65	0.999
Normal	6	14	1	21	
Total	26	55	5	86	

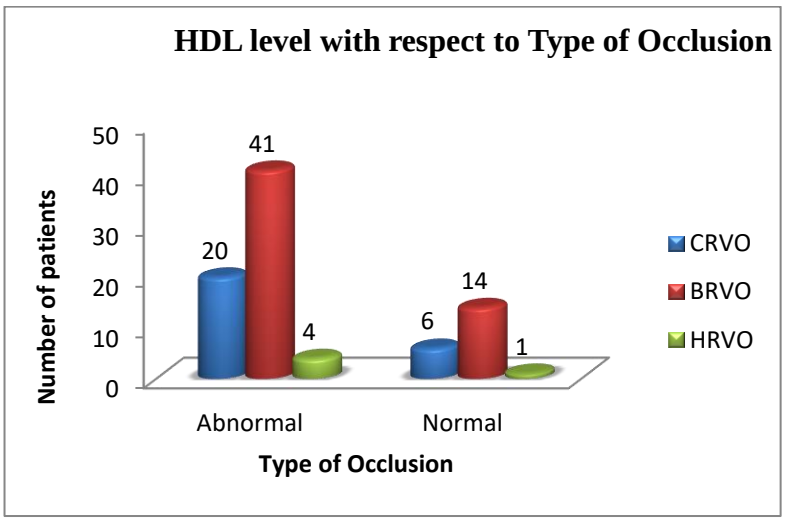

Figure 5: comparison of HDL levels with respect to type of occlusion in group1

Conclusion: - By using Chi-square test p-value > 0.05 therefore there is no significant association between HDL levels with respect to type of type retinal occlusion.

Table 9: Comparison of HDL levels in group1 and group 2

HDL	Group		Total	p-value
	Group 1	Group 2		
Abnormal	65	33	98	< 0.001
Normal	21	53	74	
Total	86	86	172	

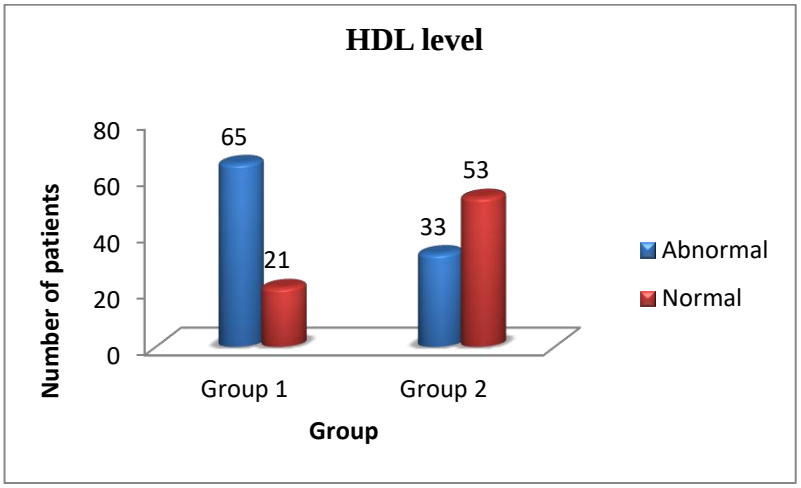

Figure 6: comparison of HDL levels between group 1 and group 2.

Conclusion :- By using Chi-square test p-value < 0.001 therefore there is significant association between HDL level in group 1 and group 2

Table 10: comparison of LDL levels with respect to type of occlusion in group 1

LDL	Type of occlusion			Total	p-value
	CRVO	BRVO	HRVO		
Abnormal	20	40	5	65	0.494
Normal	6	15	0	21	
Total	26	55	5	86	

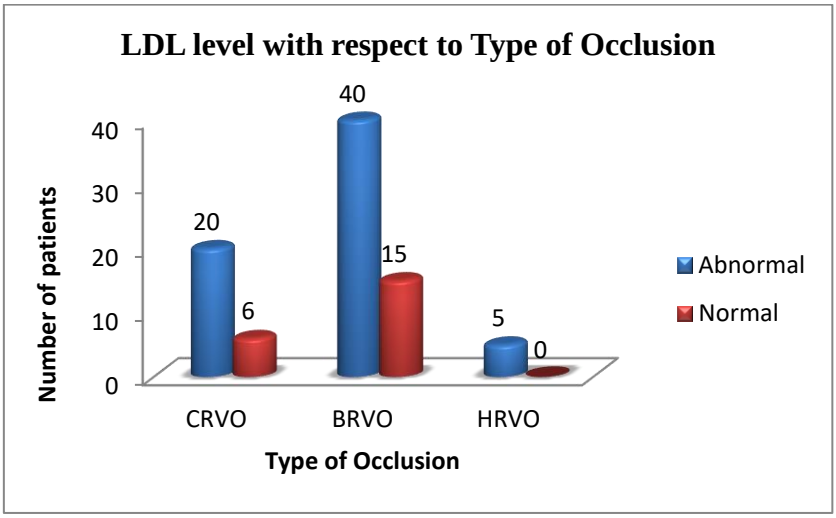

Figure 7: shows comparison of LDL levels with respect to type of occlusion in group 1

Conclusion: - By using Chi-square test p-value > 0.05 therefore there is no significant association between LDL level with respect to type of retinal occlusion.

Table 11: comparison of LDL levels between group 1 and group 2

LDL	Group		Total	p-value
	Group 1	Group 2		
Abnormal	65	30	95	< 0.001
Normal	21	56	77	
Total	86	86	172	

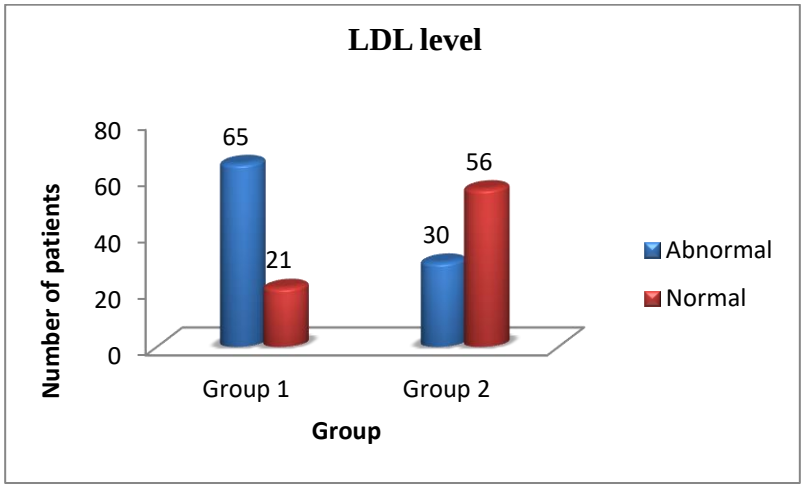

Figure 8: comparison of LDL levels between group 1 and group 2

Conclusion: - By using Chi-square test p-value < 0.05 therefore there is significant association between LDL level in group 1 and group 2.

Table 12: Comparison of systemic association between group 1 and group 2

Systemic illness	Group	
	Group 1 (n=86)	Group 2 (n=86)
Diabetes Mellitus	23	19
Hypertension	40	37

Table 13: Systemic illness with respect to type of occlusion in group 1

Systemic illlness	Type of Occlusion			Total
	CRVO	BRVO	HRVO	
Diabetes Mellitus	12	9	2	23
Hypertension	9	30	1	40

DISCUSSION

Many systemic risk factors are related to retinal vein occlusion with most typical association being older age, Hyperlipemia and Atherosclerotic Cardiovascular diseases, Hypertension, Diabetes mellitus, obesity being the common association.(2) There are lot of literature with regard to retinal vein occlusion and HTN and diabetes mellitus but hyperlipidemia is not studied independently in regard to development of retinal vein occlusion .

The fact that hyperlipidemia is a strong risk factor for CVD is well established. Hyperlipidemia refers to elevated cholesterol, elevated TG or both. The problem can be due solely to hereditary factors, but more commonly it is an acquired condition.

In the recent days, primary practitioners spend considerable time on the preventative medicine. Diagnosing and managing hyperlipidemia as a way to prevent cardiovascular disease (CVD) is a common activity for primary care physicians. According to Centers for Disease Control data from a survey of 1,492 physicians who provide ambulatory care in non-government settings, hyperlipidemia is second only to hypertension in the list of the 10 most common chronic conditions that were seen (8).

In our study, 86 eyes of 86 patients were considered in group 1 as cases, who were recently diagnosed with retinal vein occlusion. All these patients were subjected for routine slit lamp examination .A fasting lipid profile testing was done for all patients. They were also subjected to OCT examination to determine the amount of macular edema. Group 2 as controls were selective age matched patients which were taken from executive package patients coming to our hospital for routine health checkup who also underwent eye examination.

In our study , Among 86 cases in group 1 ,there were 26 cases with CRVO ,55 cases with BRVO ,5 cases were with HRVO .Most common age group affected was 61-70 years in group 1. Mean age was 58.43 years in group 1and 56.34 in group 2. Finding in group 1, According to gender, male patients were affected more than female and right eye was affected more than left eye, comparatively this was more in BRVO but these finding didn't meet statistical significance. Visual acuity was severely affected in CRVO (it was < 6/60, <n36) than in BRVO and HRVO (it was b/t (6/36-6/24, <n10). Slight male predominence can be explained by hormonal changes as (plasma viscosity) increased haematocrit in male than female.

According to beaver dam eye study, it was found that prevalence of BRVO was 0.6%, prevalence of CRVO was 0.1%. The prevalence of BRVO and CRVO varied with age which favors our study. The frequencies were similar in men and women. People more than or equal to 75 years of age were more affected by BRVO than people between 43 to 54 years of age. The overall prevalence of retinal branch vein occlusion in right eyes was similar to that in left eyes (9).

In our study, mean IOP in CRVO as 18.08 mm hg, BRVO 15.35mmhg, HRVO 17.80mmhg. Intraocular pressure was not significant statistically with respect to type of occlusion. IOP was taken to rule out neovascular glaucoma in patients with CRVO. But we didn't find significant number of patients with NVG. Primary open angle glaucoma is also a ocular risk factor for retinal vein occlusion.

In our study, comparison of retinal vein occlusion with serum lipid levels was done; Comparison of cholesterol levels with respect to type of occlusion and between group 1 and group 2 control subjects was done. There were 25 cases out of 86 with abnormal cholesterol levels in group1. Cholesterol levels were raised in group 1 but didn't meet statistical significance with respect to type of occlusion. In group2, only 6 controls showed abnormal cholesterol levels. Thus group 1 values were statistically significant when compared with age matched comparison control group 2. Similarly, Triglyceride levels were compared with respect to type of occlusion and between group 1 and group 2, there were 59 cases with abnormal triglycerides levels in group 1. Within the group 1, it didn't meet statistical significance with respect to type of occlusion. Triglyceride levels were raised in 59 cases in group1 and 18 controls in group 2 thus it was statistically significant when compared with age matched comparison control group 2. Similar finding were seen with LDL levels quite comparable to triglyceride levels than total cholesterol levels. HDL levels were reduced significantly in group 1 as opposed to age matched control group 2. Thus serum lipid levels;

Total cholesterol, Triglycerides levels, LDL levels were raised and HDL levels were reduced significantly in patients with retinal vein occlusion group 1 which was statistically significant as opposed to age matched comparison control group 2.

In a similar study conducted by kapil deb lahiri et al, also observed that total cholesterol, triglyceride, LDL cholesterol and VLDL cholesterol levels were elevated significantly (P <0.001) as well as HDL cholesterol was decreased significantly (P <0.001) in the patients with RVO as opposed to the control subjects which was consistent with our study(7) . There are various mechanisms reported regarding endothelial dysfunction by LDL Cholesterol. It is initially converted into oxidized LDL cholesterol by free radicals. The oxidized LDL is taken up by scavenger receptor on monocyte macrophages leading to foam cell. It decreases the expression of endothelial nitric oxide synthase and in turn inhibiting nitric oxide mediated vasorelaxation.(10)

In a study conducted by P M Dodson et al, it was found that Higher serum cholesterol concentrations were found in patients with central retinal vein occlusion and branch retinal vein occlusion than in the control group and similar tendencies were noted for the levels of LDL and HDL cholesterol which was statistically significant . Patients with central retinal vein occlusion also had raised levels of serum triglyceride but this was not so marked when VLDL triglyceride was measured. They thus concluded that Hyperlipidaemia is more likely to occur in patients with retinal vein occlusion than in an age-matched comparison group. Serum cholesterol and LDL cholesterol showed a stronger association with retinal vein occlusion than serum triglyceride or VLDL triglyceride. (6)

In a study conducted by W.buehl et al, a retrospective study found that, the significant difference was found between both groups that was cases and control. They found only in one parameter that was HDL phospholipid levels were significantly lower in patients with RVO than in the control group. Concentrations of several lipids and apolipoproteins associated with LDL were lower in the patient group, whereas lipids and apolipoproteins associated with VLDL were higher; however, these differences were not statistically significant .they concluded that HDL phospholipids might play a role in the development of retinal vein occlusion.(11)

In our study, systemic illnessess were considered in group 1 and group 2, There were 23 cases with DM ,40 cases with HTN in group1, which shows hypertension was most commonly associated with occurrence of RVO in our study. There were 19 controls with DM and 37 controls with HTN in group 2. Thus Systemic illnesses were comparable in both group 1 and group 2.

According to Newman-Casey PA et al, It was found that with metabolic syndrome components (hypertension, diabetes, hyperlipidemia) > 55 years, had an increased hazard of developing retinal vein occlusion compared with those with none of these conditions.(12)
Studies conducted by J. P. Ehler's et al, suggested that 48% of RVO is connected to HTN, 20% to HLD, and 50% to DM.(13)

Hyperlipedemia is a major contributory factors in causation of retinal vein occlusion in our study which was consistent with previous studies possible explanation is HLD causes increased plasma viscosity leading to increased platelet aggregation and thrombus formation.
Conclusion: Hyperlipidemia is a common independent risk factor for occurrence RVO in adults. Total cholesterol, Triglycerides, LDL levels were raised (p-value <0.001) and HDL

levels were reduced (p value <0.001) in patients with retinal vein occlusion as opposed to age matched comparison control group which was statistically significant. No statistically significant correlation was found between macular edema and serum lipid levels with p value>0.05. So serum lipid levels should be investigated for all patients with Retinal vein occlusion. While it remains to be determined whether normalizing the serum lipid levels could improve visual acuity and prevent the occurrence of RVO in the other eye or reduces complications/recurrence of RVO in the same eye. Hyperlipidemia are common risk factors for RVO in adults. It remains to be determined that serum lipid levels can improve visual acuity or the complications of RVO

References:

1. Rogers SL, McIntosh RL, Lim L, Mitchell P, Cheung N, Kowalski JW et al, Natural history of branch retinal vein occlusion: an evidence-based systematic review. Ophthalmology. 2010 Jun;117(6):1094-1101.e5.doi: 10.1016/j.ophtha.2010.01.058.
2. Bowling B. Kanski‘s Clinical Ophthalmology, systemic approach. Retinal Vascular Disease, 8th edition ;2016 Chapter 13:538-539.
3. McIntosh RL, Rogers SL, Lim L, Cheung N, Wang JJ, Mitchell P et al, Natural history of central retinal vein occlusion: an evidence-based systematic review. Ophthalmology. 2010 Jun;117(6):1113-1123.e15.doi: 10.1016/j.ophtha.2010.01.060.
4. Rogers S, McIntosh RL, Cheung N, Lim L, Wang JJ, Mitchell P et al; International Eye Disease Consortium. The prevalence of retinal vein occlusion: pooled data from population studies from the United States, Europe, Asia, and Australia. Ophthalmology. 2010 Feb;117(2):3139.e1.doi:10.1016/j.ophtha.2009.07.017.
5. Darin RG, Shah C, Michael GM, Jeffrey SH. Venous occlusive disease of the retina. In:ophthalmology Myron yanoff and Jay _s duker 4 th edition USA 2014.526-534.
6. P. M. Dodson, D. J. Galton, A. M. Hamilton, R. K. Blach. Retinal vein occlusion and the prevalence of lipoprotein abnormalities. Br J Ophthlmol. 1982; 66: 161-164.
7. Lahiri K, kundu A, gosh J, baruah M, biswas C, Das A. A Study Of Correlation Of Plasma Homocysteine With Serum Lipid Profile In Retinal Vein Occlusion. Current Indian Eye Research Journal of Ophthalmic Research Group. 2014;1(2):68.
8. Nelson RH. Hyperlipidemia as a Risk Factor for Cardiovascular Disease.Primary care. 2013;40(1):195-211. doi:10.1016/j.pop.2012.11.003.
9. Zhou JQ, Xu L, Wang S, Wang YX, You QS, Tu Y,et al The 10-year incidence and risk factors of retinal vein occlusion: the Beijing eye study.Ophthalmology. 2013 Apr;120(4):803-8. doi: 10.1016/j.ophtha.2012.09.
10. Liao JK, Shin WS, Lee WY, Clark SL. Oxidized low-density lipoprotein decreases the expression of endothelial nitric oxide synthase. J Biol Chem. 1995 Jan 6;270(1):319-24.
11. W. Buehl; E.M. Reitter; T. Stojakovic; H. Scharnagl; R. Dunavoelgyi; G. Matt; Lipid and Apolipoprotein Blood Levels in Patients With Retinal Vein Occlusion .invest ophthalmo and vis sci;april 2010:vol51, issue 13
12. Newman-Casey PA, Stem M, Talwar N, Musch DC, Besirli CG, Stein JD. Risk Factors Associated with Developing Branch Retinal VeinOcclusion Among Enrollees in a United States Managed Care Plan. Ophthalmology. 2014;121(10):1939-1948.doi:10.1016/j.ophtha.2014.04.045.
13. J. P. Ehlers and S. Fekrat, ―Retinal vein occlusion: beyond the acute event,‖ Survey of Ophthalmology, vol. 56, no. 4, pp. 281–299, 2011