# SEVERITY OF RETINOPATHY IN WELL CONTROLLED DIABETIC PATIENTS WITH AND WITHOUT DYSLIPIDEMIA

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## ABSTRACT

**Objective:** To compare the severity of diabetic retinopathy in well controlled type 2 diabetic patients with and without Dyslipidemia.

**Introduction:** Diabetic retinopathy is the most common cause of blindness influenced by the risk factors and predicated by duration of diabetes mellitus. Higher the level of HbA1C%, hypertension and abdominal obesity are risk factors for the development of retinopathy. Controlled levels of Blood pressure and hypercholesterolemia provide major clinical benefit in reducing the risk of blindness in patients with diabetic retinopathy.

**Methodology:** The study was conducted at Khyber Institute of Ophthalmic Medical Sciences (KIOMS) Hayatabad Medical Complex, Peshawar, from 4th April 2009 to 4th April 2010. It was descriptive case series study. Non probability purposive sampling technique was used.

**Results:** A total number of patients studied were 150. Age of the patients was 58.13+4.16 years. Male to female ratio was found to be 1:1. Diabetic retinopathy grading shows that NPDR was found 69(46%), PDR was 66(44%) and ADED was found 15(10%). Study group were separated into two groups on the basis of dyslipidemia. Majority of dyslipidemia was found in age range of 56-65 years (81, 54%). NPDR and ADED were more common in male while PDR was common in female diabetic patients.

**Conclusion:** It concludes that there is strong co-relation between severity of diabetic retinopathy and dyslipidemia. Patients having poor status of dyslipidemia have worse diabetic retinopathy. By keeping a good control level of serum lipid profile level in type-II diabetic, we can control the progression of severity diabetic retinopathy.

**Key Words:** Diabetic retinopathy, Dyslipidemia, NPDR, ADED.

## INTRODUCTION

The diabetes is one of major cause of irreversible blindness in the world. It is the leading cause in USA and UK at an average age of 52 years[1]. According to WHO estimates in 1995, 4.3 millions people in Pakistan had diabetes mellitus. It will swell to 11.6 millions by the year 20251. According to Pakistan national survey over all prevalence of diabetes mellitus is 11.47% and impaired glucose tolerance is 9.39%[2].

Diabetic retinopathy is the most common cause of blindness influenced by the risk factors and predicated by duration of diabetes mellitus. The incidence is 27% in 5-10 year, 71% in longer than 10 years and 90-95% after 30 years[3]. Higher the level of Glycosylated Hemoglobin (HBA1C), hypertension and abdominal obesity indicated by WHR(waist hip ratio) are risk factors for the development of retinopathy[4]. Diabetes mellitus is a disease of systemic and ocular micro-vascular abnormalities[5].

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Diabetic retinopathy occurs with duration of diabetes 10-20 years. Diabetes cause increased thickness of the basement membrane and increased permeability of the retinal capillaries, Aneurysmal dilation may occur in some vessels[6,7,8].

The following are the changes occurring in the diabetic retinopathy. Early treatment diabetic retinopathy study levels of diabetic retinopathy (ETDRS)[8].

Non proliferative diabetic retinopathy (NPDR) are Mild at least one micro-aneurysm must be present and Moderate hemorrhage or micro aneurysm (H/ma) soft exudates, venous beading (VB) to intra retinal micro vascular abnormalities (IRMA) definetly present[9].

Endothelium dysfunction in diabetes mellitus is due to increased generation of oxygen free radicals, which leads to functional consequences of endothelium dysfunction[3]. Blood pressure and cholestrolemia provides major clinical benefit in reducing the risk of blindness in patients with diabetic retinopathy[3,5].

Dyslipidemia is term used for increased triglcerides, decreased High Density Lipoprotiens (HDL) cholesterol and Low Density Lipoprotiens (LDL) particles of altered composition. The exact mechanism by which dyslipidemia may cause or induce diabetic retinopathy, is to damage endothelial cell and pericytes by oxidized low density lipoprotein cholesterol in corporation with triglycerides[10]. The antioxidant properties of

lipid lowering drugs might protect the outer retina from the oxidant damage, prevention of apoptosis of retinal cells by lipid lowering drugs[11].

Regular physical activity has been shown to be effective in reducing level of triglycerides rich VLDL. Timely and appropriate vision care can delay the onset of ocular morbidity, visual impairment, and blindness associated with diabetic retinopathy[12].

The aim of this study is to determine the relationship of Serum Lipid Profile with severity of Diabetic Retinopathy.

## METHODOLOGY

Thisdescriptive caseseries study was conducted at Khyber Institute of Ophthalmic Medical Sciences (KIOMS), Hayatabad Medical Complex, Peshawar from 4th April 2009 to 4th April 2010 over 150 patients, under significance level 0.05 with prevalence 11.74% and 5.16% margin of error using WHO sample size calculator. This was a non-Probability Purposive sampling.

The data was collected through performa. A detail history of patient's ocular and systemic status of the complaints or symptoms were collected. The duration of diabetes mellitus and its association with the diabetic retinopathy and its relation with Serum Lipid profile were collected. In Ocular Examination visual acuity of both aided and unaided of diabetic patients were recorded. Fundus Examination was done with direct ophthalmoscope and indirect ophthalmoscope with 90D, 81D and 20D lenses.The main investigation in my study was Blood sugar Level (Fasting / Random) with HBA1C. Fasting Serum Lipid profile.

All those patients who refuse to give consent for this study were excluded and the patient's age < 21 and >75 years were excluded because these patients were dependent on their families and having bad history of follow up. The data was analyzed with SPSS 10.0.

## RESULTS

Patients selected were of different age groups, with minimum age being 35 yeas and maximum age of 78 years. Mean age for first was 58.13 years+4.16SD. They were divided into four age groups and majority of the patients were found in age range of 56-65 year. Sex wise distribution shows that there were 75(50%) of male and 75(50%) were female patients with male to female ratio is 1:1.

Diabetic retinopathy grading shows that NPDR was found 69(46%), PDR was 66(44%) and ADED was found 15(10%). (Table 1)

Age wise distribution of diabetic retinopathy grading shows that majority of the patients 81(54%) have a diabetic retinopathy were in age range from 56-65year. While minimum patients 17(11.3%) were in age range from 35-45 years. (Table 2)

**Table 1: Diabetic Retinopathy Grading (n=150)**

| | Frequency | Percent |
|---|---|---|
| NPDR | 69 | 46.0 |
| PDR | 66 | 44.0 |
| ADED | 15 | 10.0 |
| Total | 150 | 100.0 |

NPDR: Non proliferative Diabetic Retinopathy
PDR: Proliferative Diabetic Retinopathy
ADED: Advanced Diabetic Eye Disease

**Table 2: Age Wise Distribution of Diabetic Retinopathy (n=150)**

| | | Diabetic Retinopathy Grading | | | |
|---|---|---|---|---|---|
| | | NDPR | PDR | ADDED | Total |
| Age | 35-45 | 5 3.3% | 12 8.0% | | 17 11.3% |
| | 46-55 | 18 12.0% | 5 3.3% | 5 3.3% | 28 18.7% |
| | 56-65 | 34 22.7% | 37 24.7% | 10 6.7% | 81 54.0% |
| | >66 | 12 8.0% | 12 8.0% | | 24 16.0% |
| Total | | 69 46.0% | 66 44.0% | 15 10.0% | 150 100.0% |

NPDR: Non proliferative Diabetic Retinopathy
PDR: Proliferative Diabetic Retinopathy
ADED: Advanced Diabetic Eye Disease

**Table 3: Sex wise distribution of Diatetic Retinopathy (n=150)**

| | | Sex | | |
|---|---|---|---|---|
| | | Male | Female | Total |
| Diabetic Retinopathy Grading | NDPR | 38 25.3% | 31 20.7% | 69 46.0% |
| | PDR | 27 18.0% | 39 26.0% | 66 44.0% |
| | ADED | 10 6.7% | 5 3.3% | 15 10.0% |
| Total | | 75 50.0% | 75 50.0% | 150 100.0% |

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**Table 4: Age wise distribution of Dyslipidemia (n+150)**

| | | Dyslipidema | | |
|---|---|---|---|---|
| | | Present | Absent | Total |
| Age | 35-45 | 16 10.7% | 1 .7% | 17 11.3% |
| | 46-55 | 22 14.7% | 6 4.0% | 28 18.7% |
| | 56-65 | 56 37.3% | 25 16.7% | 81 54.0% |
| | >66 | 22 14.7% | 2 1.3% | 24 16.0% |
| Total | | 116 77.3% | 34 22.7% | 150 100.0% |

**Table 5: Sex wise distribution of Dyslipidemia (n+150)**

| | | Sex | | |
|---|---|---|---|---|
| | | **Male** | **Female** | **Total** |
| Dyslip-idemia | Present | 52 34.7% | 64 42.7% | 116 77.3% |
| | Absent | 23 15.3% | 11 7.3% | 34 22.7% |
| Total | | 75 50.0% | 75 50.0% | 150 100.0% |

NPDR 38(25.3%) and ADED 10(6.7%) were more common in male. while PDR 39(26%) were common in female. (Table 3)

Age wise distribution of Dyslipidemia was analyzed as most of the patients 56(37.3%) having dyslipidemia were in age range 56-65 years follow by 22(14.7%) patients were in age range 46-56 and above 66 years.

**Table 6: Grading comparing Diabetic Retinopathy and Dyslipidemia**

| | | Dyslipidemia | | Total | P-value |
|---|---|---|---|---|---|
| | | **Present** | **Absent** | | 0.000 |
| Diabetic Retinopathy Grading | NDPR | 69 59.5% | | 69 46.0% | |
| | PDR | 47 40.5% | 19 55.9% | 66 44.0% | |
| | ADED | | 15 44.1% | 15 10.0% | |
| Total | | 116 100.0% | 34 100.0% | 150 100.0% | |

NPDR: Non proliferative Diabetic Retinopathy

PDR: Proliferative Diabetic Retinopathy

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While only 16(10.7%) patients were in age range 35-46 years. (Table 4)

Out of 116 (77.3%) patients having dyslipidemia, female were 64(42.7%) and male were 52(34.7%). This shows that dyslipidemia were common in female diabetic patients. (Table-5)

Dyslipidemia in Diabetic Retinopathy grading was analyzed as dyslipidemia was most common in NPDR group 69(46.0%) and PDR group having 47(31.3%) patients. Whereas dyslipidemia was absent in ADED group which was 15(10%) patients. Chi-square test shows that dyslipidemia have a significant role over diabetic retinopathy grading with p-value=0.000. (Table No 6)

## DISCUSSION

This study was conducted to see the associations between dyslipidemia and diabetic retinopathy. The findings was to see the extent of retinopathy of well controlled type-II diabetic and its association with and without dyslipidemia[13,14].

The strengths of all these studies are the extent of clinical data available in the DCCT/EDIC and the comprehensive nature of the lipid profile analyses, which included not only conventional lipid profiles, but also check HbA1 C for the status of type-II diabetic mellitus. In the present study, dyslipidemia in particular revealed associations between retinopathy status and lipoprotein subclasses that were previously unknown and could not be discerned from conventional lipid profiles. The findings are broadly consistent with those in studies by others[15,16]. In contrast, much stronger associations and gender differences were identified by the Grading of retinopathy. These associations were consistent across measures of retinopathy: Furthermore, the associations involved subclasses within all three major lipoprotein classes (total cholesterol, LDL, HDL). Retinopathy was strongly associated with small and medium, but not large, LDL in all gender. Accordingly, retinopathy was inversely associated with average LDL particle size. Associations between retinopathy and levels of triglyceride- rich lipoproteins may be partly explained by prothrombotic effects of the latter on vascular cells. For example, VLDL may increase secretion of plasminogen activator inhibitor (PAI-1) by human endothelial cells[17]. Retinopathy was also independently associated with NMR derived LDL parameters, but only in men. Thus, in men, retinopathy was positively associated with small LDL cholesterol concentration (L1, milligrams per deciliter) and LDL particle concentration (nanomolar) and negatively associated with large-LDL-cholesterol concentration (L3, milligrams per deciliter) and average LDL particle diameter (nanometers)[18]. Small LDL is known to be more atherogenic than large LDL,[19] perhaps because it more readily crosses the endothelium and/or is more readily oxidized, and these same properties may also contribute to retinal capillary injury. In the retinal capillary, oxidized LDL is toxic to both pericytes and endothelial cells[20] and may have prothrombotic effects mediated by activation of protein kinase C[21]. The conventional lipid profile demonstrates that in men and in the combined cohort there is a significant inverse association (borderline in women) of retinopathy with HDL cholesterol. The negative association of retinopathy with large HDL (corresponding to HDL 2) may be attributable in part to the paraoxonase activity associated with this

lipoprotein. Paraoxonase detoxifies lipid peroxidation products, is carried in association with large HDL, and is believed to have a protective role against retinopathy[22].

Finally, we were able to find an association of retinopathy status with the susceptibility of isolated LDL to oxidative stress.

The ETDRS showed that severity of retinal hard exudates was strongly associated with total triglycerides, total cholesterol, and LDL cholesterol[23]. Also, elevated levels of these lipids conferred increased risk for future hard exudates and subsequent visual deterioration[23]. In our study, we found associations of hard exudates with conventional lipid measures in univariate analyses, but these were lost in multivariate analyses. Again, NMR lipoprotein subclass analyses revealed associations that remained significant in the multivariate analyses. Studies using in vitro modified LDL (to simulate modified, extravasated lipoproteins such as are found in hard exudates) demonstrate adverse effects on retinal capillary pericytes and endothelial cells,[24] and so over the years, hard exudates may reflect conditions (e.g., adverse lipoprotein profile, more severe capillary leakage) that accelerate retinopathy. Hard exudates are known to improve with treatment of hyperlipidemia, but typically this improvement does not reverse visual loss, at least in the short term[18]. This supports a possible role for dyslipidemia in the development of retinopathy. Whereas one may envisage nephropathy as a cause, not a consequence, of alterations in plasma lipoproteins, it seems unlikely that retinopathy would cause dyslipidemia. Another recent study also confirm that insulin resistance in the absence of diabetes is associated with a dyslipidemia similar to that we now identify as associated with retinopathy,[22] at least for subclasses of LDL and HDL. It is of interest, however, that insulin resistance was associated with large, not medium or small, VLDL, as were retinopathy and the AER.

In summary, our data show that within all three major lipid profile classes (total cholesterol, LDL, and HDL), diabetic retinopathy is associated with a shift in subclass distribution toward smaller- diameter particles, and with an increase in LDL particle concentration. These associations cannot be detected from conventional lipid profiles, which do not discern subclass distributions. Our findings in relation to VLDL apply to both men and women, whereas those in relation to LDL and HDL apply much more strongly to men, in multivariate analyses. Because many of the alterations in lipoprotein subclasses have been shown to confer increased cardiovascular risk, our data are also consistent with the theory that dyslipoproteinemia may act as a common risk factor for retinopathy and atherosclerosis in diabetes[24]. The different associations of retinopathy with lipoprotein parameters between men and women suggest a gender differential in risk for retinopathy, because typically men have a much less favorable lipoprotein subclass profile than women. This was also the case in the DCCT/EDIC cohort[24]. Indeed, there is evidence in the literature that diabetic men may be more susceptible than women to retinopathy[24] and our data from the DCCT/EDIC cohort are in concurrence with this. When we controlled for relevant variables, men had slightly but significantly more severe retinopathy. Further prospective studies, already in progress, are needed to support or refute the possibility that lipoprotein subclass profiles contribute directly to the development of retinopathy. Future studies must also determine whether measures to modify subclass distribution, which may include use of existing insulin-sensitizing agents, may prevent or mitigate retinopathy.

## CONCLUSION

Risk factors for Diabetic retinopathy was long duration, poor glygcemic control and abnormal blood serum lipid levels. In conclusion the recognition of diabetic retinopathy as sight threatening condition. Training in ophthalmoscopy will help in early identification of diabetic retinopathy, in patients at high risk, referral for expert opinion and treatment will prevent blindness in many individuals in vulnerable communities around the world.

## RECOMENDATIONS

Blindness is almost in evitable, if left unmanaged. Regular physical activity has been shown to be effective in reducing level of triglycerides and LDL. Timely and appropriate vision care can delay the onset of ocular morbidity, visual impairment and blindness associated with diabetic retinopathy. Therefore keeping these things in mind, we can prevent the sequelae of severe blindness in already burdened economy.

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