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Study of proliferative diabetic retinopathy and its correlation with hypertension, dyslipidaemia and diabetic nephropathy

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***Abstract*---**Background: Diabetes Mellitus (DM) is a commonly encountered micro vascular disorder in ophthalmic outpatient department. It is estimated that approximately 191 million people may be suffering from this disorder by year 2030. [3] The rapid increase in number of persons with Diabetes is expected to lead to an increase in number of persons with ocular complications of diabetes. The prevalence of retinopathy changes in diabetic patients varies considerably, but is probably 20 to 30 % and out of it, 3-4% cases are of proliferative diabetic retinopathy.[4] Diabetic Retinopathy has been studied extensively in past about its effect on vision, different pathologies, incidence, prevalence, risk factors, its various diagnostic techniques and treatment modalities.[5-9] However the correlation of proliferative diabetic retinopathy with hypertension, dyslipidaemia and diabetic nephropathy and its prognosis has not been studied adequately which warrants further studies. These risk factors once accurately identified and appropriately controlled at an early stage, progression of diabetic retinopathy and its subsequent effect on vision can be effectively controlled. Aims and objectives: To study the clinical profile, presentation of proliferative diabetic retinopathy in type 2 diabetic patients and its correlation with hypertension, dyslipidaemia and diabetic nephropathy. Material and methods: *Study design*: The present study type was a cross sectional type of study conducted in patients visiting Ophthalmology OPD and admitted to the Intensive Care Units and wards in a tertiary care hospital over period of 18 months from November 2019 to May 2021. Enrolled patients underwent thorough history about visual complaints, systemic illnesses like diabetes mellitus, hypertension, nephropathy and dyslipidaemia, duration of illness, compliance to the treatment and

thorough ophthalmic examination with visual acuity and fundus examination along with vital parameters assessment and laboratory tests for diabetes, nephropathy and lipid profile. *Statistical analysis*: Appropriate statistical tests were applied using SPSS v21 for analysis;p-value<0.05 was considered statistically significant. Results: Diabetes mellitus, hypertension and dyslipidaemia had high statistical significance with proliferative diabetic retinopathy. Conclusion: Diabetes mellitus, hypertension and dyslipidaemia all 3 are identified as significant risk factors for proliferative diabetic retinopathy.

***Keywords*---**Proliferative diabetic retinopathy, Diabetes mellitus, hypertension and dyslipidaemia.

Introduction

Diabetic retinopathy (DR), a microangiopathy affecting all of the small retinal vessels, such as arterioles, capillaries and venules, is characterized by increased vascular permeability, ocular haemorrhages, lipid exudate, by vascular closure mediated by the development of new vessels on the retina and the posterior vitreous surface.[1] DR, the most common microvascular complication of DM, is predicted to be the principal reason of new blindness among working population.[2, 3] Diabetic Retinopathy has been studied extensively in past about its effect on vision, different pathologies, incidence, prevalence, risk factors, its various diagnostic techniques and treatment modalities.[3] However the correlation of proliferative diabetic retinopathy with hypertension, dyslipidaemia and diabetic nephropathy and its prognosis has not been studied adequately which warrants further studies. These risk factors once accurately identified and appropriately controlled at an early stage, progression of diabetic retinopathy and its subsequent effect on vision can be effectively controlled.

Material and Methods

Aim and objectives: To study the clinical profile, presentation of proliferative diabetic retinopathy in type 2 diabetic patients and its correlation with hypertension, dyslipidaemia and diabetic nephropathy.

Study design: The present study type was a cross sectional type of study conducted in patients visiting Ophthalmology OPD and admitted to the Intensive Care Units and wards in a tertiary care hospital over period of 18 months from November 2019 to May 2021**.** Enrolled patients underwent thorough history about visual complaints, systemic illnesses like diabetes mellitus, hypertension, nephropathy and dyslipidaemia, duration of illness, compliance to the treatment and thorough ophthalmic examination with visual acuity and fundus examination along with vital parameters assessment and laboratory tests for diabetes, nephropathy and lipid profile.

Study sample: 418 patients with diabetes mellitus were screened for proliferative diabetic retinopathy and the study was conducted in 50 patients presenting with acute proliferative diabetic retinopathy in a tertiary care hospital.

Study setting: This study was conducted in KIMS Hospital, over period of eighteen months from November 2019 to May 2021**.** The Institutional Ethical committee approval was taken.

Inclusion and exclusion criteria: All patients diagnosed with proliferative diabetic retinopathy coming to the OPD or undergoing treatment at Krishna Hospital, Karad on IPD basis were included in the study and patients with Type 1 diabetes mellitus, patients where fundus examination was difficult like patients with central corneal opacities, patients with old ocular trauma, unconscious and comatose patients, patients not willing to participate in the study, and patients with other retinal manifestations eg ARMD, glaucoma were excluded from the study.

Statistical analysis: All data was collected and complied in Microsoft excel. Results of continuous (quantitative data) measurement were presented on Mean +/- SD (min-max) and result on categorical (qualitative data) measurements was presented in percentage and proportions (%). Comparison of qualitative variable was analysed by chi-square test. Wherever necessary between groups, comparison of quantitative variables was analysed by independent student t test according to distribution. A p value of 0.05 was taken as level of significance and was considered statistically significant. Data analysis was done using open epi version 2.

Results

Majority 52.16% had age in 30 to 60 years. Mean age in years was 56.56$\pm$11.7, ranging from 15 to 75 years with majority 52.15% being males and 47.84% females. Among whole population 11.96% (50 cases) had proliferative diabetic retinopathy.

Parameters among patients with proliferative diabetic retinopathy (11.96%)

66% had duration of DM < 10 years. Mean duration of DM in years was 9.98$\pm$6.17 years. Ranging from 5 to 30 years. 62% had hypertension. High statistical significance was seen between PDR and hypertension ($p<0.0001$) Mean duration of HTN in years was 5.16$\pm$5.86 years. Ranging from 4 to 20 years. 31 patients presented with glycosuria measured by a dipstick test suggestive of deranged blood sugar levels. 16 % patients had positive ketone bodies in urine on a dipstick test suggestive of uncontrolled blood sugar levels.

20% had diabetic nephropathy. High statistical significance was seen between PDR and DN. ($p<0.001$) Urine albumin levels were detected by a dipstick test. 28% patients had albumin present in urine. 10 patients showed presence of microalbuminuria in urine detected by using Dirui Reagent Strip test. It shows altered renal function suggestive of nephropathy.

70% of PDR cases had TCL >200. 98% of PDR cases had TGR >150. 66% of PDR cases had HDL >40. 74% of PDR cases had VLDL. 76% of PDR cases had LDL

>130. High statistical significance was seen between PDR and Lipid profile. (p<0.001)
78% had macular oedema. In patients with macular oedema, 35.89 % patients had dyslipidaemia. 20 % patients having diabetic nephropathy, all had macular oedema.

Discussion

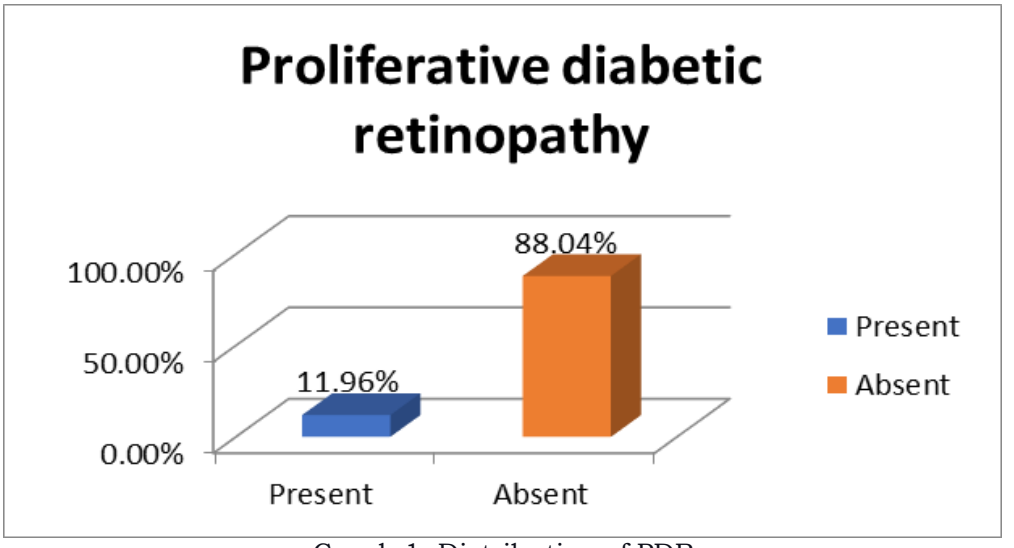
This study was a tertiary care centre based cross sectional study. We screened 418 patients with type 2 diabetes mellitus and those patients with proliferative diabetic retinopathy were included in the study population.

Age and gender distribution

Majority 52.16% had age in 30 to 60 years. Mean age in years was 56.56±11.7, ranging from 15 to 75 years. Amongst them**,** 52.15% were males and 47.84% were females showing male preponderance.

Proliferative diabetic retinopathy

Among whole population of 418 patients with type 2 diabetes mellitus screened for proliferative diabetic retinopathy, 11.96% (50 cases) had proliferative diabetic retinopathy. Study by Nwanyanwu KH et al [4] conducted a retrospective cohort analysis and found that 6.6% had PDR. Study by Baek, S.U et al [5] showed that 21.4% had PDR. Study by Giloyan A et al [6] showed that prevalence of DR was 36.2% and among them PDR was 9.8%. Study by Porta M et al [7] showed that 17.3% developed PDR. Study by Pan CW et al [8] showed that the overall prevalence of any DR was 18.0%. Study by Ossama A W El Haddada et al [9] showed that 12.8% had PDR. Similar results were found in present study.



Graph 1: Distribution of PDR

Parameters among patients with proliferative diabetic retinopathy (11.96%)
Vision

Among 11.96% of PDR cases majority 28% had lower baseline visual acuity.
Duration of DM
66% had duration of DM < 10 years. Mean duration of DM in years was 9.98±6.17 years. Ranging from 5 to 30 years.
Duration of hypertension
62% had hypertension. Mean duration of HTN in years was 5.16±5.86 years. Ranging from 4 to 20 years.
Blood pressure
Majority 24% had blood pressure 120/80. Similar findings were seen in present study.
Diabetic nephropathy
20% had diabetic nephropathy. 10 patients showed presence of microalbuminuria in urine showing altered renal function suggestive of nephropathy.
Blood sugar level
Mean fasting BSL was 167.9±46.77 and PP was 192.62±61.3. All patients were on treatment for type 2 diabetes mellitus and it was a cross sectional study. Hence the parameters were assessed at one point of time.
HbA1C
Mean HbA1C was 7.4±1.69 ranging from 5 to 12.2. Majority 46% had HBA1C in 6 to 8 range.

Parameters to diagnose diabetic nephropathy

Mean albumin/creatinine ratio was 22.42+11.63 mg/g ranging from 3 to 40 mg/g. 11 patients (20%) had deranged A/C ratio suggestive of compromised renal function. It is a positive indicator of diabetic nephropathy
Mean urea level was 34.35+56.92 mg/dL ranging from 14 to 256 mg/dL. 8 patients (16%) had deranged blood urea levels.
Mean Creatinine level was 1.44+1.29 mg/dL ranging from 0.7-7.9 mg/dL. 10 patients (20%) had deranged serum creatinine levels
31 patients presented with glycosuria measured by a dipstick test suggestive of deranged blood sugar levels.
16 % patients had positive ketone bodies in urine on a dipstick test suggestive of uncontrolled blood sugar levels.
Urine albumin levels were detected by a dipstick test. 28% patients had albumin present in urine.
10 patients showed presence of microalbuminuria in urine detected by using Dirui Reagent Strip test. It shows altered renal function suggestive of nephropathy.
Mean urine pH level was 6.62+0.96 ranging from 5 to 8 and mean Specific gravity level was 1.01+0.006 ranging from 1-1.03.

Electrolyte levels

Mean Sodium level was 134.16+4 mEq/L ranging from 122 to 144 mEq/L. Mean Potassium level was 3.94+0.46 mEq/L ranging from 3.2-5.4 mEq/L suggestive of no significant electrolyte imbalance in the study population.

Parameters to assess dyslipidaemia

Mean TCL (Total Cholesterol) level was 217.28+20.8 mg/dL ranging from 183-250 mg/dL. Majority 70% had TCL >200.
Mean TRG (Triglycerides levels) was 302.48+92.1 mg/dL ranging from 152-459 mg/dL. Majority 98% had TRG >150.
Mean HDL (High Density Lipoprotein) level was 44.67+9.63 mg/L ranging from 30-59 mg/dL. 34% had HDL <40. 66% patients had high HDL levels. Still it did not prove to be a protective factor.
Mean VLDL (Very Low Density Lipoprotein) level was 25.54+10.69 ranging from 4 to 40. 74% had VLDL <30
Mean LDL(Low Density Lipoprotein) level was 164.34+36.16 ranging from 96-220. 76% had LDL level>130.

Association between PDR and various risk factors

62% of PDR cases had hypertension. High statistical significance was seen between PDR and hypertension. ($p<0.0001$). 70% of PDR cases had TCL >200. High statistical significance was seen between PDR and TCL. ($p=0.001$). 98% of PDR cases had TGR >150. High statistical significance was seen between PDR and TGR. ($p<0.001$). 66% of PDR cases had HDL >40. No statistical significance was seen between PDR and HDL. ($p=0.13$). 74% of PDR cases had VLDL. High statistical significance was seen between PDR and VLDL. ($p<0.0003$). 76% of PDR cases had LDL >130. High statistical significance was seen between PDR and LDL. ($p<0.001$). 20% of PDR cases had DN. High statistical significance was seen between PDR and DN. ($p<0.001$).
62% of PDR cases had hypertension, 30% of PDR Cases had dyslipidaemia and 20% had diabetic nephropathy. High statistical significance was seen between PDR and all three risk factors ($p<0.0001$). High statistical significance was seen between PDR and lipid profile ($p<0.00001$).

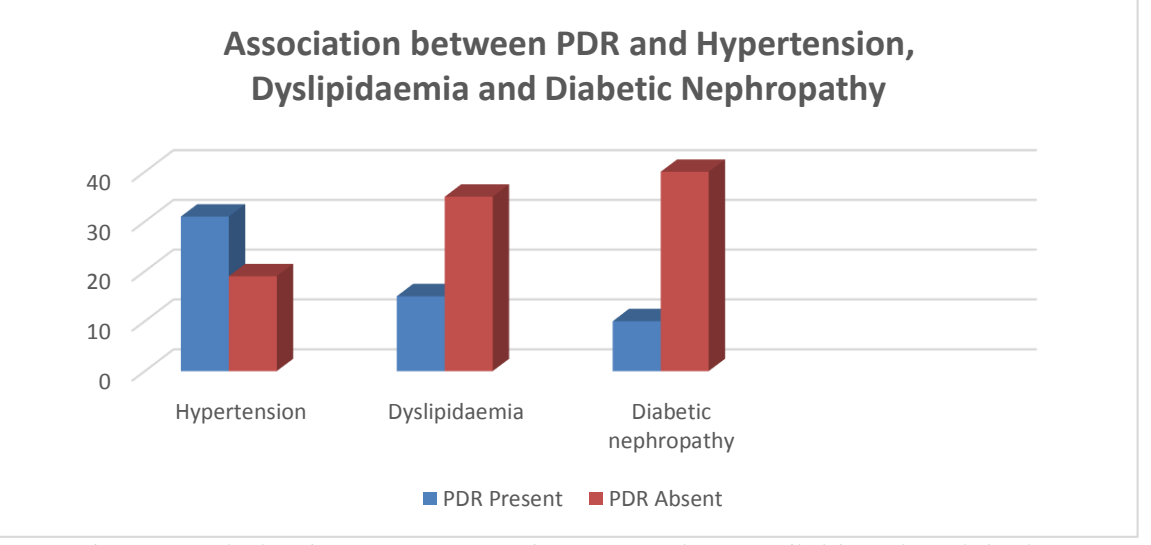
Study by Nwanyanwu KH et al [(1)] conducted a retrospective cohort analysis and found that -year probability of progression for low-risk individuals with NPDR was 5% (range 2–8) and for high-risk patients was 38% (14–55). Study by Laiginhas R et al [(10)] showed that Nephropathy was associated with prevalent DR in the late-onset group but not in the early-onset group.

Study by Cardoso CRL et al [(11)] and Diana et al [(12)] showed that baseline retinopathy prevalence, age and sex, a longer diabetes duration ($p < 0.001$), higher baseline ambulatory BPs ($p = 0.013$, for 24-hour diastolic BP), and higher mean cumulative exposure of HbA1c ($p < 0.001$), clinic diastolic BP ($p < 0.001$) and LDL-cholesterol ($p = 0.05$) during follow-up were the independent predictors of development/progression of DR. BP parameters were only predictors of DR development. Longer diabetes duration, poorer glycaemic and lipid control, and higher BPs were the main predictors of development/progression of DR. Mean cumulative clinic diastolic BP was the strongest BP related predictor.

Table 1
Association between PDR and Hypertension, Dyslipidaemia, Diabetic Nephropathy

Proliferative diabetic retinopathy	Present	%	Absent	%
Hypertension	31	62%	19	38%
Dyslipidaemia	15	30%	35	70%
Diabetic Nephropathy	10	20%	40	80%

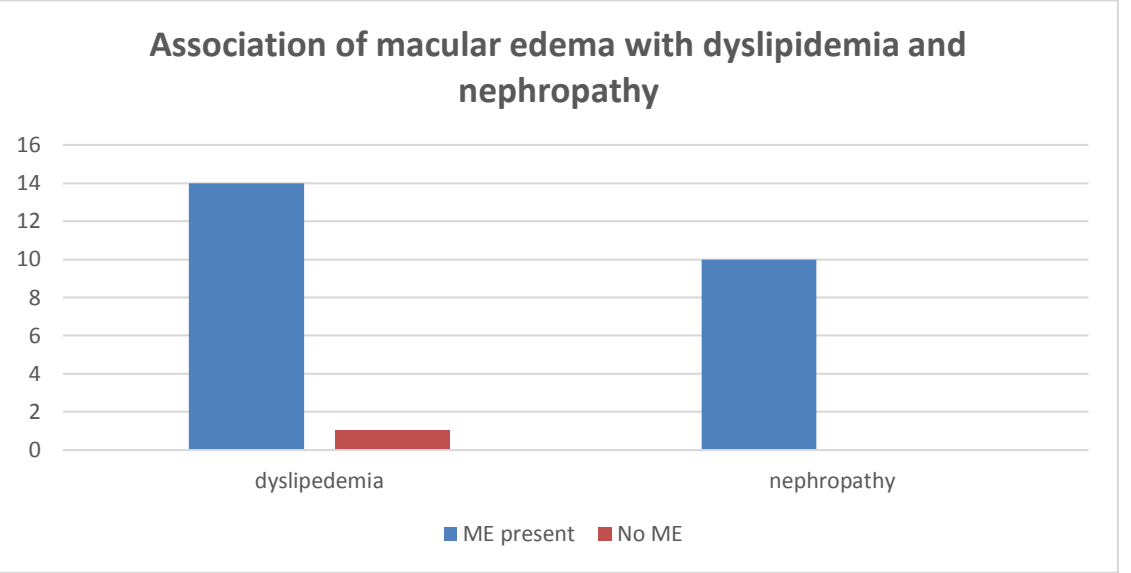
P <0.00001.



Graph 2: Association between PDR and Hypertension, Dyslipidaemia, Diabetic Nephropathy

62% of PDR cases had hypertension, 30% of PDR cases had dyslipidemia and 20% had diabetic nephropathy. High statistical significance was seen between PDR and all three risk factors (p<0.0001)

78% patients in the study population had macular oedema (ME). 35% patients with macular oedema had dyslipidaemia. 20% patients had diabetic nephropathy.



Graph 3: Association of macular edema with dyslipidemia and nephropathy

Conclusion

- Mean age of study population was 56.56 with male preponderance suggesting middle to older age population being affected who were not compliant to treatment.
- In study population, mean duration of diabetes was found out to be 9.98 years. In these patients treatment compliance was also poor.
- In patients with dyslipidaemia, 70% patients had deranged total cholesterol levels. 98 % patients had deranged triglycerides levels suggesting highest correlation with PDR. HDL was high in 66 % of patients. Still it did not prove to be a protective factor. Deranged LDL is more specific than HDL.
- Hypertension was found in 62% population. The mean duration of HTN was 5-6 years and age of onset of PDR was earlier showing positive correlation as a risk factor.
- Patient who had all 3 risk factors present showed faster progression since duration of diabetes in this patient was 5 years only.
- Only 20% patients had diabetic nephropathy. Hence it can be concluded that diabetic retinopathy and nephropathy need not go hand in hand, and other factors causing nephropathy warrants further study.
- 78% patients had macular edema. 35% patients with macular edema had dyslipidaemia. 20% patients had diabetic nephropathy and macular edema was present in all those patients showing high correlation of macular edema in nephropathy.
- One patient had no associated risk factor present, but had diabetes mellitus since 30 years. Hence duration of diabetes can be identified as isolated risk factor for PDR.
- In patients with absence of these risk factors, other risk factors like anaemia, smoking etc. should be studied and identified.
- Overall surveys to detect diabetes mellitus and identify and control the risk factors should be undertaken.

- Every diabetic patient should be screened for diabetic retinopathy early in phase.
- Counselling for treatment compliance and avoid treatment defaulters are important factors to prevent disease progression.

Conflict of interest:
Nil

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