



Original Research Article

Study of clinical correlation of diabetic retinopathy with diabetic nephropathy and diabetic neuropathy in patients with type 2 diabetes mellitus

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ABSTRACT

Purpose: To study the relationship of various stages of Diabetic Retinopathy with severity of Diabetic Nephropathy and Diabetic Neuropathy.

Materials and Methods: 120 patients of type 2 diabetic patients were screened for Retinopathy, nephropathy and neuropathy. Investigations like Fundus examination with Indirect Ophthalmoscopy, CBC, RBS, RFT – S. Creatinine, S. Urea; Urine Samples – Microalbuminuria; HbA1c; Lipid Profile and Creatinine clearance, Vitamin B12, Nerve conduction Velocity Test and Clinical Reflex Test were performed on the patients with.

Results: In present study we have found significant correlation between Retinopathy, Diabetic Nephropathy and Neuropathy. Severity of neuropathy and nephropathy increased with increase in the grade of retinopathy.

Conclusion: In our study the incidence of neuropathy and nephropathy also increases as severity of diabetic retinopathy increases. Thus, all diabetic patients must be screened for retinopathy as it can help determine the presence of other organ involvement.

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1. Introduction

Diabetes Mellitus, or simply diabetes, is a metabolic disorder characterized by high blood glucose levels resulting in damage to various organs of the human body. It is a condition fundamentally characterized by hyperglycemia due to defects in the body's ability to produce insulin giving rise to the risk of microvascular damage (retinopathy, nephropathy, and neuropathy).¹

Because of modern lifestyle diabetes mellitus prevalence is increasing worldwide. The International Diabetes Federation (IDF) has declared that the number of people suffering from diabetes is about 367 million which will rise to 553 million by 2030. 72.946.400 cases of diabetes reported in India in 2017.²

The increase in the prevalence of Diabetes Mellitus, directly leads to increases in the burden of diabetic

microvascular complications. It has been estimated that around 93 million people have diabetic retinopathy worldwide.³ Around 17.6% of people suffer diabetic retinopathy in India.³

Diabetic retinopathy is the leading cause of blindness. The rise in plasma glucose level leads to diabetic retinopathy by damaging the microvascular system of the retina. Type 1 and Type 2 diabetes mellitus both will lead to diabetic retinopathy.

One of the major complications of diabetes is End-Stage Renal Disease (ESRD) globally. Reported as an arterial blood pressure elevation persistent albuminuria, and the decline in the Glomerular Filtration Rate (GFR). This is one of the most common life threatening conditions. 20% to 40% of patients with type 1 and 20% of type II diabetic patients develop these life threatening complications.⁴ Diabetic neuropathy is condition that results from microvascular injuries of small blood vessels

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that supply nerves of the body from high hyperglycemia. The peripheral nerves of the body are most commonly affected by this conditions.

This study to find out the relationship between diabetic nephropathy, diabetic neuropathy with the severity of diabetic retinopathy in type II diabetic patients. It also aims to find out the correlation between HbA1c and severity of diabetic nephropathy, neuropathy, and retinopathy. Based on the profile of diabetic retinopathy which is easier to assess clinically, and thereby help us take timely action to prevent or reduce the severity of life threatening complications of nephropathy and neuropathy.

2. Material and Methods

This was a single centric observational, cross sectional study that was carried out prospectively in the department of the ophthalmology, Dhiraj Hospital to evaluate the correlation of diabetic retinopathy with diabetic nephropathy and diabetic peripheral neuropathy in type 2 diabetics. A total of 120 diagnosed patients of type 2 diabetes having evidence of retinopathy confirming to the inclusion-exclusion criteria, with the age more than 18 years from both genders were included.

2.1. Inclusion criteria

1. All Patients of type II diabetes mellitus found to have diabetic retinopathy irrespective of their control level and duration of disease.
2. Patients may/may not be on diabetic treatment
3. Patients who were willing to participate in the study

2.2. Exclusion criteria

1. Pre-existing nondiabetic retinopathy
2. Nondiabetic renal disorders
3. Nondiabetic neuropathy
4. Hypertension
5. Anemia
6. Unwilling Patients

After taking informed written consent, detailed ophthalmic and systemic history was taken. A complete ophthalmic evaluation was done.

Unaided and best-corrected visual acuity was recorded using Snellen's chart for distant vision. Slit lamp biomicroscopy was used to evaluate the anterior segment as well as undilated fundus with 90 D lens. A Goldmann applanation tonometer was used to measure the intraocular pressure. Dilated fundus examination was done with indirect ophthalmoscope using 20D lens. Retinopathy was diagnosed based on clinical examination (indirect ophthalmoscopy) and classified as per modified ETDRS classification.

Nephropathy was diagnosed based on investigations reports severity.

Neuropathy was diagnosed based on clinical examinations including superficial and deep tendon reflexes. Degree of sensation loss was determined on nerve conduction test.

All patients have undergone investigations like CBC, RBS, HbA1c; lipid profile, RFT including S. creatinine, S. urea and creatinine clearance; urine examination for microalbuminuria and vitamin B12.

Based on clinical examination and the results of all the tests correlation between various stages of diabetic retinopathy with peripheral neuropathy and diabetic nephropathy was determined.

2.3. Statistical analysis

SPSS 20 was used for statistical analysis of this study data.

All quantitative data were analyzed by using parametric tests whereas all qualitative data were analyzed by using nonparametric tests to find the significance level.

All data were presented in tabular and graphical presentation and p-value <0.05 was considered as significance level.

3. Result

This was a single centric observational, cross-sectional prospective study. 120 diagnosed cases of type 2 diabetes having evidence of retinopathy were enrolled.

We divided all 120 patients according to their HbA1c level such as <6%, 06-08% and > 08% to find the relationship between HbA1c and grade of retinopathy. We have observed that out of 30 patients of mild NPDR, 10.00% had HbA1c level < 06%, 30.00% had HbA1c level between 06 to 08%, and 60.00% of patients had HbA1c level more than 08%. Out of 60 patients of moderate NPDR, 20.00% had HbA1c level < 06%, 48.00% had HbA1c level between 06 to 08% and 32.00% of patients had HbA1c level more than 08%. Out of 30 patients of severe NPDR, 20.00% had HbA1c level < 06%, 70.00% had HbA1c level between 06 to 08% and 10.00% of patients had HbA1c level more than 08%. Out of 05 patients of PDR, none of the patients had HbA1c level < 06%, 40.00% had HbA1c level between 06 to 08%, and 60.00% of patients had HbA1c level more than 08%. We also applied the Chi-Square test to find the relationship between HbA1c level and retinopathy grades but we did not find a statistically significant result. p-value is 0.276.

Patients were also divided according to their blood urea level such as < 40 and > 40 and find the relationship with the grade of retinopathy. We have observed that out of 30 patients of mild NPDR, 70.00% had blood urea level < 40, and 30.00% of patients had blood urea level > 40. Out of 55 patients of moderate NPDR, 48.00% had a blood urea level < 40 and 52.00% of patients had a blood urea level > 40. Out of 30 patients of severe NPDR, 60.00% had a

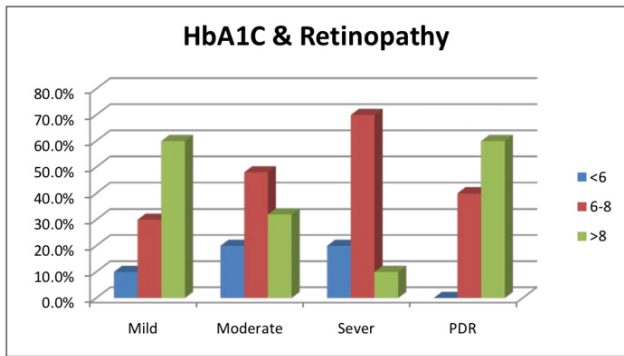


Fig. 1:

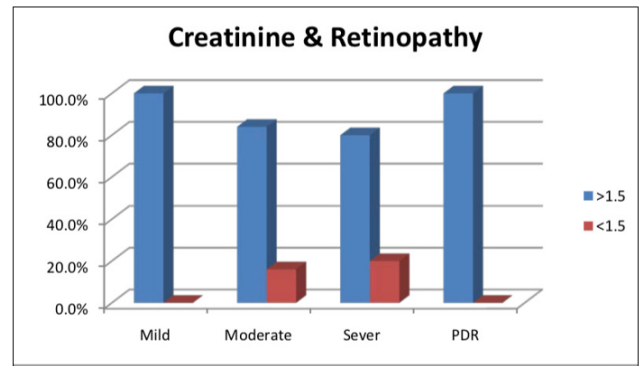


Fig. 3:

blood urea level < 40, and 40.00% of patients had a blood urea level > 40. Out of 05 patients of PDR, 80.00% had a blood urea level < 40 and 20.00% of patients had a blood urea level > 40. We also applied the Chi-Square test to find a relationship between blood urea level and retinopathy grades but we did not find a statistically significant result. The p-value is 0.590.

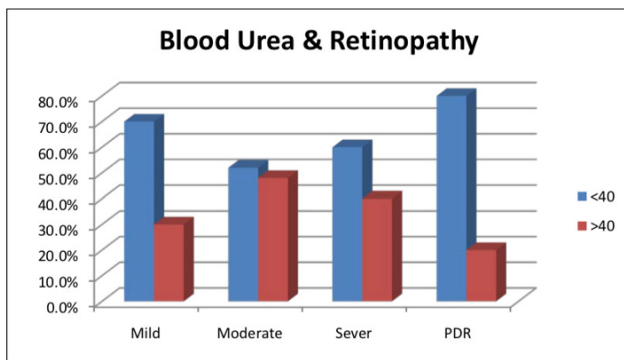


Fig. 2:

The relation between retinopathy and Creatinine was also found in our study. All the patients were divided according to their S.creatinine levels such as < 1.5 and > 1.5 and find the relationship with a grade of retinopathy. We observed that out of 30 patients of mild NPDR, 100.00% had creatinine level < 1.5 and 00.00% of patients had creatinine level > 1.5. Out of 55 patients of moderate NPDR, 16.00% had creatinine level < 1.5 and 84.00% of patients had creatinine level > 1.5. Out of 30 patients of severe NPDR, 20.00% had creatinine level < 1.5 and 80.00% of patients had creatinine level > 1.5. Out of 05 patients of PDR, 00.00% had creatinine level < 1.5 and 100.00% of patients had creatinine level > 1.5. We also applied the Chi-Square test to find the relationship between creatinine level and retinopathy grades, but we did not find a statistically significant result. The p-value is 0.387.

In the present study we have divided all enrolled 50 study participants according to their Vitamin B12 level such as

< 200 and > 200 and find the relationship with a grade of retinopathy. We have observed that out of 30 patients of mild NPDR, 30.00% had Vitamin B12 level < 200 and 70.00% of patients had Vitamin B12 level > 200. Out of 55 patients of moderate NPDR, 24.00% had Vitamin B12 level < 200 and 76.00% of patients had Vitamin B12 level > 200. Out of 30 patients of severe NPDR, 80.00% had Vitamin B12 level < 200 and 20.00% of patients had Vitamin B12 level > 200. Out of 05 patients of PDR, 60.00% had Vitamin B12 level < 200 and 40.00% of patients had Vitamin B12 level > 200. We also applied the Chi-Square test to find the relationship between Vitamin B12 level and retinopathy grades and we found statistically significant results. p-value is 0.014.

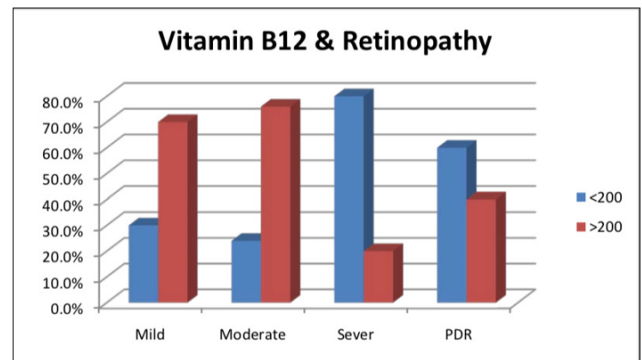


Fig. 4:

In present, we have found a significant association between retinopathy and diabetic nephropathy with the p-value 0.013 and it was concluded that with higher grading of diabetic grading i.e mild NPDR to PDR, the severity of nephropathy is also inclining. In present, we have found a significant association between retinopathy and diabetic neuropathy with the p-value 0.0001 and it was concluded that with higher grading of diabetic grading i.e mild NPDR to PDR, the severity of neuropathy is also inclining.

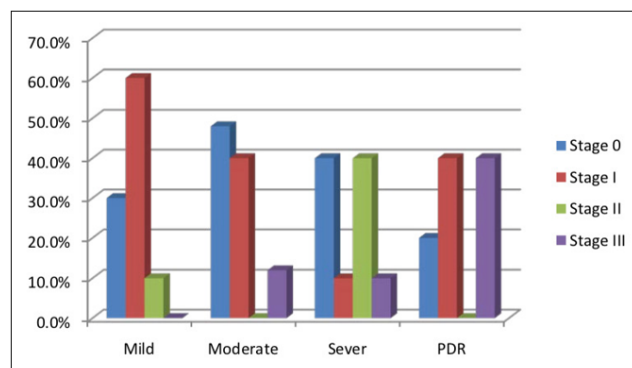


Fig. 5:

4. Discussion

Diabetes is a major cause of morbidity and mortality worldwide. The increase in the prevalence of diabetes mellitus inevitably leads to an increase in microvascular and macrovascular complications. These complications lead to serious health problems like neuropathy, renal failure, and blindness and are a major threat to the nation's public health care system.

This study aims to find out the relationship between diabetic nephropathy, diabetic neuropathy, and the severity of diabetic retinopathy in type II diabetic patients and also its relation with HbA1c. As retinal vasculature can be assessed and seen clinically, the severity of retinopathy will help in understanding the severity of diabetic nephropathy and diabetic neuropathy. Thus, it will help us take timely action to prevent or reduce the severity of life-threatening complications.

Diabetic retinopathy and diabetic nephropathy are more likely to develop in patients with poor glycemic control. Previous studies have shown that patients with HbA1C >8% are at higher risk for renal diseases. In the present study we have found that 40.33% of patients with blood urea >40 and 28.57% of patients with serum Creatinine > 1 had poor control of HbA1C. The same results have been found in Nivedita et al study and in their study they have found that 73.6% of patients with blood urea >40 and 83.3% of patients with serum creatinine > 1 had poor control of HbA1C. This shows that uncontrolled HbA1C has a relation with diabetic nephropathy.

In the present study out of total population 2/3rd were male patients and 1/3rd were female patients. Though the male population was higher in our study we did not find any significant prevalence deference between both the genders.

These results were consistent with the results published in various studies. In a study conducted by Henriesson Mother, they found an equal prevalence of microvascular changes in males and females

Poor glycemic control compared with good control helps in determining the risk of nephropathy and retinopathy

according to various clinical trials. DCCT showed a 76% reduction in the rate of development of any retinopathy and an 80% reduction in the progression of established retinopathy in patients with strict control of diabetes.⁵ However, the limitation of our study was that there was no follow up of the patient. So long term effects of glycemic control could not be assessed and hence progression of retinopathy, nephropathy, and neuropathy could not be found. The Wisconsin epidemiological study of diabetic retinopathy showed a positive correlation between the severity of retinopathy and the high level of HbA1C after 10 years of diabetes mellitus.

In the UKPDS, the risk reduction in diabetic retinopathy for every 1% decrease in HbA1C was 19%.¹ In our study (10.00%) with severe Nonproliferative diabetic retinopathy and (60.00%) patients with Proliferative diabetic retinopathy had HbA1C under poor control. Study shows that the value of HbA1C shows an increasing trend as the severity of diabetic retinopathy increases. Also patients with CSME had uncontrolled HbA1C.

A link between renal and retinal angiopathy in diabetes has been long recognized, an effect that may be mediated through an increase in blood pressure, fibrinogen levels, and lipoproteins. However, male sex has been associated with an increased risk of diabetic nephropathy in both type 1 and type 2 diabetic patients.

In the present study we have found that a total of 40.00% of the patients had Vitamin B12 deficiency. We have found that in severe nonproliferative diabetic retinopathy 80.00% and 60.00% of proliferative diabetic patients had Vitamin B12 deficiency and these results were found significant as compared to mild and moderate NPDR.

In our study we have found that the prevalence of neuropathy was higher in severe NPDR and PDR as compared to mild and moderate NPDR. In mild and moderate NPDR patients 70.00% and 76.00% of patients had vitamin B12 level of more than 200 pg/mL.

We also have found a positive significant connection between the severity of diabetic retinopathy and the incidence of diabetic nephropathy. We have found that the stage of diabetic nephropathy was increasing with the severity of diabetic retinopathy. In mild and moderate NPDR incidence of diabetic nephropathy stage 0 and 1 were higher. Whereas in severe NPDR incidence of Stage 2 was found higher. In our study among patients with severe NPDR, 40% had blood urea >40 whereas, in patients with mild NPDR and moderate NPDR, this percentage is 30.00% and 48.00% respectively. 80.00% of patients with severe NPDR had serum creatinine >1.5 and 100% of patients with PDR had serum creatinine >1.5 which shows that there is a correlation between the severity of diabetic retinopathy and diabetic nephropathy. The same results have been found in Nivedita et al study and in their study they found that patients with severe NPDR, 50% had blood urea >40.

Patients with mild NPDR and moderate NPDR it was 14.3% and 47.8 respectively. 50% of patients with severe NPDR had serum creatinine >1 and 60% of patients with PDR had serum creatinine >1.

stage III was found higher in PDR. These results found a statistically significant with a p-value of 0.013.

In the present study we have seen that there was also a positive correlation between diabetic neuropathy and diabetic retinopathy. As a similar result as with diabetic nephropathy, as the severity of diabetic retinopathy increases the incidence of diabetic neuropathy was also high... Incidence of Stage 0 and Stage 1 (A & B) of diabetic neuropathy was higher in mild and moderate NPDR whereas stage 2 of diabetic neuropathy was found higher in severe NPDR and PDR. These results found statistically significant with the p-value of 0.001. They concluded that diabetic retinopathy is one of the most important risk factors for diabetic peripheral neuropathy. Kinyoun JL et al.⁶ concluded that retinopathy to be an independent risk factor for diabetic neuropathy. He also found out that the severity of DR has a direct correlation with the presence of neuropathy in diabetic patients.

Apart from this result we also found that mean total cholesterol and VLDL were also significantly higher in severe Nonproliferative diabetic retinopathy and Proliferative diabetic retinopathy as compared to mild and moderate NPDR with a p-value of 0.001 for each respectively.

Our study suggested that early diagnosis of diabetic retinopathy can lead to preventing multi-organ damage.

5. Conclusion

In this study we concluded that patients with poor glycemic control have high chances to develop diabetic retinopathy, diabetic nephropathy, and diabetic neuropathy. Patients with HbA1c levels higher than 8, had evidence of retinopathy, nephropathy, and/or neuropathy. While uncontrolled levels showed evidence of all three microvascular changes. Patients with severe Nonproliferative diabetic retinopathy had a higher level of s. urea and s. creatinine as compared to patients with mild to moderate NPDR. Almost all patients of PDR had higher levels of s. Creatinine and s. urea. This study clearly shows that the prevalence of diabetic nephropathy in diabetic patients was more commonly present in severe NPDR and PDR.

Patients having mild to moderate NPDR had a higher incidence of stage 0 and stage 1 (A & B) of diabetic

neuropathy whereas stage 2 of diabetic neuropathy was found higher in severe NPDR and PDR. This study shows a significant connection between diabetic retinopathy and diabetic neuropathy.

Detection of diabetic retinopathy can be done on a simple clinical examination without the need for various investigations. Our study helps us in deriving the conclusion that microvascular changes involving retina co-relates with similar changes in kidney and CNS. Thus, early detection of DR changes can help us in minimizing changes in multi-organ damage.

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