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A STUDY ON NEPHROPATHY AND CONCURRENT RETINOPATHY AMONG TYPE-2 DIABETIC PATIENTS

Medicine

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ABSTRACT

Introduction: Diabetes Mellitus refers to a group of common metabolic disorders that share the phenotype of high blood sugar. Diabetes related complications affect almost every organ system and are responsible for the high morbidity and mortality associated with the disease. It can be greatly reduced by early and consistent surveillance procedures as part of comprehensive diabetes care.

Aim and Objective: To detect the presence of diabetic nephropathy and detection of retinopathy in the study population to see the concurrence rate so as to evaluate the presence of nephropathy with or without retinopathy.

Material and methods: An observational study was conducted on consecutive 200 patients with type 2 Diabetes Mellitus patients attending OPD as well as inpatients in CSTM at the School of Tropical Medicine, Kolkata from April 2015 to March 2016.

Results: Prevalence of diabetic nephropathy was 38% and that of retinopathy was 88%. Retinopathy had a very significant statistical correlation to nephropathy. Estimated GFR below 60 ml/min/1.73m2 has a strong correlation to nephropathy. Age more than 50 years and duration of disease more than 15 years was found to be statistically significant with nephropathy. Retinopathy had a strong correlation to microalbuminuria, serum creatinine, BMI more than 25, eGFR less than 60 ml/min/1.73m2 and nephropathy. Concurrent retinopathy and nephropathy were found in 37.5% and concurrent retinopathy and neuropathy increases the predictive value of nephropathy.

Conclusion: This study showed that early and consistent surveillance for organ involvement needed for patients with type 2 Diabetes Mellitus as part of comprehensive diabetes care, so that we can prevent them early.

KEYWORDS

Type 2 Diabetes Mellitus, retinopathy, nephropathy.

INTRODUCTION

Diabetes Mellitus refers to a group of common metabolic disorders whose criteria for diagnosis according to ADA guidelines, 2014 is as follows:

- Symptoms of diabetes plus random blood glucose ≥ 200mg % OR
- Fasting plasma glucose ≥ 126 mg% (No calorie intake for at least 8 hr) OR
- Hemoglobin A 1C ≥ 6.5 % OR
- 2-h plasma glucose ≥ 200mg% (after oral administration of 75g anhydrous glucose dissolved with water)

It mainly affects the vascular system in the form of microangiopathy and macroangiopathy. Diabetes related complications affect almost every organ system and are responsible for the high morbidity and mortality and that impose a high disease burden on the health care system. It can be greatly reduced by early and consistent surveillance procedures as part of comprehensive diabetes care. Diabetic nephropathy occurs in about one third patients with type II Diabetes Mellitus and is the commonest cause of chronic kidney disease and ESRD requiring renal replacement therapy. Another important micro vascular complication of type 2 Diabetes is retinopathy. Diabetic retinopathy is a highly specific vascular complication of diabetes with prevalence strongly related to the duration of diabetes. As evident from previous studies and publications worldwide, there is a significant association between nephropathy and retinopathy. It is said that in a diabetic patient with nephropathy if retinopathy is absent, diabetes being the cause of nephropathy becomes unlikely.

Our study focuses on prevalence of diabetic nephropathy and concurrent retinopathy in newly diagnosed type 2 Diabetic individuals.

MATERIALS AND METHODS

This is an observational study was conducted on consecutive 200 patients with type 2 Diabetes Mellitus patients attending OPD as well as inpatients in CSTM at the School of Tropical Medicine, Kolkata from April 2015 to March 2016. Diabetes was diagnosed according to ADA criteria. Exclusion criteria for the study were critically ill subjects, infection, ketonuria, pregnancy and lactating mother, HIV reactive, connective tissue disease, history of nephrotoxic drug intake, prior history of kidney insult and chronic kidney disease and ESRD patients on hemodialysis. A pre-designed proforma was used to collect data by proper history taking, clinical examination and investigations of total 200 patients with type 2 Diabetes Mellitus patients. Apart from routine investigations dilated retinal examination, digital fluorescence angiography of retina, optical coherence tomography and perimetry were done to detect retinopathy and urine microscopy, spot urinary albumin creatinine ratio (ACR) were done to detect nephropathy. Estimated Glomerular filtration rate (eGFR) calculation using Modified Diet in Renal Disease (MDRD) equation. Standard statistical method was used for data analysis.

RESULTS

In the present study total 200 consecutive type 2 diabetes patients were studied. Half of them (100) were from OPD and half (100) from IPD. Mean age of the population was 53.545 ± 10.5 years and mean duration of diabetes was 9.69±6.16 years. There was a female preponderance

with 59% of the population being female. Majority of the population (155/200, 77.5%) belonged to lower socio-economic status.

Figure 1: Pie chart showing gender distribution

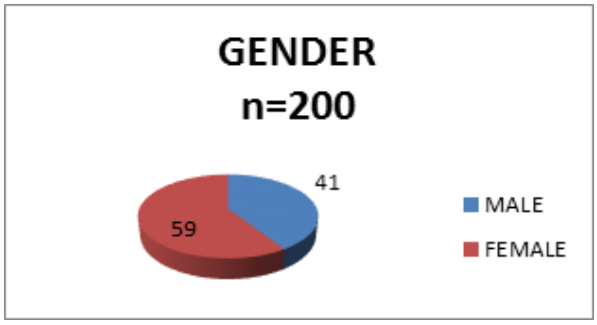
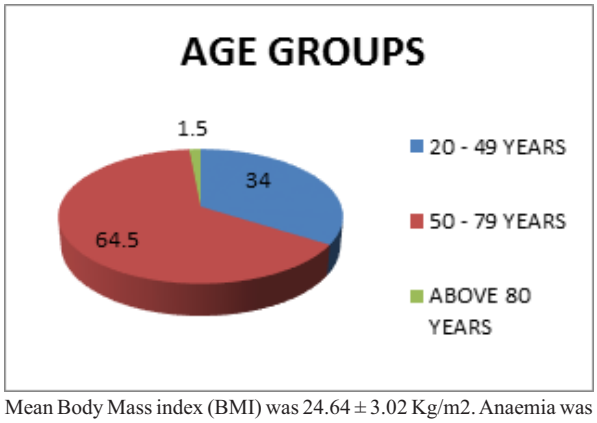
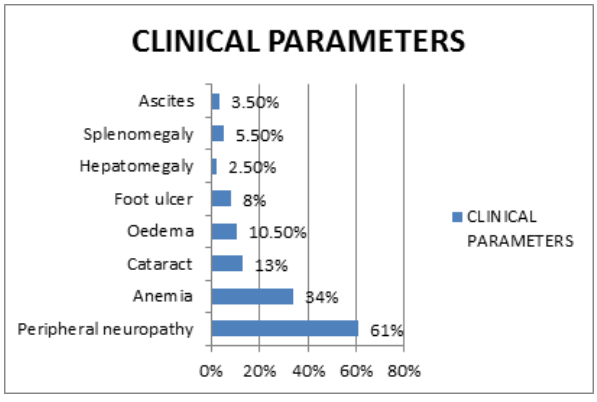


Figure 2: Pie chart showing distribution of patients according to age groups.



Mean Body Mass index (BMI) was 24.64 ± 3.02 Kg/m2. Anaemia was present in 34% of the patients. Approximately 10.5% of the patients presented with oedema of bilateral lower limbs. Foot ulcer of some duration as presenting complaint was present in 8% of the study population. History of cataract, either present or operated was found in 13% of the total population. Peripheral neuropathy was seen in 61% of the study population.

Figure 7: Bar diagram showing different clinical parameter according to frequency.



Retinopathy was observed among 176 patients accounting for 88% of the total population. Out of them, 59.09% were females and 40.90% were males. Mild Non Proliferative Diabetic Retinopathy (NPDR) was the commonest type among both males and females (F-51.4%,M-61.11%). Glycated haemoglobin percentage above 10, status of treatment, duration of diabetes and age more than 50 years did not have a significant correlation to retinopathy in this study. BMI less than 25 (p=0.0001), eGFR (measured by MDRD equation) less than 60ml/minute/1.73m2 (p=0.0141) and microalbuminuria (30-300 mg/day) (p= 0.0001) were strongly associated with retinopathy.

Figure 11: Bar diagram showing gender wise prevalence of retinopathy.

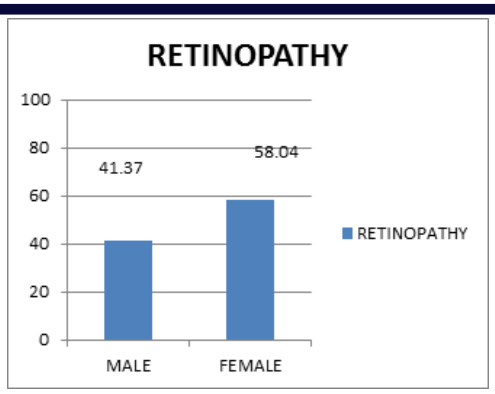


Figure 13: Bar diagram showing relationship between DR and BMI

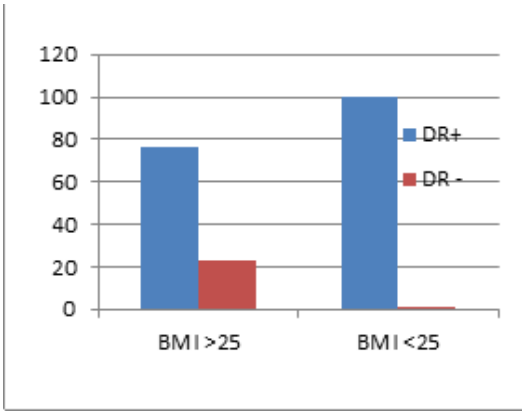


Figure 14: Bar diagram showing relationship between DR and low GFR

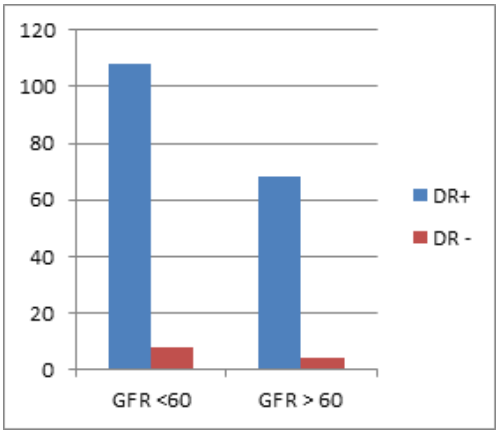
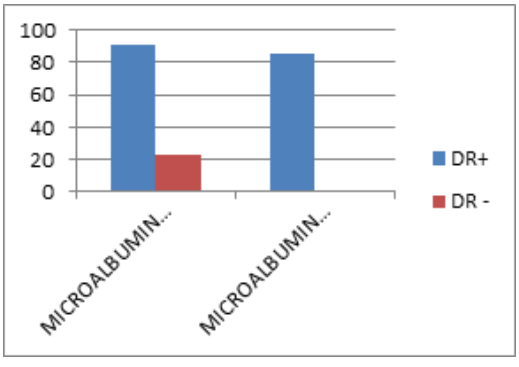


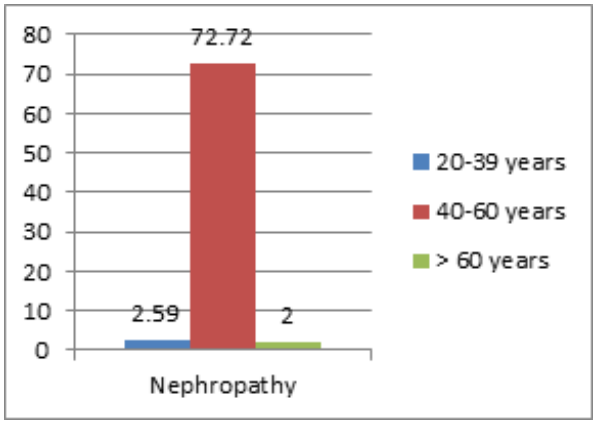
Figure 15: Bar diagram showing relationship between DR and microalbuminuria.



Kidney function decline in terms of low glomerular filtration rate (GFR) below 60 ml/minute was found in 58% of the population. Males constituted 36.84% of the total nephropathy cases while 63.15% were

females. The prevalence of nephropathy was observed highest in the age group of 40-60 years followed by patients aged more than 60 years and below 40 years in decreasing order of frequency. Mean BMI of the patients with nephropathy was 25.185± 3.515 Kg/m^2 which was higher compared to the mean BMI of 24.64± 3.02 of the population. Patients with nephropathy had a longer duration of disease and higher HBA1C compared to the study population.

Figure 16: Bar diagram showing prevalence of nephropathy according to age group.

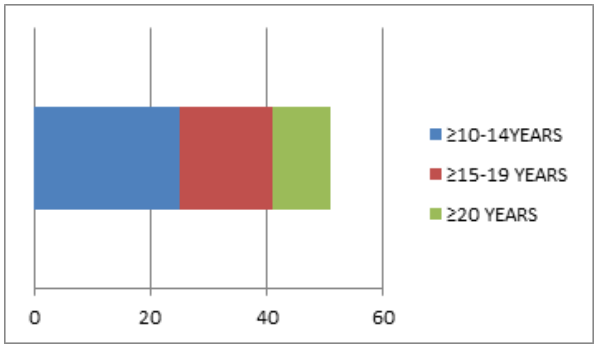


Females had higher chances of developing nephropathy compared to males. High BMI had a significant correlation to development of nephropathy. Duration of disease more than 15 years was significantly associated with occurrence of nephropathy (p=0.0140). Age more than 50 years was very significantly associated with nephropathy (p=0.0033). Dyslipidemia was present in 50% of cases of nephropathy but no statistical significance was observed as regards to occurrence of nephropathy with dyslipidemia.

Poor glycemic control in terms of glycated haemoglobin percentage more than 10 were not significantly associated with nephropathy. But the mean glycated haemoglobin level was higher in those with nephropathy. Majority (63.63%) of those who had HBA1C above 11% had nephropathy.

Serum creatinine levels above 1.5mg/dL were significantly associated with albuminuria > 500 mg/day (p= 0.0004). Macroalbuminuria also had a positive correlation to reduced glomerular filtration rate less than 60ml/minute as measured both by Cockcroft Gault equation (p= 0.0001) as well as MDRD (p= 0.0001). There was a strong correlation between microalbuminuria and creatinine >1.5 (p=0.0001). There was also a very strong correlation between microalbuminuria and eGFR below 60 ml/min/1.73m^2.

Figure 18: Prevalence of nephropathy according to duration of diabetes.



DISCUSSION

The worldwide prevalence of diabetes has risen dramatically over the past two decades. Based on current trends The International Diabetes Federation projects that 592 million individuals will have diabetes by the year 2035 [1]. An estimated 96 million people have diabetes in the region, 90% of whome have type 2, which is preventable [1]. The commonest and earliest microvascular complication of type 2 diabetes mellitus is neuropathy followed by retinopathy and nephropathy respectively. Diabetic kidney disease typically develops after a diabetes duration of 10 years, or at least 5 years in type 1 diabetes, but may be present at diagnosis of type 2 diabetes. The typical presentation of diabetic kidney disease is considered to include a long-standing duration of diabetes, retinopathy, albuminuria without hematuria, and gradually progressive kidney disease.

In this study we found that retinopathy was present in 88% of the total population, neuropathy in 61% and nephropathy was present in 38% of the population. The prevalence of nephropathy is comparable to WHO report 2016 [2]. These prevalence is quite higher than other indian studies like in North West India (Bikaner) on the prevalence of various microvascular complications in type 2 diabetes showed that retinopathy was the most common (32.5%) followed by nephropathy (30.2%) and neuropathy (26.8%) [3]; a study done on prevalence of retinopathy at a diabetes centre in South India showed the prevalence to be 34.1%. [4]; a study done on prevalence of vascular complications and their risk factors in type 2 diabetes published in JAPI showed that retinopathy(23.7%) and Neuropathy(27.5%) were commonest with nephropathy being 19.7% [5] , though all the studies showed commonest complications were retinopathy, neuropathy and nephropathy. A retrospective observational study showed that Diabetic Nephropathy (DN) patients without DR may have less serious renal damage and less diabetic complication than those with DR. In the absence of DR, there is still a lack of effective indicators suggesting diabetic nephropathy or nondiabetic glomerulopathy, and renal biopsy is needed for diagnosis in such circumstances [6]. Only one patient in our study had similar finding of progressive nephropathy without concurrent retinopathy. We planned her for a kidney biopsy but as she did not give consent for an invasive procedure, we were not able to look into the cause of progressive nephropathy.

Higher BMI was also observed in the female subjects with nephropathy compared to those females with no nephropathy. This finding is consistent with The Japan Diabetes Complications study done on type 2 diabetes mellitus patients which concluded that both past and present obesity has an increased risk of developing microvascular complications, particularly diabetic nephropathy and retinopathy.

Level of glycemic control, presence of comorbidities like dyslipidemia and hypertension , present status of treatment and duration of disease has long been known to influence the development of nephropathy and retinopathy. The United Kingdom Prospective Diabetes Study Trial (UKPDS) concluded that good glycemic control in the initial years of disease has an effect on prevention of microvascular complications later in the disease process, the so called legacy effect or metabolic memory. In this study it was seen that recent glycemic status did not have a significant correlation to nephropathy. This may be because of the fact that the HBA1C levels were checked only once and long term control was not taken into account. Also the mean age of the population was higher significantly contributing to increased prevalence of nephropathy. Hypertensives were excluded from the study and so its effect could not be evaluated. Dyslipidemia also did not have much effect on the development of nephropathy. Recent treatment status did not seem to have a significant correlation to nephropathy. This can be explained by the fact that number of patients who were treatment naive were very few (5.5%), all of whom were newly diagnosed and of relatively younger age. Age more than 50 years was significantly associated with nephropathy in this study population. This is consistent with all other existing studies. Duration of diabetes more than 15 years was also found to be very significantly associated with nephropathy which supports all other landmark trials on type 2 diabetes mellitus. Estimated GFR less than 60 ml/min/1.73 m^2 measured by MDRD equation was statistically very significant in predicting nephropathy.

Retinopathy was a very strong predictor of nephropathy particularly in those with disease duration more than 15 years and those with concurrent peripheral neuropathy and high BMI in our study. But a study done in Banaras Hindu University in the year 2007, came up with some contradictory results stating that DR was a poor predictor of type of nephropathy in proteinuric type 2 DM patients [7].

Limitations of our study were 24 hour urinary albumin detection has a wide range of variability depending on various factors like fever, exercise, infection. Absolute standardization of the test by elimination of these factors giving false positive raised urinary protein was not possible. Retinopathy cases were diagnosed by direct ophthalmoscopy

all of which could not be confirmed by optical coherence tomography. So some cases may have been missed.

CONCLUSION

Prevalence of diabetic nephropathy was 38% and that of retinopathy was 88%. Retinopathy had a very significant statistical correlation to nephropathy. Estimated GFR below 60 ml/min/1.73m^2 has a strong correlation to nephropathy. Age more than 50 years and duration of disease more than 15 years was found to be statistically significant with nephropathy. Retinopathy had a strong correlation to microalbuminuria, serum creatinine, BMI more than 25, eGFR less than 60 ml/min/1.73m^2 and nephropathy. Concurrent retinopathy and nephropathy were found in 37.5% and concurrent retinopathy and neuropathy increases the predictive value of nephropathy. So early and consistent surveillance for organ involvement needed for patients with type 2 Diabetes Mellitus as part of comprehensive diabetes care, so that we can prevent them early.

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