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MICROVASCULAR AND MACROVASCULAR COMPLICATIONS IN DIABETIC NEPHROPATHY CASES IN LOKMANYA GROUP OF HOSPITALS

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Conflicts of Interest: Nil

Abstract:

INTRODUCTION: Diabetes is a global health problem which affects all age group including children, adolescents, and adults. According to the World Health Organization (WHO), worldwide approximately 180 million people currently have type 2 DM (T2DM) and more than 95% of people with diabetes have this form. Also the number of people with type 2 DM is estimated to double by 20. According to the first WHO Global report on diabetes shown that the number of adults living with diabetes has quadrupled since 1980 to 422 million adults. This dramatic rise is largely due to the rise in type 2 diabetes and major factors driving it include overweight and obesity. In 2012 diabetes caused 1.5 million deaths and its complications can lead to heart attack, stroke, blindness, kidney failure and lower limb amputation[i]. In India, there are about 69.2 million people living with diabetes and are expected to cross 123.5 million by 2040. Intensive glycemic control lowers the incidence and progression of microvascular complications, the morbidity associated with these complications is still increasing. Diabetic microvascular which involves small vessels, such as capillaries and macrovascular complications involving large vessels, such as arteries and veins have similar etiologic characteristics. Chronic hyperglycemia plays a major role in the initiation of diabetic vascular complications through metabolic and structural derangements. Diabetic nephropathy (DN) is a progressive complication of both type1 DM and type2 DM. The first manifestation of DN is microalbuminuria, which progresses to overt albuminuria.

RESULTS: Mean age of the patients with DN was 62.54 ± 12.47. Male were 36 (72%) and female were 14 (28%) included in the study. The mean duration of nephropathy was 7.2 ± 2.9 years. Family history of DN was shown in 5 (10%). In DN Complications retinopathy was seen in 22 (44%), Stroke in 4 (8%), coronary artery disease in 29(58%), angina in (26 (52%), hypertension in 44 (88%), diabetic foot in 3 (6%) end stage renal disease in13 (26%) and death in 3 (6%) during study period. The mean proteinuria in our DN patients (gm/24 hrs) was 2.01 ± 1.99 gm/L at baseline. Protein excretion < 0.5 was found in 16 (32%) patients, mean HbA1C was 9.2 ± 1.8 % (Range 5.4-15.9) at base line and 8.93 ± 2.08 % (6.5-12.5) at the last visit.

CONCLUSION: Frequent screenings in addition to tight glycaemic, lipid, and blood pressure control may be helpful. In our study are at a higher risk of having retinopathy, CAD, angina, hypertension was observed. These complications should be studied further in future. Continuous monitoring of Blood pressure, BMI, Hypertension, HbA1C should be screened on regular basis to prevent.

KEYWORDS: Dm, DN, Glycemic, CAD, BP, BMI and HbA1C

Introduction

Diabetes mellitus (DM) has been described as a metabolic disorder which is characterized by hyperglycemia developing as a consequence of defects in insulin secretion, insulin action, or both. Type 2 diabetes encompasses individuals who have insulin resistance (IR) and usually relative or in rare cases absolute insulin deficiency[ii].DM is a global health problem which

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affects all age group including children, adolescents, and adults. According to the World Health Organization (WHO), worldwide approximately 180 million people currently have type 2 DM (T2DM) and more than 95% of people with diabetes have this form. Also the number of people with type 2 DM is estimated to double by 2030[iii].According to the first WHO Global report on diabetes shown that the number of adults living with diabetes has quadrupled since 1980 to 422 million adults. This dramatic rise is largely due to the rise in type 2 diabetes and major factors driving it include overweight and obesity.

In 2012 diabetes caused 1.5 million deaths and its complications can lead to heart attack, stroke, blindness, kidney failure and lower limb amputation[iv].In India, there are about 69.2 million people living with diabetes and are expected to cross 123.5 million by 2040 .Also, worldwide about 193 million diabetics remain undiagnosed predisposing them to the development of several long-term complications of untreated chronic hyperglycemia[v]. Intensive glycemic control lowers the incidence and progression of microvascular complications, the morbidity associated with these complications is still increasing[vi]. Diabetes is strongly associated with microvascular and macrovascular complications, which includes retinopathy, nephropathy, and microvascular neuropathy and ischemic heart disease, peripheral vascular disease, and macrovascular cerebrovascular disease which results in organ and tissue damage in approximately one third to one half of people with diabetes[vii].

Diabetic microvascular which involves small vessels, such as capillaries and macrovascular complications involving large vessels, such as arteries and veins have similar etiologic characteristics. Chronic hyperglycemia plays a major role in the initiation of diabetic vascular complications through metabolic and structural derangements, which includes the production of advanced glycation end products (AGE), abnormal activation of signalling cascades such as protein kinase C, elevated production of reactive oxygen species like ROS, oxygen-containing molecules that can interact with other biomolecules and result in damage, and abnormal stimulation of hemodynamic regulation systems (such as the renin-angiotensin system [RAS])[viii].

Diabetic nephropathy (DN) is a progressive complication of both type1 DM and type2 DM. The first manifestation of DN is microalbuminuria, which progresses to overt albuminuria (ie, increased albumin levels in the urine, indicating more severe renal dysfunction) and eventually leading to renal failure[ix]. Around one fourth of people with type 2 diabetes have microalbuminuria or a more advanced stage of DN that worsens at a rate of 2% to 3% per year[x]. Characteristic features of DN include thickening of glomerular basement membranes and glomerular hyper filtration, which leads to masengial extracellular matrix expansion and further increases in urinary albumin excretion[xi] and ultimately progressing to glomerular and tubular sclerosis and renal failure[xii].

MATERIAL AND METHODS

Present study is a cross sectional, retrospective study on patients of Lokmanya Group of Hospitals Chinchwad Nigadi Pune, a tertiary hospital in Pune. This study was carried out from March 2017 to Feb 2018. Patients screened were clinically diagnosed DN patients according to World Health Organization (WHO) criteria[xiii]. There were 50 diabetic nephropathy patients included in the study. Demographic characteristics and patients' height and weight were recorded, and body mass index (BMI) was calculated in metrics units. Blood investigations like blood glucose, HbA1C, cholesterol, Triglycerides (TG), serum creatinine, creatinine clearance, and24-hour urinary protein were investigated for each patient. Glomerular filtration rate (GFR) was calculated by using Kockroft and Gualt equation. Rate of change of GFR was calculated. Renal function was considered to be stable in patients if yearly change of GFR was 1-2.5 ml, and it was con-sidered deteriorated if yearly decrease of GFR

was > 2.5 ml. While renal function was considered improved; if yearly change of GFR was < 1 ml. Duration of follow-up, age at onset of diabetes, duration of complications, time for doubling of serum creatinine, and ESRD were recorded. Time course of all the above parameters were followed up carefully. Statistical analysis was done by using SPSS for Windows statistical package.. P value of < 0.05 was considered statistically significant. All data was entered in Excel datasheet.

OBSERVATIONS AND RESULTS

Mean age of the patients with DN was 62.54 ± 12.47. Male were 36 (72%) and female were 14 (28%) included in the study. The mean duration of nephropathy was 7.2 ± 2.9 years. Family history of DN was shown in 5 (10%)

Table 1: Characteristics of the patients at first visit

Characteristics	N=50
Mean Age	62.54 ± 12.47
Male	36 (72%)
Female	14 (28%)
Duration of nephropathy was	7.2 ± 2.9 yrs
Family history of DN	5 (10%)

Table 2: Body mass index (BMI) of the patients at first visit

BMI (kg/m^2)	N (%)
Normal (18.5-25)	5 (10%)
overweight (BMI 25.1-30)	41 (82%)
Obese (BMI 30.1-40)	6(12%)
underweight	1 (2%)

At the initial visit, BMI normal was seen in 5 (10%) patients, 41 (82%) patients were overweight, 6(12%) patients were obese, and 1 (2%) patients were underweight.

Table 3: Diabetic complications

Complications	N=50	Percentage
Retinopathy	22	44%
Stroke	4	8%
Coronary artery disease	29	58%
Angina	26	52%
Hypertension	44	88%
Diabetic foot	3	6%
End stage renal disease Blindness	13	26%
Death	3	6%

In DN Complications retinopathy was seen in 22 (44%), Stroke in 4 (8%), coronary artery disease in 29(58%), angina in (26 (52%), hypertension in 44 (88%), diabetic foot in 3 (6%) end stage renal disease in13 (26%) and death in 3 (6%) during study period.

The mean time to onset of diabetic complications from the diagnosis of diabetes in present study was 10.4 ± 3.6 years for coronary artery disease, 16.4 ± 5.9 years, for retinopathy, 10.6 ± 5.4 years for neuropathy, and 5.1 ± 3.2 years for diabetic foot. End stage renal disease was observed in patients those who were diagnosed >20 years.

25 (50%) patients had serum creatinine < 110 µmol/L, 15 (30%) between 110-140 µmol/L, 4 (8%) between 141-165 µmol/L, and 6 (12%) > 220 µmol/L. At the last visit 18 (36% of patients had their serum creatinine > 220 µmol/L.

The mean proteinuria in our DN patients (gm/24 hrs) was 2.01 ± 1.99 gm/L at baseline. Protein excretion < 0.5 was found in 16 (32%) patients, mean HbA1C was 9.2 ± 1.8 % (Range 5.4-15.9) at base line and 8.93 ± 2.08 % (6.512.5) at the last visit.

The mean cholesterol was 5.29 ± 1.3 mmol/L (range 2.1-11.6 mmol/L) at baseline versus 4.28 ± 1.0 mmol/L (1.8-9.6) at the last visit. Hypercholesteremia was seen in 42 (84%) patients at base line. At the initial visit, there were 26 (52%) patients who had cholesterol < 5.2 mmol/L; At the last visit, 21 (42%) patients had serum cholesterol < 5.2mmol/L.

DISCUSSION AND CONCLUSION

Several landmark studies like United Kingdom Prospective Diabetes Study (UKPDS) have demonstrated that strict glycemic control limit the microvascular disease while attempts to improve macrovascular outcomes through glucose-lowering interventions still remain shrouded with controversy. A relative risk (RR) reduction in myocardial infarction (MI) (P = 0.052) has been observed in the 10 years of post trial follow-up of UKPDS[xiv]. The risk of cardiovascular mortality, nonfatal MI and stroke

was reduced with pioglitazone in the Prospective Pioglitazone Clinical Trial in Macrovascular Events as compared to placebo group[xv].

In recent years, more attention has been given on the management of macrovascular complications such as stroke and acute coronary syndromes. It is well-recognized that vascular complications in a given tissue are often accompanied by evidence of pathology in other vascular regions. A linear relationship between microvascular complications and duration of disease was established by the authors where they documented the presence of microvasculopathy across different age groups in their study in 25–40% of diabetic patients aged >25 years with more than 5 years duration of diabetes[xvi]. In our study stroke was observed in 4 (8%) and coronary artery disease was seen in 29(58%) and angina in 26 (52%) patients. Matheus and Gomes described the case report of type 1 DM (T1DM) patient with early and aggressive coronary artery disease (CAD) without evidence of nephropathy, or classical risk factors for CAD. Patients with DM and associated microvascular complications appear particularly at higher risk of accelerated atherosclerosis which ultimately converts in cerebrovascular and cardiovascular events and premature death[xvii].

Diabetic retinopathy was seen in 2 (44%) and complete loss of vision was found in 3 (1.6%) patients. Prevalence of retinopathy among Saudi patients with diabetes was reported previously as 31%. In ou study hypertension was seen in 44 (88%) of the cases which was quite high. In a study by D Hirata et al[xviii] prevalence of hypertension was 62.6% which was less as compared to our study[xix].

Susceptibility for diabetic complications varies from one ethnic to another, and also from one individual to another[xx],[xxi].

According to Gross JL et al.[xxii]Proteinuria is seen in 15–40% of patients with type 1 diabetes while it ranges from 5 to 20% in patients with T2DM. The prevalence of diabetic nephropathy was higher in African Americans, Asians, and Native Americans[21]. In India, CURES 45 reported a prevalence of 2.2% for overt diabetic nephropathy and 26.9% for microalbuminuria[xxiii]. It has been seen that dyslipidemia with increased low-density lipoprotein (LDL) cholesterol and triglycerides is independently associated with diabetic kidney disease[xxiv]. In our study the mean cholesterol was 5.29 ± 1.3 mmol/L (range 2.1-11.6 mmol/L) at baseline versus 4.28 ± 1.0 mmol/L (1.8-9.6) at the last visit. Hyper-cholesteremia was seen in 42 (84%) patients at base line. At the initial visit, there were 26 (52%) patients who had cholesterol < 5.2 mmol/L; At the last visit, 21 (42%) patients had serum cholesterol < 5.2mmol/L.

End stage renal disease was seen in 13(26%) cases, Mitka M[xxv] reported 27.8% in his study in USA.

There is sharp increase in the cases of diabetes in India. Age, male gender, duration of diabetes, baseline HbA1C, systolic blood pressure, and renal function are risk factors for diabetic complications and nephropathy. Frequent screenings in addition to tight glycaemic, lipid, and blood pressure control may be helpful. In our study are at a higher risk of having retinopathy, CAD, angina, hypertension, which should be studied further in future. Continuous monitoring of Blood pressure, BMI, Hypertension, HbA1C should be screened on regular basis to prevent these complications.

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