

TO STUDY THE ASSOCIATION BETWEEN DIFFERENT TYPES OF MICROVASCULAR COMPLICATIONS WITH EACH OTHER AND DYSLIPIDEMIA IN NEWLY DIAGNOSED TYPE 2 DIABETES MELLITUS

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Abstract

Background: Diabetes is one of the commonest chronic non communicable disease affecting the society at large both in developing and developed countries. Present study aimed to study the association between different types of microvascular complications with each other and dyslipidemia in newly diagnosed type 2 diabetes mellitus.

Subjects and Methods: In this study, 100 newly diagnosed cases of type 2 diabetes mellitus patients were evaluated. A cross section of both male and female diabetes patients diagnosed within the last 3 months (new onset) was taken into study. A detailed history, clinical examination and relevant investigations were performed. Collected data were analysed by using appropriate software.

Results: In our study 60% were male and 40% were female. Majority of cases were in the age group of 46-55 years, followed by in age group 56-65 years. Association was found between Dyslipidemia and nephropathy and also between retinopathy and nephropathy.

Conclusion: Endeavour should be made to control hyperglycemia and dyslipidemia tightly by appropriate therapeutic measures so that the occurrence and worsening of complications could be mitigated.

Aims and Objectives

To study the association between different types of microvascular complications with each others and dyslipidemia in newly diagnosed type 2 diabetes mellitus.

Diabetes mellitus (D.M.) refers to a group of common metabolic disorders that share the phenotype of hyperglycemia¹. It results from a defect in insulin secretion and/or insulin action, which results in hyperglycaemia with disturbances of carbohydrate, fat and protein metabolism².

Diabetes is one of the commonest chronic non communicable disease affecting the society at large both in developing and developed countries. It is generally classified as type 1, type 2 or other specific types³.

Type 1 diabetes is generally considered a T cell mediated autoimmune disease involving destruction of the insulin secreting β cells in the pancreas, resulting in absolute insulin deficiency, whereas type 2 diabetes is characterised by resistance to the action of insulin and an inability to produce sufficient insulin to overcome this 'insulin resistance'⁴.

Globally, all types of diabetes are on the increase, type 2 diabetes in particular⁵. While diabetes has been known for many centuries, the prevalence has reached epidemic level proportion only recently⁶. The rise of prevalence has been

more alarming in developing countries than in developed countries. There has also been a trend towards a shift in the mean age of onset of type 2 diabetes to a much younger age⁷.

As per the 9th edition of International Diabetes Federation Atlas,2019,. The global diabetes prevalence is estimated to be 9.3% (463 million people), rising to 10.2% (578 million) by 2030 and 10.9% (700 million) by 2045... The major proportion of this increase will occur in developing countries of the world like India⁸. One in two (50.1%) people living with diabetes do not know that they have diabetes.

India leads the world with largest number of diabetic subjects earning the dubious distinction of being termed the "Diabetes Capital of the World".

Type 2 diabetes is accompanied by a high prevalence of associated disorders like the various components of the metabolic syndrome like hypertension, dyslipidemia and obesity; micro vascular complications like retinopathy (Rt), nephropathy (Np), neuropathy (Nu) and macro vascular complications like coronary artery disease, peripheral vascular disease and cerebrovascular disease resulting in significantly high morbidity and mortality^[9-14]. The chronic complications of diabetes mellitus translate into a significant economic burden on individuals and community at large¹⁴.

Due to its asymptomatic course, type 2 diabetes evades diagnosis for many years. Harris et al.¹⁵ estimated a gap of 9 to 12 years between the onset of type 2 diabetes and its clinical diagnosis. Long standing diabetes mellitus is associated with an increased prevalence of microvascular and macrovascular complications. The first indication of the presence of type 2 diabetes mellitus may actually be detected at the time of diagnosis of a diabetic complication.

Materials and Methods

In this study, 100 newly diagnosed cases of type 2 diabetes mellitus patients were evaluated. A cross section of both male and female diabetes patients diagnosed within the last 3 months (new onset) attending the general medicine indoor and outpatient department and other clinical departments of katihar medical college, katihar was taken into study.

A detailed history, clinical examination and relevant investigations were performed.

History

Age, sex and duration of diabetes were recorded. Family history of diabetes and personal medical history was enquired. History of symptoms suggestive of retinopathy complication like blurred vision, fluctuating vision, impaired colour vision, dark or empty area in vision, floaters in vision, vision loss were taken

Inclusion criteria

Patients with:

- Newly diagnosed case of type 2 diabetes mellitus
- Cases within 3 months of diagnosis

Exclusion criteria

Patients with:

- Type 1 diabetes mellitus
- Diagnosed type 2 diabetes of more than 3 months duration
- Previous history of any vascular disease
- End stage renal disease
- Pre existing neurological disease including stroke, dementia
- History of nephrotoxic, neurotoxic or oculotoxic drug use

Ophthalmoscopic examination included a detailed dilated fundus examination done by indirect ophthalmoscopy.

Non-proliferative diabetic retinopathy (NPDR) was diagnosed by the presence of microaneurysms, blot haemorrhages or cotton wool spots. Proliferative diabetic retinopathy (PDR) was defined as the presence of abnormal new vessels on the disc or elsewhere.

Detailed neurological examination was done. Neuropathy was diagnosed by history of numbness, paraesthesias, tingling sensation, and burning sensation and was confirmed¹⁶ by loss of touch sensation, loss of pin prick test, vibration sense testing with 128 Hz tuning fork and loss of ankle reflex. A 10gm monofilament test was done to identify foot prone to ulcer.

Biochemical analysis

Biochemical analysis of the following were done in the department of Biochemistry

American Diabetes Association Guidelines 2019 (ADA 2019)

- Fasting and/or 2 hr post 75 oral anhydrous glucose plasma glucose level was estimated by enzymatic glucose oxidation method. A basal FPG >126 mg/dl, and a plasma glucose >200 mg/dl at 2hr post 75 glucose confirmed on a second occasion was diagnostic of diabetes.
- Glycosylated haemoglobin (HbA1c) was estimated by ion exchange chromatography. In diabetes mellitus the value is ≥ 6.5 . It gives an idea of the plasma glucose control on the preceding 3 months.

Serum urea levels were determined spectrophotometrically using the product formed when urea reacted with diacetyl in the presence of a strong acid-method of Fearon. Normal value is 15 -40 mg/dl.

Serum creatinine estimation was done by the method of Brod and Sirota using Jaffe reaction. Normal value is up to 1.4 mg/dl.

Urinary albumin creatinine ratio (ACR) was done <30 $\mu\text{g}/\text{mg}$ was taken as normal, 30-300 $\mu\text{g}/\text{mg}$ and >300 $\mu\text{g}/\text{mg}$ were considered to have microalbuminuria and macroalbuminuria respectively. Presence of microalbuminuria was taken as indicative for nephropathy when at least two out of three test was positive for microalbuminuria

Lipid Profile: Blood sample was taken after 12 hours fast and the estimation of following was done – total cholesterol level, triglyceride level, HDL(high density lipoprotein) cholesterol level, LDL (low density lipoprotein) cholesterol level, VLDL(very low density lipoprotein) cholesterol level.

Data was tabulated into a master chart and mean value and standard deviation was calculated for each variable, p value was calculated using T-TEST and FISCHER EXACT TEST with the help of standard statistical software. Pearson correlation coefficient was seen to see correlation between variables.

Result and analysis

Table 1: Sex wise distribution of population

SEX	NUMBER	%AGE
MALE	60	60
FEMALE	40	40

In our study 60% were male and 40% were female

Table 2: Showing prevalence of different microvascular complications

MICROVASCULAR COMPLICATION	NO. OF PATIENTS	%AGE OF POPULATION
RETINOPATHY (RT)	7	7
NEUROPATHY (NU)	24	24
NEPHROPATHY (NP)	19	19
RETINOPATHY WITH NEPHROPATHY (RT +NP)	6	6
NEPHROPATHY (NP) + NEUROPATHY (NU)	5	5
NEUROPATHY (NU) + RETINOPATHY	2	2
RETINOPATHY WITH NEPHROPATHY WITH NEUROPATHY (RT+NP+NU)	2	2

Retinopathy was present in 7% cases, Neuropathy in 24% cases, Nephropathy in 19% cases, retinopathy with nephropathy in 6% cases and 2% were having all the three micro vascular complication.

Table 3: Prevalence of dyslipidemia in male and female

SEX	↑TG	↑TG+ ↓HDL	↑TG +↓HDL+ ↑LDL	MIXED	TOTAL	PERCENT DYSLIPIDEMIA
MALE (N=60)	6	9	3	4	22	36.66%
FEMALE (N=40)	6	3	2	3	14	35 %

Dyslipidemia was present in 36.66% of male and 35 % of female

Table 4: Association between dyslipidemia and nephropathy

	NEPHROPATHY PRESENT	NEPHROPATHY ABSENT	TOTAL	p-value
DYSLIPIDEMIA PRESENT	13	23	36	
DYSLIPIDEMIA ABSENT	6	58	64	< 0.05

36.11 % (N(13) OF DYSLIPIDEMIC PATIENTS WERE HAVING NEPHROPATHY. Fisher's Exact Test shows the two-sided P value to be less than 0.05 which is considered as significant.

Thus dyslipidemia and nephropathy were significantly associated.

Table 5: Association between retinopathy and nephropathy

	NEPHROPATHY PRESENT	NEPHROPATHY ABSENT	TOTAL	P-VALUE
RETINOPATHY PRESENT	6	1	7	< 0.05
RETINOPATHY ABSENT	13	80	93	

85.71% OF RETINOPATHY PATIENTS WERE HAVING COEXISTING NEPHROPATHY.

Fisher's Exact Test shows the two-sided P value to be less than 0.05 which is considered as significant. Thus retinopathy was significantly associated with nephropathy.

Discussion

The present cross sectional study was carried out on 100 consecutive patients of type 2 diabetes who were diagnosed recently (duration less than 3 months). The mean age at diagnosis was found to be 53.7 years. This signifies that in our hospital, diabetic patients are presenting late. Among the newly diagnosed patients 60 were male and 40 patients were female.

39% of the newly diagnosed type 2 diabetics were having one or more than one diabetic complication, this agrees well with the finding of UKPDS¹⁷ study in which up to 50 % of newly detected type 2 diabetics were having diabetic complications at the time of diagnosis. Of these 20 (33.3%) were male and 19 (47.5%) were female, so females have higher preponderance of complication than male.

Out of 7 cases of retinopathy 6 were having coexisting nephropathy. So 85.71% of retinopathy were having nephropathy. The association was statistically significant (P value < 0.05).

The above association between nephropathy with retinopathy is in concordance with the study done by Chandy et al.¹⁸ which have found the similar association and concluded that close association between diabetic nephropathy and other micro and macro vascular complications exists in our Indian patients also. Other studies^{19,20,21,22} have reported similar strong correlation between these two.

Among the dyslipidemics 16 (44.44%) patients were having diabetic complication at the time of diagnosis.

38.88% of dyslipidemic patients were having nephropathy. The association was statistically significant (P value < 0.05). A statistically significant (p value < 0.05) correlation was found between ACR and dyslipidemia. The finding agrees with the various studies which have shown that microalbuminuria is associated with lipid profile abnormalities^{23,24}. Today, it is recognized that the presence of microalbuminuria, in addition to being a marker of incipient renal disease in diabetic patients, seems to be also a marker of large vessel disease, and is associated with an increased cardiovascular disease mortality, especially coronary heart disease^{25,26,27}. This increased mortality is due, in part, to a greater prevalence of other risk factors in patients with microalbuminuria, such as lipid disorders, hypertension (H), increased fibrinogen levels and blood changes²⁸.

Summary and conclusion

The study was carried out with the intent to assess the prevalence of diabetic complications in the newly diagnosed type 2 diabetics and also to study the prevalence of lipid profile abnormalities in these patients and to assess the pattern of dyslipidemia in them.

As clear from the preceding discussion, following conclusions can be drawn

Diabetic complications are fairly common in newly diagnosed type 2 DM patients. In this study the prevalence of microvascular complication was found to be 39 %. The complications were more common in higher age group.

The prevalence of micro vascular complication was found to be 7% for retinopathy, 19% for nephropathy, 24% for neuropathy, and significant association was found between retinopathy and nephropathy.

Dyslipidemia was present in 36 % of newly diagnosed type 2 diabetics. Dyslipidemia was found to be significantly associated with nephropathy.

In summary, prevalence of complications is quite high even at the time of diagnosis of Type 2 diabetes. This is probably because of the insidious onset of diabetes and long duration of asymptomatic disease before symptoms develop. Hence screening tests for complications are strongly recommended at the time of diagnosis not only for early detection, but also to prevent the progression into end stage disease.

Endeavour should be made to control hyperglycemia and hypertension tightly by appropriate therapeutic measures so that the occurrence and worsening of complications could be mitigated.

There is an urgent need for concerted efforts by Government and Non-governmental sectors to implement national programmes aimed at prevention, management and surveillance of the disease.

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