EVALUATION OF MICROVASCULAR AND MACROVASCULAR COMPLICATIONS IN TYPE 2 DIABETES MELLITUS

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ABSTRACT

BACKGROUND

Diabetes Mellitus comprises a group of common metabolic disorder that shares the phenotype of Hyperglycaemia. Several distinct types of DM exist and is caused by complex interaction of genetic, environmental factors and lifestyle choices. The two broad categories of DM are designated as Type 1 and Type 2 Diabetes. Type 1 Diabetes occurs due to autoimmune Beta cell destruction. Type 2 DM is a heterogeneous group of disorder characterised by variable degrees of insulin resistance, impaired insulin secretion and increased glucose production.

The objective of this study is to evaluate the microvascular and macrovascular complications of Type 2 Diabetes Mellitus among patients attending the Diabetology Outpatient Department at Government Vellore Medical College and Hospital, Vellore.

MATERIALS AND METHODS

The present study was a cross-sectional study done on patients with age more than 35 years with type 2 Diabetes Mellitus attending the Diabetology Outpatient Department at Government Vellore Medical College and Hospital for a period of 6 months.

Sample Size- The sample size was estimated through convenient sampling method. After satisfying the inclusion criteria, the total number of patients included in the study was 100. The selected patients underwent detailed clinical and biochemical evaluations. The results were calculated using SPSS V 16 Software and were expressed in percentage.

RESULTS

The sample size of the study was 100. Maximum patients with diabetes were between 41 - 60 years of age. 70% of patients had duration of diabetes < 5 yrs. Of the total number of patients 72% were found to be hypertensive, 57% were found to be obese, 20% of the study population were smokers and 74% were found to have hypercholesterolaemia which was found to be the highest risk factor followed by hypertension. The prevalence of retinopathy, neuropathy and nephropathy were 34%, 20% and 32% respectively. The most common microvascular complication was retinopathy. Among the newly diagnosed DM patients, the prevalence of retinopathy, neuropathy and nephropathy were 34%, 24% and 24% respectively. Among the macrovascular complications the prevalence of coronary artery disease, peripheral vascular disease and cerebrovascular disease was found to be 36%, 6% and 10% respectively. The most common macrovascular complication was CAD.

CONCLUSION

In this study 53% of patients were males and 47% were females, all of them being above 35 years of age. The mean age of the patients was 54 years. The highest number of patients with diabetes was in the age group of 51 - 60 years. 70% of patients had duration of diabetes < 5 years. Hypertension was found in 72% of patients.

KEYWORDS

Diabetes Mellitus, Complications, Nephropathy, Neuropathy, Retinopathy, Vasculopathy.

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BACKGROUND

Diabetes Mellitus comprises a group of common metabolic disorders that shares the phenotype of hyperglycaemia. Several distinct types of DM exist and is caused by complex interaction of genetic, environmental factors and lifestyle choices.

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The Two Broad Categories of DM are designated as Type 1 and Type 2 Diabetes

- Type 1 Diabetes occurs due to auto-immune Beta cell destruction.
- Type 2 DM is a heterogeneous group of disorder characterised by variable degrees of insulin resistance, impaired insulin secretion and increased glucose production.

The chronic complication of DM affects many organ systems and is responsible for the majority of morbidity and mortality associated with the disease. The vascular complication of DM are further subdivided into Microvascular (Retinopathy, Neuropathy, Nephropathy) and Macrovascular (coronary artery disease, peripheral arterial disease and cerebrovascular disease).

The microvascular complications of both Type 1 and Type 2 DM result from chronic hyperglycaemia. Since Type 2 DM often has a long asymptomatic period of hyperglycaemia, many individuals with type 2 DM have complications at the time of diagnosis.

Evidence implicating a causative role of chronic hyperglycaemia in macrovascular complications is less conclusive. Moreover, coronary heart disease events and mortality are two to four times greater in patients with Type 2 DM. Other factors like dyslipidaemia and hypertension play an important role in macrovascular complications.

Aim of the Study

- (1) To evaluate the microvascular and macrovascular complications of Type 2 Diabetes Mellitus, attending the Diabetology Outpatient Department at Government Vellore Medical College and Hospital, Vellore. The patients were categorised according to the duration of Diabetes for the purpose of study into-
 - (a) Newly diagnosed DM.
 - (b) DM of < 5 years.
 - (c) DM for 5 - 10 years.
 - (d) DM > 10 years.
- (2) To evaluate the risk factors such as hypertension, obesity, hypercholesterolaemia and smoking.

MATERIALS AND METHODS

Study Design

The study was a cross-sectional study done on patients with age more than 35 years with type 2 Diabetes Mellitus attending the Diabetology Outpatient Department at Government Vellore Medical College and Hospital for a period of 6 months. The sample size was estimated by convenient sampling method.

Selection of Cases

Patients with type 2 DM aged more than 35 years attending the Diabetology Outpatient Department at Government Vellore Medical College and Hospital were evaluated for-

- A. Risk factors- Hypertension, Obesity, Smoking and Hypercholesterolaemia.
- B. Microvascular Complications- Retinopathy, Neuropathy and Nephropathy.
- C. Macrovascular Complications- CAD, Cerebrovascular Disease, Peripheral Vascular Disease.
- D. For evaluation of complication, they were categorised according to the duration of Diabetes.
 1. Newly diagnosed DM.
 2. DM of < 5 years.
 3. DM for 5 - 10 years.
 4. DM > 10 years.

A detailed history was recorded in respect of all the subject patients, particularly the duration of DM, Smoking, Complications, Family History of DM etc.

The following Criteria was taken/ Diagnosis of Diabetes

- Fasting Plasma Glucose > 126 mg%
- 2 hrs. Plasma Glucose > 200 mg%

Criteria for Risk Factors

Diagnosis of Hypertension²¹

Stages	Systolic	Diastolic
Pre-Hypertension	120-139	80-89
Hypertension Stage 1	140-159	90-99
Hypertension Stage 2	>160	>100

Obesity

- (a) Body Mass Index= Weight in kgs/Height in (Meter)²
 - Overweight 25-30
 - Obese >30
- (b) Waist Circumference²²
 - Male > 90 cm
 - Female > 80 cm
- (c) Total Cholesterol²³
 - < 200 Normal.
 - 200 - 239 Borderline High.
 - > 240 High.

Criteria for Microvascular Complications

1. Diabetic Retinopathy: Ocular Fundus examination by ophthalmoscope after dilatation of pupils.

(a) Non-proliferating Diabetic Retinopathy:

- Microaneurysm, Haemorrhage, Hard Exudates

(b) Proliferative Retinopathy:

- New Vessels on Disc (NVD)
- New Vessels Elsewhere (NVE)

(c) Clinically Significant Macular Oedema (CSME):

- Thickening of retina located 500 µm from the centre of macula.
- Hard exudates with thickening of adjacent retina located 500 µm from the centre of macula.
- Zone of retinal thickening of one disk area or larger in size, located one disk diameter from the centre of macula.

2. Diabetic Nephropathy:

(a) Macroproteinuria- Protein excretion of > 500 mg/day, out of which 50% is albumin. Macroalbuminuria was tested. Microalbuminuria was not tested.

(b) Serum Creatinine.

- Calculation of GFR done based on Cockcroft-Gault Formula.²⁴

$\text{Estimated creatinine clearance (ml/min)} = \frac{(140 - \text{Age}) \times \text{body weight (kg)}}{72 \times \text{P Creatinine (mg/dL)}}$
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Multiply by 0.85 for women.

3. Diabetic Neuropathy:

Symptoms of sensory and motor signs on physical examination were done.

Criteria for Macrovascular Complications

1. Cardiovascular Disease

History: Symptoms of Angina- Chest pain.

ECG:

- LVH.
- Ischaemic Heart Disease- DT - T were checked for changes.
- Features of old MI.

Echo: (Taken where necessary as follows)

- Diastolic dysfunction in HT.
 - Regional wall motion abnormalities.
 - Ejection Fraction.
2. Peripheral Vascular Disease.
Clinical examination of peripheral palpable arteries done. Doppler study was done in relevant cases.
3. Stroke.
- History and Clinical examination for stroke was done.

RESULTS AND DATA ANALYSIS

Total number of Patients= 100

Male- (53%)

Female- (47%)

Mean Age of Patients= 54 years, Mean Age of Newly Diagnosed Diabetes = 50 years.

Maximum patients with diabetes are between 41 - 60 years.

Age (Years)	Male	Female	Total N=100
34-40	3	2	5
41-50	15	16	31
51-60	22	17	39
61-70	11	10	21
>70	2	2	4

Table 1. Age and Sex Distribution

70% of Patients have duration of Diabetes of < 5 years.

Duration of DM	Male	Female	Total
New Case	19	15	34
<5	19	17	36
5-10	10	10	20
>10	5	5	10

Table 2. Duration of DM

Positive Family History of DM in 31% of Patients.

Family History of DM	Total (n=100)
Positive	31%
Negative	69%

Table 3. Positive Family History with DM

Data on Risk Factors

Total Number of Patients with Hypertension in Diabetes is 72%.

Newly diagnosed Patients with Hypertension are 65%.

Category	Newly Diagnosed (n=34)	<5 yrs. (n=36)	5-10 yrs. (n=20)	10 yrs. (n=10)	Total (n=100)
Pre-HT 120-139 80-89	5	12	3	2	22
Stage 1 140-159 90-99	11	14	10	4	39
Stage 2 160/100 and Above	6	2	1	2	11
Total	22 (65%)	28 (78%)	14 (70%)	8 (80%)	72%

Table 4. Category of Hypertension and DM

51% of Newly Diagnosed Patients are Obese/ Overweight.

Obesity BMI	Newly Diagnosed (n=34)	<5 yrs. (n=36)	5-10 yrs. (n=20)	10 yrs. (n=10)	Total (n=100)
Overweight 25-30	14	18	9	5	46(46%)
Obese >30	3	3	3	2	11(11%)
Total	17(51%)	21(59%)	12(60%)	7(69%)	57(57%)

Table 5. Obesity and Duration of DM

69% of patients have abdominal obesity based on waist circumference.

Sex	Total
Male n=53	34 (65%)
Female n=47	34 (72%)
Total n=100	68 (68%)

Table 6. DM and Abdominal Obesity

21 (61%) of newly diagnosed patients have hypercholesterolaemia.

Total Cholesterol mg/dL	Newly Diagnosed (n=34)	<5 Years (n=36)	5-10 Years (n=20)	10 Years (n=10)
200 – 239	8	14	8	5
240 and Above	13	14	9	3
Total	21 (61%)	28 (79%)	17 (83%)	8 (84%)

Table 7. DM and Hypercholesterolaemia

Most common risk factor with DM is hypercholesterolaemia- 91 (74%).

Next common risk factor is hypertension- 76 (72%).

Risk Factor	Male	Female	Total
Hypertension	42	30	72 (72%)
Obesity	30	27	57 (57%)
Smoking	24	NIL	24 (24%)
Hypercholesterolaemia	38	36	74 (74%)

Table 8. Risk Factor and DM

Data on Microvascular Complications

Retinopathy is the most common microvascular complication. Retinopathy (34%), Nephropathy (31%) and Neuropathy (20%) present at the time of DM.

Microvascular Complication	Newly Diagnosed (n=34)	<5 Years (n=36)	5-10 Years (n=20)	10 Years (n=10)	Total (n=100)
Retinopathy	12 (34%)	10 (27%)	7 (37%)	5 (50%)	34 (34%)
Neuropathy	8 (24%)	6 (18%)	4 (20%)	2 (20%)	20 (20%)
Nephropathy	8 (24%)	10 (27%)	9 (46%)	4 (40%)	31 (31%)

Table 9. Microvascular Complication and Duration on DM

Non-proliferative Retinopathy is the most common complication in Retinopathy.

Types	Total (n=34)
Non-proliferative retinopathy	29 (88%)
Proliferative retinopathy	3 (9%)
Maculopathy	2 (6%)

Table 10. Types of Diabetic Retinopathy

43% of DM patients with CKD are in stage 2. No patients with DM were found in stages 4 and 5 in this study.

GFR	Stages of CKD	Total n=32
90-120	Stage 1	7 (23%)
60- 89	Stage 2	14 (43%)
30-59	Stage 3	11(34%)
<30	Stage 4&5	Nil

Table 11. Stages of CKD in Diabetes

11% of DM patients have renal failure.

Serum Creatinine	Total N=100
<1.5 mg/dL	89 (89%)
1.5-3 mg/dL	11(11%)

Table 12. Renal Failure in DM

Data on Macrovascular Complication.

Duration	Total N=36
Newly Diagnosed	10 (28%)
<5 years	15 (42%)
5 - 10 years	6 (17%)
>10 years	5 (14%)

Table 13. CAD and DM

47% of patients with CAD are asymptomatic.

Manifestation	Total
Symptomatic	19 (53%)
Asymptomatic	17 (47%)

Table 14. Manifestation of CAD

The most common macrovascular complication is CAD (36%).

Complication	Total N= 100
CAD	36 (36%)
Peripheral Vasc. Disease	6 (6%)
CVA	10 (10%)

Table 15. Macrovascular Complications and DM

DISCUSSION

The total no. of patients analysed were 100, out of which 53% were male and 47% were female patients. The mean age of patients found in the study was 54 yrs. These findings correlate with studies done by Raheja et al,¹ which showed the mean age of 53.3 years and another study by National Rural Diabetes Survey of 1989 - 91, which showed mean age of subjects with diabetes with 52.3 yrs.² In the present study, the mean age of newly diagnosed diabetes is found to be 50 yrs.

The prevalence of diabetes increases with age. In elderly patients, the study is 39% with maximum cases in elderly being 51 - 60 years' age group. This finding correlate with studies done by Ahuja MMS.³ Epidemiological studies of DM in India showed prevalence of diabetes in elderly patients (age > 60 yrs.) in urban population as 23.4% and maximum prevalence was in age group of 61 - 69 years.

Out of 100 patients, 31% cases had positive family history of diabetes. Many Indian studies show strong association of positive family history in DM type 2. These findings correlate with study of Shah et al (1999),⁴ which showed positive family history of 24.9% and Ramachandran et al (1999)⁵

which showed strong correlation of positive family history with DM type 2.

Risk Factors/ Hypertension

The prevalence of hypertension in diabetes in the present study is 72%. Out of the total 72 patients with hypertension, 65% patients had hypertension at the time of diagnosis. CDC's National Diabetes Surveillance System 2005, USA⁶ shows 62.5% of patients have hypertension in diabetes. Among the stages of hypertension according to JNC VII report, maximum patients 53% were in Stage 1. Various Indian studies show prevalence of hypertension in DM to be around 50% - 80%.

Obesity

This study shows that 57% patients were overweight and obese according to BMI. But when waist circumference was taken, 68% patients had abdominal obesity. This correlates with a study done by Channarayana et al (2002),⁷ which showed truncal obesity based on waist circumference was 69%. Many of Indian studies showed strong correlation between obesity and DM type 2.

Smoking

20% of the patients in the present study were smokers and all of them were males. A study by SV Madhu et al (2002)⁸ showed smokers to be 15% and an International study by CDC- National Diabetes Surveillance System, 2005, USA⁶ shows smokers at 17.7% among diabetic patients.

Hypercholesterolaemia

Out of 100 patients, 74% patients had hypercholesterolaemia. 61% patients had hypercholesterolaemia at the time of diagnosis. This study correlates with a study done by CDC- National Diabetes Surveillance System, 2005, USA⁶ which showed the hypercholesterolaemia at 60% and a study done by S Shafiq et al (2001).⁹

The most common risk factor in diabetes is hypercholesterolaemia, which is 74%. Next common risk factor is hypertension. All these risk factors play a significant role in the pathogenesis of Macrovascular complications. The risk factor- Hypertension - 65%, Obesity - 51% and Hypercholesterolaemia - 61% were present at the time of diagnosis.

Microvascular Complications

Diabetic Retinopathy 34% is the most common microvascular complication. Out of the patients with Retinopathy, 88% had non-proliferative Retinopathy. The prevalence of Retinopathy increases according to the duration of diabetes. This study correlates with the study done by G Premalatha and V Mohan et al (2002)¹⁰ in Urban South Indian Population, which showed that Retinopathy was 34.1% and M Ranka et al (2004)¹¹ found it to be 28.9% in a North Indian study.

CKD in Diabetes was seen in 32% of patients in the study. Out of the patients with CKD, maximum patients i.e. 42% were in Stage 2; 18% of them had Proteinuria. Microalbuminuria was not done in this study. The finding however correlates with the study done by Ramachandra et al (1999),⁵ which showed prevalence of Proteinuria at 19.7%.

Diabetic Neuropathy was prevalent in 20% of patients. This finding however correlates with the study done by G

Premalatha and V Mohan et al (2002),¹⁰ which had 19.1% patients with Neuropathy.

A significant finding in the study of Retinopathy 34%, Neuropathy 20% and Nephropathy 31% were present at the time of diagnosis.

Macrovascular Complications

Coronary Artery Disease- 36% is the most common Macrovascular complication in the study. 47% of patients with CAD were asymptomatic in the study. 72% of patients with CAD had duration of DM of < 5 years.

Peripheral Vascular Disease was present in 6% of patients in the study. This correlates with the study by G Premalatha and V Mohan et al (2002),¹⁰ which showed 4%.

Cerebrovascular disease was found in 10% of patients in the study. This correlates with the International Study CDC- National Diabetes Surveillance System, 2005, USA,⁶ which showed 9% prevalence of stroke in DM type 2.

CONCLUSION

1. In this study 53% of patients were males and 47% were females, all of them being above 35 years of age. The mean age of the patients was 54 years.
2. The highest number of patients with diabetes was in the age group of 51 - 60 years.
3. 70% of patients had duration of diabetes < 5 years.
4. Hypertension was found in 72% of patients.
5. Obesity was found in 57% of patients.
6. 45% of the males were smokers.
7. Hypercholesterolaemia was found in 74% of patients.
8. The highest risk factor was Hypercholesterolaemia followed by Hypertension.
9. Retinopathy was found in 34% of patients.
10. Neuropathy was found in 20% of the patients.
11. Nephropathy was found in 31% of the DM patients.
12. Newly diagnosed DM patients presented with Retinopathy in 34%, Neuropathy in 24% and Nephropathy in 24%.
13. Coronary artery disease was found in 36% of patients.
14. Peripheral Vascular Disease was found in 6% of patients.
15. Cerebrovascular disease was found in 10% of patients.

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