Prevalence of Micro and Macrovascular Complications and their Risk Factors in Type-2 Diabetes Mellitus

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Abstract

Objectives: To determine the prevalence of micro and macrovascular complications in type-2 diabetes in Northwest India and its correlation with various risk factors.

Methods: In this study, total 11157 subjects (M:F 6661: 4496), attending the diabetic clinic, were analysed. The study sample resembles the population sample in anthropometric, age and socioeconomic factors. All patients had undergone the test for retinopathy by fundus examination, nephropathy by microalbuminuria, serum creatinine and blood urea, neuropathy by monofilament and biothesiometer, peripheral vascular disease (PVD) by colour doppler and cardiovascular disease by ECG.

Results: Among 11157 subjects, retinopathy was diagnosed in 32.5%, nephropathy was present in 30.2%, peripheral neuropathy was present in 26.8%, coronary heart disease (CHD) was present in 25.8% and peripheral vascular disease (PVD) was present in 28% of the subjects. Multiple logistic regression analyses showed that age had a significant association with retinopathy, neuropathy, coronary heart disease (CHD) and peripheral vascular diseases (PVD). Duration of diabetes had significant association with the neuropathy, nephropathy and PVD. Higher HbA1C increases the risk of retinopathy, neuropathy and nephropathy. Hypertension was associated with nephropathy and coronary heart disease.

Conclusion: The study highlights the high prevalence of vascular complications in type-2 diabetes in Northwest India. Retinopathy and nephropathy were the commonest complications of diabetes in our study.

Introduction

Diabetes mellitus is the most widespread affliction of mankind. Diabetes is a syndrome characterised by chronic hyperglycaemia and disturbance of carbohydrate, fat and protein metabolism associated with absolute or relative deficiencies in insulin secretion and/or insulin action. Long term complications that affect retina, kidney and nervous system are termed as microvascular complications. The macrovascular complications which include coronary artery disease, cerebrovascular disease and peripheral vascular disease also occur with higher frequency in diabetes.

Recent WHO reports show that India already has the largest number of diabetic patients in the world. The rising trend in the prevalence of type-2 diabetes has also been reported in a series of epidemiological studies. A major multicentric study was carried out on the complications of type-2 diabetes, in which India was also a participant. This WHO study showed coronary heart disease prevalence rates in diabetics between 26% and 35% with higher rates in women and with much heterogeneity among countries. Similar study carried out in south India showed high prevalence of vascular complications in type-2 diabetes. The risk of peripheral vascular diseases (PVD) in diabetic patients was found 3-5 fold higher compared to that in non-diabetics.
The risk factors for developing peripheral arterial disease are similar to those for atherosclerosis. Smoking is particularly deleterious and hyperglycaemia, hyperinsulinaemia, hypercholesterolaemia, hypertriglyceridaemia and hypertension all contribute in its pathogenesis. Peripheral neuropathy is strongly related to both age at diagnosis and duration of diabetes and usually tends to occur after age of 50 in type-2 diabetes. Prevalence of diabetic retinopathy in type-2 diabetes mellitus at a diabetic centre in south India was 34.1% which included 30.7% non proliferative diabetic retinopathy and 3.4% proliferative diabetic retinopathy. Duration of diabetes, glycosylated haemoglobin, type of treatment (Insulin treatment versus non-insulin treatment), systolic and diastolic blood pressure and serum creatinine showed a positive association while BMI has an inverse association. The selected patients were evaluated for presence of vascular (micro and macro) complications i.e. coronary artery disease, peripheral vascular disease, retinopathy, nephropathy and neuropathy by relevant investigations. Retinopathy was diagnosed by detailed fundus examination and was classified according to diabetes retinopathy study (DRS) and early treatment diabetic retinopathy study (ETDRS). Urine for microalbuminuria (30-300 mg/ 24 hrs) was tested by micral test for incipient nephropathy. Overt nephropathy was confirmed by estimation of level of blood urea, serum creatinine and macroalbuminuria.

Neuropathy was diagnosed by history of numbness, paraesthesia, tingling sensation and confirmed by touch sensation with 10 gm monofilament, vibration sense by biothesiometer and ankle reflex. PVD was considered to be present if there is definitive history of intermittent claudication and one or more of peripheral pulses is absent in both feet or ankle brachial index < 0.8 (by Doppler). Coronary artery disease was diagnosed by history of myocardial infarction or angina, documented by previous treatment records or by ECG (Minnesota codes) and chest X-ray to assess cardiac size.

Material and Method

This study was conducted in patients attending or enrolled in a diabetic clinic attached to S.P. Medical College, Bikaner (North West India) from June 2008 to December 2010. A total of 11565 type-2 diabetic patients were seen at the centre during this period. All diabetic patients registered at diabetic clinic were screened for diabetes and its complications. The present study was conducted on 11157 patients as 408 patients showed their unwillingness to give informed consent.

Each subject underwent detailed history and complete clinical examination. Details regarding age, sex, socioeconomic status, rural or urban, duration of diabetes and treatment history of diabetes were recorded for all the patients. Blood pressure was recorded in lying down, sitting and standing positions at intervals of five minutes and compared in both arms. Pregnant diabetic cases or gestational diabetics and type-1 diabetics were excluded from the study. Type-2 diabetes was differentiated from type-1 diabetes by age of onset, body habitus and evidence of ketoacidosis. Diabetes was diagnosed according to American Diabetes Association (ADA) revised criteria.

Blood glucose level estimation was done by glucose oxidase method in venous blood. Glycosylated haemoglobin (HbA1C) was measured by ion-exchange chromatography method.

Statistical Analysis

Prevalence of the complications in subgroups was compared by chi square tests. Multiple logistic regression analysis with stepwise additions of variables was performed to assess their association with each of the complication studied. Linear regression equation was used for calculation of age adjusted prevalence of complications.

Results

Total number of type-2 diabetic patients were 11157. Out of that retinopathy was found in 3621 (32.5%) patients, nephropathy was present in 3369 (30.2%) patients, neuropathy was present in 2991 (26.8%) patients, CAD was present in 2873 (25.8%) patients and PVD was found in 3125 (28%) patients.
Table 1: Results of multiple logistic regression analysis showing association of various risk factors with microvascular complications

<table>
<thead>
<tr>
<th>Diabetic Retinopathy</th>
<th>Variable</th>
<th>Odd Ratio</th>
<th>95% CI</th>
<th>Regression coefficient β</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>2.6434</td>
<td>2.341-2.985</td>
<td>3.209</td>
<td></td>
</tr>
<tr>
<td>Duration of Diabetes</td>
<td>2.6772</td>
<td>2.393-2.995</td>
<td>3.407</td>
<td></td>
</tr>
<tr>
<td>Systolic BP</td>
<td>5.1263</td>
<td>4.738-5.546</td>
<td>5.875</td>
<td></td>
</tr>
<tr>
<td>Diastolic BP</td>
<td>5.6939</td>
<td>5.308-6.108</td>
<td>5.573</td>
<td></td>
</tr>
<tr>
<td>Fasting Blood Sugar</td>
<td>2.4909</td>
<td>2.046-3.033</td>
<td>2.863</td>
<td></td>
</tr>
<tr>
<td>HbA1C</td>
<td>2.6844</td>
<td>2.283-3.157</td>
<td>3.552</td>
<td></td>
</tr>
<tr>
<td>BMI</td>
<td>4.2818</td>
<td>3.990-4.594</td>
<td>1.168</td>
<td></td>
</tr>
<tr>
<td>Serum Cholesterol</td>
<td>3.0758</td>
<td>2.883-3.281</td>
<td>0.722</td>
<td></td>
</tr>
<tr>
<td>Serum HDL</td>
<td>2.0311</td>
<td>0.181-0.228</td>
<td>1.378</td>
<td></td>
</tr>
<tr>
<td>Serum Triglyceride</td>
<td>0.8584</td>
<td>0.784-0.939</td>
<td>2.650</td>
<td></td>
</tr>
<tr>
<td>Serum LDL</td>
<td>2.1992</td>
<td>1.935-2.499</td>
<td>2.010</td>
<td></td>
</tr>
<tr>
<td>Serum VLDL</td>
<td>2.2945</td>
<td>2.144-2.456</td>
<td>0.682</td>
<td></td>
</tr>
</tbody>
</table>

Figure 1 shows relationship regarding age of patients with various vascular complications i.e. retinopathy, nephropathy, neuropathy, PVD and CAD. Total patients studied were divided in various groups according to age i.e. below 50, 51-60, 61-70, > 70 years.

Table 1 shows the association of age, duration of diabetes, systolic and diastolic blood pressure, fasting blood sugar, HbA1C, BMI, serum cholesterol, serum HDL, serum triglyceride, serum LDL and serum VLDL with retinopathy and among these factors duration of diabetes, and serum triglyceride and blood pressure showed strongest association with regression coefficient (β) 5.407 and 2.650 respectively. Regarding nephropathy, duration of diabetes and serum triglyceride were strongly associated with regression coefficient (β) 4.428 and 3.916 respectively. Among variables serum triglyceride, BMI, systolic BP and duration of diabetes had strongest association with regression coefficient (β) 1.973, 1.778, 1.756, and 1.212 respectively when neuropathy was considered.

Table 2 shows that with PVD, the factor like age, duration of diabetes, BP and HbA1C were most strongly associated with regression coefficient (β) 2.718, 3.100, 1.833 and 1.227 respectively. It was observed that with CAD, variables like duration of diabetes, systolic BP, diastolic BP, serum HDL and HbA1C shared strongest associations with regression coefficient (β) 5.332, 2.112, 1.326, 1.433 and 1.007 respectively.

Discussion

Diabetes mellitus is the commonest metabolic disorder and has a high prevalence in India. The progress of the diabetic patients largely depends on...
the complications seen in the natural course of illness. Till date, no large study was conducted regarding the microvascular and macrovascular complications in this part of India (North West), hence it was decided to undertake a cross sectional study to record various complications and the influence of various risk factors.

In the present study retinopathy was present in 3621 patients i.e. 32.5%. Our results are consistent with Ramchandran et al where they found that out of 3010 type-2 diabetics, retinopathy was present in 714 i.e. 23.7%, at a diabetes centre in Chennai.\(^5\) Knuiman et al reported prevalence of retinopathy 28% in Perth, Western Australia.\(^7\) On the contrary, Rema et al found that the prevalence of retinopathy was 34.1% in type-2 diabetes. It may be because of referral bias as this centre offers retinal services.\(^9\) On applying multiple regression analysis for diabetic retinopathy, a positive association was observed for age of patients, duration of diabetes, blood pressure, fasting blood sugar and HbA\(_1\)C.

In present investigation, evidence of nephropathy was observed in 3369 patients i.e. 30.2% (including both microalbuminuria and overt nephropathy). Klein et al in their study found that frequency of microalbuminuria was 29.2% in those taking insulin and 22.0% in those not taking insulin.\(^8\) A lower prevalence of proteinuria (19.7%) was found in the study conducted by Ramchandran et al in south Indian diabetes subjects\(^5\). Gupta et al reported prevalence of microalbuminuria in 26%.\(^10\) Schonitz from Denmark reported 27.4% prevalence, while in the WHO multicentric study of vascular disease in diabetics, a wide geographical variation was reported in prevalence of nephropathy. It ranged from 2.4% (Hong Kong), 23% (Delhi) to 37% (Oklahoma, USA).\(^4\)

This observed geographical and population variation in prevalence of diabetic nephropathy could be due to real ethnic variation in the susceptibility to diabetic nephropathy i.e. genetic, or due to poor control of diabetes, hypertension or other socioeconomic and cultural / environmental factors. Simultaneously quality and quantity of protein may also play an important role in evolution of diabetic nephropathy. On applying regression analysis for diabetic nephropathy, we found significant association of age, systolic and diastolic B.P., HbA\(_1\)C, BMI, serum cholesterol and serum triglyceride. Significant associations of duration of diabetes and nephropathy was also observed by Mohan et al (2000) and Verghese et al (2001). Systolic blood pressure was associated with high prevalence of diabetic nephropathy; however diastolic blood pressure had no significant contribution to nephropathy.\(^11,12\) Earlier, Rema et al and Ramachandran et al had also observed the positive association of hypertension with diabetic nephropathy. Poor glycaemic control indicated by raised glycosylated haemoglobin was significantly associated with increased incidences of diabetic nephropathy.\(^8,5\) Gupta et al (1991) from New Delhi found that glycosylated haemoglobin was significantly higher in microalbuminuric NIDDM patients.\(^10\)

Diabetic neuropathy is one of the commonest long term complications of diabetes mellitus. In our study neuropathy was present in 2991 (26.8%) patients. Similar prevalence was found by Ramchandran et al in southern India i.e. 27.5%,\(^5\) while Shobhana et al reported the prevalence of neuropathy as much as 70%.\(^13\) This much higher percentage of neuropathy may be due to smaller cohort, as well as referral bias which was because of large number of patients with foot complications were admitted to this centre and more sophisticated technologies were used to diagnose even sub clinical cases. Much lower prevalence of neuropathy i.e. 14% was found by Knuiman et al (West Australia) which might be due to real ethnic variation and different genetic susceptibility to develop neuropathy in presence of hyperglycaemia.\(^7\) On applying multiple regression analysis for diabetic neuropathy, a positive association revealed for duration of diabetes, blood pressure, fasting blood sugar, serum cholesterol, serum LDL and serum VLDL.

A significant association of peripheral vascular disease with the age and duration of diabetes was one of the outcomes of our study. Our findings are consistent with results of Ramachandran et al (1999) from South India.\(^5\)

Among the macrovascular complications of diabetes mellitus peripheral vascular disease (PVD) could be considered the Cindrella, as most of the interest in research and care has been cornered by coronary artery and cerebrovascular diseases. The advent of Doppler ultrasound has provided an easy means for investigating PVD. In our study we found 3125 patients suffering from PVD i.e. prevalence of PVD was 28%. In a study conducted by Ramachandran et al prevalence of peripheral vascular disease was 4% in South Indian diabetic subjects.\(^5\) Much higher prevalence in present study may be due to different genetic constitution and poor glycaemia. Similarly Palumbo et al told that at the time of diagnosis of diabetes, nearly 10% may already have lower extremity arterial disease, whose cumulative incidence rose to 45% by 20 years of duration of diabetes.\(^6\) On applying multiple regression analysis for peripheral vascular disease, variables like age, duration of diabetes, systolic and diastolic blood pressure, HbA\(_1\)C, serum cholesterol, serum triglyceride and serum VLDL were found positively associated. Present study also showed positive association of peripheral vascular disease with BMI.
Coronary artery disease was found in 2873 patients making prevalence of CAD 25.8% in present study. A study by Ramachandran et al found the prevalence of coronary artery disease as 11.4%.5

Endeavour should be made to control hyperglycaemia and hypertension tightly by appropriate therapeutic measures so that the occurrence and worsening of the complications could be mitigated. As this was a cross-sectional study, it is not possible to determine whether elevated or decreased levels of variables showing associations with complications actually preceded the development of the complications. Thus, the clinical and laboratory variables have associations with complications in this study may only be interpreted as potential risk factors. Secondly, it is a clinic based study, hence, there is a possibility of referral bias affecting the results.

References