

Complications Prevalent in Type-2 Diabetes Mellitus and Investigation of Their Risk Factors

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ABSTRACT: The present study was conducted on 12309 patients as 309 patients showed their unwillingness to give informed consent. Each subject underwent detailed history and complete clinical examination. Retinopathy was diagnosed in 34% nephropathy was present in 32% peripheral neuropathy was present in 28% coronary heart disease (CHD) was present in 26% and peripheral vascular diseases (PVD) was present in 30% of the case. Multiple logistic regression analyses showed that age had a significant association with retinopathy, neuropathy, coronary heart disease (CHD) and peripheral vascular diseases (PVD). Neuropathy was diagnosed by history of numbness, paresthesia, tingling sensation and confirmed by touch sensation by 10gm monofilament, vibration sense by biothesiometer and ankle reflex. Poor glycemic control indicated by raised glycosylated hemoglobin was significantly associated with increased incidences of diabetic nephropathy. Researchers (1995) (21) found that the initial HbA_{1c} along with initial systolic blood pressure is an important contributory factor for proteinuria. Various scientists (1991) (17) from New Delhi found that glycosylated hemoglobin was significantly higher in microalbuminuric patients.(11,12)

We found a significant association of peripheral vascular disease with the age duration of diabetes. Our findings are consistent with results of certain doctors (1997) (12) and it had been analysed (1999) (6) from South India. We did not find any association of glycemic control and hypertension and similar results were observed by scientists (1992) (13), Different researchers (1990) (14) and their supervisors (1999) (6)

I. INTRODUCTION

Diabetes mellitus (DM) is a worldwide public health problem that affects millions of people from all age, gender, and racial and ethnic groups. DM is the leading cause of blindness and amputation and contributes substantially to kidney disease, cardiomyopathy, and cerebrovascular and peripheral artery diseases. Of importance, recent advances in biology and medicine have introduced new technologies to study the molecular pathology underlying DM-related complications, the development of novel strategies to treat these conditions, and the evaluation of outcomes.

The present special issue has been designed to stimulate the continuing efforts to develop novel drugs and therapeutic targets and new perspectives of combined therapies for decreasing micro- and macrovascular complications in DM. It includes one review article and ten original research papers, from leading and emerging scientists with diverse expertise and interests, and covers three thematic areas: (a) epidemiology and pathogenesis of DM-related complications; (b) microvascular complications (nephropathy, retinopathy, and neuropathy); and (c) macrovascular complications (cardiovascular disease, stroke, and peripheral artery disease). In all these thematic areas, pathophysiological and molecular mechanisms are discussed and novel drug-target therapies, as well as stem cell-based therapy, are documented in either preclinical or clinical studies. Of importance, future preclinical studies and smaller clinical trials are warranted before proceeding to pivotal trials.

It was reported that prevalence of micro- and macrovascular complications of 2,892 patients with type 2 DM (T2DM) and their risk factors in a single center. To note, the study comprised predominantly female patients (approx 82%) which are usually underscored in epidemiologic studies. Their main findings included that increased age, disease duration, and glycated hemoglobin (HbA_{1c}) were the main risk factors for microvascular disease and diabetic foot, while age was the only risk factor for macrovascular complications. In addition, occurrence of coronary artery disease (CAD), peripheral neuropathy, diabetic foot, and lower extremity amputation was significantly higher among male individuals when compared to female individuals. Collectively, gender differences may be taken into account when providing healthcare management and allocate resources for prevention and treatment of DM-related complications.

II. OBJECTIVES

- Macro and micro vascular complications are to be determined in case of type 2 diabetes in north west India
- The correlation of type 2 diabetes and various complications are to be made with risk factors
- Major risk factors are to be identified in relation to diabetic complications

III. MATERIALS & METHODS

This study was conducted in patients attending or enrolled in a diabetic ward of SMS hospital, Jaipur, India during the year 2018-19. A total of 12765 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 12309 patients as 309 patients showed their unwillingness to give informed consent. Each subject underwent detailed history and complete clinical examination. Details regarding age, sex, socio-economic 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.

DIFFERENTIATIONS WERE MADE BETWEEN TYPE-1 AND TYPE -2 DIABETIC PATIENTS

In case of Type 1 Diabetes: Type 1 diabetes is also called insulin-dependent diabetes. It used to be called juvenile-onset diabetes, because it often begins in childhood. Type 1 diabetes is an autoimmune condition. It happens when your body attacks your pancreas with antibodies. The organ is damaged and doesn't make insulin.

It could also happen because of problems with cells in your pancreas that make insulin. Many of the health problems that can come with type 1 happen because of damage to tiny blood vessels in your eyes (called diabetic retinopathy), nerves (diabetic neuropathy), and kidneys (diabetic nephropathy). People with type 1 also have a higher risk of heart disease and stroke. Treatment for type 1 diabetes involves injecting insulin into the fatty tissue just under your skin. (1,2)

Utilization of Syringes, Insulin pens that use prefilled cartridges and a thin needle, Jet injectors that use high-pressure air to send a spray of insulin through your skin, Pumps that send insulin through a tube to a catheter under the skin of your belly, A test called the A1C blood test estimates your blood sugar levels over the previous three months. Your doctor uses it to see how well your blood sugar is controlled. That helps them know your risk of complications.

In case of Type 2 Diabetes: Type 2 diabetes used to be called non-insulin-dependent or adult-onset diabetes. But it's become more common in children and teens over the past 20 years, largely because more young people are overweight or obese. About 92% of people with diabetes have type 2. When you have type 2 diabetes, your pancreas usually creates some insulin. But either it's not enough or your body doesn't use it like it should. Insulin resistance, when your cells don't respond to insulin, usually happens in fat, liver, and muscle cells. Type 2 diabetes is often milder than type 1. But it can still cause major health complications, especially in the tiny blood vessels in your kidneys, nerves, and eyes. Type 2 also raises your risk of heart disease and stroke. (3,4)

People who are obese -- more than 23% over their target body weight for their height -- have an especially high risk of type 2 diabetes and the health problems that can follow. Obesity often causes insulin resistance, so your pancreas has to work harder to make more insulin. But it's still not enough to keep your blood sugar levels where they should be. Treatment for type 2 diabetes involves keeping a healthy weight, eating right, and exercising. Some people need medication, too.

The doctor might do an A1C test a few times a year to see how well you've been controlling your blood sugar.

Results: Retinopathy was diagnosed in 34% nephropathy was present in 32% peripheral neuropathy was present in 28% coronary heart disease (CHD) was present in 26% and peripheral vascular diseases (PVD) was present in 30% of the case. 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 complications other than coronary heart disease (CHD). Higher HbA_{1c} increased the of retinopathy, neuropathy and nephropathy. Hypertension was associated with complications except peripheral vascular diseases (PVD) and neuropathy.

This study was undertaken to define more clearly the risk factors influencing susceptibility to vascular complications in diabetic patients. There are a few clinical studies in the direction but most of them lack sufficient power and are focused only towards one specific complication. Therefore, we attempted to do a clinical study in a large cases of type-2 diabetic patients.

Blood glucose level estimation was done by glucose oxidase method in venous blood. Glycosylated hemoglobin (GHb) was measured by ion-exchange resin method with GHb kit.

Type-2 diabetes was differentiated from type diabetes by age of onset, body habitus and evidence of ketoacidosis.

Each subject underwent a 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 in all the patients. Blood pressure was recorded in lying down, sitting and standing position at intervals of five minutes and compared in both arms. Pregnant diabetic cases or gestational diabetes and type-1 diabetes were excluded from the study.(5)

The selected patients were evaluated for presence of vascular (micro and macrovascular) complications i.e. coronary artery disease, cerebrovascular 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 (30-277 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, paresthesia, tingling sensation and confirmed by touch sensation by 10gm monofilament, vibration sense by biothesiometer and ankle reflex.

PVD was considered to be present if there is definitive history of intermittent claudication or if one of more of peripheral pulses is absent in both feet or ankle brachial index < 0.78 (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.

Cerebrovascular accidents – patients were evaluated by history and examination. It will be confirmed by CT scan head.(6,7)

IV. STATISTICAL ANALYSIS

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

V. OBSERVATIONS

Total number of type-2 diabetic patients were 11157 of whom retinopathy was found in 3621 (34%) patients, nephropathy was present in 3369 (33%) patients, neuropathy was present in 2991 (29%) patients, CAD was present in 2873 (27%) patients PVD was found in 3027(30%) patients.

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 there is no large study regarding the microvascular and macrovascular complications in this part of India (North West), hence we decided to undertake a cross sectional study to record various complications and the influence of various risk factors.(8)



This study was conducted on 11157 patients of type-2 diabetes. These patients were thoroughly interrogated clinically and relevant investigations were performed. Following results were laid by this study:

- Prevalence of retinopathy was found to be 33% nephropathy was present in 35% neuropathy in 34% and CAD prevalence was 28% while PVD was found in 30%
- Multiple logistic regression analysis showed that age was significantly associated with retinopathy, nephropathy, neuropathy, PVD and CAD.
- Increased duration of diabetes had a strong relationship with all the microvascular complications and peripheral vascular disease.
- Hypertension was strongly associated with retinopathy, nephropathy (particularly systolic blood pressure) and coronary artery disease while neuropathy had a borderline significant association with hypertension.
- Poor glycemic control (increased glycosylated hemoglobin) had a definite contribution for raised prevalence of microvascular complications i.e. retinopathy, nephropathy and neuropathy.
- Body mass index was positively associated with retinopathy.(9,10)
- In our study it was obvious that those diabetic patients who were treated with insulin, had a higher rate of vascular complications but on multiple regression analysis this relationship disappeared.
- Fasting blood sugar and waist hip ratio were not found to be significantly associated with prevalence of peripheral vascular disease.
- Smoking had a definite association with peripheral vascular disease.
- Dyslipidemia was associated with retinopathy, neuropathy, nephropathy, PVD and CAD.

VI. RESULTS & DISCUSSION

This study also revealed a strong association of hypertension with nephropathy. Systolic blood pressure was associated with high prevalence of diabetic nephropathy; however diastolic blood pressures had no significant contribution to nephropathy. Earlier, it was found (12) and (6) had also observed the positive association of hypertension with diabetic nephropathy.

Poor glycemic control indicated by raised glycosylated hemoglobin was significantly associated with increased incidences of diabetic nephropathy. Researchers (1995) (21) found that the initial HbA_{1c} along with initial systolic blood pressure is an important contributory factor for proteinuria. Various scientists (1991) (17) from New Delhi found that glycosylated hemoglobin was significantly higher in microalbuminuric patients.(11,12)

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Table 1 : Results of multiple logistic regression analysis showing association of some important risk factors with microvascular complications

Diabetic retinopathy

Variable	odd ratio	95%CI	regression coefficient β
Age	2.6865	2.211-2.806	2.818
Duration of diabetes	2.3666	2.213-2.912	2.933
Systolic BP	5.113	4.323-4.987	5.076
Diastolic BP	5.203	4.879-4.999	5.111

Table 2 : Results of multiple logistic regression analysis showing association of some important risk factors with macrovascular complications

Diabetic nephropathy

Variable	odd ratio	95%CI	regression coefficient β
Age	2.5325	2.765-2.898	2.856
Duration of diabetes	2.6543	2.976-2.999	2.453
Systolic BP	7.988	6.809-6.876	6.813
Diastolic BP	6.765	6.567-6.765	6.667

Diabetic neuropathy

Variable	odd ratio	95%CI	regression coefficient β
Age	2.9876	2.456-2.765	2.675
Duration of diabetes	2.8765	2.765-2.987	2.897
Systolic BP	4.654	4.567-4.768	4.654
Diastolic BP	5.213	4.908-4.898	4.926

Table 2 : Results of multiple logistic regression analysis showing association of some important risk factors with macrovascular complications

PVD

Variable	odd ratio	95%CI	regression coefficient β
Age	2.4563	2.342-2.887	2.778
Duration of diabetes	2.7654	2.765-2.123	2.654
Systolic BP	6.876	6.908-6.999	6.786
Diastolic BP	4.532	6.547-6.821	6.546

CAD

Variable	odd ratio	95%CI	regression coefficient β
Age	2.3876	2.456-2.987	2.566
Duration of diabetes	5.8765	4.675-4.899	4.788
Systolic BP	7.909	7.572-7.854	7.556
Diastolic BP	5.604	5.342-5.667	5.567

This study projects a high prevalence of microvascular complications and CHD and PVD in diabetic patients in India (North-West region). It should be the endeavor to control hyperglycemia 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 found to 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.(13,14)

VII. CONCLUSION

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. The study highlights the high prevalence of vascular complications in type-2 diabetes in North- India. Retinopathy and nephropathy were the commonest complications of diabetes. The global burden of microvascular and macrovascular complications is substantial in these patients with type 2 diabetes who are relatively early in the disease process. These findings highlight an opportunity for aggressive early risk factor modification, particularly in regions with a high prevalence of complications. Heart involvement in diabetes may not be only a macrovascular disease where there is Orchestra of contributing factors to the development of diabetic cardiomyopathy concerning fatty acid and glucose complex structural macrovascular derangements such as hypertrophy and loss of function due to glycation but also a microvascular involvement following “common soil” hypothesis of diabetes complications. Atherosclerosis in large arteries as well as cardiomyopathy in diabetes a microvascular component may go hand in hand.

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