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Review Article

Prevalence of diabetes mellitus and its associated comorbidities: a population based study

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ABSTRACT

The purpose of this study was to quantify the prevalence and co-prevalence of common comorbidities of type 2 diabetes mellitus (T2DM). Literature search was conducted in PubMed for relevant articles published during the period from 2013 to 2023. Studies describing the prevalence rate of T2DM and its associated co-morbidities in INDIA in the past 10 years and the pharmaceutical antidiabetic treatment were identified. Out of 100 articles 10 studies conducted in India fulfilled the inclusion criteria regarding the prevalence rate of T2DM along with its associated co-morbidities. Studies revealed that comorbidity burden tended to increase in older age groups and was higher in men than women. Few studies demonstrated for the combination of hypertension (HTN) and hyperlipidaemia (67.5%), followed by overweight/obesity and HTN (66.0%), overweight/obesity and hyperlipidaemia (62.5%), HTN and chronic kidney disease (CKD) (22.4%), hyperlipidaemia and CKD (21.1%), HTN and cardiovascular disease (CVD) (20.2%), hyperlipidaemia and CVD (20.1%), overweight/obesity and CKD (19.1%) and overweight/obesity and CVD (17.0%). The most common conditions in patients with T2DM included HTN in 82.1%; overweight/obesity in 78.2%; hyperlipidaemia in 77.2%; CKD in 24.1%; and CVD in 21.6%. It was concluded from the study that the vast majority of patients with T2DM have multiple comorbidities. To ensure a comprehensive approach to patient management, the presence of multimorbidity should be considered in the context of clinical decision making.

Keywords: Type 2 diabetes mellitus, Multimorbidity, Hyperlipidaemia

INTRODUCTION

Type 2 diabetes mellitus (T2DM) is a progressive metabolic disorder that develops in the case of insulin resistance and reduced insulin secretion, leading to chronic hyperglycaemia. Comorbidities such as cardiovascular disease (CVD), hypertension (HTN), dyslipidaemia, and renal insufficiency, among others, are commonly seen in conjunction with a diagnosis of T2DM.[1]

The burden of diabetes is huge and continues to put pressure on the economy of the developing and underdeveloped nations. India is one of the top ten diabetic countries in the world with 31.7 million diabetic people in the year 2002 and WHO treatment of concurrent conditions can lead to more effective disease management and, in turn, improve patient functioning, quality of life, and mortality risk. The American Diabetes Association guidelines stresses the importance of modifying a patient's therapy, including pharmacologic treatment, based on their individual clinical profile, including comorbidities.[3]

Antihyperglycemic agents used for the treatment of T2DM each have a specific safety and tolerability profile that may impact the suitability for use depending upon the clinical characteristics and personal medical history of the individual being treated. For example, metformin is commonly used as the first line of therapy in patients with T2DM; however, this medication is not suitable for

patients with more advanced stages of renal insufficiency. Sulfonylureas can cause weight gain, leading to hypoglycaemia.

Incretin-based therapies, including dipeptidyl peptidase-4 inhibitors (DPP-4i) and glucagon-like peptide-1 receptor agonists, have been associated with a slightly increased risk of pancreatitis. A small, but significant, increased risk of hospitalization for heart failure has been observed with one DPP-4 inhibitor, but not with other members of the class. Selective sodium glucose co-transporter 2 inhibitors (SGLT2i) represent the newest class of oral antihyperglycemic agents for patients with T2DM.[4] This class of drugs is contraindicated in patients with severe renal impairment and warrants caution when being used in patients with moderate renal insufficiency. In addition, their use is associated with an increased risk of genital mycotic infections, as well as urinary tract infections (UTI).

An increasing prevalence of diabetes and its complications in the Indian society have focused on the need for more research work to be performed in this area. Appropriate tools need to be designed and implemented in the affected population. With this background the present study sought to quantify the prevalence and co-prevalence of several common comorbidities in the patient population, including congestive heart failure (CHF), Chronic kidney disease (CKD), retinopathy, neuropathy, cardiovascular disease (CVD), Uterine tract infection (UTI), genital mycotic infections, hypoglycaemia, pancreatitis, liver disease, Hypertension (HTN), hyperlipidaemia and overweight/obesity in the context of India and other developing countries.

Objectives

The objectives of this study were to study the (a) prevalence of T2DM and the comorbidities associated with it; (b) occurrence of pairs of comorbidities in the diabetic population; and (c) association of T2DM and its co-morbidities in the given treatment procedures.

METHODS

Search strategy

A search was carried out in PubMed for studying the prevalence and co-prevalence of T2DM and its associated co-morbidities in past ten years covering India and other developing countries. A broad search criteria was used to retrieve as many relevant articles as possible. The references for retrieved publications were also reviewed to identify further relevant studies.

Selection criteria

Studies were considered to be relevant if they involved patients with T2DM, factors affecting T2DM and its associated co-morbidities shown in the past ten years. Those studies were excluded from the analysis where the age group was below 18 years, because the juvenile stage was not considered in the study.

Data extraction

The extracted data included the country where the study was performed, number of patients, patient's characteristics at baseline, data source, study design, the duration of follow up.

RESULTS

Search results

A total of 100 titles were identified and their abstracts were reviewed independently based on their pre-defined selection criteria. Based on the relevant information from abstracts, full texts for 23 abstracts were retrieved and reviewed. The reasons that papers were found to be ineligible included the population without T2DM, published protocol or the study design without the results.

Patient populations and its associated co-morbidities

All studies were carried out in India and involved analysis of inpatient and outpatients. Patient population size ranged between 100 to 1,389,016 eligible patients.[5] Mean age of patients across the studies ranged between 41 and 68 years.[6] Percentage of female ranged between 33% to 53% and percentage of male ranged between 45% to 67%. One of the studies showed that the comorbidity burden tended to increase in older age groups and was higher in men than women. The most common conditions in patients with T2DM included hypertension (HTN) (82.1%); overweight/obesity in 78.2%; hyperlipidaemia in 77.2%; chronic kidney disease (CKD) in 24.1%; and cardiovascular disease (CVD) in 21.6%. The highest co-prevalence was demonstrated for the combination of HTN and hyperlipidaemia (67.5%), followed by overweight/obesity and HTN (66.0%), overweight/obesity and hyperlipidaemia (62.5%), HTN and CKD (22.4%), hyperlipidaemia and CKD (21.1%), HTN and CVD (20.2%), hyperlipidaemia and CVD (20.1%), overweight/obesity and CKD (19.1%) and overweight/obesity and CVD (17.0%).[5]

In some studies, neuropathy was present in 33% patients; retinopathy was present in 6% of patients and nephropathy was present in 50% patients. Microalbuminuria was present in 44% patients, whereas macroalbuminuria was present in 6 % patients. Subjects were classified into two groups on the basis of glycated haemoglobin (HbA1C) levels. Subjects with HbA1C > 7.5% had more microvascular complications than with HbA1C 6.5-7.5%, the association was statistically significant.[7]

Over the past few decades, integrated health delivery systems have evolved, and continue to increase in number. As a result of the evolution of these systems, the way that

diabetes-related care is delivered and management of its comorbid conditions have changed considerably.[8] The result of the current review suggest that T2DM is a leading cause of certain comorbidities such as retinopathy, nephropathy, hypertension, obesity and hyperlipidaemia. Few studies showed that in the newly diagnosed patients with T2DM, majority were from the age group 41-50 years (40%) among 210 populations (13.15%) of newly detected in India T2D had neuropathy 6.1% had retinopathy and 1.06% had nephropathy. Risk factors of macro vascular complication such as hypertension, obesity, and dyslipidaemia were observed in 23.3%, 26%, and 27% of patients respectively. Ischemic heart disease was noticed in 6% (WHO, 2014). One-third of the study population had microvascular complications, predominantly neuropathy. Nearly 76.6% of patients had uncontrolled glycated haemoglobin (HbA1c) ≥7% (53 mmol/mol); 62% of these patients had HbA1c between 7% and 8% (53-64 mmol/mol). Glycaemic control from combination of oral hypoglycaemic agents (OHAs) with or without insulin varied between 14.2% and 24.8%.[8]

Glycaemic control

The mean±SD HbA1c, fasting plasma glucose (FPG), and postprandial glucose (PPG) values were 7.7% (61 mmol/mol)±1.09, 126.8 mg/dl (7.03 mmol/l)±19.02, and 198.27 mg/dl (11.0 mmol/l)±43.51, respectively. Nearly three-fourths (76.6%) of patients had uncontrolled HbA1c ≥7% (≥53 mmol/mol). Of patients with uncontrolled diabetes, a substantial proportion (62%) had HbA1c between 7% and 8% (53-64 mmol/mol), 33.6% had HbA1c between 8% and 10% (64-86 mmol/mol), while a minor proportion (4.4%) had HbA1c >10% (86 mmol/mol) (Figure 1). Overall, 42.4% of patients had FBG>130 mg/dl (7.2 mmol/l), of which 87.0% had HbA1c≥7% (53 mmol/mol). However, among patients FBG <130 mg/dl (7.2 mmol/l) (57.6%), 68.9% had HbA1c ≥7% (53 mmol/mol). Similarly, 62.9% of patients had PPG>180 mg/dl (10.0 mmol/l), of which 85.7% had HbA1c ≥7% (>53 mmol/mol). Of patients with obesity, 77.6% had uncontrolled HbA1c and of patients with hypertension, 81% had HbA1c ≥7% (≥53 mmol/mol). Of patients with diabetes duration >2 years, HbA1c was under control in only 21.8% (2-5 years: 22.7% and >5 years: 21.1%).[9]

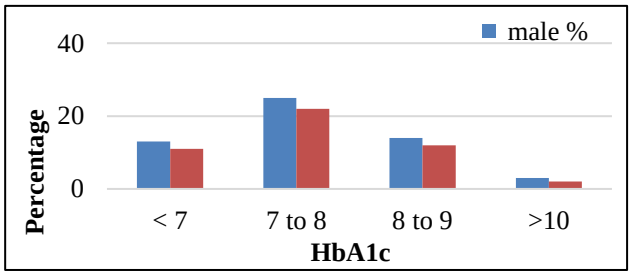

Figure 1: Percentage of patients with glycated haemoglobin (HbA1c) categories showing glycaemic control status of study population grouped by gender.

Antidiabetic therapy

Most of the patients (73%) were taking dual or triple therapy, followed by monotherapy (14%), and 12% patients were taking more than three OHAs. Insulin use was reported among 17.2% of overall patients. Of the OHAs, 83.1% were taking metformin as monotherapy or combination therapy. Multiple therapies comprised sulfonylurea + metformin pill (60%) and combinations of different drugs including gliptins (53.1%), alpha-glucosidase inhibitors (15.5%), and thiazolidinediones 10%. Most patients (86.6%) diagnosed within 2 years were on metformin therapy either alone or as combination in accordance with the recent guidelines. Of patients taking monotherapy, 33% had good glycaemic control as compared with 21.7% among patients on combination therapies. Overall, the range of glycaemic control for different combinations of OHAs with or without insulin varied between 14.2% and 24.8%. Irrespective of diabetes duration, patients on three or more OHAs and uncontrolled HbA1c levels had greater proportion of any microvascular complications (Figure 2).[8]

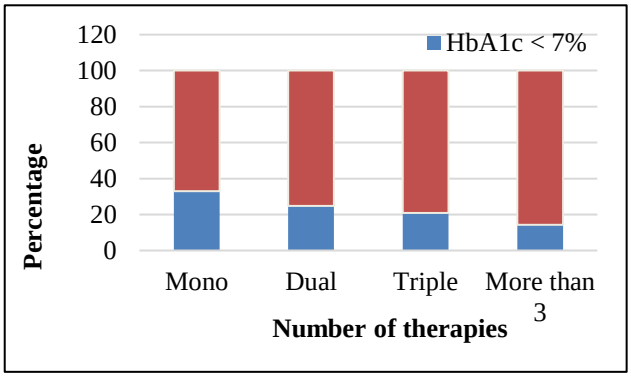

Figure 2: HbA1c status and number of hypoglycaemic therapies used (dual, triple, and more than three therapies include patients with or without insulin).

About 35.7% of the patients had at least one microvascular complication the proportion was higher for neuropathy (26.9%), followed by nephropathy (8.6%) and retinopathy (7.1%), and 15.4% patients had two or more complications. Good glycaemic control among patients with type 2 diabetes reduces the risk of diabetes-related microvascular complications.[9-11]

Overall, 80.4% of patients with any microvascular complication had uncontrolled diabetes status. The proportion of patients with microvascular complications progressively increased with duration of diabetes, especially neuropathy showing a steep rise compared with nephropathy and retinopathy. The multivariate analysis demonstrated increasing odds of having any microvascular complication with longer duration of type 2 diabetes compared with recently diagnosed diabetes (past 1-2 years, OR 1.67 (95% CI 1.52 to 1.84); past 2-5 years, OR 2.53 (95% CI 2.31 to 2.78); >5 years, OR 4.01 (95% CI 3.66 to 4.39)). Furthermore, patients with hypertension (stage I

OR=1.18 and stage II OR=1.34; p<0.05) and uncontrolled HbA1c (OR=1.28, p<0.0001) had significantly increased risk of any microvascular complication (Figure 3).[9]

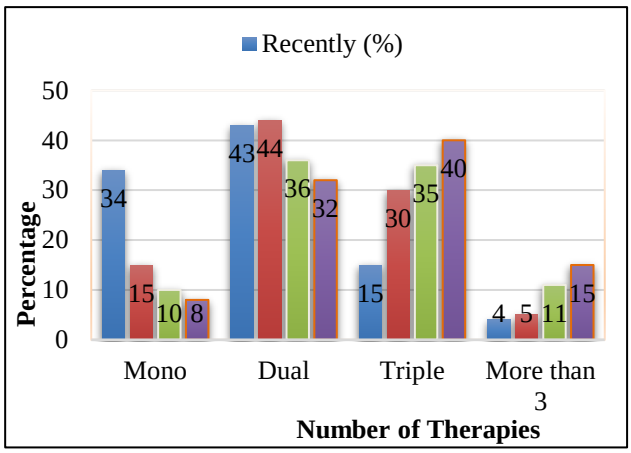

Figure 3: Percentage of patients with different duration of diabetes grouped by number of hypoglycaemic therapies.

Diabetes-related follow-up and health maintenance

In 2008 and 2013, the mean numbers of diabetes-related office visits were 2.6 and 2.5; p<0.0001, and of missed appointments were 1.2±1.9 and 1.5±1.9; p<0.0001, respectively. The percentages (%) of patients, in 2008 and 2013, who received the recommended influenza vaccine in the prior season and pneumonia vaccine within the past 10 years, were 32.7 and 38.8 and 51.8 and 61.7, respectively. Dilated eye examinations were not tracked by the electronic heath record (EHR) in 2008. This has since become more standard practice, yet the number of patients with the structured documentation of yearly dilated eye examinations remains low; only 12.9% of patients with diabetes in 2013 had a dilated eye examination documented in the structured health maintenance section of the HER.[12,13]

Thyroid dysfunction

8.33% diabetic patients had known history of hypothyroidism; 17 (1.5%) persons were diagnosed to have newly detected hypothyroidism (TSH>10 µIU/ml) during the study period. Hence, the prevalence of clinical hypothyroidism was 9.83%.

68 (5.9%) patients were newly found to have subclinical hypothyroidism. When comparison was done between the clinical hypothyroid (pre-existing and newly detected) and euthyroid persons the presence of hypothyroidism was found to be associated with female sex, hypertension, dyslipidaemia, obesity, a duration of diabetes more than 2 years, anaemia, and an elevated ESR. Alcohol intake was found to have a protective effect, but it could be due to a lower rate of alcoholism among females who were more likely to suffer from hypothyroidism due to other reasons.

When alcoholism and ESR were adjusted for sex by logistic regression analysis no significant association of alcoholism and ESR with hypothyroidism remained. No difference was found in the prevalence of abdominal obesity, poor control of hypertension or lipid parameters, microalbuminuria, renal dysfunction, plasma glucose levels, HbA1c, or hyperuricemia among patients with hypothyroidism and those without. On logistic regression analysis, only 3 parameters, namely, known dyslipidaemia (OR=1.99), overweight/obese status (OR=2.07), and anaemia (OR=2.19), were found to be more common in patients with hypothyroidism. When subclinical hypothyroid patients were compared with the euthyroid group none of the variables analysed showed a significant difference.[14,15]

Diabetic risk in depressed patients

Several studies showed that people who suffer from depression are more likely to develop T2DM.[16,17] According to a recent study antidepressant treatment may be a risk factor for suboptimal glycaemic control on the relationship between antidepressant use and glycaemic control. The study found that using multiple antidepressant subclasses significantly increased the levels of HbA1C in adults with diabetes.[18] Previous research indicated that, although the short-term antidepressant therapy of nondiabetic depression patients improves insulin sensitivity along with depression, the long-term effects may be the reverse.[19]

The exception is noradrenergic antidepressants, which can reduce insulin sensitivity in people who are not diabetic.[19] Selective serotonin re-uptake inhibitor treatment may improve the glycaemic control in depressed T2DM patients and is the only class of antidepressants with confirmed favourable effects on glycaemic control on both short and long term use.[20]

Antidepressant use over time is substantially associated with a lower risk of diabetes, suggesting that antidepressants, not depression, are linked to the incidence of DM2.[21] Antidepressant use over time is substantially associated with a lower risk of diabetes suggesting that antidepressants are linked to the incidence of T2DM. A study conducted in 2015 on 200936 depressed patients examined the impact of diabetes on depression and found that T2DM may raise the risk of complications from depression.[22]

CONCLUSION

Based on recent researches it is evident that a large population of India is suffering from diabetes and its

comorbidities on a wide scale. The increasing diabetes epidemic could have a profound impact on morbidity and mortality rates which in turn can lead to increased healthcare expenditure. Its management needs a multi-factorial approach involving primary, secondary and tertiary prevention of diabetes involving multiple stake holders. These include stimulating a healthy lifestyle to prevent diabetes (primary prevention), certifying universal healthcare coverage and access to inexpensive medicines to prevent complications (secondary prevention) and early detection and management of the complications of diabetes (tertiary prevention). These measures could help to reduce the economic costs due to diabetes and related complications.

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