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Prevalence and clinical profile of metabolic syndrome among type 1 diabetes mellitus patients in southern India

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ABSTRACT

Aim: To assess the prevalence of metabolic syndrome (MetS) among patients with type 1 diabetes mellitus(T1DM) and to look at prevalence of diabetes complications in T1DM with and without MetS.
Methods: We studied 451 T1DM patients attending a tertiary diabetes centre in Chennai, South India. T1DM was diagnosed based on absence of beta cell reserve and requirement of insulin from the time of diagnosis. Data on clinical and biochemical characteristics as well as complications details to study the prevalence were also extracted from electronic records. T1DM patients were divided into those with and without MetS[diagnosed according to the harmonizing the metabolic syndrome criteria(IDF/NHLBI/AHA/WHF/IAS/IASO)].
Results: The overall prevalence of MetS among T1DM was 22.2%(100/451). Patients with MetS were older, had longer diabetes duration, acanthosis nigricans, and increased serum cholesterol. In the unadjusted logistic regression analysis, retinopathy, nephropathy and neuropathy were associated with MetS. However after adjustment for age, gender, diabetes duration, HbA1C and BMI significant association was seen only between MetS and retinopathy [odds ratio (OR) 2.82, 95% CI 1.18–6.74, $p = 0.020$] and nephropathy [OR 4.92, 95% CI 2.59–9.33, $p < 0.001$].
Conclusion: Prevalence of MetS is high among Asian Indian T1DM patients, and its presence is associated with increased risk of diabetic retinopathy and nephropathy.

1. Introduction

The clustering of metabolic abnormalities with central obesity, glucose intolerance, hypertension and dyslipidemia is known as metabolic syndrome (MetS) (Alberti, Zimmet, & Shaw, 2006). Although there is controversy regarding the clinical significance of MetS, there is growing evidence that it is a highly prevalent condition and that it is strongly linked to future type 2 diabetes(T2DM) (Lorenzo, Okoloise, Williams, Stern, & Haffner, 2003) and cardiovascular disease (Isomaa et al., 2001). Studies from the United States and Europe have shown high prevalence rates of MetS among patients with T2DM, ranging from 70 to 89% (Beltrán-Sánchez, Harhay, Harhay, & McElligott, 2013; McGill, Molyneaux, Twigg, & Yue, 2008; Povel et al., 2013). A population-based study from Chennai, in southern India, reported a MetS prevalence of 25.8% in the general population (Deepa, Farooq, Datta, Deepa, & Mohan, 2007) and over 50% in the T2DM cohort (Enas et al., 2007). There is also evidence for ethnic diversity in co-morbid conditions associated with MetS across various populations (Shadmi, 2013).

Studies on prevalence of MetS among patients with type 1 diabetes mellitus (T1DM) are more limited in comparison to T2DM, and concern mainly patients of European origin. Studies on adults with T1DM from Finland, Scotland and Spain indicate that prevalence of MetS is around 30 to 40% (Chillarón et al., 2010; Ghosh, Collier, Hair, Malika, & Elhadda, 2010; Thorn et al., 2005). However, in studies that include children, prevalence rates of MetS are significantly lower with15.0% and 9.5% reported in Australian and Italian studies respectively (McGill et al., 2008; Valerio et al., 2014).

Obesity and insulin resistance which are typically risk factors for T2DM are considered to be the main drivers of MetS (Ghosh et al., 2010; Gordon Smith & Robinson Singleton, 2006; Valerio et al., 2014). However, nowadays due to the rapidly spreading obesity epidemic, subjects with T1DM are also showing signs of obesity and insulin resistance (Ghosh et al., 2010; Thorn et al., 2005). These subjects

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conjunctly also develop a secondary resistance to their injected insulin. This clinical condition is termed as "double diabetes", as it alludes to the fact that there is a shift from a T1DM to a T2DM clinical profile. Such individuals typically tend to have an increased risk of MetS (Kilpatrick, Rigby, & Atkin, 2007; Teupe & Bergis, 1991). There is a lack of studies on MetS in T1DM from developing countries where obesity rates are in general, far lower and where there is limited data on the association between MetS and the vascular complications of T1DM.

The aim of this study is to assess the prevalence of MetS in T1DM patients attending a tertiary centre in southern India, and to look at the prevalence of diabetes-related complications in T1DM subjects with and without MetS.

2. Methods

2.1. Selection of subjects

Data for this study were extracted from the diabetes electronic medical record (DEMR) system at Dr. Mohan's Diabetes Specialties Center (DMDSC), a tertiary diabetes centre at Chennai in southern India. Since the inception of DMDSC in 1991, approximately 275,000 diabetic patients have been registered, of whom around 1665 (0.60%) were diagnosed to have T1DM based on criteria given below. The present study population was selected from those T1DM patients who satisfied the following criteria: age 10 years and above at first visit and having documented measurements for all five MetS criteria (waist circumference, blood pressure, HDL cholesterol, serum triglyceride, and fasting plasma glucose levels) at first visit (Fig. 1). All relevant data from the 451 T1DM patients who met these criteria were retrieved from the electronic database, and used in this study. Informed consent was obtained from all study subjects who were above 18 years of age. For those below 18 years of age assent was obtained from the patient and consent from the parent. The study was approved by the institutional ethics committee.

2.2. Clinic procedures

At first visit to our centre, every patient is registered with a unique identifier number, enabling detailed tracking of patients over time. Following initial diagnosis and receipt of this unique DEMR registration number, each patient undergoes a set of standard procedures. The patient is first seen by a dietician or diabetes educator, who procures an in-depth medical history, including current diabetes symptoms, past illness, dietary details, family history of diabetes, current medications, and past surgical procedures. This is followed by a complete physical examination by the physician, specifically looking for signs of insulin resistance like acanthosis nigricans and skin tags. Detailed anthropometric measurements are then collected using standardized techniques. Height is measured in centimeters using a stadiometer, weight is measured in kilograms using an electronic scale, and waist circumference is measured in centimeters using a non-stretchable fiber measuring tape. The body mass index (BMI) is calculated as weight in (kg) divided by height in meters squared. Blood pressure is measured with a mercury sphygmomanometer, in the sitting position, and is rounded off to the nearest 2 mmHg.

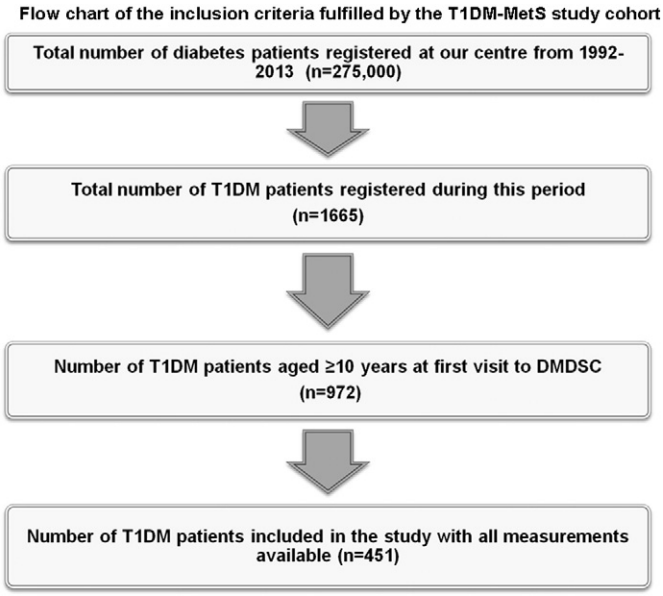

Fig. 1. Flow chart of the inclusion criteria fulfilled by the T1DM-MetS study cohort.

All biochemical tests are performed in our laboratory, which is certified by the College of American Pathologists (CAP) and the National Accreditation Board for Testing and Calibration of Laboratories (NABL). Fasting plasma glucose samples are collected after an overnight fast for a minimum of 8 hours. The post-prandial samples are obtained 90 minutes after consumption of a standard south Indian breakfast for glucose and stimulated C-peptide measurement (Snehalatha, Ramachandran, Mohan, & Viswanathan, 1987).

Up until 2008, the glucose oxidase method was performed to measure plasma glucose levels, the CHOD-PAP and GPO-PAP methods were utilized for serum cholesterol and triglycerides levels, respectively, and the modified kinetic method of Jaffe was conducted to measure serum creatinine levels using a CIBA Corning Express Plus Auto Analyzer (Corning, USA). Currently, plasma glucose measurements are done by the hexokinase method, while total cholesterol, triglycerides, HDL, and serum creatinine are measured using a Hitachi 912 Autoanalyzer employing commercial kits (Mannheim, Germany). Glycated hemoglobin (HbA1c) is analyzed by the Bio-Rad HPLC method with the Variant machine (Bio-Rad, Hercules, CA, USA). LDL cholesterol is calculated using the Friedewald formula (Friedewald, Levy, & Fredrickson, 1972).

2.3. Diagnosis of T1DM and MetS

Diabetes was diagnosed based on either a fasting plasma glucose (FPG) level [≥126 mg/dl (7.0 mmol/L)] or a 2-hour post glucose level [≥200 mg/dL (11.1 mmol/L)] or if they were receiving antidiabetic drugs (Alberti & Zimmet, 1998). T1DM was defined based on the sudden onset of symptoms such as polyuria, polydipsia, unexplained weight loss, and/or diabetic ketoacidosis, a fasting C-peptide assay < 0.3 pmol/ml and stimulated C-peptide <0.6pmol/ml, and continuous need for insulin injections from the time of diagnosis of diabetes (Fida et al., 2001).

According to the current harmonizing criteria, developed jointly by the International Diabetes Federation Task Force on Epidemiology and Prevention; National Heart, Lung, and Blood Institute; American Heart Association; World Heart Federation; International Atherosclerosis Society; and international association for the study of obesity, any 3 of the following 5 components constitutes metabolic syndrome (Alberti et al., 2009):

1) Elevated waist circumference – for children and adolescents, if waist circumference was ≥ 90th percentile, which was defined based on a prior study on the Asian Indian population, in which age-and gender-specific percentiles were determined (Kuriyan et al., 2011). For adults, ethnic specific cutoff points of >90 cm and >80 cm for men and women, respectively, were used to define elevated waist circumference (WHO, 2000).
2) Elevated serum triglyceride levels ≥1.7 mmol/L (150 mg/dl) or treatment for hypertriglyceridemia.