Review Article

Metabolic Syndrome and Diabetes: A Review

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ABSTRACT

The prevalence of metabolic syndrome is increasing worldwide. Several factors such as hyperglycemia are associated with risk of developing metabolic syndrome. Metabolic syndrome is a clinical tool for identification of subjects at risk of diseases such as type 2 diabetes mellitus, which could be a predictor of metabolic syndrome. There may be an association between diabetes, metabolic syndrome and cardiovascular morbidity and mortality. This study aimed to review the literature on diabetes, as a component of metabolic syndrome.

KEYWORDS: Metabolic syndrome; Diabetes; Diseases

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INTRODUCTION

Metabolic syndrome (MetS) is a major public-health problem worldwide. It increases the risk of developing type 2 diabetes mellitus (T2DM) and cardiovascular disease (CVD) by 5- and 2-fold, respectively [1]. Many studies have shown that patients with MetS are at greater risk of stroke (2-4 fold), myocardial infarction (3-4 fold) and mortality (2-fold) compared to those without the syndrome [2]. In 1920, Kylin, a Swedish physician, showed the association of hypertension, hyperglycemia and gout [3]. In 1947, Vague indicated that visceral obesity is associated with metabolic disorders in patients with CVD and T2DM [4]. In 1965, Avogaro and Crepaldi revealed a syndrome that included hypertension, hyperglycemia and obesity [5]. In 1988, Reaven demonstrated "Syndrome X" as a concept of insulin resistance [6]. In 1989, Kaplan introduced the syndrome "The Deadly Quartet", which is due to upper body obesity, glucose intolerance, hypertriglyceridemia, and hypertension [7]. In 1992, Haffnerre introduced "The Insulin Resistance Syndrome" [8].

There are several criteria for diagnosis of MetS [9]. The World Health Organization (WHO) in 1998 and European Group for the Study of Insulin Resistance in 1999 provided definitions for MetS [10, 11]. The National Cholesterol Education Program-Adult Treatment Panel (NCEP/ATP) in 2001 [12], the American Association of Clinical Endocrinologists in 2003 [13] and the International Diabetes Federation (IDF) in 2005 [14] also reported their definitions.

It has believed that high prevalence of MetS is the reason for more recent study. Many studies have shown that the worldwide prevalence of MetS ranges from almost 10% to 84%. The prevalence of MetS is affected by geographic location, sex, age, race, sedentary lifestyle, high body mass index and ethnicity [15, 16]. Study of Cameron et al. indicated that the prevalence of MetS and its components is associated with genetic background, diet, levels of physical activity, smoking, family history of diabetes, and education level [17]. Age-related study of Park et al. have revealed that the prevalence of MetS ranges from 20 to 70 years in males and females [18], while findings of Ponholzer et al. showed that prevalence of MetS ranges from 32.6% to 41.5% among

postmenopausal females [19]. Study of Marjani et al. showed that the prevalence of MetS in patients with T2DM is higher in females (53.27%) than in males (48.71%) [20]. Marjani et al. also indicated that the frequency of MetS in T2DM patients was 75.42% and 76.79% according to ATPIII and IDF diagnostic criteria, respectively. In addition, females have been affected more than men according to both criteria [21]. The frequency of MetS in Fars and Sistani ethnic groups in Gorgan (Iran) was 20.62% and 23.75%, respectively [22,23]. The prevalence of MetS in Korean and Chinese females was 13.8% [24] and 17.8% [25], respectively. Studies of Eshtiaghi [26], Ainy [27], Deilbert [28], Figueiredo Neto [29] and Heidari et al. [30] indicated that the prevalence of MetS is 18.3%, 53%, 23%, 24% and 44.9%, respectively. The aim of this study was to review the literature on the association of diabetes with MetS.

Diabetes, a component of MetS

T2DM is a chronic and fatal disease with an increasing prevalence worldwide [31]. MetS is a clinical tool for identification of subjects at risk of some diseases such as CVD and T2DM. Several factors may lead to development of MetS [32]. MetS is associated with insulin resistance, visceral adiposity, atherogenic dyslipidemia, endothelial dysfunction, genetic susceptibility, hypertension, thrombophilia, and chronic stress [33]. According to the WHO, diabetes in defined as fasting plasma glucose of ≥7.0mmol/l (126mg/dl) or 2-h venous plasma glucose ≥11.1 mmol/l (200mg/dl) following ingestion of 75g oral glucose load [34]. The number of patients with T2DM worldwide has been estimated to increase to 300 million by 2025 [35].

High glucose level is a component of MetS [1, 36]. Many studies have reported insulin resistance as a risk factor for MetS [37]. It is well demonstrated that insulin resistance causes hyperglycemia. A study has shown that insulin resistant was considered in most subjects with the MetS [38]. Moreover, there seems to be an association between MetS and pre-diabetes. In addition, MetS increases the risk of developing diabetes by 5-fold [39]. Impaired fasting glucose (IFG) or impaired glucose tolerance (IGT) in patients with MetS may also increase the risk of developing diabetes. Some findings have indicated that MetS without diabetes may increase the risk of diabetes by almost 5-fold, whereas in patients with IFG or IGT, the risk of diabetes is 5- to 7-fold higher compared to subjects with normal blood glucose [40]. Thus, there may be an association between IFG or IGT, MetS and the increased risk of diabetes. Diabetologists believe that diabetes is a risk factor for CVD and microangiopathic disease. CVD is the most important complication of diabetes. It is accounted for up to 80% of the macrovascular complications [41,42]. Diabetic patients also have higher risk of developing hypertension, dyslipidemia, and obesity. They may also be at risk of coronary heart disease, stroke, and peripheral vascular disease along with retinopathy, chronic kidney disease, bladder dysfunction, erectile dysfunction, orthostatic hypotension, gastroparesis, and skin disorders [33]. Studies have revealed that there is an association between increased glucose level and incidence of microangiopathy (diabetic nephropathy, retinopathy, and neuropathy). Many molecular mechanisms have been suggested to explain the effect of increased glucose levels in microangiopathy. These mechanisms include protein kinase C activation, formation of advanced glycation end products, formation of reactive oxygen species, flux through the hexosamine pathway, the polyol pathway induction, overexpression of growth factors and inflammatory cytokines, and defective

insulin signaling [43, 44]. The prevalence of metabolic disorders is increasing worldwide [45]. Several risk factors are associated with this increase [46]. MetS with or without diabetes, is a predictor of coronary heart disease and premature mortality [47-49]. In diabetic patients, MetS is considered a risk factor for chronic microvascular complications [47-48, 50-52]. Some studies have shown association of MetS and microvascular complications in diabetics [53, 54].

Clinical identification of MetS patients is important for management and treatment to reduce the potential risk of subsequent diseases [55]. Lifestyle changes, primarily weight loss, change in diet, exercise, and pharmacological treatment are effective for controlling the risk of complications [56]. However, the clinical management of patients with MetS is not easy. This may be due to lack of a known method for prevention or improvement of all risk factors (components of MetS) of MetS.

Physicians use different methods to treat each component of MetS. For example, drug therapy is used to reduce blood pressure, blood glucose, and triglycerides. Lifestyle modification is another method that can be advised by physicians and dieticians [57]. Although the impact of lifestyle modification is less than that of drug therapy, it can be useful for controlling the metabolic risk factors [58]. Weight loss is also suggested for treatment of patients with MetS, which can be carried out by limiting calorie intake, behavioral change, physical activity and anti-obesity medications [58]. Studies have shown that weight loss can lower blood pressure, affect lipid profile (decrease triglyceride and increase high-density lipoprotein levels), and improve insulin resistance [59-60]. Weight loss could also reduce fasting blood glucose, insulin, hemoglobinA1c levels, and contribute to abdominal fat loss [61, 62]. It seems to improve an unusual component of MetS and limit the progression of diabetes [63]. According to the Finnish Diabetes Prevention Study [64] and the US Diabetes Prevention Program [65], diet and exercise have significant effects on the progression of IGT to T2DM. Some studies have revealed association of hyperlipidemia and hyperglycemia (the components of the MetS) with low glycemic index foods [66], while the prevalence of insulin resistance and MetS is associated with high glycemic index foods [67].

Implementation of treatment guidelines provided by the NCEP [68], the seventh Joint National Commission for treatment of high blood pressure [69], the American Diabetes Association [70], the American Heart Association [36], and the National Institute of Health Obesity Initiative [71] could also be used to prevent risk factors of MetS.

CONCLUSION

Several factors can prevent the development of MetS. T2DM is suggested as a predictor of MetS. There is an association between diabetes, MetS and cardiovascular morbidity and mortality.

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