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Renal damage in the metabolic syndrome (MetSx): Disorders implicated

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ABSTRACT

The prevalence of metabolic syndrome is increasing worldwide and has become a risk factor for the development of chronic kidney disease. The complex linkage between metabolic syndrome and chronic kidney disease is under research and the factors involved beyond the biological pathogenesis include demographic, sociological and psychological factors that are related to the metabolic syndrome prevalence. The social context of disease causation is as relevant to today's clinical scientist and practitioner as biomarker-directed risk stratification and therapy. The aim of this review is to compare the criteria for diagnosis among different international health organizations, identifying all factors that contribute to the development of this association between metabolic syndrome and chronic kidney disease, and categorizing them by those that could be useful for preventive strategies. In addition, patients with metabolic syndrome have microvascular disease characterized by microalbuminuria, decreased glomerular filtration rate, tubular atrophy, interstitial fibrosis, and glomerulosclerosis. These effects may be due to insulin resistance, hypertension, dyslipidemias, activation of inflammatory processes, fibrotic, dysbiosis and generation of oxidative stress; which cause an imbalance in the main vasoactive factors and thus endothelial dysfunction, deteriorating the renal function. Furthermore, since unhealthy eating habits and a sedentary lifestyle are among the strongest risk factors related to these diseases, lifestyle interventions programs have been recommended for facilitating positive changes in behavior at the individual level. However, further research is needed to promote multiple social, economic and political transformations, shifting the intervention emphasis from individual education, counseling, regimens and medications to community, national and global institutions.

1. Introduction

Metabolic syndrome (MetSx) is a set of metabolic abnormalities that Avogaro et al. described for the first time as an association between obesity, hyperlipidemia, hypertension, diabetes and cardiovascular diseases defined as a plurimetabolic syndrome (Avogaro et al., 1967). Haller described MetSx (Haller, 1977), called "Syndrome X" (Reaven, 1995, 2004), and included insulin resistance as a central player. Multiple international health organizations define the presence of MetSx in individuals with insulin resistance, plus another two out of four following conditions: (1) visceral obesity, (2) elevated levels of triglycerides and/or low-density lipoprotein-Cholesterol (LDL-C), 3) hypertension and 4) elevated serum glucose levels (hyperglycemia) on fasting (Table 1). Numerous studies reported that the distribution of visceral fat is a major risk factor for cardiovascular diseases (Masson et al., 2017) and chronic kidney disease (CKD) (Huh et al., 2016); also obesity by itself is considered an independent risk factor for the development of the CKD (Panwar et al., 2015; Prasad, 2014) and breast, ovary, testicular and bladder cancers (Bogefors et al., 2017; Esposito et al., 2012). Thereby, MetSx is a specific set of abnormalities that contribute to cardiovascular morbimortality and type 2 diabetes mellitus (Reaven, 2004; Xanthakis et al., 2015). More recently, a group of researchers reported that the MetSx is a multifactorial disease caused by a complex interaction of genetics and environmental factors, and contributes to the deterioration of the disorders related to this syndrome (Mazidi et al., 2016).

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Table 1
Criteria for diagnosing metabolic syndrome.

Criteria	WHO	EGIR	NCEP-ATP III	AHA	IDF
	Individuals with three or more of the following conditions:				
1) Hypertension	≥140/≥90 mmHg	≥140/≥90 mmHg	≥130/≥85 mmHg	≥130/≥85 mmHg	≥130/≥85 mmHg
2) HDL cholesterol	♀ ≤ 39 mg/dl ♂ ≤ 35 mg/dl	♀ ≤ 39 mg/dl ♂ ≤ 39 mg/dl	♀ ≤ 50 mg/dl ♂ ≤ 40 mg/dl	♀ ≤ 50 mg/dl ♂ ≤ 40 mg/dl	♀ ≤ 50 mg/dl ♂ ≤ 40 mg/dl
3) Triglycerides	≥ 150 mg/dl	≥ 150 mg/dl	≥ 150 mg/dl	≥ 150 mg/dl	≥ 150 mg/dl
4) Serum glucose levels on fasting			> 110 mg/dl	> 100 mg/dl	> 100 mg/dl
5) Visceral obesity	♀ ≥ 88 cm ♂ ≥ 90 cm	♀ ≥ 80 cm ♂ ≥ 94 cm	♀ ≥ 88 cm ♂ ≥ 102 cm	♀ ≥ 88 cm ♂ ≥ 102 cm	♀ ≥ 80 cm ♂ ≥ 94 cm

World Health Organization (WHO, 1998); European Group for the study of Insulin Resistance (EGIR, 1999); National Cholesterol Education/Adult Treatment Panel III (NCEP-ATPIII, 2004); American Heart Association (AHA, 2005) and International Diabetes Federation (IDF, 2005).

Recently, CKD has gained attention because kidney function deteriorates rapidly in those patients with MetSx. The mechanisms by which MetSx is associated with a decrease in kidney function have been described, and while some literature attributes it more to metabolic dysfunction, for instance insulin resistance, there is also literature that has identified adipokine disturbances and lately, dysbiosis as important contributors. However, the current definition of both diseases depends on the criteria of health organizations or institutions in each country or region, leading to the question of whether the criteria for diagnosis can be compared around the world. Additionally, one of the main concerns about the association between MetSx and CKD is the deterioration of the patients' health, which in severe cases might end up in disabilities beyond the economic impact not only for the patients themselves but for the health system of each country. Chronic diseases affect the quality of life and functional status of patients, thus substantially increasing the use of healthcare services and the costs of secondary health care (Anderson, 2009). Yet at the same time the economic and political forces of globalization are responsible for the changed living conditions and behaviors leading to the risk factors for chronic diseases (Manderson, 2010; Wiedman, 2010).

In this review, we first compare the criteria for diagnosis among different international health organizations. Secondly, we identify all factors that contribute to the development of the association between MetSx and CKD and then we categorize them by those that could be useful for preventive strategies for early detection or potential targets for treatment.

2. Prevalence of metabolic syndrome in the world

MetSx constitutes an economic and public health problem that adversely affects life quality (measured by 36 items that explore eight dimensions of health (Donini et al., 2016)) and is associated with risk factors such as gender, age, ethnicity[1] (Gravlee and Sweet, 2008), sedentism[2] (Ricciardi, 2005), lifestyle and diet (Donini et al., 2016). Also, in the last decade, intestinal microbiota has been identified as a significant player (Bischoff et al., 2016; Org et al., 2017). However, prevalence statistics depend on the criteria for clinical diagnosis of the World Health Organization (WHO, 1998), the European Group for the study of Insulin Resistance (EGIR, 1999), the National Cholesterol Education/Adult Treatment Panel III (NCEP-ATPIII, 2004), the American Heart Association (AHA, 2005) and the International Diabetes Federation (IDF, 2005; Lopes et al., 2016; Pucci et al., 2017) (Table 1).

An updated study from 2003 to 2012 showed a MetSx prevalence of 33% in the United States (Aguilar et al., 2015), 26.6% in Europe (Vishram et al., 2014), 49.5% in the Middle East (Hajat and Shather, 2012), 24% in China (Pan et al., 2016), 32% in Brazil (De Carvalho Vidigal et al., 2013) and 36.8% in Mexico (Rojas et al., 2010); all countries indicated significant variable impact by gender and age (Table 2). According to NCEP-ATPIII, the MetSx is present in 82% of cases with type 2 diabetes mellitus, 64.7% of hypertensive patients, 54.5% of hypertriglyceridemic patients and 61.5% of individuals with microalbuminuria, defined as excretion of albumin in urine (González and Lavalle, 2009).

A homogenization in the definition adjusted to gender and ethnicity was carried out in 2009; however, the criteria mostly used in clinical studies are the NCEP-ATPIII and IDF, where a higher prevalence of MetSx associated to factors such as age and gender has generally been

[1] See (Gravlee and Sweet, 2008) for a discussion about the use of the concepts 'race' and 'ethnicity' and the importance of identifying the sociocultural processes that generate health inequalities.

[2] See (Ricciardi, 2005) for a thorough discussion on this concept and its implications for identifying effective intervention strategies and public policy changes to promote a physically active lifestyle.