

Prevalence of metabolic syndrome and level of serum testosterone among erectile dysfunction patients attending kasr Alaini hospital

THESIS

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Abstract

The aim of this work was to determine the influence of metabolic syndrome (MS) and serum testosterone in patients with erectile dysfunction (ED) and their possible association. This cross sectional study included 100 patients suffering from erectile dysfunction. Patients subjected to full history taking, full examination, investigation and, evaluation by IIEF-5, the results of the present study revealed that: Prevalence of metabolic syndrome among erectile dysfunction patients was 35% according to NCEP ATP III and 42% according to IDF, The presence of metabolic syndrome is associated with more severe erectile dysfunction. Total testosterone was significantly lower in metabolic syndrome patients.

Key word:

Metabolic syndrome,
Erectile dysfunction.

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Introduction

The Metabolic syndrome has received considerable attention in recent years due to its association with increasingly common pathophysiological states such as heart failure (**Ingelsson et al., 2006**), type 2 diabetes mellitus (**Imam et al., 2007**), and erectile dysfunction (ED) (**Bansal et al., 2005**). Metabolic syndrome is considered the main threat for public health in the 21st century (**Taskinen. 2007**) and is associated with an increased risk of CVD, irrespective of which metabolic syndrome definition is used (**Table 1**). **Bataille et al., (2006)** studied over 10,000 men in France and Northern Ireland, and found that metabolic syndrome predicts the risk of having coronary heart disease in multiple areas of Europe. Obesity and physical inactivity are known to be risk factors for the development of metabolic syndrome (**Ford & Li. 2006**) and it is well known that obese individuals are more likely to develop insulin resistance than non-obese individuals. This insulin resistance predisposes these individuals to metabolic risk factors such as elevated serum TG, reduced HDL levels, elevated fasting glucose levels, and high blood pressure (**Hu et al., 2004**). These metabolic abnormalities, in conjunction with abdominal (visceral) obesity, represent the classical symptoms of metabolic syndrome. According to the third National Health and Nutrition Examination Survey (**Ford et al., 2002**), the age-adjusted prevalence of metabolic syndrome in American men was 23.7%. There is considerable evidence linking metabolic syndrome to androgen deficiency.

Metabolic syndrome

The “metabolic syndrome” (MS) is a clustering of components that reflect overnutrition, sedentary lifestyles, and resultant excess adiposity. The metabolic syndrome includes the clustering of abdominal obesity, insulin resistance, dyslipidemia, and elevated blood pressure and is associated with other comorbidities including the prothrombotic state, proinflammatory state, nonalcoholic fatty liver disease, and reproductive disorders **(Marc-Andre et al., 2008)**.

It is estimated that around 20-25 percent of the world's adult population have the metabolic syndrome and they are twice as likely to die from and three times as likely to have a heart attack or stroke compared with people without the syndrome **(Stern et al., 2004)**.

In addition, people with metabolic syndrome have a fivefold greater risk of developing type 2 diabetes. They would add to the 230 million people worldwide who already have diabetes, one of the most common chronic diseases worldwide and the fourth or fifth leading cause of death in the developed world. The clustering of cardiovascular diseases (CVD) risk factors that typifies the metabolic syndrome is considered to be the driving force for a new CVD epidemic **(diabetes Atlas, third edition, IDF, 2006)**.

Historical background

In 1988 Gerald Reaven presented the Banting Lecture at the American Diabetes Association meeting. The title of his lecture was “The Role of Insulin Resistance in Human Disease”, and the corresponding article was published in the same year **(Reaven, 1988)**. He gave pathophysiological arguments for the existence of a “syndrome X”, in which he included insulin resistance, hyperinsulinaemia, hyperglycaemia, dyslipidaemia, arterial hypertension.

Several years later, during the Claude Bernard Lecture of the European Society for the Study of Diabetes (EASD), Reaven included central adiposity in the syndrome, and noted the importance of free fatty acids **(Reaven, 1995)**. While Reaven’s description was based on the pathophysiology of insulin resistance, the syndrome that he described was not precise and it was not possible to identify individuals as having the syndrome: the combination of abnormalities, the numbers of abnormalities, the thresholds defining the abnormalities were not given. The only abnormality Reaven quantified was insulin resistance, which he affirmed to be present in 25% of the adult population.

Reaven was not the first to propose such a syndrome. Kylin, in 1923, described the clustering of hypertension, hyperglycaemia and gout **(Kylin, 1923)**. In France, Jean Vague, at the end of the 1940s, documented the association between central adiposity, diabetes, atherosclerosis and gout **(Vague, 1947)**. Later, **Avogaro et al. (1967)** described a metabolic syndrome and in 1985 Michaela Modan proposed that hyperinsulinaemia was the link between hypertension, obesity and glucose intolerance **(Modan et al., 1985)**.

Following the description of the syndrome by Reaven, it has become a major theme of research and of public health interest. The number of publications on the subject is ample evidence of the importance given to the syndrome by clinicians and researchers (over 18000 citations to the “metabolic syndrome” in PubMed, December 2006 – with more than 3000 citations in 2006 alone).

Components of Metabolic Syndrome

There are 6 components of the metabolic syndrome that relate to CVD:

- Abdominal obesity
- Atherogenic dyslipidemia
- Raised blood pressure
- Insulin resistance $\pm$ glucose intolerance
- Proinflammatory state
- Prothrombotic state

These components of the metabolic syndrome constitute a particular combination of what adult treatment panel III (ATP III) terms *underlying*, *major*, and *emerging* risk factors. According to ATP III, *underlying* risk factors for CVD are obesity (especially abdominal obesity), physical inactivity, and atherogenic diet; the *major* risk factors are cigarette smoking, hypertension, elevated LDL cholesterol, low HDL cholesterol, family history of premature coronary heart disease (CHD), and aging; and the *emerging* risk factors include elevated triglycerides, small LDL particles, insulin resistance, glucose intolerance, proinflammatory state, and prothrombotic state **(Adult Treatment Panel III 2002)**.

For present purposes, the latter 6 components are designated *metabolic risk factors*. Each component of the metabolic syndrome will be briefly defined.

- ***Abdominal obesity*** is the form of obesity most strongly associated with the metabolic syndrome. It presents clinically as increased waist circumference.
- ***Atherogenic dyslipidemia*** Lipid abnormalities, particularly high triglycerides and low HDL-C, are strongly associated with insulin resistance and are criteria for the metabolic syndrome (**Lewis et al., 2002**). Studies in rats have shown that hyperinsulinemia stimulates the synthesis of fatty acids by increasing the transcription of genes for lipogenic enzymes in the liver, Fatty acids in turn stimulate increased production of very-low-density lipoprotein. It is unknown whether insulin resistance induces dyslipidemia or whether insulin resistance and dyslipidemia are associated via an underlying cause. (**Assimacopoulos et al., 1995**).
- ***Elevated blood pressure*** The relation between hypertension and insulin resistance is confounded by the significant independent relation between hypertension and obesity. Increased sympathetic tone has been associated with obesity, and both insulin and leptin appear to have a direct effect on sympathetic nervous system activity. Insulin infusions stimulate sodium retention by the kidney, and insulin stimulates vascular smooth muscle growth. Fasting insulin, used as an estimate of insulin resistance, has been significantly correlated with blood pressure (**Haynes et al., 1997**). Similarly, leptin has direct central effects that increase sympathetic

outflow to the kidney. It has been hypothesized that selective leptin resistance maintains leptin-induced sympathetic activation in obesity, which permits leptin to play an important role in the pathogenesis of obesity-related hypertension and metabolic syndrome (**Correia and Rahmouni. 2006**).

- ***Insulin resistance*** is present in the majority of people with the metabolic syndrome. It strongly associates with other metabolic risk factors and correlates univariately with CVD risk. These associations, combined with belief in its priority, account for the term insulin resistance syndrome. Even so, mechanisms underlying the link to CVD risk factors are uncertain. Patients with longstanding insulin resistance frequently manifest glucose intolerance, another emerging risk factor. When glucose intolerance evolves into diabetes-level hyperglycemia, elevated glucose constitutes a major, independent risk factor for CVD.
- ***A proinflammatory state***, recognized clinically by elevations of C-reactive protein (CRP), is commonly present in persons with metabolic syndrome. Multiple mechanisms seemingly underlie elevations of CRP. One cause is obesity, because excess adipose tissue releases inflammatory cytokines that may elicit higher CRP levels.
- ***A prothrombotic state***, characterized by increased plasma plasminogen activator inhibitor (PAI)-1 and fibrinogen, also associates with the metabolic syndrome. Fibrinogen, an acute-phase reactant like CRP, rises in response to a high-cytokine state. Thus, prothrombotic and proinflammatory states may be metabolically interconnected.

Criteria for Clinical Diagnosis of Metabolic Syndrome

At least 3 organizations have recommended clinical criteria for the diagnosis of the metabolic syndrome. Their criteria are similar in many aspects, but they also reveal fundamental differences in positioning of the predominant causes of the syndrome. Each will be reviewed briefly.

(1) World Health Organization

In 1998, a World Health Organization (WHO) consultation group outlined a provisional classification of diabetes that included a working definition of the metabolic syndrome **(Alberti and Zimmet. 1998)**. This report was finalized in 1999 and placed on the WHO website (see Table 1). The guideline group also recognized CVD as the primary outcome of the metabolic syndrome. However, it viewed insulin resistance as a required component for diagnosis. Insulin resistance was defined as 1 of the following: type 2 diabetes; impaired fasting glucose (IFG); impaired glucose tolerance (IGT), or for those with normal fasting glucose values (≥ 110 mg/dL), a glucose uptake below the lowest quartile for background population under hyperinsulinemic, euglycemic conditions. In addition to insulin resistance, 2 other risk factors are sufficient for a diagnosis of metabolic syndrome. A higher blood pressure was required than in ATP III. BMI (or increased waist:hip ratio) was used instead of waist circumference, and microalbuminuria was listed as one criterion. The requirement of objective evidence of insulin resistance should give more power to predict diabetes than does ATP III, but like ATP III, the presence of type 2 diabetes does not exclude a diagnosis of metabolic syndrome. A potential disadvantage of the WHO criteria is that special testing of glucose status beyond routine clinical assessment may be necessary to diagnose metabolic syndrome **(World Health Organization report.1999)**.

(2) National cholesterol education programme ATP III

Criteria of ATP III are shown in **Table 1**. When 3 of 5 of the listed characteristics are present, a diagnosis of metabolic syndrome can be made. The primary clinical outcome of metabolic syndrome was identified as Coronary heart disease/Cardiovascular disease. Abdominal obesity, recognized by increased waist circumference, is the first criterion listed. Also listed are raised triglycerides, reduced HDL cholesterol, elevated blood pressure, and raised plasma glucose. Cutpoints for several of these are less stringent than usually required to identify a categorical risk factor, because multiple marginal risk factors can impart significantly increased risk for CVD. Explicit demonstration of insulin resistance is not required for diagnosis; however, most persons meeting ATP III criteria will be insulin resistant. Finally, the presence of type 2 diabetes does not exclude a diagnosis of metabolic syndrome (**Adult Treatment Panel III 2002**).

(3) International Diabetes Federation (IDF) criteria

According to IDF definition, for a person to be defined as having the metabolic syndrome they must have: Central obesity (defined as waist circumference ≥ 94 cm for European men and ≥ 80 cm for European women, with ethnicity specific values for other groups, (**Table 2**) plus any two of the following four factors: blood pressure $\geq 130/85$ mmHg, fasting plasma glucose ≥ 100 mg/dl, serum triglyceride ≥ 150 mg/dl, and HDL cholesterol < 40 mg/dl (**Alberti et al., 2005**). (**TABLE 1**)