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LIST OF ABBREVIATIONS

AACE	the American Association of Clinical Endocrinologists
ADA	American Diabetes Association
Pk	protein kinase
BMI	body mass index
BP	blood pressure
BPA	bisphenol A
CETP	cholesterol ester transfer protein
CNS	central nervous system
CRP	C-reactive protein
CVD	cardiovascular disease
DBP	diastolic blood pressure
DHEA	Dehydroepiandrosterone
DHT	Dihydrotestosterone
E2	estradiol
EGIR	The European Group for the Study of Insulin Resistance
ERs	Estrogen receptors
ET-1	Endothelin-1
FFAs	free fatty acids
FIELD	Fenofibrate Intervention and Event Lowering in Diabetes

FMD	flow-mediated dilation
GLUT4	glucose transporter 4
HDL	high-density lipoprotein
HDL-C	high-density lipoprotein cholesterol
HOMA	homeostatic model assessment
$HOMA_{IR}$	homeostatic model assessment of insulin resistance
HSL	hormone-sensitive lipase
IDF	International Diabetes Federation
IGT	impaired glucose tolerance
IL	interleukin
IRS	insulin receptor substrate
LDL	low-density lipoprotein
MetS	metabolic syndrome
NCEP	National Cholesterol Education Program Adult
NFk-B	nuclear factor kappa-beta
NHANES	National Health and Examination Survey
NO	nitric oxide
NOS	nitric oxide synthase
PDE	Phosphodiesterase
PI3K	phosphoinositide 3-kinases
PRA	Plasma rennin activity
RAS	renal artery stenosis
RCT	randomized clinical trials
SBP	systolic blood pressure

SHBG	sex hormone-binding globulin
ICAM-1	Intercellular Adhesion Molecule 1
sVCAM-1	vascular cell adhesion molecule-1
TAG	triacylglycerol
TG	Triglycerides
TNF-α	tumour necrosis factor alpha
tPA	tissue-type plasminogen activator
TRT	testosterone replacement therapy
VLDL	very low density lipoprotein
VSM	vascular smooth muscle
vWF	Von Willebrand factor
WC	Waist Circumference
WHO	the World Health Organization
WHR	waist/hip ratio

Association of sex hormones with metabolic syndrome among Egyptian males

Thesis

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Introduction

Metabolic syndrome is associated with increased risk of cardiovascular disease (CVD) and mortality ***(Aijaz et al., 2008).*** In fact, the presence of even 1 or 2 components of the metabolic syndrome increases overall mortality compared with the absence of any component of the metabolic syndrome. Metabolic syndrome even predicts the occurrence of sudden death, independent of the presence of other cardiovascular risk factors. ***(Escobedo et al., 2009).***

Epidemiological studies have shown that low testosterone is associated with metabolic syndrome (MetS) in Caucasian and middle- aged Japanese men. ***(Akishita et al., 2010)***. In addition, numerous studies have found inverse associations between the severity of features of the metabolic syndrome and plasma testosrerone ***(Saad and Gooren., 2011)*** .

Men show higher rates of cardiovascular morbidity and mortality than pre- menopausal women and this sexual dimorphism may be related to sex- specific effects of sex steroids on cardiovascular risk factors ***(Tomaszewski et al ., 2009).***

Endogenous estrongen levels among females have been linked to several components of the metabolic syndrome, including glucose tolerance, lipid metabolism and blood pressure, free estradiol levels were significantly higher among women with the metabolic syndrome than in women without metabolic syndrome in two separate studies ***(Goulart et al., 2009)***.

The increasing prevalence of metabolic syndrome (MS) with age in older men has been linked with decreasing testosterone levels. Interestingly,while testosterone levels decline with age, estradiol (E2) levels remain relatively stable, resulting in a decreased testosterone : E2 ratio. Because E2 levels tend to be elevated in morbid obesity, insulin resistance, and diabetes, it is reasonable to hypothesize that high E2 levels are associated with MS in older men. Whether changes in this hormonal pattern play a role in the development of MS should be further tested ***(Maggio et al., 2008).***

It is likely that sex steroids are involved in the male and female patterns of fat deposition. The sex steroid- induced regional distribution is not an all- or- none mechanism. It is a preferential accumulation of excess fat. Obese men and women still show their sex- specific fat accumulation but store their fat also in the fat depots of the other a preferential accumulation of fat in the abdominal region is associated with an increased risk of type 2 DM and

cardiovascular disease , not only in obese supjects but even in non-obese subjects***(Saad and Gooren, 2011).***

Sex hormone levels and androgen/estrogen balance may play an important role in determining MS and future cardiovascular risk among children and adolescents ***(Agirbasli et al ., 2009).***

Androgens, estrogens were not extensively **investigated** in relation to cardiovascular phenotypes in men ***(Tomaszeweski et al., 2009).***

Aim of the work

1-Examine the relation of endogenous sex hormone levels with components of metabolic syndrome in a cohort of apparently healthy males.

2-Comparison of the level of endogenous sex hormone levels between males with metabolic syndrome and healthy males.

THE METABOLIC SYNDROME

Definitions of Metabolic Syndrome

The clinical utility of identifying people with the metabolic syndrome (MetS) has raised concerns from many scientific groups. In particular, the use of the term "syndrome" was examined and discussed by the International Diabetes Federation (IDF) ***(Alberti et al., 2006).*** The IDF described a syndrome as *"a recognizable complex of symptoms and physical or biochemical findings for which a direct cause is not understood. When causal mechanisms are identified, the syndrome becomes a disease."* Although insulin resistance is present in a majority of people with the MetS, the IDF found insufficient evidence for a causal link between the two, a statement that agreed with the American Diabetes Association (ADA), which published its concerns about the lack of certainty regarding the causative pathogenesis of insulin resistance and its utility as a marker for cardiovascular diseases (CVD) ***(Kahn et al., 2005).***

In particular, the ADA emphasized the lack of clarity in the MetS definition and cautioned clinicians not to assume that the MetS is well characterized ***(Kahn et al., 2005)***. Although there are divergent criteria for the identification of the MetS, they all tend to agree that the MetS core components include obesity, insulin resistance, dyslipidemia, and hypertension ***(Alberti et al., 2006).***