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## Review Article

### METABOLIC SYNDROME AND ITS ASSOCIATION WITH BENIGN PROSTATIC HYPERPLASIA WITH SPECIAL REFERENCE TO UNANI SYSTEM OF MEDICINE: A REVIEW

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#### ABSTRACT

Metabolic syndrome (MetS) is a group of morbid pathological conditions with high socioeconomic burdens on society. It includes Obesity, Diabetes Mellitus, Dyslipidemia and Hypertension etc. According to recent studies all these components of MetS are directly associated with prostate volume, transitional zone volume, prostate specific antigen and Lower Urinary Tract Symptoms (LUTS) due to Benign Prostatic Hyperplasia (BPH). About 25% of men above 40 years of age and about 70% of men above 70 years of age are suffering from BPH. It is a very common and irritating problem of aging males. Size of the prostate and its symptoms are not directly related. Clinical features of BPH are usually summarized as irritative and obstructive symptoms. Irritative symptoms include raised frequency of urine, nocturia, urgency etc and obstructive symptoms include straining, intermittency, weak stream and retention etc. The exact etiology of the prostatomegaly is still not clear but age related hormonal and neoplastic theories are very popular and widely accepted (non modifiable risk factors). Besides these two theories, there are some modifiable risk factors such as MetS, Dietary imbalances and Inflammatory factors etc which also play very important role in the development of prostatomegaly. In the management of BPH, besides the medical management, modifications in the lifestyle of the patients (Tasarruf in Asbabe Sitta Zaruriya) provide better and faster recovery and delay the development of serious health problems. So the BPH with MetS must be managed with a multidisciplinary approach.

**Keywords:** metabolic syndrome, benign prostatic hyperplasia, sue mizaj barid umoomi, asbabe sitta zaruriya

#### INTRODUCTION

##### Metabolic Syndrome (Sue Mizaj Barid Umoomi)

The Metabolic syndrome (Sue Mizaj Barid Umoomi) is not a specific disease; actually it is a group of symptoms and a worldwide epidemic disorder with a high socioeconomic burden due to its association with increased morbidity and mortality. This clinical term "Metabolic syndrome" was first proposed by an American endocrinologist Gerald Reaven in 1998<sup>1</sup>. It is also known as metabolic syndrome X, Reaven syndrome, polymetabolic syndrome, insulin resistance syndrome, dysmetabolic syndrome and deadly quarter syndrome due to its grave socioeconomic impacts<sup>2</sup>.

MetS is a group of medical conditions including abdominal (Visceral) obesity, impaired glucose metabolism, hypertriglyceridaemia, low high-density lipoprotein (HDL) cholesterol and arterial hypertension, which increase the odds for type 2 diabetes mellitus (T2DM) and cardiovascular (CV) diseases. Besides T2DM and CV diseases, several other pathological conditions are also associated with MetS, e.g. non-alcoholic fatty liver disease, obstructive sleep apnoea, polycystic ovarian syndrome, micro vascular disease and lipodystrophy etc.

In addition, in males, erectile dysfunctions, infertility and hypogonadism as well as psychological disturbances are often considered co morbid factors with MetS<sup>3</sup>. Underlying risk factors for MetS include (abdominal) obesity, an atherogenic diet, and physical inactivity, alcohol consumption, tobacco chewing, decreased serum concentration of high-density lipoprotein (HDL) cholesterol, increased serum concentration of low-density lipoprotein (LDL) cholesterol, hypertriglyceridaemia, insulin resistance with glucose intolerance, high blood pressure (HTN), chronic and subclinical inflammations and a prothrombotic state etc<sup>4</sup>.

Various criteria's have been developed by expert groups for clinical diagnosis of the metabolic syndrome. The most widely accepted of these were produced by the World Health Organization (WHO 1999), the National Cholesterol Education "Program – Adult Treatment Panel Third (NCEP ATP III, 2001)". Therefore, the International Diabetes Federation (IDF) brought together various groups recommending a diagnostic set which was similar to the updated version of adult treatment panel III. All groups established that the core components of the metabolic syndrome are obesity, insulin resistance, dyslipidemia and hypertension etc as summarized in table 1 below.

**Table 1: Definition and diagnostic criteria of metabolic syndrome<sup>5</sup>**

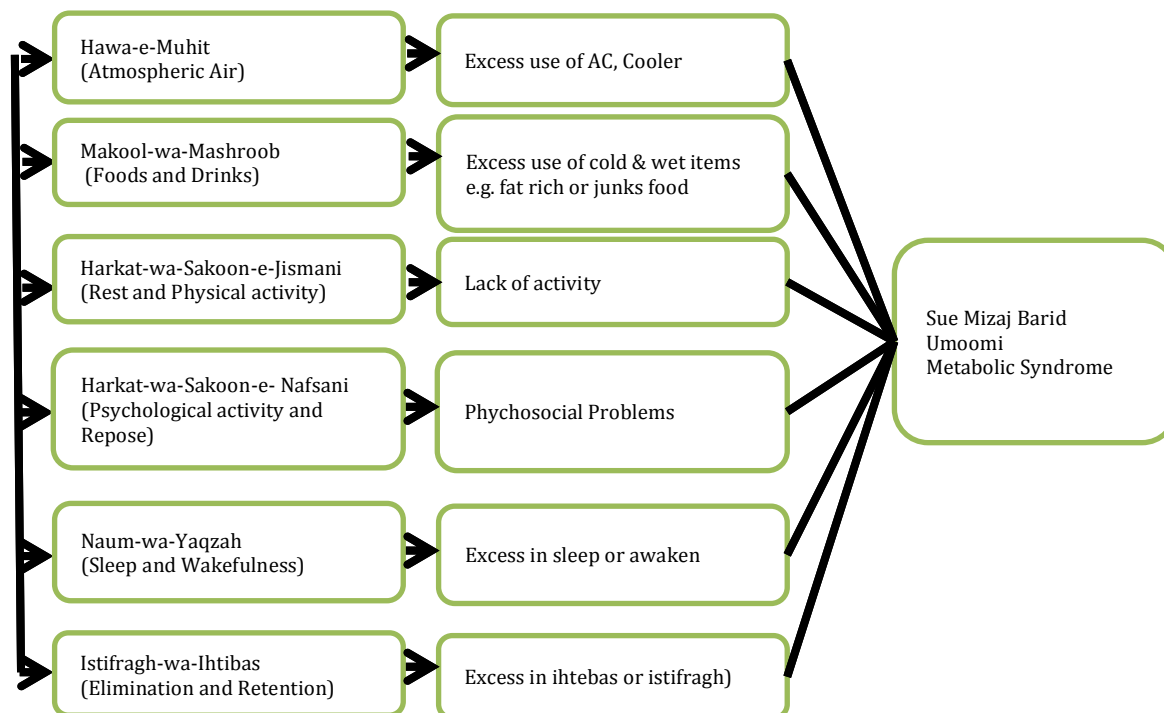
Clinical Measure	WHO 1998	ATPIII 2004	IDF 2005
Insulin Resistance	Impaired glucose tolerance (IGT), Impaired fasting glucose (IFG), Insulin resistance (IR) plus any two of the following;	None Any three of the following five features;-	None Any three of the following five features;-
Dyslipidaemia	Triglycerides (TG)>1.695mmol/L, High density lipoprotein cholesterol (HDL-C) <0.9mmol/L (males) <1.0mmol/L (females)	TG >1.695mmol/L, HDL-C < 40mg/dL (males) < 50mg/dL (females)	TG >1.7mmol/L or on TG Rx, HDL-C < 1.03mmol or on HDL-C Rx
Blood pressure	>140/90mmHg	>130/85mmHg	>130/85mmHg
Plasma glucose	>7.0mmol/L (fasting)	>5.5mmol	>5.5mmol/L (includes diabetes)
Central obesity	Waist/Hip ratio(WHR) > 0.90(males); 0.85(females) and or Body mass index(BMI) >30kg/m <sup>2</sup>	Waist circumference >102cm (males); > 88cm (females)	Waist circumference >94 cm
Others	Urinary albumin excretion ratio> 20mg/min or albumin/creatinine ratio> 30mg/g		

**ASBABA SITTA ZARURIYA (SIX ESSENTIALS OF LIFE) AND METS**

This is one of the basic and unique concept of Unani Syatem of Medicine (USM) regarding health and disease of the mankind which makes the USM more prominent and distinguishable among all pathies of the world. Asbabe Sitta Zaruriya are basically the six essentials of life without which human life is impossible. These are as follows:

- 1)Hawa-e-Muheet (Atmospheric Air)
- 2)Makool-wa-Mashroob (Foods and Drinks)
- 3) Harkat-wa-Sukoon-e-Badani (Rest and Physical activity)
- 4)Harkat-wa-Sukoon-e- Nafsani (Psychological activity and Repose)
- 5) Naum-wa-Yaqzah (Sleep and Wakefulness)
- 6) Ihtibas -wa- Istifragh (Retention and Elimination)

Asbabe Sitta Zaruriya (ASZ) are the most important and initial regimen of USM for the preservation and restoration of health i.e when all the six factors are in equilibrium, health is maintained; otherwise it needs moderation and modification<sup>6-10</sup>. The excess or lack in any factor harbours the various kinds of diseases and leads to physical, mental or social problems. These problems are due to the imbalance of ASZ. These imbalances are termed as Sue Mizaj and it may be of four types (1) Sue Mizaj Haar Ratab (2) Sue Mizaj Haar Yabis (3) Sue Mizaj Barid Ratab and (4) Sue Mizaj Barid Yabis. Sue Mizaj can be further divided into two groups (1) Sue Mizaj Maqami and (2) Sue Mizaj Umoomi (localized or generalized abnormal Mizaj of the body) but here in this article we are only concerned with the Sue Mizaj Barid Umoomi as it is directly related to MetS as summarized in Picture below.



**Picture 1: Etiopathogenesis and risk factors of the Sue Mizaj Barid Umoomi (MetS) in USM**

Picture 1 is showing the etiopathogenesis and risk factors of the Sue Mizaj Barid Umoomi. The picture also explains that the moderation and modification of these factors is the actual treatment for the MetS therefore its management guidelines should be considered and followed accordingly.

### **BENIGN PROSTATIC HYPERPLASIA (WARME GHUDDAE MAZI SULB)**

Warme Ghuddae Mazi Sulb- the Benign Prostatic Hyperplasia (BPH) is very common and irritating problem of males. About 25% of men above 40 years of age and about 70% of men above 70 years of age are suffering from BPH. It is a very common and irritating problem of aging males. Size of the prostate and its symptoms are not directly related. Clinical features of BPH are usually summarized as irritative and obstructive symptoms. Irritative symptoms include raised frequency of urine, nocturia, urgency etc and obstructive symptoms include straining, intermittency, weak stream and retention etc<sup>11</sup>. A few other names have been given to this condition. These are: Senile enlargement of the prostate, benign enlargement of the prostate, Adenoma, Adenomyoma, Fibroadenomyoma, and Nodular Hyperplasia.

The pathological changes in the prostate during the process of BPH are of two types—overgrowth of the glandular substance and overgrowth of connective tissue element, depending upon which of the element predominates; the consistency of the enlarged prostate will vary. In case of overgrowth of glandular elements the consistency is softer in comparison to the overgrowth of the connective tissue elements in which the consistency will be firmer<sup>12</sup>.

The exact etiology of the prostatomegaly is still not clear but age related hormonal and neoplastic theory is very popular and widely accepted (non modifiable risk factors). Besides these two theories there are some modifiable risk factors such as all the components of the MetS play very important role in the prostatomegaly.

### **CORRELATION BETWEEN THE METS AND BPH**

Nandeesh H et al (2006) who found that patients with prostatic hyperplasia had a much higher concentration of Cholesterol (ChT) and LDL and lower levels of HDL in plasma compared to patients without prostatic hyperplasia. In that study the concentration of insulin in patients with diagnosed BPH were significantly related with ChT and Triglycerides (TAG) levels<sup>13</sup>.

Ozden C et al (2006) investigated lipid parameters in patients with diagnosed BPH. The analysis showed a relationship between MetS in patients with BPH and lower-than-standard HDL level and a higher TAG. Their experiment suggested that atherogenic dyslipidemia, which is one of the diagnostic indicators of MetS, has an impact on the growth of the prostate<sup>14</sup>.

Vignozzi et al (2014) proposed an interesting three hits hypothesis on the development of BPH, which may also be helpful in understating the multifactorial relationship between BPH and MetS. According to this hypothesis, a chronic and subclinical inflammation (first hit) could be the first point for the metabolic alternations (second hit) and changes in the sex-hormone levels i.e. testosterone, dihydrotestosterone, estrogen, and progesterone levels (third hit). The combined effects of these may result in over expression of toll-like receptors and transformation of the prostatic cells into antigen-presenting cells leads to prostate enlargement<sup>15</sup>.

Ryl et al (2015) conducted a study on 128 males with BPH and 141 without BPH to clear that whether the metabolic syndrome and benign prostatic hyperplasia is in association or coincidence and he found a high prevalence of MetS and its individual components among patients with BPH who were referred for TURP. He also suggested that age and levels of HDL cholesterol, fasting insulin and sex hormones were significantly associated with the pathogenesis and progression of the BPH<sup>16</sup>.

Yongqiang fu et al (2016) conducted a long term prospective study on 525 diagnosed patients of LUTS due to BPH between 45-78 years of age in China to investigate whether MetS may be associated with clinical progression of BPH or not. Patients were divided into BPH with MetS group and another BPH without MetS group. After 3 years follow up he concluded that the clinical progression rate was significantly ( $p < 0.05$ ) higher in BPH with MetS group in contrast with BPH without MetS group. T2DM and HTN were related to increase the risk of BPH progression. He also suggested that MetS especially T2DM and HTN may accelerate the clinical progression of BPH<sup>17</sup>.

### **MANAGEMENT OF METS**

The underlying conditions that promote the development of MetS are overweight and obesity (dyslipidemia), physical inactivity (lack of physical exercise), sedentary lifestyle, excess use of low residue (high proteinous and fatty diets) excess use of cold and freezed dietary items, excess consumption of alcohol and red meats (all types of mentioned diets are atherogenic diets) and excess use of air condition and cooler, smoking, long term exposure of cold environment etc<sup>6-10&15-18</sup>. Therefore, lifestyle modification is first-line therapy to prevent and treat MetS. The most important therapeutic intervention in subjects with MetS is to focus not only on a single component but it should be managed with a multidisciplinary approach to overcome the MetS such as use of high fibrous diets, weight reduction, regular exercise and physical activities and the psychosocial modifications. According to USM, all these modifications come under the interventions in Asbabe Sitta Zaruriya and termed as Ilaj Bil-Tadbeer<sup>19,20,21</sup>.

### **CONCLUSION**

Managements of BPH/LUTS in subjects with MetS the only treatment of the prostate disease and ignoring the components of MetS is highly insufficient and this attitude usually leads to progression of the diseases and its related complications and makes the patient's quality of life worse. So the best management for long term effects of such cases requires proper life style modifications first to control the MetS like weight reduction, regular exercise, dietary modification, decreasing the effect of insulin resistance, discouraging the habits of alcohol and smoking etc as well as the psychosocial counselling along with the medical treatments. By this multidisciplinary approach we can treat very easily and successfully the all cases of BPH with MetS.

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