

## Effects of metabolic syndrome on prostate specific antigen level, prostate volume and international prostate symptom scores in patients with benign prostatic hyperplasia

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### Abstract

**Background and objective:** Benign prostatic hyperplasia involves the enlargement of prostatic glandular tissue and narrowing of the urethra. It affects bladder storage or emptying. Most of the men with benign prostatic hyperplasia have no symptoms. This study aimed to compare international prostate symptom scores, prostate specific antigen level and prostate volume in patients having benign prostatic hyperplasia with and without metabolic syndrome.

**Methods:** This study involved 85 patients with benign prostatic hyperplasia who were divided into two groups. The first group included 40 participants who were only suffering from benign prostatic hyperplasia and the second group involved 45 participants who were suffering from both metabolic syndrome and benign prostatic hyperplasia. The division of subjects was performed depending on three abnormal parameters out of five parameters, such as body mass index (BMI >25kg/m<sup>2</sup>), dyslipidemia (Triglyceride ≥150 mg/dl, High density lipoprotein-C <40 mg/dl), blood pressure (BP ≥130/85 mmHg), fasting plasma glucose (PG ≥110 mg/dl).

**Results:** Patients with metabolic syndrome at diagnosis appears to have significantly higher levels of prostate specific antigen comparing with patients without metabolic syndrome, 3.9±0.26 and 2.7±0.21, respectively. Similarly, patients with metabolic syndrome at diagnosis had significantly higher prostate volume levels (72.69 ± 2.69 ml) comparing to patients without metabolic syndrome (46 ± 2.44 ml). Patients with metabolic syndrome at diagnosis showed considerable higher international prostate symptom scores level (23.62 ± 0.62) compared to patients without metabolic syndrome (18.87 ± 0.327).

**Conclusions:** benign prostatic hyperplasia patients having metabolic syndrome have significantly higher values of prostate specific antigen levels, prostate volume and international prostate symptom scores compared to benign prostate hyperplasia patients without metabolic syndrome.

**Keywords:** Prostate; prostatic antigen; hyperplasia; metabolic syndrome.

### Introduction

Benign prostatic hyperplasia (BPH) involves enlargement of prostatic glandular tissue and narrowing of the urethra. Lower urinary tract symptoms, generally regarded as a hallmark of significant BPH, encompasses disorders of bladder storage or emptying, and is further divided into irritative and obstructive symptoms.<sup>1</sup> BPH subjects usually present with lower urinary tract symptoms comprising of frequency,

nocturia, intermittency, hesitancy, weak urine stream and incomplete evacuation often progressing to acute urinary retention. The metabolic syndrome (MetS) is a cluster of cardiovascular risk factors, which includes central obesity, hypertension, hyperglycemia, dyslipidemia, and insulin resistance, with subsequent development of hyperinsulinemia and impaired glucose metabolism.<sup>2</sup> The exact mechanisms of the complex pathways of

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MetS are not completely understood. The pathophysiology is extremely complex and has been only partially elucidated. The most important factors are weight, genetics, Endocrine disorders, aging, and sedentary lifestyle. Recent studies indicate that prolonged stress can be an underlying cause of metabolic syndrome by disregulating the hormonal balance of the hypothalamic-pituitary-adrenal axis.<sup>2</sup> Recent studies have suggested a possible relationship between MetS and BPH. Obesity, dyslipidemia, hypertension, and insulin resistance, as well as MetS itself, may contribute to the risk factors of BPH and lower urinary tract symptoms. This may be related to changes in insulin resistance, increased autonomic activity, impaired nitrenergic innervation, increased Rho kinase activity, pro-inflammatory status, and changes in sex hormones that occur in association with MetS. Studies elucidated that physical activity and dietary strategies may help in decreasing the incidence of MetS and its impact on BPH and lower urinary tract symptoms.<sup>3,4</sup> Other studies demonstrated that obesity and dyslipidemia might be associated risk factor of BPH. While Central obesity, dyslipidemia, and hyperinsulinemia could be associated with high-grade prostate cancer.<sup>5,6</sup> Previous studies have demonstrated that prostate size and prostate specific antigen level (PSA) are strong predictors of acute urinary retention and progression of BPH5----- . This study aimed to examine the relationship between MetS and indicative BPH parameters (prostate specific antigen level, prostate volume and international prostate symptom scores) in symptomatic BPH patients.

### Methods

Eighty-five male patients suffering from BPH were enrolled in this study in Rizgary Teaching Hospital at the capital of Iraqi Kurdistan region, Erbil. Their ages were between 55 and 85 years. Patients were divided into two groups. The first group

included 40 participants, who only suffered from BPH and the second group involved 45 participants suffering from both MetS and BPH. BPH patients were having international prostate symptom scores (IPSS) equal or greater than 13 and prostate volume (PV) were equal or greater than 25ml. In the second group, five parameters were addressed, patients have three out of five parameters regarded as MetS. These parameters included body mass index (BMI >25kg/m<sup>2</sup>), dyslipidemia (Triglyceride ≥150 mg/dl, high density lipoprotein-C <40 mg/dl), blood pressure (BP ≥130/85 mmHg), fasting plasma glucose levels (PG ≥110 mg/dl). Only 76 out of 85 patients were cooperative and completed the study successfully; 38 patients from group one and 38 patients from the second group. Eight milliliters of venous blood from a fasted patient (at least 8 hours) was collected into "Clot Activator and Gel (ZS)" tube through using a sterile disposable 21G×1.5 (vacuette) visio plus needle. The eight ml of venous blood was separated into two tubes 5ml and 3ml. LDL, cholesterol, HDL (high density lipoprotein), TG (triglyceride), were measured by using the 5ml of venous blood. For biochemical analysis, commercially available kits were used (Bilimsel Tibbi uruler Paz. Tic. Ltd, Sti/Turkey). Serum PSA was measured using the 3ml blood sample, after centrifuging at 3000 rpm for 5 minutes (Marubeni, Hitachi/ Japan). This assay employs the quantitative sandwich enzyme immunoassay technique (Stat fax / USA). Antibody specific for PSA has been pre-coated onto a microplate. Standards and samples are pipetted into the wells with a Horseradish Peroxidase (HRP) conjugated antibody specific for PSA. Following a wash to remove any unbound reagent, a substrate solution is added to the wells and color develops in proportion to the amount of PSA bound in the initial step. The color development is stopped and the intensity of the color is measured using a microplate reader (Roche / USA). Prostate gland volume was estimated

through transabdominal ultrasound (Siemens/Germany), by department experienced radiologists. International prostate symptom score (I-PSS) were measured in all patients at diagnosis according to previous literature.<sup>5</sup> I-PSS is based on the answers to seven questions concerning urinary symptoms and one question concerning the quality of life. The questionnaire table includes (Incomplete emptying, Frequency, Intermittency, Urgency, Weak Stream, Straining, Nocturia). Each question concerning urinary symptoms allows the patient to choose one out of six answers indicating increasing severity of the particular symptom. The answers are assigned points from 0 to 5. The total score can, therefore, range from 0 to 35 (asymptomatic to very symptomatic). Data are presented as mean  $\pm$  standard error of mean (SEM). Statistical evaluation was performed using the t-test for two independent groups. Results were considered statistically significant when *P* value  $\leq 0.05$ . The data were processed in software Sigma Stat for windows version 3-5 (systal software, Chicago, Illinois, USA).

### Results

Table 1 shows the mean comparison of PSA, PV, and IPSS in patients with and without metabolic syndrome at diagnosis of BPH. Data demonstrates that patients with metabolic syndrome at diagnosis had significantly higher levels of PSA comparing with patients without metabolic

syndrome,  $3.9 \pm 0.26$  and  $2.7 \pm 0.21$ , respectively. Similarly, patients with metabolic syndrome at diagnosis had significantly higher PV levels ( $72.69 \pm 2.69$  ml) comparing to patients without metabolic syndrome ( $46 \pm 2.44$  ml). Patients with metabolic syndrome at diagnosis had considerable higher IPSS ( $23.62 \pm 0.62$ ) compared to patients without metabolic syndrome ( $18.87 \pm 0.327$ ).

### Discussion

To differentiate between patients with and those without metabolic syndrome, BMI, LDL and TG parameters were abnormal in patients with metabolic syndrome whereas those three parameters were normal in patients without metabolic syndrome. As a consequence, in the current study, it was revealed that patients with metabolic syndrome at diagnosis had significantly higher levels of PSA, PV and IPSS compare with those patients without metabolic syndrome. In the present study, the mean PSA value was not lower in the obese group. In the univariate analysis by Pearson's correlation coefficient, BMI correlated positively with PSA (*P* <0.001). Over the past decades, there have been different studies investigated the influence of obesity on the development of BPH with conflicting results.<sup>6,7</sup> As the same result in the current study, Freedland with his colleagues examined the association between BMI and PSA among men who underwent radical prostatectomy for prostate cancer. They found no correlation

**Table 1:** Comparison of prostatic specific antigen (PSA), prostate volume (PV) and International prostate symptom score (IPSS) in patients with and without metabolic syndrome (MetS).

Parameters	Without Metabolic syndrome N=38	With Metabolic syndrome N=38	<i>P</i> value
PSA (ng/ml) $\pm$ SEM	$2.70 \pm 0.21$	$3.90 \pm 0.26$	<0.001
PV (ml) $\pm$ SEM	$46.0 \pm 2.44$	$72.69 \pm 2.69$	<0.001
IPSS $\pm$ SEM	$18.87 \pm 0.3270$	$23.62 \pm 0.62$	<0.001

between BMI and PSA.<sup>8</sup> Banz et al. found that men underwent radical prostatectomy with higher BMI were associated with higher prostate volume but lower PSA which may be related to hemodilution among obese men.<sup>9</sup> Sohn et al. investigated the association between BMI and PSA among 26,912 Korean men who visited health promotion centers. They noted that BMI was inversely correlated with PSA. Their result demonstrated that the mean PSA value was the lowest in the obese group.<sup>10</sup> One of the reasons behind this discrepancy data among these studies is genetic variation, which means that all of the studies have not been conducted in the same country or population or area. Besides, subjects in this study were diabetic patients or hypertensive patients and/or both of them. Moreover, Ochiai et al. demonstrated that the metabolic syndrome parameters were inversely correlated to the PSA level. Nonetheless, the metabolic syndrome parameters considerably affected the PSA level indirectly by its relationship to the prostate volume.<sup>11</sup> With regards to the correlation between PV and MetS, the current study revealed that PV was positively correlated with MetS. There was a significant difference in PV of the patients with metabolic syndrome compared to that of the patients without metabolic syndrome at diagnosis. On the other hand, other studies support our data. For instances, Kim et al. examined the relationship of PV with metabolic and anthropometric parameters.<sup>12</sup> They reported that PV was correlated positively with weight and height, but there was no statistical correlation between PV and BMI in their multivariable linear regression analysis. A recent study that recruited 465 men shows that PV was positively correlated with central obesity, as represented by waist circumference, but not with overall obesity, as represented by BMI.<sup>12</sup> Furthermore, other researchers from the USA studied men underwent radical prostatectomy. They reported that BMI was positively associated with PV in

those patients younger than 63 years.<sup>8</sup> Ochiai et al. found a direct correlation between BMI and PV.<sup>11</sup> They concluded that BMI could be the reason behind this positive result, which PV was enlarged with increasing BMI, since patients with Metabolic syndrome have higher BMI compared to patients without metabolic syndrome. Kristal et al. and Dahle et al. demonstrated that obesity may influence prostatic enlargement and may also worsen urinary obstructive symptoms by increasing the activity of sympathetic nervous systems.<sup>6,13</sup> They studied several modifiable lifestyle factors related to the development of symptomatic BPH in 5,600 men. They reported significant increases in symptomatic BPH (IPSS >14) with obesity. Therefore, they suggested that obesity in adulthood was associated with a higher prevalence of lower urinary tract symptoms (including frequency, nocturia, intermittency, hesitancy, weak urine stream and incomplete evacuation often progressing to acute urinary retention). Rohrmann et al. investigated the association between obesity and lower urinary tract symptoms in the national health and nutrition examination Survey. They recognized that an increase in BMI after age 25 was positively associated with lower urinary tract symptoms.<sup>14</sup> Several other studies evaluated the relationships between BMI and BPH parameters, but these studies included healthy populations of men who visited a health promotion center.<sup>9,12,13</sup> In the present study we included symptomatic BPH patients who visited the department of urology for evaluation or treatment.

## Conclusions

The present study concludes that BPH patients with metabolic syndrome had a significantly higher value of PSA, PV and IPSS compared to BPH patients without metabolic syndrome.

## Conflicts of interest

The authors report no conflicts of interest.



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