Body Mass Index (BMI), lipid profile, leptin level and their correlation with Prostate Specific Antigen (PSA) in Iraqi patients with Benign Prostatic Hyperplasia (BPH)

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Key word: Body Mass Index, lipid profile, leptin level

(Received: Aug 2012, Accepted: Oct 2012)

Abstract:
Background: Benign prostatic hyperplasia (BPH) is a prevalent problem among older men. There is controversy about the risk factors that contribute to the development and aggravation of BPH, diet and obesity may have a major role in the development of BPH. This study investigate body mass index (BMI) as a marker of obesity, leptin level, and lipid profile in correlation with the prostate-specific antigen PSA in symptomatic BPH Iraqi patients.

Patients and Methods: Randomly selected twenty patients newly diagnosed with BPH visited Baghdad hospital for special surgery, including 10 non-obese patients with BPH, and 10 overweight or obese patients with BPH. Body mass index (BMI) was calculated and blood samples were drawn to determine fasting blood glucose (FBG), total cholesterol, triglycerides, HDL cholesterol, serum leptin, and prostate-specific antigen (PSA).

Results: BMI value, Triglycerides, and serum leptin was significantly higher in overweight or obese patients (p < 0.05), and there was non significant high level of FBG, PSA, total cholesterol compared to non obese (p >0.05). Significant lower level of HDL cholesterol was also noticed in obese patients (p <0.5). In non obese patients, PSA correlated negatively with BMI, leptin, triglycerides and FBG, positively with total cholesterol and HDL cholesterol. While in obese patients, PSA correlated negatively with BMI, leptin, HDL cholesterol, and FBG. PSA correlated positively with total cholesterol and triglycerides.

Conclusion: In this study, obesity marker like serum leptin, BMI and triglycerides was significantly higher in overweight/obese BPH patients compared to non obese, but correlated negatively with PSA (except with triglycerides). Further research exploring relationship of diet, obesity with prostate cancer and BPH will lead to understanding of the complex inter-relationship.
Introduction

Benign prostatic hyperplasia (BPH) is a prevalent problem among older men, and its incidence is expected to increase as the human lifespan is prolonged. Symptoms of BPH, such as lower urinary tract symptoms (LUTS), have a negative impact on quality of life [1].

About 60% of men aged >50 years have histologic evidence of BPH; characterized by the presence of nonmalignant, unregulated overgrowth of the prostate gland. This prevalence increases to 80% in patients aged ≥70 years [2]. Currently, BPH is the fourth most prevalent disease in men >50 years [3].

There is controversy about the risk factors that contribute to the development and aggravation of BPH [4]. Recent studies concerning the pathophysiology of BPH have suggested that in addition to the conventional risk factors, such as age, family history and androgen activity, newly identified risk factors, such as smoking, diet and obesity may have a major role in the development of BPH [4, 5].
Prostate-specific antigen (PSA) is the most important prostate cancer screening tool and the majority of prostate cancers are detected with biopsy after abnormal PSA. Several studies have found that obese men have lower PSA values than do nonobese men [6]. Because of hemodilution by the large plasma volume in obese men, some investigators have hypothesized that the PSA value is underestimated in obesity [7].

Multiple studies have reported that obese men have a larger prostate volume (PV) [8], and recently some studies have also revealed that a relationship exists between obesity and LUTS [8, 10].

Large cohort studies have consistently demonstrated that obese men are at increased risk for BPH and LUTS. Furthermore, a (BMI 35 kg/m2 or greater) were at 3.5-fold increased risk for BPH (defined as total prostate volume 40 cc or greater) than non-obese participants (BMI less than 25 kg/m2) [11].

Similar to obesity, the relationship between BPH and dyslipidemia has been documented in several studies. Rahman et al [12] observed that prostate weight was significantly higher in hyperlipidemic rats than in controls [12].

In addition to animal models, the relationship between BPH and dyslipidemia has been documented in epidemiologic studies. Hammarsten et al [13] examined the data of 158 men and reported that individuals with a low level of high-density lipoprotein (HDL) cholesterol (<1.18 mmol/l) had a larger prostate volume (mean: 49.0 vs 39.0 ml) and a higher annual BPH growth rate (mean: 1.02 vs 0.78 ml/y) than did individuals with a high level of HDL cholesterol (≥1.18 mmol/l) [13].

In a subsequent report, Nandeesha et al [14] observed that men with BPH had a significantly higher total cholesterol (mean: 4.5 vs 4.2 mmol/l) and low-density lipoprotein (LDL) cholesterol levels (mean: 2.8 vs 2.2 mmol/l) than did men without BPH [14].

Leptin is a hormone secreted from adipose tissue that affects the ingestion of food and body weight [15]. Furthermore, it plays a role in keeping the energy balance in the body by stimulating the generation of heat through activation of the sympathetic nerve system [16].

According to a recent study, the higher the blood leptin concentration, the greater the negative effect on cellular differentiation and cancer progression in prostate cancer (PCa) It is also known that leptin stimulates the cellular proliferation of benign prostatic hyperplasia (BPH) [17].

There have been few studies, however, concerning the effect of obesity on BPH parameters particularly PSA in Iraqi men, especially symptomatic BPH patients. Furthermore, we think it might be meaningful to investigate body mass index (BMI) as a marker of obesity, leptin level, and lipid profile in correlation with the PSA in symptomatic BPH Iraqi patients.

**Patients and Methods**

This study was done over a period from Jan 2012 to June 2012. Randomly selected twenty patients newly diagnosed with BPH visited Baghdad hospital for specialized surgery, were allocated into two groups:

- Group A: Include 10 non-obese patients newly diagnosed with BPH.
- Group B: Include 10 overweight or obese patients newly diagnosed with BPH.
Body mass index (BMI) was calculated as weight in kilograms divided by height in meters squared (kg/m²). Our BMI ranged from 20.1 to 32.2 kg/m². Normal weight is defined as BMI < 25 kg/m². Overweight was defined as BMI ≥ 26 kg/m², and obesity was defined as BMI ≥ 30 kg/m².

Blood samples were drawn from fasting patients to determine fasting blood glucose (FBG), total cholesterol, triglycerides, HDL cholesterol, serum leptin, and prostate-specific antigen (PSA).

The digital rectal exam (DRE) was performed by senior urologists. Patients with elevated PSA values (PSA greater than 4.0). Total PSA levels were analyzed using ELISA. Acon USA. (Awareness technology INC).

FBS was measured using glucose oxidase (glucinate) enzymatic method (Biolabo Reagents / France), lipid profile was measured using Rflotron plus (ROSCH), and serum leptin level was measured using ELISA. DRG.Germany (DRG Instrument GmbH / Germany).

Statistical analysis was performed using t-tests, as well as regression analysis as appropriate to evaluate any associations. Data was analyzed using SPSS computer software and P-values <0.05 were considered to be statistically significant.

**Results**

1. **Mean BMI, PSA, leptin, FBG, and lipids:**
   - Table 1 shows that the mean BMI was 22.61 ± 1.56 kg/m² in group A patients, and 29.14 ± 1.73 kg/m² in group B. BMI value in group B was very significantly higher compared to group A (p < 0.001).
   - The mean PSA was 3.88 ± 1.61 ng/ml in group A patients, and 5.80 ± 4.14 ng/ml in group B. PSA value was higher in group B compared to group A (p > 0.05) (table 1).
   - The mean serum leptin was 9.81 ± 1.51 ng/ml in group A patients, and 11.71 ± 1.71 ng/ml in group B. Serum leptin value was significantly higher in group B patients compared to group A (p < 0.05) (table 1).
   - The mean FBS was 125.55 ± 0.05 mg/dl in group A patients, and 136.40 ± 1.40 mg/dl in group B. There was non-significant higher FBS level in group B patients compared to group A (p > 0.05) (table 1).
   - The mean total cholesterol value was 277.44 ± 0.75 mg/dl in group A patients, and 261.5 ± 1.27 mg/dl in group B. Higher but non-significant total cholesterol level was noticed in group B patients compared to group A (p = 0.54) (table 1).
   - The mean HDL cholesterol was 36.22 ± 0.68 mg/dl in group A patients, and 28.40 ± 1.18 mg/dl in group B. Significant lower level of HDL cholesterol was noticed in group B compared to group A (p < 0.5) (table 1).
   - The mean value of triglycerides was 206.44 ± 0.63 mg/dl in group A patients, and 305.40 ± 1.11 mg/dl in group B. Triglycerides level was very significantly higher in group B compared to group A (p < 0.001) (table 1).

2. **Association of PSA level with BMI, leptin, FBG, and lipids:**
   - We examined the relationship between PSA and BMI, leptin, FBG, and lipids using regression analysis. Table (2) presents the association in group A patient. PSA correlated negatively with BMI (r= -0.45), negatively with leptin (r=-0.72 , positively with total cholesterol (r= 0.03), negatively with triglycerides (r= 0.71), positively with HDL cholesterol (r=0.23), and negatively with FBG (r=-0.05). The regression correlation were (r= -0.04 , - 0.106 , 0.39 , - 0.105, 0.068 , -0.096)
In group B patients, table (3), PSA correlated negatively with BMI (p=0.91), negatively with leptin (p=0.82), positively with total cholesterol (p=0.068), positively with triglycerides (p=0.14), negatively with HDL cholesterol (p=0.94), and negatively with FBG (p=0.51). The regression correlation were (r=-0.12, -0.11, 0.27, 0.15, -0.12, -0.06) (figures 1, 2, 3, 4, 5, 6) respectively.

Discussion

Several large scale studies have investigated the influence of obesity on the development of BPH with conflicting results [18,19,20,21,22]. Obese men were 2.4 folds more likely to undergo BPH surgery [23]. Freedland et al examined the association between BMI and PSA among men who underwent prostatectomy for prostate cancer. They found no association between them [24]. This association was also examined by Zilli et al, he found no association between obesity indices in younger age diagnosed with greater prostate volume, and surrogate markers of biochemical failure as PSA nadir (n PSA) [25]. Sohn et al investigated the association between BMI and PSA among 26.912 Korean men who visited health centers. They noted inverse correlation between BMI and PSA [26]. Furthermore, the mean PSA value decreased in a linear fashion with an increase in BMI category from 1.01 ng/ml in normal weight men to 0.69 ng/ml in obese men in adjusted age/race population [27]. In a subsequent report, Jong et al found negative correlation between PSA and BMI and positive correlation between BMI and prostate volume (PV) and International Prostate Symptom Score (IPSS) in symptomatic BPH patients [28]. In study cohort, obese men had a 17% lower age-adjusted PSA level compared to normal weight men. This relationship was non-significant [29]. In this study, increased values of PSA was noticed among obese newly diagnosed BPH patients compared with non-obese although non-significant (p=0.18). Negative correlation was found between BMI and PSA (p=0.91), scoring better correlation among obese patients compared to non-obese (r=-0.12, -0.04) respectively. Banez et al suggested that PSA value was underestimated in obesity, and lower PSA levels were largely due to hemodilution by the large plasma volume in obese men [7].

Obesity and dyslipidemia have been well reported to increase risk of BPH and high grad CaP [30,31]. Although there are contradictory reports stating no association between serum lipids and histological BPH [32,33,34]. Many other cohort and case controlled studies show strong correlation between BPH and lipid profile [13, 14, 35]. Similarly, Hammarsten and Hogstedt observed that the of HDL –C was significantly lower in men with BPH than in those without BPH in a large sample (n=307) [36]. Mydle et al found high level of triglycerides (but not cholesterol) and low HDL concentration in overweight white men with CaP compared to men with normal weight CaP [37]. Ozden et al examined BPH patients with some metabolic syndrome component. He found significantly higher median body weight, BMI, serum glucose, serum triglycerides, and PSA level, but lower serum HDL-C level compared to patients without metabolic syndrome [9]. Han et al found that PSA is negatively correlated with HDL and FBG in BPH patients with metabolic syndrome [38]. This study show very significantly high level of triglycerides (p<0.001), and significantly low HDL concentration (p<0.05) among overweight/obese BPH patients compared to controls. High but non significant total cholesterol and FBG levels was noticed in this group. Furthermore, a positive correlation was found in this study between PSA and triglycerides (p=0.14) and cholesterol (p=0.06), and strong negative correlation with...
HDL cholesterol (p = 0.94) in overweight/obese BPH patients compared to controls. PSA was also negatively correlated with FBG (p = 0.5). Parsons et al observed no overall association between LDL cholesterol and BPH (p=0.2). However, when men were stratified according to diabetes status, individuals with diabetes who had the highest LDL cholesterol had a 4-fold higher risk of reporting BPH than did those with the lowest LDL cholesterol. This observation suggests that dyslipidemia may interact with other components of metabolic syndrome to increase BPH risk [11,30]. This may at least partially explain why other investigators observed no significant relationship between dyslipidemia and BPH/LUTS [39].

Few epidemiological studies have investigated the association of leptin, C peptide, and risk of BPH, but due to less sample size and cross sectional study design, investigators found no definite correlation [40,23,14]. Dahle et al examined the association between abdominal obesity, increased insulin, and overall obesity with higher risk of BPH. They found that overall obesity but not leptin are associated with higher risk of BPH [41]. Inversly, Seung et al observed that central obesity rather than overall obesity seems to be more predictere of LUTs correlated with BPH in Korean population [42]. Singh et al found no correlation between leptin and PSA in 30 prospective cases of cancer prostate in India [43]. Lopez et al observed that body composition and leptin are related to prostate cancer (CaP) aggressiveness but not prevalence, and raised serum leptin is independent of obesity and PSA [44]. In this study, serum leptin was significantly higher in overweight/obese BPH patients compared to non obese (p< 0.05). Leptin was negatively correlated with PSA (p= 0.82) in both study groups. Till date it is not clear whether leptin is an independent risk factor or it is a risk factor in association with obesity for progression of prostate cancer [45].

Further research exploring this relationship may give birth to many new preventive strategies to be added to the standard treatment package to retard progression.

Acknowledgments: We gratefully acknowledge a considerable debt to Dr. Nawfal Fahad Abdulkarem, a senior Urologist at Baghdad hospital for special surgery for his kind contribution in this study.

References:


Table (1): Mean BMI, PSA, Leptin & lipids in non obese & over weight/obese newly diagnosed BPH patients.

<table>
<thead>
<tr>
<th></th>
<th>Group A</th>
<th>Group B</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Non obese BPH patients (n=10)</td>
<td>Obese BPH patients (n=10)</td>
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</tr>
<tr>
<td>BMI (kg/m²)</td>
<td>22.61 ±1.56</td>
<td>29.14 ±1.73</td>
<td>7.46 × 10⁻⁸***</td>
</tr>
<tr>
<td>PSA (ng/ml)</td>
<td>3.88 ± 1.61</td>
<td>5.8 ± 4.14</td>
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<tr>
<td>Serum leptin (ng/ml)</td>
<td>9.81 ± 1.51</td>
<td>11.71 ± 1.70</td>
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<td>FBS (mg/dl)</td>
<td>125.55 ± 0.05</td>
<td>136.40 ± 1.40</td>
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<td>Total cholesterol (mg/dl)</td>
<td>277.44 ± 0.75</td>
<td>261.50 ± 1.27</td>
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<td>HDL (mg/dl)</td>
<td>35.22 ± 0.68</td>
<td>28.40 ± 1.18</td>
<td>0.0128*</td>
</tr>
<tr>
<td>TG (mg/dl)</td>
<td>206.44 ± 0.63</td>
<td>305.4 ± 1.11</td>
<td>0.00024***</td>
</tr>
</tbody>
</table>

P < 0.05 *significant,
P < 0.001 ** high significant,
P < 0.0001 *** very high significant.

n=number of patient.
Table (2): Association of PSA level with BMI, leptin, FBG, and lipids in non-obese patients newly diagnosed with BPH:

<table>
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<tr>
<th>PSA (ng/ml)</th>
<th>BMI (Kg/m²)</th>
<th>Serum Leptin (ng/ml)</th>
<th>FBS (mg/dl)</th>
<th>Chol. (mg/dl)</th>
<th>HDL (mg/dl)</th>
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<td>23.8</td>
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<tr>
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<td>23.5</td>
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<td>4</td>
<td>21.3</td>
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<td>8</td>
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<td>8.8</td>
<td>133</td>
<td>330</td>
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<td>3</td>
<td>20.1</td>
<td>9.2</td>
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<td>7.7</td>
<td>115</td>
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<tr>
<td>Mean ± SD</td>
<td>3.88 ± 1.61</td>
<td>22.61 ± 1.56</td>
<td>9.81 ± 1.51</td>
<td>125.55 ± 0.75</td>
<td>35.22 ± 0.68</td>
<td>206.44 ± 0.63</td>
</tr>
</tbody>
</table>

P value 0.450 0.723 0.658 0.031* 0.233 0.714

P < 0.05 *, significant,

Table (3): Association of PSA level with BMI, leptin, FBG, and lipids in overweight/obese patients newly diagnosed with BPH:

<table>
<thead>
<tr>
<th>PSA (ng/ml)</th>
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<th>Serum Leptin (ng/ml)</th>
<th>FBS (mg/dl)</th>
<th>Chol. (mg/dl)</th>
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<tr>
<td>Mean ± SD</td>
<td>5.8 ± 4.14</td>
<td>29.14 ± 1.73</td>
<td>11.71 ± 1.70</td>
<td>136.40 ± 1.40</td>
<td>28.40 ± 1.18</td>
<td>305.4 ± 1.11</td>
</tr>
</tbody>
</table>

P value 0.916 0.828 0.510 0.068 0.946 0.141
Figure [1]: Correlation between PSA levels and BMI in both non-obese and overweight / obese BPH patients.

Figure [2]: Correlation between PSA levels and Leptin in both non-obese and overweight / obese BPH patients.
Figure [3]: Correlation between PSA levels and total cholesterol in both non-obese and overweight / obese BPH patients.

Figure [4]: Correlation between PSA levels and triglycerides in both non-obese and overweight / obese BPH patients.
Figure [5]: Correlation between PSA levels and HDL cholesterol in both non-obese and overweight / obese BPH patients.

Figure [6]: Correlation between PSA levels and FBG in both non-obese and overweight / obese BPH patients.