ORIGINAL ARTICLE

Association Between Metabolic Syndrome and Benign Prostate Hyperplasia

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ABSTRACT

Metabolic syndrome (MetS) is a highly prevalent complex disorder among adults worldwide which includes cardiovascular risk factors such as central obesity, insulin resistance, dyslipidemia and hypertension. MetS or its components are prevalent in patients with benign prostate hyperplasia (BPH), a common urogenital disorder of adult male with increasing age. This cross-sectional study was conducted in the Department of Biochemistry, Dhaka Medical College, Dhaka from July 2014 to June 2015 with a total of 100 subjects. Of these 50 patients of BPH attending the Department of Urology, Dhaka Medical College Hospital, Dhaka was taken as Group I and 50 age-matched apparently healthy adults was taken as Group II. According to the National Cholesterol Education Program Adult Treatment Panel (NCEP-ATP III, 2005) criteria, components of MetS as fasting plasma glucose, serum triglyceride, serum HDL-C level, blood pressure, waist circumference were assessed and compared between groups by chi-square (x^2) tests and unpaired student's 't' test as appropriate. A p value <0.05 at 95% CI was considered as significant. Metabolic Syndrome was significantly more common in BPH patients than that of healthy individuals (72% VS 38%, p=0.001). Mean$\pm$SD of fasting plasma glucose and serum triglycerides were significantly higher in Group I than that of Group II (5.7$\pm$0.6 mmol/l vs 5.13$\pm$0.97 mmol/l, p=0.001; and 191.3$\pm$33.9 mg/dl vs 159.2$\pm$45.5 mg/dl, p=0.001, respectively). Percentage of subjects having high blood pressure, high serum triglyceride and low serum HDL-C were significantly high in BPH patients (Group I) than that of healthy individuals of Group II (BP: 72% VS 44%, p=0.005, TG: 90% vs 54%, p=0.001, HDL-C: 72% VS 54%,p=0.001). Metabolic syndrome or its components are more common among patients with benign prostate hyperplasia. Routine investigations to detect MetS can be done to reduce the risk of cerebrovascular diseases, cardiovascular diseases and type 2 diabetes mellitus in BPH patients.

Key Words: Metabolic syndrome, Benign prostate hyperplasia

Introduction

Benign prostate hyperplasia (BPH) is a focal enlargement of the peri-urethral region of the prostate seen in most aging men, which results in symptoms requiring clinical intervention in approximately one-third of men over the age of 60 years. BPH is now the fourth most prevalent disease in men aged more than 50 years[1].

Though a highly prevalent disorder, the pathogenesis of BPH is not yet well understood. In the past decade an increasing number of reports have suggested a possible relationship between BPH and several metabolic disturbances, known as metabolic syndrome[2,3].

Co-morbidities commonly seen in patient with BPH/LUTS include obesity and type 2 diabetes mellitus which are the inevitable outcome of MetS. Both diabetes and obesity alter sex steroid hormone metabolism and both may be considered to be pro-inflammatory conditions releasing chemokines that may well contribute to prostate growth[4]. In aging males, significant tissue remodeling and apoptosis process that take place within the prostate may be associated with BPH[5]. The metabolic syndrome (MetS) is a cluster of risk factors including obesity, atherogenic dyslipidemia, hypertension, glucose

intolerance and a pro-inflammatory and pro-thrombotic state that predispose a patient to the risk of developing cardiovascular diseases (CVD), type 2 diabetes mellitus (T2DM), renal failure and stroke[6]. Worldwide, the prevalence of MetS ranges from 10% to 50%. The MetS as a driver of current epidemics of diabetes and cardiovascular diseases which have become a major challenge to public health around the world[7]. An increasing trend of this syndrome has been observed in Asian population also. One meta-analysis in 2007 had shown that approximately 10% -13% of adult Asian people have MetS[8].

A number of expert groups and several organizations have attempted to develop a unifying definition for the metabolic syndrome (MetS) such as WHO, EGIR, NCEP-ATP III. All groups agree on the core components of MetS: obesity, insulin resistance/impaired glucose regulation, dyslipidemia and hypertension, marker of systemic inflammation such as elevated C-reactive protein and autonomic sympathetic over activity[9]. According to US National Cholesterol Education program, at least three of the following for adult man must be present to identy as having MetS. These are Central obesity: WC ⩾ 102 cm, Dyslipidemia: TG ⩾ 150 mg/dl, Dyslipidemia: HDL-C < 40 mg/dl, Blood pressure ⩾ 130/85 mmHg and Fasting plasma glucose ⩾ 6.1 mmol/l. But for South Asians WC ⩾ 90 cm for men recommended as a components of Mets by joint venture of WHO and IDF in 2005.

The association between Metabolic Syndrome and BPH has also been studied recently. Non-insulin dependent diabetes mellitus (NIDDM), hypertension, obesity and low level of high density lipoprotein cholesterol (HDL-C) levels constitute risk factors for the development of BPH. Men with fast growing BPH had a higher prevalence of NIDDM, hypertension, elevated fasting insulin level and lower HDL-C level than men with slow growing BPH[10].

Several anthropometric measurements have been used to define obesity including waist circumference, waist to hip ratio and body mass index (BMI). Similar to obesity the relationship between BPH and dyslipidemia has been documented in several studies. Men with BPH had significantly higher total cholesterol, low-density lipoprotein cholesterol (LDL-C) level and lower the level of HDL-C compared to those in men without BPH[11]. This observation suggests that dyslipidemia per se is not sufficient enough to concur with BPH determinism, but the presence of other metabolic derangements, like T2DM, favor the process, because of an unfavorable total and LDL cholesterol particle size and density[12].

Hyperglycemia may play a role by increasing cytosolic-free calcium in smooth muscle cells and neural tissue, leading to sympathetic nervous system activation. The IGF pathway may also contribute to the association between insulin resistance and BPH. Insulin shows a structural similarity to IGF-1 and combines with its receptor, which may activate a complex pathway influencing prostate cell growth and proliferation. Alternatively, as insulin level increases, IGF-1 binding protein-1 decreases, thus increasing IGF bioavailability[13].

The present study was designed in a small group of Bangladeshi population to observe the association of anthropometric and biometrical parameters of metabolic syndrome in patients with benign prostate hyperplasia. However, to our knowledge no such study has yet been done in Bangladesh, though several studies have been done in abroad to establish the association between metabolic syndrome and benign prostate hyperplasia. So this study was designed to see the association of metabolic syndrome with benign prostate hyperplasia which might play some role to reduce the cardiovascular risk in BPH patient by appropriate intervention.

Materials and Method

This observational cross-sectional study was carried out in the Department of Biochemistry, Dhaka Medical College, Dhaka during the period from July 2014 to June 2015. A total of 100 male subjects selected for the study were

divided into two Groups. Group I consisted of 50 subjects having BPH and Group II consisted of age-matched 50 apparently healthy subjects. Along with anthropometric measurements (WC, BMI, and WHR) BP, fasting blood glucose and lipid profile were assessed and compared between Groups to observe the association between MetS and BPH. A preformed data collection sheet was used to record the data.

After 10-12 hours of overnight fasting, 5 ml of venous blood was collected from median cubital vein of each study participants by disposable syringe with all aseptic precautions. The needle was detached from the nozzle and 3 ml of blood was transferred immediately into a dry and clean plain test tube and rest 2 ml of blood was collected in a Na-Fluoride containing tube. Separated serum and plasma were preserved in eppendorff tube for biochemical assay. All the biochemical tests were performed in the Department of Biochemistry, Dhaka Medical College, Dhaka.

Laboratory Method

- Estimation of fasting plasma glucose was done by 'Glucose Oxidase' (GOD-PAP) method.
- Estimation of fasting serum total cholesterol was done by enzymatic end-point (CHOD-PAP) method.
- Estimation of fasting serum triglycerides (TG) was done by enzymatic (GPO-PAP) method.
- Estimation of fasting serum high density lipoprotein (HDL) cholesterol was done by enzymatic end point (CHOD-PAP) method.
- Estimation of fasting serum Low-density lipoprotein (LDL) cholesterol was calculated by using Friedwald's formula.

Metabolic syndrome was diagnosed using the National Cholesterol Education Program (NCEP), Adult Treatment Panel, ATP III Guideline (2005). If three or more of the criteria were present, the subject was diagnosed as having metabolic syndrome. Qualitative data were expressed as frequency distribution and percentage and quantitative data were expressed as mean±SD. Data were analysed using windows based computer software device with Statistical Package for Social Science (SPSS) version 20.0. Comparison between groups was done by chi square (x^2) test and unpaired student's 't' test as appropriate. The p value <0.05 was taken as level significance.

Results

As shown in table-I, mean±SD of age was 59.8±5.1 years in Group I and 58.7±5.7years in Group II. There was no statistically significant difference in age between Groups ($p>0.05$). Waist circumference was significantly higher in Group II (93.5.±11.0 cm) than in Group I (85.9±9.4 cm) and p-value was 0.001. But waist-hip ratio (Group I: 0.85±0.06 and Group II: 0.86±0.05) and BMI (group I: 26.9±3.8 kg/m^2 and Group II: 27.5±3.9 kg/m^2) were almost same in both Groups and the differences were not statistically significant ($p>0.05$). Systolic BP was slightly higher in group I (125±15 mmHg) than that of Group II (122±7 mmHg) and diastolic BP was also slightly higher in group I (84±9 mmHg), than that of Group II (82±5.0 mmHg) but differences were not statistically significant ($p>0.05$).

Table I: Comparison of various components of metabolic syndrome (Anthropometric measurements) in group I and group II

Components of metabolic syndr ome (Anthropometric measurements)	Group I (n=50) Mean ± SD	Group II (n=50) Mean ± SD	p value
Age (years)	59.8±5.1	58.7±5.7	0.349
Waist circumference (WC)	85.9 ± 9.4	93.5 ± 11.0	0.001
Waist-hip ratio (WHR)	0.85 ± 0. 06	0.86 ± 0.05	0.668
BMI (kg/m^2)	26.9 ± 3.8	27.5 ± 3.9	0.438
Systolic BP (mmHg)	125 ± 15	122 ± 7	0.190
Diastolic BP (mmHg)	84 ± 9	82 ± 5.0	0.279

Table II shows lipid profile and FPG of the study groups. Triglyceride was significantly higher in group I (191.3±33.9 mg/dl) than in group II (159.2±45.5 mg/dl) and HDL-C was significantly lower (37.8±3.1 mg/dl) in group I than in group II (41.3±5.2 mg/dl), $p<0.05$. Fasting plasma glucose was significantly higher in group I (5.70±0.60mmol/l) than in group II (5.13±0.97mmol/l), $p<0.05$. Differences in TC and LDL-C was not significant between groups, $p>0.05$.

Table II: Comparison of lipid profile and FPG in group I and group II

Components of metabolic syndrome (Lipid profile)	Group I (n=50) Mean ± SD	Group II (n=50) Mean ± SD	p value
Total cholesterol (mg/dl)	167.8 ±37.1	179.8 ±67.8	0.277
HDL-C (mg/dl)	37.8 ±3.1	41.3 ±5.2	0.001*
LDL-C (mg/dl)	105.8 ±29.9	110.9 ±25.4	0.358
Triglyceride (mg/dl)	191.3 ±33.9	159.2 ±45.5	0.001*
Fasting plasma glucose (mmol/l)	5.70 ±0.60	5.13 ±0.97	0.001*

Table III shows comparison of various components of MetS according to NCEP-ATP III (2005) criteria among group I and group II. There were significant differences in all of the components of metabolic syndrome between group I and group II. Hypertension was present in 72% (n = 36) and 44% (n = 22) of subjects in group I and group II respectively. FPG was high in group I, 24% (n = 12) and in group II it was 12% (n = 6). WC was low in group I 26% (n = 13) and in group II it was 62% (n = 31). HDL-C was low in group I, 80% (n = 40) and in group II, 40% (n = 20). TG was high in group I, 90% (n = 45) and in group II, 54% (n = 27). All these results were statistically significant except FPG (p value in BP= 0.005; in FPG= 0.118; in WC= 0.001; in HDL-C= 0.001 and in TG= 0.001).

Table III: Comparison of components of MetS according to NCEP-ATP III (2005) criteria in group I and group II

Component of metabolic syndrome		Group I (n=50) n (%)	Group II (n=50) n (%)	p value	OR (95% CI)
BP	⩾130/85	36 (72)	22 (44)	0.005	3.27 (1.42 - 7.52)
	<130/85	14 (28)	28 (56)		
FPG	⩾6.1 mmol/L	12 (24)	6 (12)	0.118	2.31 (0.79 – 6.76)
	< 6.1 mmol/L	38 (76)	44 (88)		
WC	⩾90 cm	13 (26)	31 (62)	0.001	0.21 (0.09 – 0.50)
	< 90 cm	37 (74)	19 (38)		
HDL-C	⩾40 mg/dl	40 (80)	20 (40)	0.001	6.00 (2.45 – 14.67)
	> 40 mg/dl	10 (20)	30 (60)		
TG	⩾150 mg/dl	45 (90)	27 (54)	0.001	7.66 (2.61 – 22.54)
	< 150 mg/dl	05 (10)	23 (46)		

Table IV shows that prevalence of metabolic syndrome in benign prostate hyperplasia was 72% (36 out of 50 study subjects) in group I. In Group II it was 38% (19 out of 50 persons) and OR: 4.19 (1.81-9.72) at 95% CI, $p=0.001$.

Table IV: Prevalence of metabolic syndrome in group I and group II

Group I n = 50	Group II n = 50	Total	OR	p-value	95%CI
36 (72.0%)	19 (38.0%)	55 (55.0%)	4.19	0.001*	1.81 – 9.72

Discussion

Benign prostate hyperplasia (BPH) is a progressive condition characterised by prostate enlargement leading to lower urinary tract symptoms (LUTS). Metabolic Syndrome is a cluster of cardiovascular risk factors including central obesity, atherogenic dyslipidemia, hypertension, insulin resistance with compensatory hyperinsulinemia and glucose intolerance. Metabolic Syndrome has been associated with an increased risk of BPH in several observational studies done in abroad but no published data was found about the association between MetS and BPH in Bangladesh[14,15]. We tried to determine the metabolic syndrome or its components among benign prostate hyperplasia patients and apparently healthy men for

assessment of association of MetS with BPH.

To establish the purpose of this cross-sectional study, 50 BPH patients and 50 apparently healthy individuals were taken as group I and group II respectively. The serum lipid profile, fasting plasma glucose and several anthropometric measurements were assessed and statistically compared between groups to observe the association between metabolic syndrome and benign prostate hyperplasia.

Benign prostate hyperplasia (BPH) was seen among elderly people. In this study, age was matched in both groups and age range was 40-70 years. Mean (±SD) age was 59.8±5. 1 years in group I and 58.7±5.7 years in Group II and the difference was not statistically significant ($p>0.05$). Isa MM et al. also found the similar results in their findings[1]. In the study conducted by Jeon et al[16] it was shown that prevalence of BPH increases with increase in age which is similar to our study.

In our study different anthropometric measurements of components of MetS were taken to observe the association between MetS and BPH. WC was significantly higher in Group II (93.5 ± 11.0 cm) than that in Group I (85.9 ± 9.4 cm) and p-value was 0.001. So, WC was significantly increased in healthy individuals of our study. This may be due to sampling bias where maximum admitted patients in Group I came to DMCH from low socioeconomic Group, mostly living in rural areas and generally have ill health. But the participants of Group II were taken by personal contact from Dhaka city, which were mixed urban and rural population of mixed socioeconomic condition and with average health status. A study reported that waist circumference >90 cm is an important risk factor for prostate hyperplasia[17] which was not consistent with our study.

Waist-hip ratio (Group I: 0.85±0.06 and Group II: 0.86±0.05) was almost same in both the groups in our study and the difference was not statistically significant ($p>0.05$). The study observed the small but statistically insignificant difference in BMI among participants (mean±SD:26.9±3.8 kg/m^2 in group I vs 27.5±3.9 kg/m2 for group II), $p=0.438$, which agree with another study done the abroad[2]. This study showed that systolic BP was slightly higher in group I (125 ± 15 mmHg) than that of Group II (122±7 mmHg) but the difference was not statistically significant ($p>0.05$). Similarly, diastolic BP was non-significantly slightly higher in Group I (84±9 mmHg) than that of Group II (82±5.0 mmHg). Similarly, a study reported that men with a history of hypertension had a 1.5 fold higher risk of developing moderate-to-severe BPH/LUTS[18].

In our study mean±SD of fasting plasma glucose was significantly higher in Group I than that in Group II (5.7±0.60 mmol/l vs 5.13±0.97 mmol/l and $p=0.001$). A similar conclusion was drawn by a population based study of African-American men aged 40-79 years and BPH patients reporting a diabetic history and high fasting plasma glucose have a 2 fold increase in risk of developing moderate to severe LUTS[18].

In this study lipid profile of the study Groups were assessed. Triglyceride was higher in Group I (191.3±33.9 mg/dl) than in Group II (159.2±45.5mg/dl) and HDL-C was lower (37.8±3.1 mg/dl) in Group I than that in Group II (41.3±5.2 mg/dl) and both results were statistically significant ($p<0.05$). Non-significant($p>0.05$) differences were observed in total cholesterol (Group I: 167.8 ±37.1 mg/dl; group II: 179.8 ± 67.8 mg/dl) and LDL-C (Group I:105.8 ± 29.9 mg/dl; Group II : 110.9 ± 25.4 mg/dl) between Groups. This study observed that the level of HDL-C was significantly lower in men with BPH (37.8±3.1mg/dl vs 41.3±5.2 mg/dl, $p<0.001$)11. This study showed that reduced HDL-C and increased TG level were noted to be the main determinants of MetS related prostate enlargement[19].

Our study showed significant differences of

various components of metabolic syndrome according to NCEP-ATP III (2005) criteria between study Groups. Hypertension was significantly higher in Group I: 36 (72%) than that in Group II: 22 (44%) with OR (95% CI): 3.27 (1.42-7.52); p=0.005. FPG was non-significantly higher in Group I: 12 (24%) than that in Group II: 6 (12%)OR:2.31 (0.79-6.76); p=0.118. HDL-C was low in Group I: 40 (80%) than Group II: 20 (40%) which was statistically significance as OR: 6.00(2.45-44.67); p=0.001. TG was higher in Group I: 45 (90%) than that in Group II: 27 (54%) as OR: 7.66(2.61-22.54); p=0.001. All the results were statistically significant except FPG (p value in BP: 0.005; in FPG: 0.118; in HDL-C: 0.001; in TG: 0.001). But WC was higher in Group II: 31 (62%) than in Group I: 13 (26%), p= 0.001. Many other studies observed similar findings showing that metabolic syndrome or components of metabolic syndrome are risk factors for prostate hyperplasia[2,14]. But some studies from Asian populations failed to show possible association between metabolic syndrome and benign prostate hyperplasia[20,21].

The prevalence of metabolic syndrome in benign prostate hyperplasia was 72% (36 out of 50 patients) and in healthy adults it was 38% (19 out of 50 persons) with OR: 4.19 (1.81-9.72) at 95% CI. Total prevalence of metabolic syndrome in both BPH patients and healthy adults was 55% (55 out of 100 study subjects). This finding supported that there seems to be an association between metabolic syndrome and benign prostate hyperplasia.

It may be concluded that Metabolic syndrome or its components are more common in benign prostate hyperplasia patients. Routine investigations to detect MetS in BPH patients may help to reduce the risk of cerebrovascular diseases, cardiovascular diseases and type 2 diabetes mellitus with appropriate and timely intervention.

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