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Original Article

The Influencing Role of Diabetes Mellitus and Hypertension in the Establishment of Benign Prostatic Hyperplasia

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Abstract

Background
Benign prostatic hyperplasia is regarded as non-malignant growth of prostatic tissue. It is the most common benign tumor in men, and the incidence is age related. In men aged more than 50 years, it is the fourth most prevalent disease. This study aim to determine the association of benign prostatic hyperplasia with diabetes mellitus and/or hypertension and this may help to bring out new dimensions in management of benign prostatic hyperplasia.

Materials and Methods
Five hundred forty patients, diagnosed as benign enlargement of prostate with control group 270 at Urology out patient door between May 2018 to February 2019 with approval of Institutional review committee, were included. Patient with history of prostate cancer, neurogenic bladder, those who had undergone surgical intervention for prostate, not willing to take part in study were excluded.

Results
Age range in cases and control were from 41–94 years. Diabetes was present in 14.63% of cases and 11.85% of controls. The positive association was established between prostatic hyperplasia and Diabetes (P-0.27). Hypertension was present in 37.96% of cases and 29.63% of controls (P-0.019). Diabetes and Hypertension were present in 56.48% in cases and 43.33% in control (P-0.001).

Conclusion
Study suggests that benign prostatic hyperplasia is associated with diabetes mellitus and hypertension and may help to bring out new dimensions in management of benign prostatic hyperplasia.

Keywords: *Benign prostatic hyperplasia, Diabetes mellitus, Hypertension*

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Introduction

Benign prostatic hyperplasia (BPH) is regarded as non-malignant growth of prostatic tissue [1]. In men aged more than 50 years, it is the fourth most prevalent disease [2]. BPH has substantial adverse effects on the public health. Its prevalence is anticipated to grow abruptly in the coming years [3]. Health-related quality of life including work productivity, social and family relationships, mental health and sleep quality are affected by BPH [4, 5]. Increased risks of prostate enlargement and clinical BPH are associated with diabetes [6]. Approximately 25-35% of all men over 60 years of age have concomitant BPH and hypertension. The reason implicated in their development is increased sympathetic activity [7]. However, a study demonstrated that much lower urinary tract symptoms (LUTS) and large prostate volume are present in men with hypertension (HTN) than without HTN [8].

Altered serum levels of androgenic and estrogenic steroid hormones among smokers play role in the induction and maintenance of BPH [9]. A study hypothesized that sustained smoking resulting in elevations in intra-prostatic androgens, mainly dihydrotestosterone, may be associated with prostate enlargement [10]. Another study concluded that irritative symptoms have positive correlation with the number of cigarettes smoked per day [11]. In study done by fu Y in 2016 showed DM and HTN was related to increased risk of BPH [12]. Body mass index (BMI) and fasting blood glucose were positively correlated with total prostate volume [13].

Several modifiable, age-related metabolic aberrations like diabetes and obesity were important determinants in both the development and the progression of BPH [14]. In addition, Nandy and Saha established positive association between prostate volume with raised blood pressure and fasting blood glucose [15]. Likewise hypertension was also not associated with BPH in the studies carried out by Guess and Zucchetto [16, 17]. There is no study done regarding the association of BPH with DM and/or HTN in Nepal as far as best of our literature search. This study is conducted with an aim to determine the association of BPH with diabetes mellitus (DM) and/or HTN. This may help to bring out new dimensions in management of BPH.

Materials and Methods

This Case control study was conducted from February 2018 to March 2019 with approval by 'Institutional Review Committee' of Nobel Medical College and Teaching Hospital, Biratnagar. A prior written informed and well understood consent was taken from all eligible patients. All male patients diagnosed as BEP were included in the study. Patient with history of prostate cancer, neurogenic bladder, those who had undergone surgical intervention for prostate, not willing to take part in study were excluded. Age matched male population without lower urinary tract symptoms and normal range blood pressure and blood sugar admitted in urology in patient department were taken as control. A sample size was estimated on the basis of literature [6], considering DM/HTN in normal population (P2 = 32.3%), Odds ratio (OR= 1.54), expected proportion of diabetes/hypertension in BPH patients (P1 = 42%). With power 80% and alpha error 5% two sided and ratio of case to control (2:1), a total of 540 cases and 270 controls was required for the study.

A detailed clinical history with respect to LUTS, duration of illness, past history and thorough clinical examination were recorded in a specifically designed proforma. The diagnosis of BPH was based on following clinical markers: LUTS severity was measured by the American Urological Association Symptom Index (AUA-SI) score, and I-PSS score Prostate volume (ml) greater than 20ml was considered enlarged, Prostatic Serum Antigen (PSA) concentrations 4ng/ml for BPH. The cases were then assessed for maximum urinary flow rate (Qmax) to determine the obstructive features of BPH. IPSS score was graded as follows: Mild: 0 – 7, Moderate: 8 – 19, Severe: 20 – 35.Prostate volume was measured by abdominal ultrasonography. The subjects were instructed to fill their urinary bladder by consuming water. The ellipsoid formula was used to calculate the size by multiplying the largest antero-posterior height (H), transverse width (W), cephalo-caudal length (L) and diameters by 0.524 (H X W X L X π/6). Prostatic volume in subjects undergoing clinical examination was categorized as enlarged if it's greater than 20 ml. Urine flow rate was measured by uroflowmetry (NIDHI flow 814). Patient was advised to come with full bladder and urinate in special toilet without attempting to manipulate the speed or flow in any way. BPH was defined as maximum flow rate (Qmax) less than 15 mL/s on a voided volume of at least 125–150 mL.Serum PSA was measured and cut off value was 4 ng/mL. The sensitivity of PSA more than 4ng/ml in detecting carcinoma

prostate was 100% and the positive predictive value for serum PSA was 19.0%.

Control subjects were age matched and selected from patients admitted in urology ward. They were assessed for BPH through LUTS questionnaire and those with I-PSS score less than 7 were included in the study. Cases and control subjects completed the voiding evaluation by I-PSS. The I-PSS comprises of 7 items scored from 0 to 5, giving maximum global score of 35 points. All the subjects were assessed for HTN and DM. Patient was categorized as case of HTN if blood pressure ≥140/90 mmHg (According to JNC 7 classification). Blood pressure was measured after 5 minutes rest and again 10 minutes later, also recording the mean value. For those undiagnosed cases of diabetes: Fasting blood sugar was sent after no caloric intake for at least 8 h., FPG ≥126 mg/dl (7.0 mmol/l) was included in DM. Previously diagnosed cases of DM. Data was entered in Microsoft Excel 2010 and all analyses were performed using the Statistical Package for the Social Sciences (SPSS 11.5).

Results

Total patients admitted to urology department with diagnosis of benign enlargement of prostate were 540 among this 305 patients had diabetes and hypertension.

Table 1: Association of Benign Prostatic Hyperplasia with Diabetes

Diabetes	Cases, n(%)	Control, n(%)	Total	OR (95% CI)	P value*
Present	79(14.63%)	32(11.85%)	111(13.70%)	1.27	
Not present	461(85.37%)	238(88.15%)	699(86.30%)	(0.82–1.99)	0.279
Total	540(100%)	270(100%)	810(100%)		

DM was present in 14.63% of cases and 11.85% of controls. The positive association was established between BPH and DM but it was statistically not significant (OR: 1.27; 95% CI: 0.82 – 1.99; P = 0.279).

Table 2: Association of Benign Prostatic Hyperplasia with Hypertension

Hypertension	Cases, n (%)	Controls, n (%)	Total	OR (95% CI)	P value*
Present	205(37.96%)	80(29.63%)	285(35.19%)	1.45	
Not present	335(62.04%)	190(70.37%)	525(64.81%)	(1.06–1.99)	0.019
Total	540(100%)	270(100%)	810		

HTN was present in 37.96% of cases and 29.63% of controls. The positive association was found between BPH and HTN, which was statistically significant (OR: 1.45; 95% CI: 1.06 – 1.99; P = 0.0195).

Table 3: Association of Benign Prostatic Hyperplasia with Hypertension and Diabetes Concomitant

Concomitant hypertension and diabetes	Cases, n (%)	Control, n (%)	Total	OR (95% CI)	P value*
Present	21(3.89%)	5(1.85%)	26(3.21%)	2.14	
Not present	519(96.11%)	265(98.15%)	784(96.79%)	(0.79–5.75)	0.129
Total	540(100%)	270(100%)	810(100%)		

DM and HTN both were concomitantly present in 3.89% of cases and 1.85% of the controls. The positive association of BPH was found with DM and HTN but it was statistically not significant (OR: 2.14; 95% CI: 0.79 – 5.75; P = 0.1296).

Table 4: Association of Benign Prostatic Hyperplasia with Hypertension and/or Diabetes

Hypertension and /or diabetes	Cases, n(%)	Control, n(%)	Total	OR (95% CI)	P value*
Present	305 (56.48%)	117 (43.33%)	422 (52.09%)	1.70	
Not present	235 (43.52%)	153 (56.67%)	388 (47.91%)	(1.26–2.27)	0.000
Total	540 (100%)	270 (100%)	810 (100%)		

DM and/or HTN was present in 56.48% in cases and 43.33% in control. The positive association was found between BPH and DM and/or HTN and it was statistically significant (OR: 1.697, 95% CI: 1.26 – 2.27, P=0.0004).

Table 5: Risk factors of BPH

Variables associated	Multivariate analysis OR (95% CI)	P Value*
Diabetes	1.61 (1.02 – 2.54)	0.042
Hypertension	1.67 (1.20 – 2.31)	0.002
Concomitant diabetes and hypertension	2.73 (1.01 – 7.4)	0.048

Discussion

BPH is regarded as non-malignant growth of periurethral transition zone of prostatic tissue [1]. It is the most common benign tumor in men, and the incidence is age related [2]. The incidence of BPH increases by 10 % per decade and reaches 80% at approximately 80 year of age [18]. Its prevalence worldwide is 26.2% and in Nepal is 39.6% [19]. The mean age of presentation of the patient with BPH is 65.2 years. LUTS which are the most common presentation of BPH are measured by the AUA-SI and its internationally validated counterpart, the International Prostate Symptom Score (I-PSS). LUTS can be classified as mild, moderate and severe grade. Association of LUTS with enlarged prostate (volume more than 20 ml) along with PSA value less than 4ng/ml can be used to diagnose BPH with higher accuracy [20]. There are various risk factors such

as sex steroid hormones, the metabolic syndrome, obesity, DM, physical activity, HTN, diet, and inflammation which appear to potentially influence the natural history of BPH. Though DM and HTN which are the burning problems of modern world have been linked to the progression of BPH but still, the association has been the topic of controversy. Therefore, in this study, we have tried to find whether BPH is associated with DM and / or HTN.

In our study, 14.63% of cases of BPH and 11.85% of controls had DM. In study done by Rohrmann in 405 American men in 2005, DM was present in 15.5% of cases and 9% of controls [21]. As both DM and BPH are the diseases of elderly group of people, they are likely to be present at the same time. In contrast to our study, a study demonstrated no statistical difference in BPH (defined by IPSS score) in the group of men with DM as a risk factor and without DM [22]. Similarly, in the population-based Massachusetts Male Aging Study, DM could not predict clinical BPH. In our study, 37.96% (205) of cases and 29.63% (80) of control had HTN. In the study done by Rohrmann, HTN was present in 40.8% of cases and in 27.7% of controls [21]. Similarly, in study by Chiu, HTN was present in 62.3% of cases and 54.3% of controls [23].

In a study by Maruenda, they found that an estimated 25% of men more than 60 years were found to have concomitant BPH and HTN [24]. This concomitancy is credited to the fact that both HTN and BPH are the diseases of elderly. Our study showed that there is statistically significant age independent positive association between HTN and BPH (OR: 1.67; 95% CI: 1.20 – 2.31; p value: 0.002). Similar to our study, a study by Chen in 130 patients demonstrated BPH patients on an average have 1.42 ± 1.28 risk factors for cardiovascular factors including HTN and DM [25]. Our study showed that 3.89% of cases and 1.85% of control had concomitant HTN and DM demonstrating positive association between BPH and concomitant HTN and DM (OR: 2.73; 95% CI: 1.01 – 7.4; p value: 0.048) but it's not statistically significant as the sample size is less for this concomitancy.

As far as literature search is concerned, association of BPH with concomitant DM and HTN has not been studied before and hence, no comparison could be done. Our study showed that 56.48% of cases and 43.33% of control had DM and/or HTN. In addition our study demons-trated age independent positive association between BPH and DM and/or HTN which was statistically significant (OR: 1.70; 95% CI: 1.26 – 2.27; p value: 0.0004).

Conclusion

BPH is associated with DM, HTN, concomitant DM and HTN and DM and/or HTN, So, prevention of hypertension and / or diabetes can prevent BPH and its progression. The prevention of risk factors of DM and HTN can prevent the progression of BPH and its related complications.

Conflicts of interests: None

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