SAS Journal of Surgery
Abbreviated Key Title: SAS J Surg
ISSN 2454-5104
Journal homepage: https://www.saspublishers.com

OPEN ACCESS

Surgery

Association between Diabetes Mellitus and Benign Prostatic Hyperplasia

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DOI: 10.36347/sasjs.2022.v08i12.006 | **Received:** 09.09.2022 | **Accepted:** 16.10.2022 | **Published:** 07.12.2022

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Abstract | **Original Research Article**

Background: Previous studies had documented a causal relationship between diabetes mellitus (DM) and benign prostatic hyperplasia (BPH) through hyperinsulinaemia and increased serum levels of insulin-like growth factor-1 (IGF-1). These growth factors contribute to prostatic enlargement and may cause lower urinary tract symptoms (LUTS) and increase symptom severity in BPH patients. This study was aimed at associating DM with clinical parameters of BPH. ***Materials and Method*:** This was a retrospective study of one hundred and sixteen (116) BPH patients carried out over a year period. Their clinical, laboratory and imaging study results were retrieved from their case files. Eligible patients were taken through a structured questionnaire during their clinic visits. This questionnaire assesses severity of LUTS in BPH patients called the International Prostate Symptom Score (IPSS) and quality of life scale. All data were entered into a structured proforma and analyzed using the statistical package for social sciences (SPSS) version 20.0 software. Diabetic patients were selected based on the clinical history of diabetes mellitus (DM). ***Results:*** One hundred and Sixteen (116) patients aged between 43 and 82 years with a mean age of 63.10±8.89 years were studied. Diabetic patients were older than non-diabetics. They also had higher clinical parameters of BPH namely; higher prostate volume (PV), higher symptom scores both voiding and storage and a poorer quality of life from symptom-bother. ***Conclusion*:** Diabetic men have higher prostate volume which can precipitate LUTS, cause BPH progression and symptom severity.

Keywords: Diabetes mellitus, Benign prostatic hyperplasia, Lower Urinary tract symptoms, International Prostate Symptom Score.

INTRODUCTION

Over the years, researchers have observed similarities in symptomatology between DM and BPH. More studies revealed that the prevalence of both conditions occurs in similar ages and DM has been demonstrated to contribute to the development and progression of BPH [1, 2]. In a consecutive series of patients with LUTS referred for prostate surgery, cross-sectional studies in Sweden showed that DM, hypertension, obesity, low high density lipo-protein, plasma cholesterol and high plasma insulin levels correlated significantly with the diagnosis of BPH [1, 3]. Further studies specific to DM and increasing LUTS from the Massachusetts male aging study [4], the finish male health study FMHS [5] and Sandfeldt *et al*., [6] had consistently reported a highly significant association. LUTS common in both DM and BPH are often classified as voiding and storage symptoms.

There are several hypothesized mechanisms put forward to explain how DM produces and worsens LUTS especially in BPH patients. DM causes impairment of detrusor function through neuropathies and this leads to lower maximal flow rate for any given level of bladder outlet resistance resulting in increased post void residual volume and LUTS severity [7]. Apart from diabetic-induced neuropathies leading to LUTS, other mechanisms include hyperinsulinaemia and increased levels of serum IGF-1. Hyperinsulinaemia causes enhanced glucose metabolism in the ventro-medial neurons of the hypothalamus leading to activation of α-adrenergic pathways resulting in smooth muscle contraction in the bladder neck and the prostate contributing to the development of LUTS [8]. Again hyperinsulinaemia is associated with raised serum IGF-1; both are noted to be involved in prostate cell growth [9]. A study by Sarma *et al*., [10] demonstrated a positive correlation between DM and prostate volume and PV had been implicated in the Static component of BPH- related LUTS. Uncontrolled DM can cause

osmotic diuresis, increased thirst with consequent worsening urinary frequency and nocturia especially in BPH patients resulting in perceived poor quality of life. BPH in the same vein, produces LUTS by enhancing outlet resistance through both the static and dynamic components but does not primarily impair detrusor function, unlike what is observed in DM-induced LUTS [7]. The distinction between LUTS caused by DM and BPH is difficult to appreciate due to greater power of overlap, however, degree of diabetic control has been shown to affect the progress of BPH with improvement in BPH markers such as prostate volume, maximum flow rate (Qmax) and IPSS. This study was aimed at associating DM with clinical parameters of BPH.

MATERIALS AND METHOD

This study was carried out in 2021 (Jan-Dec. 2021) in the urology clinic of our facility. The study population was restricted to patients with clinical and or histological diagnosis of BPH who also had complete clinical, laboratory and radiological information. Exclusion criteria were patients suspicious of prostate cancer (Pca) on rectal examination, elevated prostate specific antigen (PSA), trans-rectal ultra-sound guided biopsy results of Pca, patients with urethral stricture, urethral or bladder cancer. Diabetic men were recruited based on medical history of diabetes. Patients were grouped into 2; diabetics were in group 1 and non-diabetics in group 2.

Measurements

Eligible patients were assessed on the day of their clinic visits and such case files were coded to avoid duplication of information. One hundred and sixteen (116) selected patients were taken through a well-structured questionnaire (IPSS and quality of life scale) to assess LUTS severity. The interviews were conducted by surgery residents and supervised by consultant urologists. The questionnaire usually consists of seven questions namely incomplete bladder emptying of urine, urinary frequency, intermittency, urgency, weak stream, straining and nocturia. Each symptom is scored from zero to five depending on its severity. The minimum total score is zero and maximum score is thirty-five (35). This is further divided into the 3 groups: 0-7 (mild), 8-19 (moderate) and 20-35 (severe) symptoms. A drill on six questions to test the degree of bother and quality of life from these symptoms was also done. Information on digital rectal examination findings of the prostate was documented. Laboratory investigations included fasting blood sugar (FBS), serum PSA and Trans-rectal ultrasound scan (TRUS) of the prostate for volume measurement using the ellipsoid formula by multiplying the largest antero-posterior (height), transverse (width) and cephalo-caudal (length) prostate diameters by 0.52, ($H \times W \times L \times {}^{\pi}/_{6}$).

Statistical Analysis

Collated data was entered into a spread sheet and analysed using the SPSS version 20.0 software. Descriptive statistics was used for continuous variables to calculate their means and Standard deviation. Frequency table was constructed for categorical variables. Students T-test was used to compare means of variables while Pearson correlation was used to test the extent of linear relationship between variables. P value was set at less than 0.05 for statistical significance.

RESULTS

The mean age of all patients was 63.10±8.89 years ranging from 43 to 82years. The mean age of diabetic men was 66.36 ± 8.52 years and 61.7± 8.65 years for non-diabetics. There was a significant statistical difference in age between the two groups ($P < 0.05$). Table 1 shows descriptive statistics for all patients. Tables 2 and 3 present frequency of categorical variables. Men in their 6^{th} decade of life formed the majority (Table 2). Prevalence of DM was 24.1% (Table 3). More men (65.5%) had PSA in the range of 0-4ng/ml. Prostate volume in excess of 50mls were observed in most of the patients (44.8%) and IPSS of 8-19 (Moderate severity) was found in the majority (70.7%) of patients, followed by Score of 20-35 (19.8%) and least by score of 0-7 (9.5%). Table 4 features means of age in diabetics and non-diabetics and baseline prostate characteristics in both groups. Table 5 shows Correlation of variables.

Table 1: Descriptive Statistics:

Variable	Mean ± Std	Min	Max
Age (Years)	63.10 ± 8.89	43	82
PSA (ng/ml)	5.07± 5.6	0.10	25.90
PV (mls)	61.01 ± 46.09	14.40	313.32
IPSS	14.46 ± 5.98	3	34
Voiding Symptoms	5.04 ± 4.22	0	19
Storage Symptoms	9.41 ± 2.91	3	15
Qol	4.46 ± 0.94	2	6

Table 2: Age Category:

Age range	Frequency (n)	Valid (%)	Cumulative (%)
40-49	4	3.4	3.4
50-59	42	36.2	39.7
60-69	37	31.9	71.6
70-79	28	24.1	95.7
80-89	5	4.3	100.0
90 and above	0	0.0	100.0
Total	116	100.0	

Table 3: Diabetic Status

	Frequency (n)	Valid (%)	Cumulative (%)
DM	28	24.1	24.1
Non- DM	88	75.9	100.0
Total	116	100.0	

Table 4: T-test of Variables

Variables	DM	Non-DM	T-test Statistics
Age (Years)	66.36 ± 8.52	61.87 ± 8.65	P < .05*
PSA (mg/ml)	4.12 ± 4.11	5.41 ± 6.01	P > .05
PV (mls)	79.55 ± 68.61	55.39 ± 34.77	P < .05*
IPSS	16.00 ± 4.83	13.91 ± 6.27	P > .05
Voiding Score	5.79 ± 3.53	4.80 ± 4.43	P > .05
Storage score	10.25 ± 2.38	9.08 ± 3.00	P > .05
Qol Scale	4.71 ± 0.89	4.37 ± 0.95	P > .05

* Statistical Significance at P < 0.05

Table 5: Correlation Table

PV vs DM	r = .225,	P = 0.015*
PV vs PSA	r = .235,	P = 0.01*
IPSS vs PV	r = .282,	P = 0.002*
Storage vs PV	r = .125,	P = 0.000*
Voiding vs PV	r = .310,	P = 0.001*

* Statistical Significance at P < 0.05

DISCUSSION

Bourke and Griffin were the first researchers that suggested an association between DM and BPH aetiology owing to high prevalence of DM in BPH patients referred for prostate surgery [12]. Both disease entities occur in similar ages and DM has been demonstrated to contribute to the development and progression of BPH [1, 2]. Many reports have suggested a causal relationship between high plasma insulin level typical of DM and the development of BPH [13, 14]. BPH generally enhances bladder outlet resistance by both the static and dynamic components leading to LUTS and Ozcan *et al*., [15] in their study demonstrated a direct association between static and dynamic components of BPH and DM. Higher prostate volume (PV) is implicated in the static components of the bladder outlet obstruction and in a study by Hammarsten et al., [1], it was reported that DM patients with LUTS had higher PV than non-diabetics. Larger PV in diabetics have been explained as contributed by hyperinsulinaemia and increased IGF-1 levels in the blood of diabetics as both are known prostate cell growth promoters [9]. A decrease in insulin concentration was demonstrated in studies of rats to correlate positively with reduction in PV [16, 17], Barnard *et al*., [18] also associated the reduction of epithelial prostate stem cells with the reduction of plasma insulin. DM has also been reportedly involved in the dynamic component of bladder outlet obstruction by way of hyperinsulinaemic activation of the autonomic neural pathways leading to α-adrenergic stimulation of the smooth muscles of the bladder neck and the prostate causing LUTS [8]. Again DM can cause LUTS through neuropathies [7]. Although, both DM and BPH cause LUTS by the static and dynamic means, BPH does not primarily cause LUTS by impairing detrusor function [7]. It is quite difficult to differentiate LUTS caused by DM and BPH as the mechanisms overlap.

In this study, PV in diabetics was higher than in non-diabetics with a statistically significant mean difference (P < 0.5). PV also correlated positively with the diabetic population (r = .225, P< 0.5). Previous studies reported same findings [1, 10]. The prevalence of DM was noted to be higher than in the general population in same locality (24.1% vs 7.0%) [19]. Apart from age-related increase prevalence of both DM and

BPH, the observed prevalence may suggest a causal relationship of these conditions. Serum PSA concentration was lower in diabetics than non-diabetics. This has been consistently reported by previous studies and thought to be related to lower androgen levels in DM [20-22] since PSA is androgen regulated [23]. Further work on this subject showed that the inverse relationship between PSA and DM was more pronounced in long standing DM [24] as plasma insulin decreases in these patients leading to subsequent decrease in serum PSA [25].

International prostate symptom score (IPSS) represented by 7 symptoms and composed of both voiding and storage symptoms of the lower urinary tract usually measures the degree of severity of bladder outlet obstruction caused by BPH. It also relates directly with the health-related quality of life of the sufferer. IPSS in this study was higher in diabetics even when stratified into voiding and storage components. It therefore follows that diabetes can influence symptom severity in BPH patients. Another study had documented same finding [10]. The mechanism is likely due to diabetic cystopathy producing both storage and voiding LUTS [7]. Again, hyperglycaemia in diabetics could cause osmotic diuresis, increased thirst and fluid intake with increase urinary frequency. Activation of the sympathetic nervous system and subsequent α-adrenergic stimulation of the smooth muscles of the bladder neck and prostate together with higher PV in diabetics had been advocated to contribute to both the dynamic and static components of bladder outlet resistance exaggerating symptoms of BPH [8]. Quality of life assessment was worse in the diabetic arm informing greater degree of symptom-bother imposed by diabetes on BPH sufferers.

Although the causal relationship between DM and BPH has been suggested through high plasma insulin and IGF-1 levels contributing to higher prostate volume and generating static component of bladder outlet resistance, the use of LUTS to associate DM and BPH may be limited as DM has only been shown to aggravate symptom severity in established BPH patients while on the other hand, BPH is not always accompanied by symptoms.

This study was limited by lack of other information associated with DM that could also influence LUTS due to BPH. Body Mass Index (BMI) was not recorded. Diabetic individuals are likely to be obese and a direct relationship between obesity and LUTS due to BPH had been demonstrated via hyperinsulinaemia and an increased oestrogen to androgen ratio [3, 5, 26]. Information on duration of diabetes and medications use were somewhat misleading because of poor information recall and was not recorded. According to previous studies, a good diabetic control was associated with reduction in symptom severity among BPH patients [11]. Post void residual volume of urine on ultrasound scan was not also recorded which could have strengthened the already suggested association between LUTS due to DM and BPH. In a study by Ozcan *et al*., [15] post void residual volume was significantly higher in diabetics than in non-diabetics (Pvalue=0.000). This variable characterizes bladder outlet obstruction due to symptomatic BPH. Beyond the inherent flaws of a retrospective study, the strength of this work confirms in part that DM could double as one of the risk factors for BPH develpoment as well as increased propensity to worsen symptom severity in established BPH.

CONCLUSION

This study shows that DM could be associated with BPH development through enhanced prostate enlargement that could lead to static components of BPH-induced outlet obstruction and an inherent capacity to increase symptom severity measured by IPSS in BPH patients.

Authors Contribution:

Elijah Asuquo Udoh: Substantial contributions to conception and design, Acquisition of data, Drafting the article, revising it critically for important intellectual content, data analysis and Final approval of the version to be published.

Anthony Joseph Usoro: Substantial contributions to conception and design, revising it critically for important intellectual content and final approval of the version to be published.

Ifiok Udo Essiet: Substantial contributions to conception and design, revising it critically for important intellectual content and final approval of the version to be published.

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