

City Research Online

City, University of London Institutional Repository

Citation: Asare, G. A., Sule, D. S., Oblitey, J. N., Ntiforo, R., Asiedu, B., Amoah, B. Y., Lamptey, E. L., Afriyie, D. K. & Ohene-Botwe, B. (2021). High degree of prostate related LUTS in a prospective cross-sectional community study in Ghana (Mamprobi). Heliyon, 7(11), e08391. doi: 10.1016/j.heliyon.2021.e08391

This is the published version of the paper.

This version of the publication may differ from the final published version.

Permanent repository link: https://openaccess.city.ac.uk/id/eprint/29557/

Link to published version: https://doi.org/10.1016/j.heliyon.2021.e08391

Copyright: City Research Online aims to make research outputs of City, University of London available to a wider audience. Copyright and Moral Rights remain with the author(s) and/or copyright holders. URLs from City Research Online may be freely distributed and linked to.

Reuse: Copies of full items can be used for personal research or study, educational, or not-for-profit purposes without prior permission or charge. Provided that the authors, title and full bibliographic details are credited, a hyperlink and/or URL is given for the original metadata page and the content is not changed in any way.

City Research Online: http://openaccess.city.ac.uk/ publications@city.ac.uk/



Contents lists available at ScienceDirect

Heliyon

journal homepage: www.cell.com/heliyon



Research article

High degree of prostate related LUTS in a prospective cross-sectional community study in Ghana (Mamprobi)



George A. Asare ^{a,**}, Derick S. Sule ^b, Jared N. Oblitey ^b, Reese Ntiforo ^b, Bernice Asiedu ^a, Brodrick Y. Amoah ^a, Emmanuel L. Lamptey ^b, Daniel K. Afriyie ^c, Benard Ohene Botwe ^{b,*}

- ^a Chemical Pathology Unit, Department of Medical Laboratory Sciences, School of Biomedical & Allied Health Sciences (SBAHS), University of Ghana, P. O Box KB 143, Korle Bu Campus, Ghana
- b Department of Radiography, School of Biomedical & Allied Health Sciences (SBAHS), University of Ghana, P. O Box KB 143, Korle Bu Campus, Ghana
- ^c Department of Pharmacy, Ghana Police Hospital, Cantonments, Accra, Ghana

ARTICLE INFO

Keywords:

Lower urinary tract symptoms (LUTS) Benign prostatic hyperplasia (BPH) Prostate volume Metabolic syndrome (MetS)

ABSTRACT

Background: Changing voiding patterns, volume and frequency, may sometimes be mistaken for anxiety, stress or increase in fluid consumption. In the aging male population, the commencement of lower urinary tract symptoms (LUTS) may be silent and perceived as "normal" and unrelated to Benign prostatic enlargement (BPE). The purpose of the study was to determine the prevalence of apparently "silent LUTS" (perceived asymptomatic LUTS) in men in a Ghanaian Community as well as its underlying risk factors.

Methods: One hundred and eleven (111) men (40–70 years) were recruited from a community in Ghana. The International Prostate Symptoms Score (IPSS) questionnaire (administered in the local language and English) and ultrasonographic imaging of the prostate volume (PV) were utilized to collect data. IPSS score >7 plus PV > 30 cm³ was definitive of lower urinary tract symptoms. Eighty-one (81) participants were classified "LUTS Negative" (LN) and 30, "LUTS Positive" (LP). Risk factors i.e., cholesterol (CHOL), triglyceride (TG), high density lipoprotein cholesterol (HDL-C), low density lipoprotein cholesterol (LDL-C), very low-density lipoprotein (VLDL), coronary risk (CR), BMI and Blood Pressure were also determined.

Results: The prevalence of LUTS using only IPSS definition alone was 42.3%. However, IPSS in combination with Prostate Volume gave a prevalence of 27.0%. LN subjects had enlarged prostate (41.98%) and LP, 100%. Quality of life (QoL) was better in the LUTS Negative than LUTS Positive group (p < 0.001). In the univariant analysis coronary risk, triglyceride and VLDL contributed to LUTS (p = 0.023, 0.22, 0.22, respectively). In a multivariant analysis HDL-C (p = 0.027), BMI (p = 0.047) and triglyceride (p = 0.019) significantly contributed to LUTS. **Conclusions:** The prevalence of LUTS (42.3%) is high. Components of Metabolic Syndrome- HDL-C, BMI, and coronary risk were associated with LUTS. This emphasizes the need for community education.

1. Introduction

Male populations in their mid-years need to pay extra attention to physiological changes including urodynamics. Changing voiding patterns, volume and frequency, may sometimes be mistaken for anxiety, stress or increase in fluid consumption. However, the occurrence of poor voiding characteristics such as nocturia, frequency, urgency are suggestive of lower urinary tract symptoms (LUTS) [1]. With time as symptoms advance, LUTS become obvious and the quality of life (QoL) is affected. Asymptomatic bladder outlet obstruction (BOO) may therefore be

ignored, while sub-clinical benign prostatic hyperplasia or enlargement (BPH/BPE) may be over-treated for LUTS [2]. BPH is a laboratory diagnosis which is histologically determined, whiles prostate enlargement is clinically diagnosed [3, 4]. The severity and impact of these conditions can be assessed using the International Prostate Symptoms Score (IPSS) where a score >7 is considered symptomatic and QoL score more >3, a significant bother (Madersbacher *et al.*, 2004). A combination of IPSS and enlarged prostate >30 cm is definitive of the presence of LUTS [5].

Metabolic syndrome (MetS), comprising obesity and abnormalities of triglyceride (TG), high density lipoprotein cholesterol (HDL-C), fasting

E-mail addresses: george.asare@gmail.com (G.A. Asare), sirbenard13@gmail.com, bebotwe@gmail.com (B.O. Botwe).

^{*} Corresponding author.

^{**} Corresponding author.

plasma glucose (FBG) and blood pressure (BP), correlate strongly with LUTS and BPH (NCEP ATP III) [6]. Prostate enlargement leads to a protrusion into the bladder, bladder neck or urethral lumen. The severity of the symptoms do not correlate well with the degree of enlargement as well as prostate specific antigen (PSA) levels [7, 8]. BPH may arise from the transition zone or the periurethral glands, causing LUTS and subsequently obstructing urinary and ejaculatory flow. In order to evaluate LUTS qualitatively, the IPSS questionnaire was adopted [6, 9]. In the aging male population, the commencement of LUTS may be silent and perceived as "normal" and unrelated to BPE. The study aimed at determining the magnitude of apparently "silent LUTS" (perceived asymptomatic LUTS; the presence of partial indicators of the classic clinical symptoms, without the respondent being aware of the impingement upon the quality of life that we used the term "silent LUTS) in men in a Ghanaian community as well as the risk factors. In this study, a combination of IPSS >7 and enlarged prostate >30 cm³ was definitive of the presence of LUTS [6].

2. Methods

This was a prospective study involving residents of a small suburb of Accra. Male participants aged 40–70 years were invited to freely participate. One hundred and eleven (111) participants were recruited. Participants filled the necessary consent forms. The study was approved and ethics clearance number SBAHS-MLS/10570421/SA/2018–2019 issued. Furthermore, the study was conducted in accordance with the Helsinki Declaration of 1964 (revised in October, 2008).

Men on catheter or those who had undergone prostatectomy; those with associated anal lesion precluding such as third-degree hemorrhoids, prostate cancer, were also excluded.

The IPSS questionnaire is made up of eight (8) major questions. Seven questions focused on incomplete emptying, frequency, intermittency, urgency, weak stream, straining and nocturia. Answers were graded from zero (0) to five (5) representing the increasing severity of the symptoms of urinary dysfunction. The eighth question sought to elicit answers such as, being delighted, pleased, mostly satisfied, mixedabout equally satisfied and dissatisfied, mostly dissatisfied, unhappy and terrible, if the person had to spend the rest of his life with the condition. This was scored on a scale of zero (0) to six (6). The higher the score, the poorer the QoL. IPSS was administered both in the English language and local language for clarity and emphasis in order to remove every shadow of doubt.

An amount of 3 mL of (10–12 h) fasting venous blood was collected from each participant between 6:30 and 9:00 am. Blood was discharged into a fluoride and serum separator tubes. Fluoride tube samples were centrifuged at 3000 rpm for 15 min within the shortest possible time. Plasma was aliquoted. Gel separator tube samples were centrifuged at 5000 rpm for 10 min and sera aliquoted into Eppendorf tubes. Both plasma and sera were stored at -20 $^{\circ}\text{C}$ for later analysis.

Participants stood barefooted on the Seca stadiometer (Hamburg, Germany). Height was obtained to the nearest 0.1 cm. For weight, participants retained light clothing while the sole of each foot made contact with the bio-impedance zones of the Seca 770 scale (Hamburg, Germany). Weight was measured to the nearest 0.1kg. BMI was calculated as the ratio of weight (kg) to height (m) square. Systolic and diastolic blood pressure was measured twice (5 min apart) after participants sat for at least 15 min, using Omrion 785 auto-inflating BP machine and the mean recorded.

Prostate specific antigen (PSA) concentration was measured using a 96-well enzyme-linked immunosorbent assay (ELISA) test kit from Human (Germany). The test was conducted according to the manufacturer's instructions using the principle of sandwich ELISA technique. The final chromogen was read at 450 nm.

Plasma glucose determination using the Mindray glucose hexokinase (HK) method on Mindray BS-400 Chemistry Analyzer (Shenzen, China) was performed according to the manufacturer's instructions.

Lipid profile consisting of Total Cholesterol (TC), Triglycerides (TG), HDL, LDL and VLDL and was performed on sera using a VITROS 5.1 FS Chemistry Analyzer (Rochester, NY, United States of America). The VITROS 5.1 FS Chemistry Analyzer uses the enzymatic method and was used to determine the concentration of the various parameters in the serum samples at particular wavelengths. The tests were carried out on the analyzer using the manufacturer's protocol.

The participants were evaluated using a Siemens SONOLINE SSI-6000 ultrasound machine with a 7.5-MHz transrectal end fire probe and a 3.5MHz curvilinear probe. The prostate was imaged in its entirety in at least 2 orthogonal planes (longitudinal and coronal) from the apex to the base of the gland. Color and power Doppler sonography was used in detecting areas of increased vascularity. The periprostatic fat and neurovascular bundle was evaluated for symmetry and echogenicity. The transverse, anteroposterior, and longitudinal dimensions of the transition zone (TZ) were measured in the same planes in which the total prostate dimension was determined. The total prostate volume and TZ volume were calculated electronically using the Prolate Ellipsoid Formula (length \times height \times width \times 0.5236 (pi/6) in-built into the ultrasound machine.

Categorical data were presented as frequencies and percentages. For continuous variables, means and standard deviations were compared with students' t-test when normally distributed. For skewed data, median and interquartile ranges were compared using Mann-Whitney test. Additionally, simple and multiple logistic regression analyses with forward stepwise procedure was used. Univariate analysis and multiple linear regression were performed to reveal the relationships among different clinical parameters and PV. Pearson correlation analysis was performed to determine the association of risk factors with IPSS and Prostate Volume. The analyses were conducted with Statistical package for the Social Sciences (SPSS) V.22.0 software (IBM Corporation). Two-side $p \leq .05$ was considered statistically significant.

3. Results

The peak age was in the 61–70 years category (35.14%0 which was closely followed by 51–60 years (34.23%). Majority of the participants were married (76.57%). With regard to education, about 40% (39.64%) completed Junior High School, and about a quarter received tertiary education (22.5%). Majority of the participants (39.64) were retired people and only 9% were unemployed. More than half (54.95) belonged to the low income bracket and 10% earned high income. Only 2.2% of the respondents were smokers (Table 1).

From the frequency figure, abnormal IPSS levels in the LP group was 5 times that of LN (100.0% and 20.99%, respectively). For high PSA 77.7% was found in the LN group compared to 56.67% in the LP group. Obesity was slightly lower in the LN group compared to the LP group (21.25% and 26.67%, respectively) group. Pre-diabetes was 73.75% in the LN group compared to 60.0% in the LP (Figure 1).

When the data was stratified according to age (<50 years and ≥50 years) alongside possible LUTS risk factors, blood pressure was significantly different (p = 0.003) with those below 50 years having a higher blood pressure. For all other parameters except fasting plasma glucose (FPG), those at 50 years and above had higher results, though not significant (Table 2).

From Table 3, continuous variables such as age was significantly different (p = 0.003) with LP being higher than LN (57.69 \pm 10.92 and 63.96 \pm 8.95 years, respectively). Triglyceride, CR, and VLDL were significantly higher in the LP group compared to the LN group (p = 0.036, p = 0.041 and p = 0.36, respectively). BMI was higher in the LP group than the LN group (p = 0.037).

Data from Table 4 showed significant differences (p < 0.001) in PSA of LN and LP groups [2.68 (2.25, 3.48) and 3.5 (2.77, 9.59) ng/ml, respectively]. Prostate volume was $34.28 \pm 15.06 \text{ cm}^3$ for LN and $53.94 \pm 32.02 \text{ cm}^3$ for LP (p < 0.001). Transrectal ultrasound (TRUS) prostate volume was 34.75 ± 14.76 and $54.71 \pm 33.15 \text{ cm}^3$ for LN and LP, respectively (P < 0.001). The TZ volume followed a similar pattern with

Table 1. Sociodemographic characteristics of the cross-sectional male participants of the study within the Community-Frequencies of Categorical Data.

		n (%)
Age class (years)	40–50	20 (18.02)
	51–60	38 (34.23)
	61–70	39 (35.14)
	>70	14 (12.61)
Marital status	Married	85 (76.57)
	Single	9 (8.12)
	Divorced	7 (6.31)
	Widowed	10 (9.00)
Level of education	Primary	4 (3.60)
	Junior High School	44 (39.64)
	Senior High School	38 (34.23)
	Tertiary	25 (22.52)
Employment status	Unemployed	10 (9.01)
	Self-employed	21 (18.92)
	Government employed	24 (21.62)
	Non-government employed	12 (10.81)
	Retired	44 (39.64)
Income status	Low income	61 (54.95)
	Middle income	38 (34.23)
	High income	12 (10.91)
Smoking habits	Never smoked	81 (73.2)
	Previously smoked	27 (24.6)
	Currently smokes	3 (2.2)

Key: Low income \leq \$500/mo; Middle income >\$500 - \$1500/mo; High income >\$1500/mo

higher values in the LP compared to the LN groups (p < 0.001). IPSS and QoL were significantly different in the LP group, compared to the LN group (p < 0.001).

Lipid profile parameters were significantly contributors to LUTS (p < 0.05) apart from HDL and LDL cholesterol. PSA and age were also significant factors predictive of LUTS (p = 0.017, p = 0.008, respectively (Table 5).

Multivariate factors related to LUTS and prostate volume included PSA (p = 0.007), elements of MetS [FPG (p = 0.023), HDL-C (p = 0.027), TG (p = 0.019), and BMI (p = 0.047)] (Table 6).

In Table 7 PSA for normal prostate volume (NV) ($<30~\text{cm}^3$) was 2.57 (2.16, 3.06) cm³ and abnormal volume (AV) ($>30~\text{cm}^3$) 2.96 (2.66, 7.55) cm³ (p < 0.002). TRUS PV was 26.8 \pm 5.97 cm³ (NV) and 49.83 \pm 25.75 cm³ (AV) (p < 0.001). The TRUS TZ was 8.17 \pm 3.58 cm³ and 22.58 \pm 21.93 cm³ for NV and AV, respectively (p < 0.001).

Factors correlating with PV and IPSS are presented in Table 8. Common parameters between the two such as age and PSA correlated fairly with IPSS and PV, although PV correlations were more than IPSS. There was a slight correlation between IPSS and CR (r = 0.174, p = 0.041). However, BMI correlated with PV (p = 0.046). Others were systolic blood pressure (r = 0.340, p = 0.000) and diastolic blood pressure (r = 0.293, p = 0.002).

4. Discussion

The prevalence of LUTS using IPSS alone was 42.3%. However, IPSS in combination with Prostate Volume gave a prevalence of 27.0%. In a 2004–2006 population-based study of 950 men (50–74 years) conducted in Accra had a prevalence of 19% using IPSS [10]. In a 2016 hospital-based study at the second largest teaching hospital in Ghana (Komfo Anokye Teaching Hospital) LUTS was reported to be 88.89%. This high figure may be attributed to the nature of the study which was cross-sectional and hospital based [11]. A study done in Uganda, had a prevalence rate of 40.5% with a cohort of 415 men aged >55 years [12].

In Nigeria the prevalence of LUTS suggesting BPH in a clinic-based study was 72.2. [13] From the afore-mention it is obvious that clinic/hospital-based studies have a higher prevalence than community-based studies. Our prevalence of 42.3% is close to that of the Uganda studies (40.5%).

Studies have demonstrated that MetS as well as its individual components are independent risk factors for LUTS/BPH [14].

In our study, the use of TRUS was advantageous, as this scanning technique allowed a better visualization of the central, transition and peripheral zones of the prostate gland. Both the univariate and multivariate analysis did not show cholesterol to be a risk factor for LUTS and enlarged PV (Tables 5 & 6). However, HDL-C was (Table 6). Similarly, in the REDUCE study, total cholesterol was not a risk factor for LUTS development but HDL-C was significantly associated with LUTS [15]. On the contrary, some clinical and epidemiological studies seem to suggest a positive association between high serum cholesterol levels and LUTS [16]. Elevated cholesterol is associated with prostate cell proliferation [17]. Perhaps cholesterol alone may not be the culprit, but detrusor overreaction and poor bladder control occurs with hyperlipidaemia [18].

VLDL, was significantly associated with LUTS (p=0.022) (Table 5). Over production of VLDL is as a result of increased triglyceride and a reduced lipoprotein lipase in the peripheral tissue, mostly associated with insulin resistance, and diabetes, a factor for MetS [19].

Pre-diabetes twice higher in the LP group compared to the LN group (Figure 1). Obesity on the other hand was thrice higher in the LN group than the LP group. However, BMI was significantly higher in the LP group than the LN group (Table 3). Fowke et al. [20] also showed that obesity was independently associated with prostate volume and a possible underpinning mechanism shown animal studies [21].

Although none of the lipid profile parameters had a significant correlation with prostate volume, CR (CHOL/HDL-C) correlated with IPSS (Table 6). Cardiovascular disease (CD) risk, assessed by the TG/HDL-C ratio is related to MetS. In one study, both univariate and multivariate analysis demonstrated that CD risk factor correlated with PV [22]. Others did not find any association of LUTS and MetS or the components thereof [23]. However, in our univariate analysis, CR was further associated with LUTS (p=0.023) (Table 3). Similarly, in the study of Sandfeldt and Hahn [24], large prostate glands posed a high risk to cardiovascular disease development compared with men who had smaller prostate glands. Our results are consistent with that of Parsons et al. [25] who observed that CR was associated with the pathogenesis of BPH and significant positive associations of IPSS and CVD risk [26]. Endothelial dysfunction has been assigned as one possible reason for this [27].

A significant correlation existed between systolic/diastolic blood pressure and prostate volume (Table 6). Guven et al. [28] also observed that increasing blood pressure correlated with increasing LUTS perhaps through inducing bladder sympathetic hyperactivity.

Systolic and diastolic blood pressure significantly correlated prostate volume (p < 0.000 and p = 0.002, respectively) but not IPSS score (Table 8). One study has reported a probability of 1.54 times higher chance of increased prostate volume with higher blood pressure [29] and another study however, indicated that hypertensives had higher IPSS and prostate volume [30] and worsen LUTS. Blood catecholamine levels are reported to be higher in systolic BP patients [31]. Such high levels affect the lumbosacral cord which in turn affects voiding frequency as well as prostatic smooth muscle tone [31]. The linear regression analysis of this study significantly linked BP to prostate volume. Similar results were obtained by others where an association was obtained between hypertension and BPH independent of age [28]. On the contrary Zeng et al. [32] have proposed no association between hypertension and BPH.

In this study we investigated 111 apparently healthy men who were classified as either LN or LP, based on IPSS >7 and prostate volume >30 cm³. Those without LUTS were slightly younger than those with LUTS (51–60 years). It does appear that at a lower age, LUTS symptoms maybe occult or silent or "normal" as described by others. In this study, participants were allowed to fill their own IPSS questionnaire and this

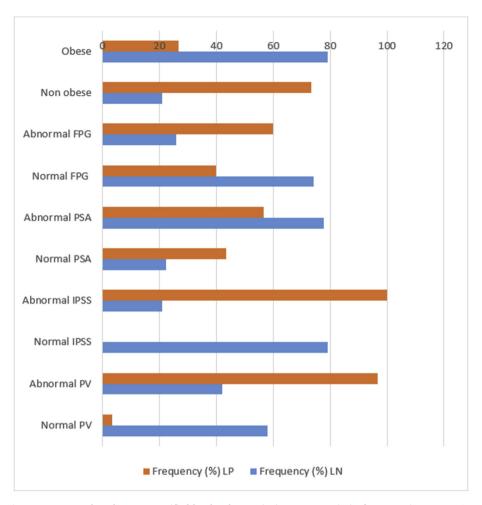


Figure 1. Frequency of various parameters when data was stratified by the absence (LN) or presence (LP) of Lower Urinary Tract Symptoms (LUTS). IPSS = International Prostate Symptoms Score, PSA = Prostate Specific Antigen (ng/ml), BMI = Body Mass Index (Kg/m 2), FPG = Fasting Plasma Glucose (mmol/l), Normal PV - Prostate Volume \leq 30 cm 3 , Normal IPSS - \leq 7.

Table 2. Showing possible Risk Factors associated with LUTS when stratified by age using Students t test on descriptive data of participants.

	Age (Years)	N	Mean \pm SD	p-value
Total Cholesterol (mmol/L)	>50	91	4.81 ± 1.18	0.090
	≤50	20	5.22 ± 1.12	
Triglyceride (mmol/L)	>50	91	$1.85\pm0.~45$	0.090
	≤50	20	2.01 ± 0.43	
LDL (mmol/L)	>50	91	3.47 ± 0.94	0.687
	≤50	20	3.55 ± 0.91	
HDL-C (mmol/L)	>50	91	0.89 ± 0.24	0.687
	≤50	20	0.92 ± 0.24	
Systolic BP (mmHg)	>50	91	147.01 ± 27.68	0.003
	≤50	20	132.93 ± 20.03	
FPG mmol/L	>50	91	5.71 ± 1.78	0.849
	≤50	20	5.66 ± 1.04	

 $LDL = Low \ density \ lipoprotein, \ HDL = High \ Density \ Lipoprotein, \ FPG = Fasting \ plasma \ glucose, \ BP = Blood \ pressure.$

approach of patient-reporting assessment has been validated as better by Viktrup et al. [33].

Although LUTS might affect QoL, poor bladder emptying could lead to an increase in the sympathetic nervous system activity, hence high blood pressure [28]. Historically LUTS has been associated with bladder outlet obstruction/prostate enlargement. The causal relationship has however not been established even though both conditions are

age-related. Furthermore, not all issues related to bladder symptoms are linked to prostate enlargement.

The reliability of the bladder volume alone in the analysis of LUTS is questionable, as LUTS are not disease specific. However, the bladder may be central as over-reactivity of the detrusor and may be the culprit through the malfunction of the detrusor muscle. Recent studies further support the idea of asymptotic histological inflammation of the prostate

Table 3. Statistical analysis of factors related to metabolic syndrome (MetS) stratified by the absence or presence of Lower Urinary Tract Symptoms (LUTS) using Students *t* test on descriptive data of participants.

	LUTS	N	Mean	SD	P-value
Age (years)	Negative	81	57.69	10.92	0.003
	Positive	30	63.96	8.95	
FPG (mmol/L)	Negative	81	5.23	0.59	0.442
	Positive	30	5.35	0.75	
Total cholesterol (mmol/L)	Negative	76	4.90	1.17	0.143
	Positive	27	5.32	1.30	
HDL-C (mmol/L)	Negative	76	0.92	0.24	0.402
	Positive	27	0.87	0.26	
Triglyceride (mmol/L)	Negative	76	1.11	0.58	0.036
	Positive	27	1.47	0.78	
Coronary risk	Negative	76	7.68	2.22	0.041
	Positive	27	9.01	2.97	
VLDL (mmol/L)	Negative	76	0.50	0.26	0.036
	Positive	27	0.67	0.35	
LDL-C (mmol/L)	Negative	76	3.25	1.36	0.658
	Positive	27	3.40	1.61	
Systolic BP (mmHg)	Negative	77	138.82	23.61	0.119
	Positive	29	149.68	33.75	
Diastolic (mmHg)	Negative	77	86.53	19.41	0.503
	Positive	29	89.58	20.82	
BMI (Kg/m ²)	Negative	81	26.43	4.09	0.037
	Positive	30	28.26	4.13	

FPG = Fasting Plasma Glucose, BMI = Body Mass Index, HDL-C=High density lipoprotein, VLDL = Very Low density Lipoprotein, LDL-C = Low density lipoprotein, BP = Blood pressure.

Table 4. Statistical analysis of parameters related to prostate enlargement when data was stratified according to the absence of presence of Lower Urinary Tract Symptoms (LUTS) using Mann-Whitney test.

	LUTS	LUTS			
	Negative		Positive		
	Mean (SD)	Median	Mean (SD)	Median	
PSA (ng/mL)	5.56 (8.49)	2.68 (2.25,3.48)	11.71 (15.82)	3.5 (2.77, 9.59)	0.001
Full_BV(cc)	266.42 (160.45)	225.24 (160.82, 308.23)	194.11 (106.66)	185.96 (115.01, 232.88)	0.019
Total_PV (cc)	34.28 (15.06)	28.51 (24.16,37.66)	53.94 (32.02)	45.36 (35.46, 61.30)	< 0.001
IPSS_Score	5.7 (4.48)	5 (3, 7)	12.8 (5.73)	12 (10.0, 14.0)	< 0.001
RUV (cc)	33.67 (63.91)	11 (1.50, 35.82)	26.85 (40.91)	9.48 (0.73, 45.45)	0.846
TRUS_PV_mean (cc)	34.75 (14.76)	31.73 (24.61, 40.57)	54.71 (33.15)	45.29 (35.70, 63.48)	< 0.001
TRUS_TZV (cc)	12.3 (9.13)	9.48 (6.66, 27.23)	27.23 (29.50)	20.09 (14.50, 26.40)	< 0.001
QoL	1.73 (1.73)	1 (0, 2.50)	3.23 (1.91)	3 (2.0, 5.0)	< 0.001

PSA = Prostate specific antigen, Full BV = Full Bladder volume, PV = prostate volume, IPSS = International Prostate Score, RUV = Residual urine volume, TRUZ PV = Transrectal ultrasound of prostate volume, TRUZ_TZV = Transrectal ultrasound of transition zone prostate, QoL = Quality of life.

 Table 5. Inferential statistics - Univariate Analysis of parameters in relation to Lower Urinary Tract Symptoms (LUTS).

Variables	in	the	Equation

variables in the Equation				
			95% C.I. for EXP(B)	
	Sig	Exp (β)	Lower	Upper
Age (years)	0.008	1.063	1.016	1.112
PSA (ng/mL)	0.017	1.044	1.008	1.081
FPG (mmol/L)	0.388	1.341	0.688	2.614
Total cholesterol (mmol/L)	0.121	1.336	0.927	1.926
HDL-C (mmol/L)	0.376	0.445	0.074	2.672
Triglyceride (mmol/L)	0.022	2.153	1.117	4.152
Coronary risk (CR)	0.023	1.234	1.029	1.480
VLDL (mmol/L)	0.022	5.364	1.269	22.674
LDL-C (mmol/L)	0.627	1.077	0.799	1.451
Systolic BP (mmHg)	0.071	1.014	0.999	1.030

(continued on next page)

Table 5 (continued)

Variables in the Equation

			95% C.I. for EXP(B)	
	Sig	Exp (β)	Lower	Upper
Diastolic BP (mmHg)	0.484	1.008	0.986	1.030
Body Mass Index (Kg/m²)	0.037	1.121	1.007	1.248

PSA = Prostate specific antigen, FPG = Fasting plasma glucose, HDL-C=High density lipoprotein cholesterol, LDL-C = Low density lipoprotein cholesterol, VLDL = Very low-density lipoprotein, BP = Blood pressure.

Table 6. Inferential Statistics - Multivariate Analysis of parameters in relation to Lower Urinary Tract Symptoms (LUTS).

Variables in the Equation

			95% C.I. for EXP(B)	
	Sig	Exp (β)	Lower	Upper
Age (years)	0.865	0.994	0.922	1.070
PSA (ng/mL)	0.007	1.098	1.026	1.174
FPG (mmol/L)	0.023	4.166	1.217	14.254
Total Cholesterol (mmol/L)	0.105	1.545	0.914	2.612
HDL-C (mmol/L)	0.027	0.031	0.001	0.676
Triglyceride (mmol/L)	0.019	3.478	1.224	9.880
Systolic BP (mmHg)	0.226	1.021	0.987	1.056
Diastolic BP (mmHg)	0.485	0.981	0.931	1.034
Body Mass Index (Kg/m²)	0.047	1.310	1.003	1.711

PSA = Prostate specific antigen, FPG = Fasting plasma glucose, HDL-C=High density lipoprotein cholesterol, BP = Blood pressure.

Table 7. Non-parametric data analysis of factors stratified by prostate volume by the Mann-Whitney test.

	PV GRADE	PV GRADE			P-value
	<30 cm		>30 cm		
	Mean (SD)	Median	Mean (SD)	Median	
PSA	4.35 (5.86)	2.57 (2.16, 3.06)	8.7 (12.88)	2.96 (2.66,7.55)	0.002
Full_BV	271.56 (166.03)	228.9 (168.55, 314.7)	225.98 (136.76)	207.2 (137.16, 270.69)	0.098
Total_PV	24.94 (3.37)	24.89 (22.31, 28.09)	50.33 (24.6)	44.21 (34.84, 60.74)	< 0.001
IPSS_Score	6.55 (5.53)	5 (3,9)	8.51 (5.84)	7 (5,12)	0.016
RUV	32.82 (69.38)	9.32 (1.44, 37.56)	30.81 (48.95)	12.06 (1.48,37.87)	0.814
TRUS_PV_mean	26.8 (5.97)	25.58 (22.47, 31.5)	49.83 (25.74)	42.61 (36.16, 58)	< 0.001
TRUS_TZV	8.17 (3.58)	7.62 (5.81, 9.62)	22.58 (21.93)	17.88 (13.5, 24.46)	< 0.001
Triglyceride	1.1 (0.63)	0.85 (0.73, 1.29)	1.3 (0.67)	1.1 (0.82, 1.58)	0.042
CR	7.82 (1.87)	7.44 (6.7, 9.22)	8.14 (2.92)	7.48 (5.65, 9.96)	0.881
VLDL	0.5 (0.29)	0.39 (0.33, 0.59)	0.59 (0.3)	0.5 (0.37, 0.72)	0.042
LDL-C	3.41 (1.22)	3.28 (2.73, 4.14)	3.22 (1.57)	3.36 (2.24, 4.36)	0.569

 $PSA = prostate \ specific \ antigen \ (ng/ml), \ BV = Bladder \ volume \ (cm^3), \ PV = Prostate \ volume \ (cm^3), \ IPSS = International \ prostate \ Symptoms \ Score, \ RUV = Residual \ Urine \ Volume \ (cm^3), \ TRUS \ PV = transrectal \ ultrasound \ prostate \ volume \ (cm^3), \ TRUS \ PV = transrectal \ ultrasound \ transition \ zone \ volume \ (cm^3), \ Triglyceride \ (mmol/l), \ CR = coronary \ risk, \ VLDL = very \ low \ density \ lipoprotein \ (mmol/l), \ LDL-C = low \ density \ lipoprotein \ cholesterol \ (mmol/l).$

Table 8. Correlational analysis between prostate volume (PV) and the International Prostate Symptoms Score (IPSS) against measured parameters using Pearson correlation analysis.

	IPSS		PV GRADE	
	r	p-value	r	p-value
Age (years)	0.185	0.033	0.388	0.000
PSA (ng/mL)	0.165	0.050	0.217	0.017
FPG (mmol/L)	0.139	0.084	-0.046	0.327
Total-cholesterol (mmol/L)	0.044	0.333	0.058	0.287
HDL-C (mmol/L)	-0.156	0.060	-0.052	0.308
Triglyceride (mmol/L)	0.115	0.127	0.163	0.056
CR	0.174	0.041	0.117	0.128
VLDL (mmol/L)	0.115	0.128	0.163	0.057
LDL-C (mmol/L)	0.052	0.304	0.030	0.386

(continued on next page)

Table 8 (continued)

	IPSS		PV GRADE	
	r	p-value	r	p-value
Systolic BP (mmHg)	0.149	0.070	0.341	0.000
Diastolic BP (mmHg)	0.062	0.271	0.293	0.002
Body Mass Index (Kg/m²)	0.039	0.349	0.172	0.046

PSA = prostate specific antigen, FPG = fasting plasma glucose, HDL-C = high density lipoprotein cholesterol, LDL-C = low density lipoprotein cholesterol, CR = coronary risk, VLDL = Very low density lipoprotein, BP = Blood pressure.

(asymptotic BPH) which goes through the process of healing, tissue remodeling by stromal cells [34], eventual enlargement and the occurrence of LUTS. Conversely some patients with histologic BPH do not show signs of LUTS or have silent LUTS [34].

5. Conclusions

In conclusion, components of MetS that were associated with LUTS included HDL-C, BMI, BP and CR. There was a sizable percentage (41.8%) of participants who experienced no symptoms of LUTS and yet had an enlarged prostate, and increased PSA. The prevalence of LUTS (42.3%) as observed in this study is high. Components of Metabolic Syndrome- HDL-C, BMI, blood pressure and coronary risk were associated with LUTS.

Declarations

Author contribution statement

George A. Asare and Derick S. Sule: Conceived and designed the experiments; Performed the experiments; Analyzed and interpreted the data; Contributed reagents, materials, analysis tools or data; Wrote the paper.

Jared N. Oblitey, Reese Ntiforo, Bernice Asiedu, Brodrick Y. Lamptey, Emmanuel L. Lamptey and Daniel K. Afriyie: Performed the experiments; Analyzed and interpreted the data; Contributed reagents, materials, analysis tools or data; Wrote the paper.

Benard Ohene Botwe: Performed the experiments; Analyzed and interpreted the data; Wrote the paper.

Funding statement

This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

Data availability statement

Data will be made available on request.

Declaration of interests statement

The authors declare no conflict of interest.

Additional information

No additional information is available for this paper.

References

- [1] M. Speakman, R. Kirby, S. Doyle, C. Ioannou, Burden of male lower urinary tract symptoms (LUTS) suggestive of benign prostatic hyperplasia (BPH) – focus on the UK, BJU Int. 115 (2015) 508–519.
- [2] R. Taoka, Y. Kakehi, The influence of asymptomatic inflammatory prostatitis on the onset and progression of lower urinary tract symptoms in men with histologic benign prostatic hyperplasia, Asi. J. Urolog. 4 (3) (2017) 158–163.

- [3] S.J. Berry, D.S. Coffey, P.C. Walsh, L.L. Ewing, The development of human benign prostatic hyperplasia with age, J. Urol. 132 (1984) 474–479.
- [4] C.J. Nickel, Inflammation and benign prostatic hyperplasia, Urol. Clin. 35 (1) (2008) 109–115.
- [5] H.J. Park, J.E. Won, S. Sorsaburu, P.D. Rivera, S.W. Lee, Urinary tract symptoms (LUTS) secondary to benign prostatic hyperplasia (BPH) and LUTS/BPH with erectile dysfunction in Asian men: a systematic review focusing on tadalafil, World J. Mens. Health. 31 (3) (2013) 193–207.
- [6] J.S. Park, K.C. Koo, H.K. Kim, B.H. Chung, K.S. Lee, Impact of metabolic syndromerelated factors on the development of benign prostatic hyperplasia and lower urinary tract symptoms in Asian population, Medicine 98 (42) (2019), e17635.
- [7] K.B. Sasanka, J.N. Simanta, T.P. Rajeev, J.B. Saumar, M.D. Phanindra, B. Bikash, Correlation of age, prostate volume, serum prostate-specific antigen, and serum testosterone in Indian, benign prostatic hyperplasia patients, UroToday Int. J. 5 (5) (2012) art 43.
- [8] I.B.O.W. Putra, A.R.A.H. Hamid, C.A. Mochtar, R. Umbas, Relationship of age, prostate-specific antigen, and prostate volume in Indonesian men with benign prostatic hyperplasia, Prostate Int. 4 (2016) 43–48.
- [9] S. Madersbacher, G. Alivizatos, J. Nordling, C.R. Sanz, M. Emberton, J.J. de la Rosette, EAU 2004 guidelines on assessment, therapy and follow-up of men with lower urinary tract symptoms suggestive of benign prostatic obstruction (BPH guidelines), Eur. Urol. 46 (5) (2004) 547–554.
- [10] A.P. Chokkalingam, A DeMarzo Ed Yeboah, G. Netto, K. Yu, R.B. Biritwum, Y. Tettey, A. Adjei, S. Jadallah, Y. Li, L.W. Chu, D. Chia, S. Niwa, A. Partin, I.M. Thompson, C. Roehrborn, R.N. Hoover, A.W. Hsing, Prevalence of BPH and lower urinary tract symptoms in West Africans, Prostate Cancer Prostatic Dis. 15 (2) (2012 June) 170–176.
- [11] K. Aboah, F. Agyemang-Yeboah, C.K. Gyase-Sarpong, F.F. Laing, E. Acheampong, B.F. Twumasi, G. Amoah, E.N. Batu, A.P. Asamoah, Lower urinary tract symptoms suggestive of benign prostatic hyperplasia among Ghanaian men: a cross-sectional prospective study, Int. J. Res. Med. Sci. 4 (9) (2016).
- [12] F. Bajunirwe, L. Stothers, J. Berkowitz, A.J. Macnab, Prevalence estimates for lower urinary tract symptom severity among men in Uganda and sub-Saharan Africa based on regional prevalence data, Can. Urol. Assoc. J. 12 (11) (2018) E447–E452.
- [13] A.A. Bock-Oruma, I.S. Oghu, Prevalence of lower urinary tract symptoms suggestive of benign prostatic hyperplasia in primary care, Port Harcourt, Nigeria, S. Afr. Fam. Pract. 55 (5) (2013) 467–472.
- [14] C. De nunzio, L. Cindolo, M. Gacci, F. Pellegrini, M. Carini, R. Lombardo, et al., Metabolic syndrome and lower urinary tract symptoms in patients with benign prostatic enlargement: a possible link to storage symptoms, Urology 2014 (84) (2014) 1181–1187.
- [15] T.L. Feng, E. Howard, A.C. Vidal, D.M. Moreira, R. Castro-Santamaria, G.L. Andriole, et al., Serum cholesterol and risk of lower urinary tract symptoms progression: results from the reduction by dutasteride of prostate cancer events study, Int. J. Urol. 24 (2) (2017) 151–156.
- [16] S. Rohrmann, E. Smit, E. Giovannucci, E.A. Platz, Association between markers of the metabolic syndrome and lower urinary tract symptoms in the Third National Health and Nutrition Examination Survey (NHANES III), Int. J. Obes. 29 (3) (2005) 310–316
- [17] K. Pelton, D. Di Vizio, L. Insabato, C.P. Schaffner, M.R. Freeman, K.R. Solomon, Ezetimibe reduces enlarged prostate in an animal model of benign prostatic hyperplasia, J. Urol. 184 (2010) 1555–1559.
- [18] X.G. Liu, Y. Tang, W. Yu, S.L. Wu, J. Jin, Effects of diabetic hyperlipidemia on bladder function and its possible mechanisms in a male rabbit model, Zhonghua Yixue Zazhi 93 (2013) 3338–3342.
- [19] C.A. Aguilar-Salinas, T. Viveros-Ruiz, Recent advances in managing/understanding the metabolic syndrome, F1000Res 3 (2019), 8: F1000 Faculty Rev-370.
- [20] J.H. Fowke, S.S. Motley, M.S. Cookson, R. Concepcion, S.S. Chang, M.L. Wills, et al., The association between body size, prostate volume and prostate-specific antigen, Prostate Cancer Prostatic Dis. 10 (2007) 137–142.
- [21] M. Jiang, D.W. Strand, O.E. Franco, P.E. Clark, S.W. Hayward, PPAR gamma: a molecular link between systemic metabolic disease and benign prostate hyperplasia, Differentiation 82 (4-5) (2011) 220–236.
- [22] H. Besiroglu, M. Dursun, A. Otunctemur, E. Ozbek, The association between triglyceride high density lipoprotein cholesterol ratio and benign prostate hyperplasia in non-diabetic patients: a cross-sectional study, Aging Male 3 (2017) 198–204.
- [23] O. Telli, A. Demirbas, M. Kabar, M.A. Karagoz, H. Sarici, B. Resorlu, Does metabolic syndrome or its components correlate with lower urinary tract symptoms in benign prostatic hyperplasia patients? Nephrourol 7 (3) (2015), e27253.
- [24] L. Sandfeldt, R.G. Hahn, Cardiovascular risk factors correlate with prostate size in men with bladder outlet obstruction, BJU Int. 92 (2003) 64–68.

- [25] J.K. Parsons, J. Bergstrom, E. Barrett-Connor, Lipids, lipoproteins and the risk of benign prostatic hyperplasia in community-dwelling men, BJU Int. 101 (3) (2008) 212 218
- [26] L. Bora, W.L. Sang, R.K. Hye, I.K. Dae, Y.S. Hwa, H.K. Jae, Relationship between lower urinary tract symptoms and cardiovascular risk scores including Framingham Risk Score and ACC/AHA Risk Score, Neurourol. Urodyn. 37 (1) (2018) 426–433.
- [27] S. Matsui, M. Kajikawa, T. Maruhashi, Y. Iwamoto, N. Oda, S. Kishimoto, et al., Combination of flow-mediated vasodilation and nitroglycerine-induced vasodilation is more effective for prediction of cardiovascular events, Hypertension 67 (2016) 1045–1052.
- [28] O. Guven, I. Selvi, Karaismailoğlu Eda, Association between benign prostate enlargement-related storage and voiding symptoms and systolic blood pressure: a single-center cross-sectional study, Sao Paulo Med. J. 137 (2019) 446–453.
- [29] N. Gondžetović, Z. Jatić, A. Omerbašić, Assessment of lower urinary tract symptoms (LUTS) in hypertensive men, Folia Medica Facultatis Medicinae Universitatis Saraeviensis 53 (1) (2018) 3–6.

- [30] E.C. Hwang, S.O. Kim, D.H. Nam, H.S. Yu, I. Hwang, S. Jung, et al., Men with hypertension are more likely to have severe lower urinary tract symptoms and large prostate volume, Low. Urin. Tract. Symptoms 7 (1) (2015) 32–36.
- [31] M. Esler, M. Rumantir, D. Kaye, G. Jennings, J. Hastings, F. Socratous, et al., Sympathetic nerve biology in essential hypertension, Clin. Exp. Pharmacol. Physiol. 28 (2001) 986–989.
- [32] X.-T. Zeng, H. Weng, J. Xiong, Q. Huang, L.-L. Ma, Y.-H. Ji, et al., Comparison of clinical and physiological parameters for benign prostatic hyperplasia in hypertensive and normotensive patients, Front. Physiol. 9 (2018) 1330.
- [33] L. Viktrup, R.P. Hayes, P. Wang, W. Shen, Construct validation of patient global impression of severity (PGI-S) and improvement (PGI-I) questionnaires in the treatment of men with lower urinary tract symptoms secondary to benign prostatic hyperplasia, BMC Urol. 7 (12) (2012) 30.
- [34] C.G. Roehrborn, Pathology of benign prostatic hyperplasia, Int. J. Impot. Res. (Suppl. 3) (2008) S11e8.