

Original Research Article

Association of male lower urinary tract symptoms with metabolic syndrome: a prospective study from tertiary care centre

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ABSTRACT

Background: The exact nature of the association between metabolic syndrome (MetS) and lower urinary tract symptoms (LUTS) is still not completely understood. There appears to be support for the hypothesis that metabolic and pathological derangements characterizing MetS can promote the development and progression of Benign Prostatic Enlargement and LUTS.

Methods: A total of 212 patients were included in the study, of whom 106 (50%) had LUTS and metabolic syndrome and 106 (50%) had LUTS without metabolic syndrome. The severity of the patient's lower urinary tract symptoms was assessed by the International Prostate Symptom Score (IPSS). Erectile function was assessed by a 5 question International Index of Erectile Function (IIEF) Questionnaire. MetS was defined according to the National Cholesterol Education Program-Adult Treatment Panel III (NCEP-ATPIII).

Results: The study showed a statistically significant association between prostate volume, IPSS score, and each individual component of metabolic syndrome. There is a significant association between metabolic syndrome and sexual dysfunction in men, and the severity of lower urinary tract symptoms is correlated with the severity of erectile dysfunction in the age group in the department of urology.

Conclusions: Patients with MetS, characterized by increased waist circumference, BMI, triglycerides, and decreased HDL levels, exhibited more severe Lower urinary tract symptoms, along with heightened sexual dysfunction, particularly erectile and ejaculatory dysfunction.

Keywords: IIEF, IPSS, Lower urinary tract symptoms, Metabolic syndrome, Prostate volume

INTRODUCTION

The exact nature of the association between metabolic syndrome (MetS) and lower urinary tract symptoms (LUTS) is still not completely understood.¹ Studies show that men with metabolic alterations experience faster-developing LUTS or are more frequently candidates for benign prostatic enlargement (BPE) surgery.^{2,3} Vignozzi et al. found support for the hypothesis that metabolic and pathological derangements characterizing MetS can

promote the development and progression of BPE and LUTS.⁴ Because of its link to increased morbidity and mortality, metabolic syndrome (MetS) is a complicated and widespread pandemic condition with a high socioeconomic effect. A substantial amount of epidemiological research suggests a link between MetS and LUTS. Erectile dysfunction (ED) affects more than half of males over the age of 50 years.⁵ Men's health is becoming more popular, and the problem of sexual dysfunction is becoming more prevalent. Despite intense

research efforts in the past five decades to elucidate the underlying etiology of prostatic growth and LUTS in older men, cause-and-effect relationships have not been established. The importance of these two conditions in terms of their public health impact remains significant. Therefore, this study attempts to prospectively evaluate the association between Metabolic Syndrome and risk of Lower Urinary Tract Symptoms (LUTS) and BPE to find out effects of Metabolic Syndrome on prostatic parameters/LUTS.

METHODS

Sample size

Total 212 patients were included for the study.

Study method

Prospective observational single centre study was done.

Study place

The study was carried out at Kasturba Medical College, Manipal.

Study duration

The duration of the study was from September 2020 to March 2022.

Inclusion criteria

All adult male patients who were present with LUTS with metabolic syndrome were eligible for study.

Exclusion criteria

Patients having Carcinoma prostate, Stricture urethra, Hematuria, History of previous surgical treatment for BPH, Men with history of pelvic radiotherapy, Patients not willing to participate in study, Patients with calculus disease/neurogenic disease/pediatric patients were excluded. The purpose of the study was explained to the patient, and informed consent was obtained for the collection of data in the patient's own vernacular language. A detailed history and clinical examination were conducted. The severity of the patient's LUTS was assessed by the International Prostate Symptom Score (IPSS). Using the IPSS questionnaire, symptoms were further categorized as voiding (incomplete emptying, weak stream, intermittency, straining) and storage (frequency, urgency and nocturia).

Finally, each symptom of the IPSS questionnaire was categorized into no symptoms (0 points), mild (0-7), moderate (8-19), and severe (20-35). Anthropometric parameters like height, weight, and waist circumference were calculated. A transabdominal ultrasound was done to assess prostate volume and post void residual urine

(PVRU). Blood samples were taken for serum prostate specific antigen (PSA), fasting blood glucose, urea, creatinine, and lipid profile. Erectile function was assessed by 5 question International Index of Erectile Function (IIEF) Questionnaire. A score of 1-5 is awarded to each of the 5 questions and graded as follows: No ED score is 22-25; Mild ED score is 17-21; Mild to Moderate ED score is 12-16; Moderate ED score is 8-11; Severe ED score is 1-7. Ejaculatory function was assessed using Male Sexual Health Questionnaire (MSHQ-EjD) short form questionnaire. A score of 1-5 is awarded to four questions. 11-14; Mild EjD, 5-10; Moderate EjD, 1-4; severe EjD. MetS was defined according to the National Cholesterol Education Program-Adult Treatment Panel III (NCEP-ATPIII), which requires at least three of the following five components: central obesity (waist circumference of >102 cm), elevated triglycerides (≥ 1.7 mmol/l or 150 mg/dL), elevated blood pressure ($\geq 130/85$ mmHg), elevated fasting glucose (≥ 6.1 mmol/l or 110 mg/dl) and reduced HDL cholesterol (< 1.03 mmol/l or 40 mg/dl). Patients were commenced on medical management for LUTS or counselled on appropriate life-style changes as clinically indicated. LUTS were assessed using the IPSS.

Ethical approval

The study was approved by the Institutional Ethics Committee KMC Manipal, approval number 242/2020. The study is compliant with all the ethical standards. Informed research consent to participate was taken from all participants. Due consideration has been given not to ill harm or deprive any participant of the study via direct or indirect actions of the investigators or via conduct of the research.

Statistical analysis

Chi-square test was applied for qualitative variables. Independent sample t test was applied to compare the statistical difference of quantitative variables between the groups. The level of significance is set at 5%.

RESULTS

Demographic data of patients

A total of 212 patients were included in the study, of whom 106 (50%) had LUTS and metabolic syndrome and 106 (50%) had LUTS without metabolic syndrome.

Table 1: Division of patients based on metabolic syndrome.

Total patients	LUTS with Mets patients	LUTS without Mets patients
212 (100%)	106 (50%)	106 (50%)

Mean age of the study population was 63.71 years with minimum age of patient was 49 and maximum age of patient in study was 89 years.

Patients of 60 to 69 years was found to most common age group in this study with 37.26 % followed by 70-79 years age group patients contributing to 31.13%.

Table 2: Division of patients based on age.

	N (%)	Min	Max	Mean	SD
Age	212	51	89	63.71	8.614
Age groups (in years)	Frequency	Percent			
50 to 59	51	24.05			
60 to 69	79	37.26			
70 to 79	66	31.13			
> 80	16	7.54			
Total	212	100.0			

Out of total 212 patients 108 patients were Hypertensive accounting for most common comorbidity with 50.94%, 102 patients were Diabetic, 86 was Obese, 42 had Dyslipidemia.

Table 3: Division of patients based on comorbidities.

		Frequency	Percent
Diabetes mellitus	Yes	102	48.11
Hypertension	Yes	108	50.94
Obesity	Yes	86	40.56
Dyslipidemia	Yes	42	19.81

The mean prostate volume measured was 41.32gms in LUTS patients with metabolic syndrome and 24.73 gms in LUTS patients without metabolic syndrome.

Table 4: Mean prostate volume.

	LUTS with Mets	LUTS without Mets
Mean prostate volume	41.32 gms	24.73 gms

Mean voiding symptoms in LUTS patients with metabolic syndrome is 2.78 higher than in LUTS patients without metabolic syndrome which is statistically significant with a Pvalue of 0.001. Mean storage symptoms in LUTS patients with metabolic syndrome is 1.69 higher than in LUTS patients without metabolic

syndrome which is statistically significant with a Pvalue of 0.001. Mean MFR in LUTS patients with metabolic syndrome is 4.37 ml/sec lower than in LUTS patients without metabolic syndrome which is statistically significant with a Pvalue of 0.0001. Mean Post void residue (PVR) in LUTS patients with metabolic syndrome is 12.28 ml more than in LUTS patients without metabolic syndrome which is statistically significant with a Pvalue of 0.001. Mean HDL cholesterol in LUTS patients with metabolic syndrome is 3.4 mg/dl more than in LUTS patients without metabolic syndrome which is statistically significant with a Pvalue of 0.001.

Mean Triglyceride level in LUTS patients with metabolic syndrome is 11.30 mg/dl more than in LUTS patients without metabolic syndrome which is statistically significant with a Pvalue of 0.001. Mean FBS in LUTS patients with metabolic syndrome is 27.59 mg/dl higher than in LUTS patients without metabolic syndrome which is statistically significant with a Pvalue of 0.001. Mean Systolic blood pressure (SBP) levels in LUTS patients with metabolic syndrome is 17.53mmhg higher than in LUTS patients without metabolic syndrome which is statistically significant with a P value of 0.001. Mean Systolic blood pressure (SBP) levels in LUTS patients with metabolic syndrome is 9.13 mmhg higher than in LUTS patients without metabolic syndrome which is statistically significant with a Pvalue of 0.001. Mean BMI levels in LUTS patients with metabolic syndrome is 4.60 kg/m² higher than in LUTS patients without metabolic syndrome which is statistically significant with a Pvalue of 0.001.

Mean IIEF score in LUTS patients with metabolic syndrome is 8.89 lower than in LUTS patients without metabolic syndrome which is statistically significant with a Pvalue of 0.001. Mean Ejaculatory function score in LUTS patients with metabolic syndrome is 1.72 lower than in LUTS patients without metabolic syndrome which is statistically significant with a Pvalue of 0.001. Mean Ejaculation bother score in LUTS patients with metabolic syndrome is 1.17 higher than in LUTS patients without metabolic syndrome which is statistically significant with a Pvalue of 0.001. Mean waist circumference in LUTS patients with metabolic syndrome is 12.64 higher than in LUTS patients without metabolic syndrome which is Statistically significant with a Pvalue of 0.001.

Table 5: Comparison of the quantitative parameters between the groups using independent sample t test.

	Groups	N	Min	Max	Mean	SD	Mean diff	P value
Voiding Symptoms	LUTS with MetS	106	4	14	8.59	1.57	2.78	0.001*
	LUTS without MetS	106	3	9	5.81	0.92		
Storage symptoms	LUTS with MetS	106	3	10	6.92	0.99	1.69	0.001*
	LUTS without MetS	106	3	7	5.32	0.82		
Total IPSS score	LUTS with MetS	106	7	24	15.52	1.47	4.48	0.001*
	LUTS without MetS	106	6	16	11.02	2.43		

Continued.

	Groups	N	Min	Max	Mean	SD	Mean diff	P value
QOL	LUTS with MetS	106	2	5	3.85	0.79	1.41	0.001*
	LUTS without MetS	106	2	4	2.43	0.57		
MFR	LUTS with MetS	106	5.0	12.8	8.50	1.58	-4.37	0.001*
	LUTS without MetS	106	10.4	15.0	12.88	1.07		
PVR	LUTS with MetS	106	10	120	40.09	16.69	12.28	0.001*
	LUTS without MetS	106	10	40	27.81	6.97		
HDL cholesterol	LUTS with MetS	106	23	44	31.85	4.971	-3.4	0.01*
	LUTS without MetS	106	24	40	34.55	5.271		
Triglyceride	LUTS with MetS	73	136	220	185.64	21.17	11.30	0.01*
	LUTS without MetS	69	145	246	174.34	29.09		
FBS	LUTS with MetS	106	85	236	157.03	35.284	27.59	0.01*
	LUTS without MetS	106	82	248	129.44	35.862		
SBP	LUTS with MetS	106	110	150	137.53	10.00	17.53	0.001*
	LUTS without MetS	106	108	146	120.08	8.44		
DBP	LUTS with MetS	106	70	100	88.15	6.52	9.13	0.001*
	LUTS without MetS	106	60	94	79.02	6.49		
BMI	LUTS with MetS	106	30	33	31.49	0.89	4.60	0.001*
	LUTS without MetS	106	25	28	26.89	0.87		
IIEF score	LUTS with MetS	86	7	24	11.23	2.92	-8.89	0.001*
	LUTS without MetS	99	14	24	20.13	2.24		
Ejaculatory function	LUTS with MetS	86	12	15	13.00	0.87	-1.72	0.001*
	LUTS without MetS	99	13	15	14.73	0.49		
Ejaculation Bother/satisfaction	LUTS with MetS	86	0	2	1.49	0.70	1.17	0.001*
	LUTS without MetS	99	0	2	0.31	0.55		
Waist Circumference	LUTS with MetS	106	73	103	93.21	5.60	12.64	0.001*
	LUTS without MetS	106	70	90	80.57	3.46		

QOL - Quality of life , MFR - Mean flow rate in ml/sec , PVR-Post void residue in ML units , SBP-Systolic blood pressure in mmHg, DBP-Diastolic blood pressure in mmHg, HDL-High density lipoprotein in mg/dl, IIEF-International index of erectile function , FBS-Fasting blood sugar in mg/dl BMI-body mass index in kg/m² All the seven symptoms in IPSS were found to be higher in LUTS patients with metabolic syndrome compared to LUTS patients without metabolic syndrome. * - Significant

Table 6: Distribution of the subjects based on the individual IPSS symptom score.

		Groups			Chi-square value	P value
		LUTS with MetS	LUTS without MetS	Total		
Q1: Incomplete emptying	1	Count	44	4	71.52	0.001*
		%	41.5%	3.8%		
	2	Count	48	34		
		%	45.3%	32.1%		
	3	Count	14	66		
		%	13.2%	62.3%		
Q2: Frequency	4	Count	0	2	72.6	0.001*
		%	0.0%	1.9%		
	1	Count	0	4		
		%	0.0%	3.8%		
	2	Count	60	4		
		%	56.6%	3.8%		
	3	Count	46	96		
		%	43.4%	90.6%		
Q3: Intermittency	4	Count	0	2	111.9	0.001*
		%	0.0%	1.9%		
	1	Count	76	10		
		%	71.7%	9.4%		

Continued.

		Groups				Chi-square value	P value
			LUTS with MetS	LUTS without MetS	Total		
	2	Count	28	29	57		
		%	26.4%	27.4%	26.9%		
	3	Count	2	65	67		
		%	1.9%	61.3%	31.6%		
	4	Count	0	2	2		
		%	0.0%	1.9%	.9%		
Q4: Urgency	0	Count	20	2	22	32.72	0.001*
		%	18.9%	1.9%	10.4%		
	1	Count	86	86	172		
		%	81.1%	81.1%	81.1%		
	2	Count	0	18	18		
		%	0.0%	17.0%	8.5%		
Q5: Weak stream	1	Count	22	4	26	26.55	0.001*
		%	20.8%	3.8%	12.3%		
	2	Count	84	88	172		
		%	79.2%	83.0%	81.1%		
	3	Count	0	14	14		
		%	0.0%	13.2%	6.6%		
Q6: Straining	1	Count	106	86	192	22.08	0.001*
		%	100.0%	81.1%	90.6%		
	2	Count	0	20	20		
		%	0.0%	18.9%	9.4%		
Q7: Nocturia	1	Count	12	2	14	133.24	0.001*
		%	11.3%	1.9%	6.6%		
	2	Count	84	10	94		
		%	79.2%	9.4%	44.3%		
	3	Count	10	94	104		
		%	9.4%	88.7%	49.1%		

DISCUSSION

Lower urinary tract symptoms

Paul Abrams coined the term "lower urinary tract symptoms." Lower urinary tract symptoms are divided into three categories: storage, voiding, and post-micturition symptoms. Nearly fifty percent of all men who are diagnosed with BPH have a moderate-to-severe degree of LUTS. LUTS is the predominant symptoms in patients with BPE above 40 years of age (Figure 1).

Metabolic syndrome

The metabolic syndrome (MetS) is a multi-factorial disorder that increases the risk of diabetes and death from cardiovascular and non-cardiovascular causes (Figure 2). According to Parsons and Kashefi's et al physical activity appears to minimize the chances of BPH and LUTS, comprehensive literature analysis.⁶ Currently, the research supports a link between LUTS and a lack of physical activity, obesity, BMI, and other metabolic syndrome indicators. Increased physical activity, on the other hand, tends to protect against BPH. Diokno et al.

According to F. Abdollah et al individual components of MetS (obesity, dyslipidemia, hypertension, and insulin resistance) as well as the syndrome itself may increase the incidence of BPH and lower urinary tract symptoms in individuals.⁷ Kyprianou N et al found alterations in insulin resistance, increased autonomic activity, poor nitrenergic innervation, increased Rho kinase activity, pro-inflammatory states, and sex hormone changes are all linked to MetS.⁸

IPSS score and Metabolic syndrome

The International Prostate Symptom Score is an eight-question screening tool (seven symptom related and one QOL, or quality of life question). The International Prostate Symptom Score has been instrumental in the clinical investigation of lower urinary tract symptoms and benign prostatic hyperplasia. De Nunzio C et al in a population-based European study by demonstrated a strong positive association between MetS (defined using NCEP-ATPIII criteria) and LUTS severity.⁹ The presence of MetS was correlated not only with total IPSS score but also with voiding and storage sub scores, as well as each single question of the IPSS questionnaire. Moreover,

higher IPSS scores were positively associated with each component of MetS, and a higher risk of LUTS treatment was associated with MetS severity. Indeed, the presence of two components was associated with a 51% higher risk of being treated for LUTS, rising to nearly 250% when all five components were present. Men with a waist circumference >102 cm were 39% more likely to report a voiding IPSS sub score >5 and 40% more likely to report a storage IPSS sub score >4. Our study found a significantly positive correlation between IPSS score or its individual components and metabolic syndrome (Table 6), even though we included waist circumference as a component of metabolic syndrome.

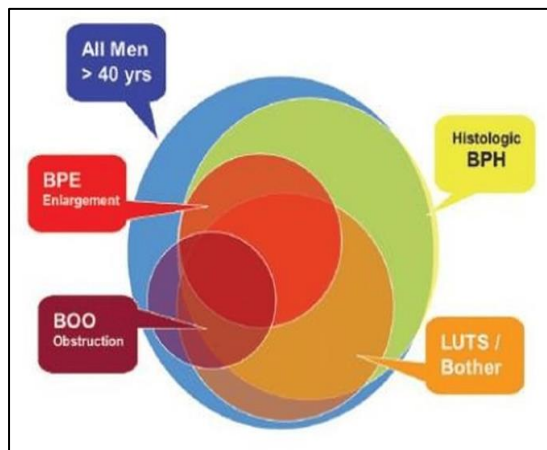
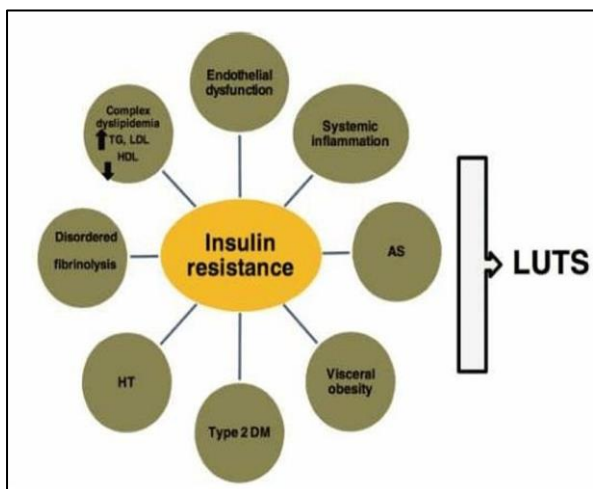


Figure 1: Diagram interpreting the relationship between BPE, LUTS and BOO.

We also looked at the relationship between individual components of metabolic syndrome and IPSS scores, as well as prostate gland volume and found a positive correlation. We were also able to show a statistically significant positive correlation between MetS and voiding and storage sub scores separately (Table 5).



HT-Hypertension AS-Atherosclerosis TG- Triglycerides

Figure 2: Components of metabolic syndrome and their pathogenic connections to development of lower urinary tract symptoms.

Prostate volume and Metabolic syndrome

In a recent metaanalysis Gacci M et al. eight studies were included for a total of 5403 patients, of which 1426 (26.4%) had MetS defined according to current classification and prostate volume difference between patients with MetS versus patients without MetS was evaluated: the combination of results of trials showed that patients with MetS have significantly higher total prostate volume versus those without MetS (+1.8 mL).¹⁰ In our study overall mean prostate volume measured was 41.32 grams whereas in men with LUTS and metabolic syndrome and 24.73 in patients without metabolic syndrome (Table 4).

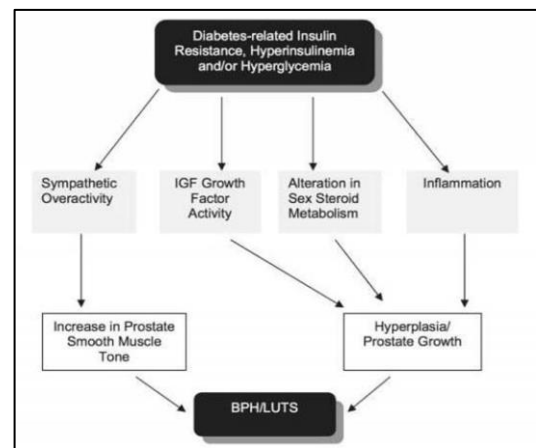


Figure 3: Hypothesized mechanisms of BPH/LUTS in Diabetic patients

Obesity and LUTS

In our study, Obesity was seen in 86 patients was considered based on BMI and Waist circumference (W.C). we discovered that a waist circumference of more than 90 cm was associated with an increase in IPSS score (Table 5). According to Parsons et al men who were above the 50th percentile of waist circumference (96.5 cm) had an increased risk of prostate enlargement compared to those who were below this threshold. BMI did have a statistically significant correlation with IPSS Score in our study and it was a risk factor for increased LUTS.¹¹

Diabetes and LUTS

Several mechanisms link diabetes with LUTS (Figure 3). Parson et al found fasting blood glucose and prostatic gland volume to have a significant positive relationship.¹¹ Dahle et al discovered a significant link between fasting sugar levels and BPH in a study.¹² In our study 102 patients had DM. Significant positive correlation was found between fasting blood sugar level and IPSS Score, higher the blood sugar levels, more severe were the LUTS (Table 1).

Hypertension and LUTS

According to Hammarsten et al. in 158 patients with LUTS prostate gland volume was positively correlated with Systolic Blood Pressure level.¹³ In our study 108 patients were hypertensive. Our findings are suggestive of more severe LUTS and higher IPSS scores in patients with LUTS and metabolic syndrome than in patients without metabolic syndrome (Table 5).

Dyslipidemia and LUTS

Parsons et al in the Rancho Bernardo cohort study found a fourfold increased risk of BPH among diabetic men with LDL cholesterol in the highest tertile, but not in the overall cohort.¹¹ This observation suggests that dyslipidemia itself is not strong enough to induce prostate enlargement, but the concomitant presence of other metabolic derangements, such as diabetes or those concurring with the MetS construct, favors the process. In our study Dyslipidemia was seen in 42 patients and were considered using HDL cholesterol and Serum triglyceride levels, there was a significant inverse relationship between IPSS scores and HDL levels. There was significant positive relationship between serum triglyceride levels and LUTS. Patients with dyslipidemia had less severe LUTS when compared to patients without dyslipidemia (Table 5).

Most studies have used the IPSS alone or in conjunction with transrectal ultrasound to assess LUTS/BPH. There is little information available about uroflowmetry or postvoid residual urine volume. In our study, we aimed to compare objective parameters such as Uroflowmetry values, postvoid residual urine volume, and metabolic syndrome. There is significant decrease in peak flow rate on uroflowmetry and increase in postvoid residual urine volume in patients with Metabolic syndrome, according to our findings.

Metabolic syndrome and Sexual dysfunction and LUTS

The link between lower urinary tract symptoms and erectile dysfunction has recently gained attention because both disorders are not only common, but also affect men of the same age group. Rosen et al found that the risks of erectile dysfunction and ejaculatory dysfunction are double in men with severe lower urinary tract symptoms than those without severe lower urinary tract symptoms.¹⁴ Abnormal erectile and ejaculatory responses have a considerable adverse effect on the QoL (quality of life) of those men who were sexually active previously. This causes significantly increased levels of anxiety and depression in these people. Lower urinary tract symptoms (LUTS) and sexual dysfunction are common problem of the aging population. Ours is the first study evaluating patients with lower urinary tract symptoms and sexual dysfunction with metabolic syndrome. The exact pathway of sexual dysfunction in men with LUTS is not well

understood. Diokno et al. has proposed three common pathophysiologic mechanisms.¹⁵

The change in the NO (nitric oxide) pathway in the prostate. Atherosclerosis of pelvic vessels. Hyperactivity of the autonomic nervous system. Our study discovered a clear association between sexual dysfunction and the lower urinary tract symptoms. For measuring lower urinary tract symptoms and sexual dysfunction, we employed standardized and validated scales. In every case, the principal investigator administered these scales. Rosen et al. found prevalence of 36% of sexual dysfunction in LUTS patients in the western literature.¹⁴ In this study, the incidence of moderate sexual dysfunction with lower urinary tract symptoms was 32 percent. Our study showed that sexual dysfunction was more prevalent in men with LUTS and metabolic syndrome than in patients without metabolic syndrome (Table 4).

Limitations of the study

We would like to emphasize that we were unable to study the impact of metabolic syndrome on prostate growth rate. Age was not matched; however, a multivariate analysis was done to overcome this limitation. The present study was not powered to study the associated risk factors for sexual dysfunction.

CONCLUSION

Our study established a significant association between lower urinary tract symptoms (LUTS) and Metabolic Syndrome (MetS), as evidenced by a positive correlation between IPSS scores, individual MetS components, and prostate gland volume. Patients with MetS, characterized by increased waist circumference, BMI, triglycerides, and decreased HDL levels, exhibited more severe LUTS, along with heightened sexual dysfunction, particularly erectile and ejaculatory dysfunction. These findings underscore the complex relationship between MetS, LUTS, and sexual function, highlighting the need for holistic management strategies to address these interconnected conditions effectively.

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Conflict of interest: None declared

Ethical approval: The study was approved by the Institutional Ethics Committee

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