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Original Research Paper

General Surgery

"ASSOCIATION OF LOWER URINARY TRACT SYMPTOMS WITH METABOLIC SYNDROME IN MALE PATIENTS OF AGE MORE THAN 45 YEARS."

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ABSTRACT

Objective: The association of Lower Urinary Tract Symptoms with Metabolic Syndrome in male patients of age more than 45 years since there is insufficient data about LUTS and MetS in Indian population and contradicting reports in various studies regarding the correlation of LUTS and MetS worldwide.

Methods- 152 men aged >45 years with symptoms of LUTS during a 365 period from 1st June 2019 to 31st May 2020 have been included in this observational study. LUTS were defined according to the International Prostate Symptom Score (IPSS) and metabolic syndrome with the National Cholesterol Education Program/Adult Treatment Panel III definition. We studied the correlation between metabolic syndrome and its individual components, and the severity of LUTS (IPSS and treatment for LUTS). Analyses were adjusted for body mass index, age, and prostate-specific antigen level.

Results-. About one third of LUTS patients were between 60-69 years of age (33.6%), more than half moderate LUTS (65.8%)patients. Severe LUTS was most common in age ≥80 years (41.7%). MetS in LUTS patients was 33.6% highest in age 50-59 years (42.1%) and was lowest in age ≥80 (16.7%). Prevalence of MetS in LUTS patients was 3.63 times higher in age 50-59 years than ≥80 years (OR=3.63, 95%CI=0.89-14.86).

Conclusion- Our results suggest a significant relationship between LUTS linked to benign prostatic hyperplasia and metabolic syndrome, in terms of frequency and severity. The risk of being treated for LUTS also increased with an increasing number of metabolic syndrome components present. The prevention of such modifiable factors by the promotion of dietary changes and regular physical activity practice may be of great importance for public health.

KEYWORDS : LUTS, Metabolic Syndrome,Obesity, IPSS, Benign Prostatic Hyperplasia,

INTRODUCTION-

Lower urinary tract symptoms (LUTS) are defined as a complex of symptoms that may affect storage or voiding. Symptoms of LUTS are largely classified into irritative symptoms and obstructive symptoms. Irritative symptoms include frequency, urgency and nocturia. Obstructive symptoms include intermittency, weak stream, straining as well as incomplete emptying (Haider et al, 2009)[1]

Prevalence report suggests that the rate can be as high as 79% in males more than 70 years of age. This report is from African countries where population dynamics tend to change with time. The prevalence rate for LUTS among South Africans aged 65 years of age and older is estimated to rise from 3.4% in 1995 to 7.5% in 2025. (Litman et al, 2007; Favilla et al, 2010)[2,3].

Metabolic syndrome (MetS) includes a cluster of diseases which includes central obesity, dyslipidemia, hypertension, and insulin resistance. The discovery of Metabolic syndrome (MetS) can be traced back to early 20th century when Kylin (1923)[4] described the condition of metabolic disturbances which includes hyperglycemia, gout and hypertension.

Since there's no universally accepted diagnostic criteria for the definition of MetS; different guidelines proposed by the International Diabetes Federation (IDF), National Cholesterol Education Program Adult Treatment Panel III (NCEP ATP III) and World Health Organization (WHO) are generally employed to distinguish this condition in medical practice (Alberti et al, 2006; Expert Panel on Detection, Evaluation, and Treatment of High Blood Cholesterol in Adults, 2001; Consultation, 1999)[5,6,7].

There are number of epidemiological reports that signify the possible association between Lower Urinary Tract Symptoms (LUTS) and Metabolic Syndrome (MetS). LUTS are the outcome of mainly benign prostatic hyperplasia (static),α-adrenergic receptor-mediated muscle tension(dynamic) and inflammatory determinants. (Donnell, 2011; Moul and McVary, 2010)[8,9].

Moreover, studies of association between LUTS, BPH and its urodynamic parameters are unconvincing in identifying the causal association between the urodynamic parameters of BPH severity and symptoms which show that BPH is not the only factor in defining LUTS. Nowadays, LUTS is acknowledged to be a non–organ-specific, non–sex-specific and global term that comprises all urinary symptoms, as well as its post-micturition symptoms, storage symptoms and voiding symptoms with a substantial undesirable effect on patients' quality of life (Welch et al, 2002)[10].

AIMS and Objectives-.

To evaluate the association of Lower Urinary Tract Symptoms with Metabolic Syndrome in male patients of age more than 45 years since there is insufficient data about LUTS and MetS in Indian population and contradicting reports in various studies regarding the correlation of LUTS and MetS worldwide..

MATERIAL AND METHODS-.

Study design: Prospective observational study

Study duration: 1st June 2019 to 31st May 2020

Study place: Surgical wards of department of surgery, SSMC and associated SGMH, Rewa.

INCLUSION CRITERIA:
All male patients aged more than 45 years presenting with symptoms of LUTS

EXCLUSION CRITERIA:
1. Patients with history of carcinoma or known carcinoma of lower urinary tract.
2. Patients with LUTS with history of trauma.
3. All patients with upper urinary tract infection.
4. Critically ill patients.
5. Patients diagnosed with urological diseases which include urethral stricture, urologic infections or neurologic bladder.

Study Population All patients aged 45 years and above admitted from Surgery OPD, Superspeciality OPD, Casualty or patients transferred from other departments with complains of lower urinary tract symptoms were selected. In order to minimize the confounding factor and bias, the above mentioned exclusion criteria were used. A total of 152 patients were selected for the study after obtaining informed and written consent.

Assessment of LUTS
IPSS was used to assessed the severity of LUTS. It contains seven set of questions : i) frequency, ii) urgency, iii) nocturia, iv) weak stream, v) intermittency, vi) straining and vii) incomplete emptying. Each set of questions can be scored from 0 to 5, with a total score of 35. Based on this total score, IPSS was then categorized into mild (0-7), moderate (8-19) and severe (20-35). Symptoms of LUTS were further classified using IPSS into storage symptoms which includes – frequency, urgency and nocturia and voiding symptoms which includes – weak stream, intermittency, straining and incomplete emptying.

Assessment of Metabolic Syndrome
National Cholesterol Education Program/Adult Treatment Panel III (NCEP/ATP III) was used to define metabolic syndrome. Metabolic syndrome is defined as any of the patients who have the following three or more out of the following five criteria: (i) waist circumference ≥90 cm; (adjusted for asian men) (ii) triglyceride ≥150mg/dl or on drug treatment for elevated triglycerides; (iii) reduced HDL-cholesterol < 40mg/dl or on drug treatment to reduced HDL-cholesterol; (iv) SBP ≥130 mmHg and/or DBP ≥85 mmHg or treated; (v) elevated fasting glucose ≥ 100mg/dl or on drug treatment for elevated glucose.

Data Collection
The questionnaire collected the following information: presence and severity of LUTS according to the IPSS, anthropometric characteristics (height, weight and waist circumference), age, body mass index (BMI), systolic/diastolic blood pressure (SBP/DBP) and biological parameters [triglycerides, high-density lipoprotein (HDL)-cholesterol, blood glucose level, PSA level], and whether the patient was treated for hypertension, dyslipidaemia, diabetes, or LUTS.

STATISTICAL ANALYSIS
Correlation between the individual components of metabolic syndrome and lower urinary tract symptoms and was studied. The severity of LUTS in those with or without metabolic syndrome and in different age group was examined using Mantel-Haenszel chi-square test. The magnitude of association between LUTS and MetS were estimated using binary logistic regression methods for Odds ratios and 95% confidence intervals (95% CI) to permit the exploration of varied covariates simultaneously. All statistical test were two-tailed, with a P value of _0.05 considered statistically significant. All the analysis were carried out on SPSS 16.0 version (Chicago, Inc, USA).

RESULTS-

Table-1: Age distribution of LUTS patients

Age in years	No. (n=152)	%
45-49	11	7.2
50-59	19	12.5
60-69	51	33.6
70-79	47	30.9
≥80	24	15.8
Mean±SD (Range)	67.66±10.64 (45-92)	
Severity of LUTS		
Mild LUTS	7	4.6
Moderate LUTS	100	65.8
Severe LUTS	45	29.6
Prevalence of MetS		
With MetS	51	33.6
Without MetS	101	66.4

Table-1 shows the age distribution of LUTS patients. About one third of LUTS patients were between 60-69 years of age (33.6%) followed by 70-79 (30.9%), ≥80 (15.8%), 50-59 (12.5%) and 45-49 (7.2%). The mean age of patients was 67.66±10.64 years ranging from 45-92 years. severity of LUTS patients. More than half of LUTS patients were moderate LUTS (65.8%) followed by severe (29.6%) and mild (4.6%). The prevalence of MetS in LUTS patients was 33.6%.

Table-2: Association of Prevalence of MetS with age

Age in years	No. of patients	With MetS		Without MetS		OR (95%CI)	p- value[1]
		No.	%	No.	%		
45-49	11	2	18.2	9	81.8	1.11 (0.17-7.21)	0.91
50-59	19	8	42.1	11	57.9	3.63 (0.89-14.86)	0.07
60-69	51	19	37.3	32	62.7	2.96 (0.88-9.99)	0.08
70-79	47	18	38.3	29	61.7	3.10 (0.91-10.55)	0.07
≥80	24	4	16.7	20	83.3	1.00 (Ref.)	
Storage symptoms							
Nocturia							
Present	108	38	35.2	70	64.8	1.29 (0.60-2.76)	0.50
Absent	44	13	29.5	31	70.5	1.00 (Ref.)	
Frequency							
Present	47	15	31.9	32	68.1	0.89 (0.43-1.87)	0.77
Absent	105	36	34.3	69	65.7	1.00 (Ref.)	
Urgency							
Present	40	13	32.5	27	67.5	0.93 (0.43-2.02)	0.87
Absent	112	38	33.9	74	66.1	1.00 (Ref.)	
Voiding symptoms							
Weak Stream							

Present	57	19	33.3	38	66.7	0.98 (0.49-1.97)	0.96
Absent	95	32	33.7	63	66.3	1.00 (Ref.)	
Straining							
Present	61	21	34.4	40	65.6	1.06 (0.53-2.11)	0.85
Absent	91	30	33.0	61	67.0	1.00 (Ref.)	
Incomplete emptying							
Present	42	13	31.0	29	69.0	0.84 (0.39-1.82)	0.67
Absent	110	38	34.5	72	65.5	1.00 (Ref.)	
Intermittency							
Present	43	16	37.2	27	62.8	1.25 (0.59-2.62)	0.54
Absent	109	35	32.1	74	67.9	1.00 (Ref.)	
Voiding symptoms							
BP							
Increased	59	38.8	51	86.4	8	13.6	-
Normal	93	61.2	0	0.0	93	100.0	1.00 (Ref.)
FBS							
Increased	27	17.8	26	96.3	1	3.7	104.00 (13.45-803.68)
Normal	125	82.2	25	20.0	100	80.0	1.00 (Ref.)
TG							
Increased	43	28.3	33	76.7	10	23.3	16.68 (6.99-39.80)
Normal	109	71.7	18	16.5	91	83.5	1.00 (Ref.)
HDL							
Decreased	14	9.2	13	92.9	1	7.1	34.21 (4.32-270.56)
Normal	138	90.8	38	27.5	100	72.5	1.00 (Ref.)
Waist Circumference							
Increased	34	22.4	28	82.4	6	17.6	19.27 (7.14-52.00)
Normal	118	77.6	23	19.5	95	80.5	1.00 (Ref.)

[1]Binary logistic regression, OR-Odds ratio, CI-Confidence interval, Ref.: Reference category

Table-2 shows the association of prevalence of MetS with age. The prevalence of MetS in LUTS patients was highest in age 50-59 years (42.1%) and was lowest in age ≥80 (16.7%). The prevalence of MetS in LUTS patients was 3.63 times higher in age 50-59 years than ≥80 years (OR=3.63, 95%CI=0.89-14.86). However, there was no significant (p>0.05) association of prevalence of MetS with age. The association of prevalence of MetS with storage symptoms. The prevalence of MetS in LUTS patients was higher among patients whom nocturia was present (35.2%) than absent (29.5%). However, there was no significant (p>0.05) association of prevalence of MetS with storage symptoms. Prevalence of MetS with storage symptoms. However, there was no significant (p>0.05) association of prevalence of MetS with voiding symptoms. The prevalence of MetS was significantly (p=0.0001) whom FBS, TG and waist circumference was increased than normal. The prevalence of MetS was significantly (p=0.0001) associated whom HDL was decreased than normal.

DISCUSSION-

Age distribution of LUTS patients

In this study, about one third of LUTS patients were between 60-69 years of age (33.6%) followed by 70-79 (30.9%), ≥80 (15.8%), 50-59 (12.5%) and 45-49 (7.2%). The mean age of patients was 67.66±10.64 years ranging from 45-92 years.

Various demographic studies of LUTS have been conducted over the past years. Nancy N. Maserejian et al. (2013)[11] conducted a study on 1305 patents and reported that age between 40-49 years contribute the highest number of LUTS(30.7%) patients while the incidence is decrease gradually with age. Varant Kupelian et al[12, 13] also conducted two studies in 2006 and 2008 but reported conflicting result regarding the prevalence of LUTS in different age groups. U Chung Lai et al (2011)[14] also found out that incidence of LUTS was most common in 50-59 years of age(38.6%) and least common in age more than 70 years of age.

This study found that more than half of LUTS patients were moderate LUTS (65.8%) followed by severe (29.6%) and mild (4.6%). Telli et al (2015)[15] informed that 74 patients (31.3%) with mild IPSS (0-7) was group 1; 97 patients (40.9%) with moderate IPSS (8 - 19) group 2 and 66 patients (27.8%) with severe IPSS (20-35) were defined as group 3. group 4 consisted of 117 healthy controls.

Severity of LUTS patients

Different researches have been conducted for the distribution of severity of LUTS patients. Tae Heon Kim et al (2014)[16] stated that moderate LUTS is more common than severe LUTS and mild LUTS is least common in korean population. However, Sabine Rohrmann et al (2016)[17] reported that severe LUTS is the least common LUTS (2.7%) while mild LUTS(75.3%) is the most common LUTS. S Madersbacher et al(1998)[18] reported the gradual increase in percentage of moderate/severe LUTS from age group 40-49 years to 70-79 years of age. In 2004, AsenOlof Anderson et al[19] demonstrated the gradual increase of severity of LUTS.

This study showed that mild LUTS was most common in age 45-49 years (9.1%) and moderate LUTS was also most common in age 45-49 years (81.8%). Severe LUTS was most common in age ≥80 years (41.7%). However, there was no significant (p>0.05) association of severity of LUTS patients with age.

Comparison of Voiding Symptoms of LUTS patients with age

The current study demonstrated that weak stream was most common in age ≥80 years (50%) and staining was also most common in age ≥80 years (45.8%). In complete emptying was most common in age ≥80 years (33.3%). Intermittency was most common in age 45-49 (36.4%). However, there was no significant (p>0.05) voiding symptoms of LUTS patients with age.

The prevalence of MetS in LUTS patients was 33.6% in the present study. Telli et al (2015)[15] revealed that MetS was determined at 37 patients (50%) in group 1, 45 patients (46.5%) in group 2, 32 patients (48%) in group 3 and 52 patients (44.4%) in controls and no statistically significant correlation was detected between LUTS and MS in BPH (P = 0.113). Lee et al (2015)[20] tested the hypothesis that the metabolic syndrome (MS) is linked to lower urinary tract symptoms (LUTS) in

Korean men and found that The prevalence of the MetS was 187/328 (57.0%) in 2004 and 125/224 (55.8%) in 2007 among men, respectively. Pashootan et al (2015)[21] found that metabolic syndrome was in 51.5% of the patients and 47% were treated for LUTS.

Association of Prevalence of MetS with metabolic components

Bashu Dev et al in (2017)[22] studied on 429 patients and found out that among metabolic components, low HDL (69.8%) was the most common components, followed by hypertrigl yceridemia (60.27%), hypertension (56.1%) and central obesity (30.1%). James Osei-Yeboah et al[23] on the other hand reported in 2017 that hypertension (63.93%) was the most common metabolic components while hypertriglyceridemia (6.56%) was the least common components. Felix Val K et al[24] in 2008 found out that low in HDL(47.4%) was more common than hypertension(46.9%) among the 456 patients. In other study, Mawuli Gyakobo et al[25] in 2012 also found out that hypoalphalipoproteinemia (42.7%) was more common than hypertension (39.5%) in metabolic syndrome patients. F KowNanse in 2013[26] also reported that both central obesity and hypertension (64%) each are the most common metabolic components among the study group while hypertriglyc eridemia (9.6%) was the least common.

Unfortunately, despite the importance of the public health impact of these two pathologies, correlation between MetS and BPH/LUTS has not been thoroughly studied. A systematic review identified eight eligible studies showing the role of MetS in the development of BPH (Gacci et al, 2015)[27], whereas only the correlation between MetS and prostate volume has been assessed, without strong available evidence regarding the frequency and severity of LUTS. Theoretically LUTS are considered as a substitute for the course of BPH and often resulting from an enlarged prostate and heightened tone of the prostate and bladder smooth muscle.

Pathophysiological mechanisms to explain the relationship between MetS and LUTS include the influence of sustained hyperglycemia on the viability of parasympathetic neurons in the pelvic ganglion. Animal studies demonstrated that long-term increased serum glucose initiates neuronal apoptosis that favors parasympathetic neuron when compared to sympathetic neuron (Cellek et al, 1999)[28]. This unbalanced loss of autonomic neurons induces an oversupply of sympathetic tone compared to parasympathetic efferent activity. In addition, hypertension also increases sympathetic tone and α1-adrenoceptor function (Michel et al, 1990)[29].

So it is presumed that an increased sympathetic tone results in increased bladder neck obstruction and reduced bladder power. All these together collaboratively culminate in increased voiding symptoms as reported in the present study. In addition, the Rho kinase system has a very important role in prostate contractility which is by modifying the calcium sensitivity of the contractile muscles (Rees et al, 2003; Takahashi et al, 2007)[30-31].

Higher levels of interleukin (IL)-8 and of the vasoconstrictor endothelin-1, which are usually elevated in men with MetS, may lead to an increased activity of the Rho kinase system that in turn may result in prostate contractility, including voiding symptoms. In a previous clinical study, doxazosin, an α-blocker used for symptomatic prostatic hyperplasia treatment, which increases insulin sensitivity and reduce insulin levels (Khan and Chakrabarti, 2003; Penna et al, 2009)[32,33].

However, a few studies do not support the association between MetS and LUTS. Gao and colleagues (2012)[34] retrospectively evaluated the effect of MetS on the severity of LUTS with data from a healthy and examination survey project in China, they concluded that no significant were found in the severity of LUTS in men with or without MetS. However, their study is difficult to compare with our results as they took the whole man population as the study objects, regardless of whether or not there was a concomitant BPH existed, and their subjects are younger (median age were 39 vs. 65 of the present study) and less symptomatic (92.1% participants with mild LUTS). Even so, their study found moderate or severe storage symptoms were inversely correlated with MetS. The same considerations are also valid for similar studies performed in an Asian population where no significant differences were found in the severity of LUTS between the MetS and non-MetS group (Park et al, 2008)[35].

One of the limitations of this study was small sample size and short duration of study period. Further investigations with long-term follow-up are needed to better understand the role of MetS as a potential risk factor for BPH/LUTS progression and to identify new possible therapeutic targets and open novel strategies for the management of BPH/LUTS.

CONCLUSION-

In conclusion, the results of the present study confirm the significant relationship between LUTS and metabolic syndrome in men, in terms of frequency and severity. The risk of being treated for LUTS also increased with an increasing number of metabolic syndrome components present. The prevention of such modifiable factors by the promotion of dietary changes and regular physical activity practice may be of great importance for public health.

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