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ASSOCIATION BETWEEN BENIGN PROSTATIC ENLARGEMENT, ERECTILE DYSFUNCTION AND METABOLIC SYNDROME

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ABSTRACT
The overwhelming evidence of a connection between lower urinary tract symptoms (LUTS) and erectile dysfunction (ED) comes from numerous major epidemiological research. Clinical data indicates that the development of ED, LUTS, and metabolic syndrome is caused by a number of shared pathophysiological pathways. The association between ED and metabolic syndrome in patients presenting with LUTS due to BPE was conducted at the Department of Urology, Saveetha Medical College. The study comprised 100 patients, whose ages ranged from 45 to 84 years old, with a mean age of 63.8 years. The physical attributes and laboratory results of the patients were tabulated. Based on the IPSS classification of patients' LUTS, 15%, 46% and 39% were found in the mild, moderate and severe LUTS patient groups. It was found that the severity of LUTS increased as people aged, but statistically insignificant($p>0.05$). Regarding the severity of LUTS, there was no discernible difference in LUTS between the groups with mild/no ED and moderate/severe ED ($p=0.314$). 25% had diabetes mellitus, 48% had central obesity, 40% had increased triglycerides, 65% had lower HDL cholesterol, and 24% had systemic hypertension. Out of 100 patients, 36 patients satisfied three out of the five criteria and were diagnosed with metabolic syndrome. 11% had no ED, whereas 58% had mild ED, 23% had moderate ED, and 8% had severe ED. An increase in ED severity was noted with increasing age($p=0.01$). There was a significant difference in the presence of metabolic syndrome between the groups with mild/no ED and moderate/severe ED ($p=0.029$). It was discovered that there was no correlation between the severity of LUTS and the existence of metabolic syndrome ($p=0.152$). Regarding the occurrence of metabolic syndrome, there is a substantial difference between the groups with mild or no ED and those with moderate or severe ED. A BPE patient was more likely to have ED than a patient without metabolic syndrome if they also had an additional diagnosis of this condition. In a patient with BPE, the existence of ED may be a predictor of metabolic syndrome.

KEYWORDS
lower urinary tract symptoms, autonomic hyperactivity, erectile dysfunction, metabolic syndrome.

INTRODUCTION

The overwhelming evidence of a connection between lower urinary tract symptoms (LUTS) and erectile dysfunction (ED) comes from numerous major epidemiological research. Clinical evidence suggests that several common pathophysiological mechanisms lead to the development of ED, LUTS, and metabolic syndrome.

OBJECTIVE

To determine the association between ED and metabolic syndrome in patients presenting with LUTS due to BPE

MATERIAL AND METHODS

This study was conducted at the Department of Urology, Saveetha Medical College, between November 2022 and October 2023. Inclusion criteria included patients with a clinical diagnosis of BPE (Benign Prostatic Enlargement). A clinical diagnosis of BPE was made with the following criteria - males aged 45 years and above with voiding or storage LUTS or acute urinary retention, low Qmax on uroflowmetry. Exclusion criteria included males with LUTS already on medical treatment or previous surgical treatment like TURP, visual internal urethrotomy, etc., males with LUTS due to causes other than BPE such as urinary tract calculus, urinary tract cancer, urethral stricture, prostatic abscess, urtehritis, etc. 100 consecutive patients with BPE related LUTS qualified for the study. The following data such as age, blood pressure, plasma fasting glucose level, serum HDL cholesterol level, serum triglyceride level, waist circumference, prostate volume (measured by ultrasonogram abdomen), uroflowmetry and post void residual urine volume were obtainerd. The National Cholesterol Education program -Adult Treatment Panel III (NCEP ATP III) defined three or more of the following clinical criteria for a diagnosis of metabolic syndrome: waist circumference (men >102 cm, women > 88 cm), fasting blood triglyceride level ≥150 mg/dL, HDL-cholesterol (men <40 mg/dL, women <50 mg/dL), fasting blood glucose ≥110 mg/dL, and blood pressure ≥130/85 mmHg. The International Prostate Symptom Score (IPSS) was used to stratify the patients' LUTS, and the International Index for Erectile Dysfunction Index-5 (IIEF-5) was used to stratify their erectile dysfunction. According to IPSS, we had three groups such as mild LUTS (<8 points), moderate LUTS (8-18) points and severe LUTS (>19 points). Patients with IIEF-5 scores ranging from 6 to 25 were classified as having mild or no ED, and patients with IIEF scores ranging from 26 to 30 were classified as moderate/severe ED group. The following tests were run using SPSS (Statistical Package for the Social Sciences) v11.0 for statistical evaluation: Pearson correlation analysis, ANOVA, Chi-square, and Student's t test. The accepted threshold for a statistically significant difference was $p<0.05$.

RESULTS

The study included 100 patients, with a mean age of 63.8 years and ages ranging from 45 to 84. The physical attributes and laboratory results of the patients were tabulated (Table 1). Based on the IPSS classification of patients' LUTS, 15%, 46% and 39% were found in the mild, moderate and severe LUTS patient groups (Table 2). It was found that the severity of LUTS increased as people aged, but statistically insignificant($p>0.05$). Regarding the severity of LUTS, there was no discernible difference in LUTS between the groups with mild/no ED and moderate/severe ED ($p=0.314$). 25% had diabetes mellitus, 48% had central obesity, 40% had increased triglycerides, 65% had lower HDL cholesterol, and 24% had hypertension. Out of 100 patients, 36 patients satisfied three out of the five criteria and were diagnosed with metabolic syndrome. 11% had no erectile dysfunction, 58% had mild erectile dysfunction, 23% had moderate erectile dysfunction, and 8% had severe erectile dysfunction (Table 3). An increase in ED severity was noted with increasing age ($p=0.01$). There was a significant difference in the presence of metabolic syndrome between the groups with mild/no ED and moderate/severe ED ($p=0.029$). The degree of LUTS was not observed to be correlated with the existence of metabolic syndrome ($p=0.152$) (Table 4)

TABLE 1: PHYSICAL ATTRIBUTES AND LABARATORY RESULTS

DEMOGRAPHIC DATA	MEAN
Age (year)	63.8
Plasma fasting glucose (mg/dl)	102.19
High Density lipoprotein- cholesterol (mg/dl)	40.07
Volume of the prostate (ml)	38.71
Serum triglyceride level (mg/dl)	154.38
Maximal urine flow rate (ml/sec)	14.37
Residual urine voluime after voiding (ml)	98.69
International Index for Erectile Dysfunction Index-5 scores	18.58

International Prostate Symptom Score	10.76	5.31

TABLE 2: CORRELATION BETWEEN LOWER URINARY TRACT SYMPTOMS AND ERECTILE DYSFUNCTION

SEVERITY OF LUTS	MILD/NO ERECTILE DYSFUNCTION n=69	MODERATE/SEVERE ERECTILE DYSFUNCTION n=31	p value
Mild (n=15)	27%	9%	0.314
Moderate (n=46)	31%	17%	
Severe (n=39)	11%	5%	

TABLE 3: CORRELATION BETWEEN ERECTILE DYSFUNCTION AND METABOLIC SYNDROME

SEVERITY OF ERECTILE DYSFUNCTION	METABOLIC SYNDROME PRESENT n=36	METABOLIC SYNDROME ABSENT n=64	p Va
Mild/No ED (IIEF 6-11) n=69	21%	58%	0.02
Moderate/Severe ED (IIEF 17-30) n=31	15%	6%	

TABLE 4: CORRELATION BETWEEN LOWER URINARY TRACT SYMPTOMS AND METABO SYNDROME

SEVERITY OF LUTS	METABOLIC SYNDROME PRESENT n=36	METABOLIC SYNDROME ABSENT n=64	p Value
Mild n=15	6%	9%	0.152
Moderate n=46	16%	30%	
Severe n=39	14%	15%	

DISCUSSION

Male aging patients frequently experience erectile dysfunction (ED) and lower urinary tract symptoms (LUTS) (1). Although research has shown an association between LUTS and ED that is unrelated to advanced age, advanced age is a significant component in the concomitancy between LUTS and ED (2). These complaints have a complex aetiology; changes in neuroregulatory variables including nitric oxide and RhoA kinase, as well as innervation of the lower urinary tract. Comorbid diseases including metabolic syndrome, diabetes, and hypogonadism that impact these neuroregulatory systems can also be held accountable for the onset of these issues in addition to aging. The significance of this specific neural circuit is demonstrated by the beneficial effects of widely used medications on the previously stated neural pathways (3). Metabolic syndrome can cause abnormalities in neuroregulatory circuits related to the lower urinary system, which can result in problems with ejaculatory, erectile, and urine storage (2). In our investigation, 36% of the patients had metabolic syndrome. The rates of metabolic syndrome were reported to be 14 and 15%, respectively, in our patients with severe LUTS and ED. Our study's findings regarding the frequencies of metabolic syndrome in patients with severe LUTS and ED were consistent with previous research, which lends credence to the theory that the aforementioned symptoms could arise through comparable mechanisms. A complex illness associated with insulin resistance, metabolic syndrome has an unclear underlying cause. Prostate volume growth each year, LUTS, and components of metabolic syndrome have all been shown to significantly correlate (4). It was shown in an animal experiment that long-term exposure to hyperglycemia causes neuronal cells to undergo apoptosis. Ultimately, this has a significant effect on the parasympathetic nervous system, which causes autonomic hyperactivity that may contribute to the development of LUTS (5). Endothelial dysfunction, associated with metabolic syndrome and resulting from many etiological causes, can also give rise to ED. In a study looking at ED and endothelial dysfunction as indicators of impaired endothelial function, proinflammatory cytokines were detected more often in men who were obese than in men who were not obese. Moreover, male patients with ED had greater CRP levels than non-ED patients (6). Bal et al.'s research on 393 patients between the ages of 40 and 70 revealed a prevalence of 39.9% for metabolic syndrome and 79.8% for ED. They found a substantial association between blood pressure, ED, fasting blood glucose, and waist circumference in their investigation (7). However, none of the etiological indicators for ED—higher trigyceride levels, lower HDL values, and ED rates—showed a significant association in our investigation. In addition,

there was no discernible relationship between IIEF scores and waist circumference. The incidence of ED was shown to be 6.2 times higher in cases of severe LUTS and 4.4 times higher in cases of mild LUTS in a Turkish patient group with LUTS (8). 83% of LUTS patients were still able to engage in sexual activity, 48.7% had some erectile impairment, and 10% had no erectile dysfunction as all, according to the MSAM-7 research (9). No significant association between LUTS, diabetes mellitus, hypertension, and abdominal obesity could be found by Demir et al. (10). In their study, the frequency of lower urinary tract symptoms was substantially higher in those with hypertriglyceridemia (28.8% vs. 53.8%). Temml et al. examined the role of metabolic syndrome in 2371 males and discovered that 33.8% of the patients had it (11). Nevertheless, no meaningful association was discovered between metabolic syndrome and an IPSS score higher than 7. In our investigation, there was no significant difference in the incidence of LUTS between those with and without metabolic syndrome. Severe LUTS cases made up 39% of the study group. In individuals with overactive bladder, Dagdeviren et al. discovered a correlation between serum nerve growth factor levels and metabolic syndrome (12). De Nunzio et al. observed that patients with benign prostatic enlargement who had metabolic syndrome were more likely to experience storage symptoms (13). Dogan Y et al. measured the correlation of LUTS/BPH, metabolic syndrome incidence and severe ED. They observed a negative link between age and IIEF scores, erectile dysfunction IIEF scores declined with aging, and metabolic syndrome criteria—aside from triglyceride level—did not correspond with IPSS (14). In their investigation of the connection between metabolic syndrome and overactive bladder (OAB), Lai et al. found that there was a positive correlation between the incidence of urge urine incontinence and waist circumference. The incidence of nocturia and overactive bladder was positively linked with waist circumference (15). Mitsui et al. used metabolomics to determine that male LUTS was related with increased glutamate and decreased levels of arginine, asparagines, and inosine monophosphate (16). Papaefstathiou et al. examined the effects of diabetes mellitus on LUTS in both males and females. They found that while moderate-to-severe LUTS was more common in women with diabetes mellitus, there was no statistically significant association between LUTS and males with diabetes mellitus (17). Park et al. examined the relationship between the metabolic syndrome and LUTS and BPE in Asian males. They found that the metabolic syndrome characteristics were highly correlated with LUTS and that lowering LDL-C and fat mass levels might stop the development of BPE in healthy Korean guys in five years (18). Plata et al. published that metabolic syndrome correlated with LUTS but not with erectile dysfunction, but a possitive correlation between diabetes mellitus with LUTS and erectile dysfunction (19). The effect of insulin resistance on LUTS was studied by Russo et al., who noted that insulin resistance accounted for a higher incidence of LUTS and that severe LUTS was independently predicted by insulin resistance (20). Zhao et al. in his study found out a positive correlation between metabolic syndrome and severity of LUTS. Additionally, he demonstrated how each component of the metabolic syndrome stood alone as a risk factor for severe LUTS (21). Zorba et al. published that in patients with metabolic syndrome, prostate volume, serum PSA (Prostate Specific Antigen) and residual urine voluime after voiding were significantly higher (22). Additionally, Li et al. found a strong correlation between metabolic syndrome and increased prostate volume and annual growth rate (23). He discovered no connection between IPSS/IPSS subgroups and metabolic syndrome. As opposed to our finding, he found a positive correlation between metabolic syndrome and uroflowmetry parameters such as reduced Vmax and increased post void residue.

CONCLUSION

Regarding the occurrence of metabolic syndrome, there is a substantial difference between the groups with mild or no ED and those with moderate or severe ED. A BPE patient was more likely to have ED than a patient without metabolic syndrome if they also had a additional diagnosis of this condition. In a patient with BPE, the existence of ED may be a predictor of metabolic syndrome.

REFERENCES

1. Mondul AM, Rimm EB, Giovannucci E, Glasser DB, Platz EA. A prospective study of lower urinary tract symptoms and erectile dysfunction. J Urol. 2008 Jun;179(6):2321-6. doi: 10.1016/j.juro.2008.01.150. Epub 2008 Apr 18. PMID: 18423761; PMCID: PMC3217213.

2. Mazur DJ, Helfand BT, McVary KT. Influences of neuroregulatory factors on the development of lower urinary tract symptoms/benign prostatic hyperplasia and erectile dysfunction in aging men. Urol Clin North Am. 2012 Feb;39(1):77-88. doi: 10.1016/j.ucl.2011.09.005. Epub 2011 Oct 13. PMID: 22118347.

3. Agochukwu-Mmonu N, Pop-Busui R, Wessells H, Sarma AV. Autonomic neuropathy

and urologic complications in diabetes. Auton Neurosci. 2020 Dec;229:102736. doi: 10.1016/j.autneu.2020.102736. Epub 2020 Oct 16. PMID: 33197694; PMCID: PMC10248950.
4. Hammarsten J, Högstedt B. Hyperinsulinaemia as a risk factor for developing benign prostatic hyperplasia. Eur Urol. 2001 Feb;39(2):151-8. doi: 10.1159/000052430. PMID: 11223674.
5. Cellek S, Rodrigo J, Lobos E, Fernández P, Serrano J, Moncada S. Selective nitrergic neurodegeneration in diabetes mellitus - a nitric oxide-dependent phenomenon. Br J Pharmacol. 1999 Dec;128(8):1804-12. doi: 10.1038/sj.bjp.0702981. PMID: 10588937; PMCID: PMC1571816.
6. Giugliano F, Esposito K, Di Palo C, Ciotola M, Giugliano G, Marfella R, D'Armiento M, Giugliano D. Erectile dysfunction associates with endothelial dysfunction and raised proinflammatory cytokine levels in obese men. J Endocrinol Invest. 2004 Jul-Aug;27(7):665-9. doi: 10.1007/BF03347500. PMID: 15505991.
7. Bal K, Oder M, Sahin AS, Karataş CT, Demir O, Can E, Gümüş BH, Ozer K, Sahin O, Esen AA. Prevalence of metabolic syndrome and its association with erectile dysfunction among urologic patients: metabolic backgrounds of erectile dysfunction. Urology. 2007 Feb;69(2):356-60. doi: 10.1016/j.urology.2006.09.057. Epub 2007 Jan 31. PMID: 17275074.
8. Akkus E, Kadioglu A, Esen A, Doran S, Ergen A, Anafarta K, Hattat H; Turkish Erectile Dysfunction Prevalence Study Group. Prevalence and correlates of erectile dysfunction in Turkey: a population-based study. Eur Urol. 2002 Mar;41(3):298-304. doi: 10.1016/s0302-2838(02)00027-1. PMID: 12180232.
9. Rosen R, Altwein J, Boyle P, Kirby RS, Lukacs B, Meuleman E, O'Leary MP, Puppo P, Robertson C, Giuliano F. Lower urinary tract symptoms and male sexual dysfunction: the multinational survey of the aging male (MSAM-7). Eur Urol. 2003 Dec;44(6):637-49. doi: 10.1016/j.eururo.2003.08.015. PMID: 14644114.
10. Demir O, Akgul K, Akar Z, Cakmak O, Ozdemir I, Bolukbasi A, Can E, Gumus BH. Association between severity of lower urinary tract symptoms, erectile dysfunction and metabolic syndrome. Aging Male. 2009 Mar;12(1):29-34. doi: 10.1080/13685530902777425. PMID: 19326294.
11. Temml C, Obermayr R, Marszalek M, Rauchenwald M, Madersbacher S, Ponholzer A. Are lower urinary tract symptoms influenced by metabolic syndrome? Urology. 2009 Mar;73(3):544-8. doi: 10.1016/j.urology.2008.10.027. Epub 2009 Jan 1. PMID: 19118873.
12. Dagdeviren H, Cengiz H. Association between Metabolic Syndrome and Serum Nerve Growth Factor Levels in Women with Overactive Bladder. Gynecol Obstet Invest. 2018;83(2):140-144. doi: 10.1159/000477170. Epub 2017 Jun 22. PMID: 28637031.
13. De Nunzio C, Brassetti A, Proietti F, Deroma M, Esperto F, Tubaro A. Metabolic syndrome and smoking are associated with an increased risk of nocturia in male patients with benign prostatic enlargement. Prostate Cancer Prostatic Dis. 2018 Jun;21(2):287-292. doi: 10.1038/s41391-017-0003-z. Epub 2017 Dec 4. PMID: 29203892.
14. Doğan Y, Uruç F, Aras B, Şahin A, Kıvrak M, Ürkmez A, Güner ND, Aydın S. The relationships between metabolic syndrome, erectile dysfunction and lower urinary tract symptoms associated with benign prostatic hyperplasia. Turk J Urol. 2015 Mar;41(1):7-12. doi: 10.5152/tud.2015.99997. PMID: 26328190; PMCID: PMC4548658.
15. Lai HH, Helmuth ME, Smith AR, Wiseman JB, Gillespie BW, Kirkali Z; Symptoms of Lower Urinary Tract Dysfunction Research Network (LURN). Relationship Between Central Obesity, General Obesity, Overactive Bladder Syndrome and Urinary Incontinence Among Male and Female Patients Seeking Care for Their Lower Urinary Tract Symptoms. Urology. 2019 Jan;123:34-43. doi: 10.1016/j.urology.2018.09.012. Epub 2018 Oct 28. PMID: 30393054; PMCID: PMC6312730.
16. Mitsui T, Kira S, Ihara T, Sawada N, Nakagomi H, Miyamoto T, Shimura H, Yokomichi H, Takeda M. Metabolomics Approach to Male Lower Urinary Tract Symptoms: Identification of Possible Biomarkers and Potential Targets for New Treatments. J Urol. 2018 May;199(5):1312-1318. doi: 10.1016/j.juro.2017.11.070. Epub 2017 Nov 22. PMID: 29175111.
17. Papaefstathiou E, Moysidis K, Sarafis P, Ioannidis E, Hatzimouratidis K. The impact of Diabetes Mellitus on Lower urinary tract symptoms (LUTS) in both male and female patients. Diabetes Metab Syndr. 2019 Jan-Feb;13(1):454-457. doi: 10.1016/j.dsx.2018.11.009. Epub 2018 Nov 3. PMID: 30641743.
18. Park JS, Koo KC, Kim HK, Chung BH, Lee KS. Impact of metabolic syndrome-related factors on the development of benign prostatic hyperplasia and lower urinary tract symptoms in Asian population. Medicine (Baltimore). 2019 Oct;98(42):e17635. doi:

10.1097/MD.0000000000017635. PMID: 31626149; PMCID: PMC6824778.

19. Plata M, Caicedo JI, Trujillo CG, Mariño-Alvarez ÁM, Fernandez N, Gutierrez A, Godoy F, Cabrera M, Cataño-Cataño JG, Robledo D. Prevalence of metabolic syndrome and its association with lower urinary tract symptoms and sexual function. Actas Urol Esp. 2017 Oct;41(8):522-528. English, Spanish. doi: 10.1016/j.acuro.2016.12.009. Epub 2017 Apr 5. PMID: 28390836.
20. Russo GI, Regis F, Spatafora P, Frizzi J, Urzì D, Cimino S, Serni S, Carini M, Gacci M, Morgia G. Association between metabolic syndrome and intravesical prostatic protrusion in patients with benign prostatic enlargement and lower urinary tract symptoms (MIPS Study). BJU Int. 2018 May;121(5):799-804. doi: 10.1111/bju.14007. Epub 2017 Sep 28. PMID: 28872764.
21. Zhao S, Chen C, Chen Z, Xia M, Tang J, Shao S, Yan Y. Relationship between Metabolic Syndrome and Predictors for Clinical Benign Prostatic Hyperplasia Progression and International Prostate Symptom Score in Patients with Moderate to Severe Lower Urinary Tract Symptoms. Urol J. 2016 Jun 28;13(3):2717-26. PMID: 27351328.
22. Zorba OÜ, Uzun H, Akça G, Yazar S. The Effect of Different Metabolic Syndrome: Definitions on the Relationship Between Metabolic Syndrome and LUTS in Men With Benign Prostatic Enlargement. Am J Mens Health. 2017 Jan;11(1):158-163. doi: 10.1177/1557988316638654. Epub 2016 Jun 23. PMID: 26993995; PMCID: PMC5675180.
23. Li J, Peng L, Cao D, Gou H, Li Y, Wei Q. The association between metabolic syndrome and benign prostatic hyperplasia: a systematic review and meta-analysis. Aging Male. 2020 Dec;23(5):1388-1399. doi: 10.1080/13685538.2020.1771552. Epub 2020 Jun 2. PMID: 32482153.