

<http://www.pjbs.org>

PJBS

ISSN 1028-8880

**Pakistan
Journal of Biological Sciences**

ANSI*net*

Asian Network for Scientific Information
308 Lasani Town, Sargodha Road, Faisalabad - Pakistan

Non-obstructive Lower Urinary Tract Symptoms Versus Prostate Volume in Benign Prostatic Hyperplasia

¹K. Hassanzadeh, ²P. Yavari-kia, ¹Y. Ahmadi-Asrbadr and ³F. Nader-Abbasi

¹Department of Urology, Imam Reza Hospital, Tabriz University of Medical Sciences, Tabriz, Iran

²Medical Journal, Tabriz University of Medical Sciences, Tabriz, Iran

³Tabriz University of Medical Sciences, Tabriz, Iran

Abstract: This study was aimed to determine the relation between sonographically measured prostate volume and the severity of non-obstructive Lower Urinary Tract Symptoms (LUTS) in Benign Prostatic Hyperplasia (BPH). This was an analytic-descriptive, cross-sectional and prospective study which was carried out on a sequential sample of 60 male patients since 2006 to 2008. The patients were divided to three groups (prostate volume < 40 cc; 40 cc ≤ prostate volume ≤ 59 cc; prostate volume ≥ 60 cc) based on the ultrasonographic volume of the prostate. The American Urological Association scores of frequency, urgency, nocturia and dysuria were compared between three groups. The mean age and the mean total score of non-obstructive symptoms of BPH of the patients were 71.18±8.74 and 13.38±2.96, respectively. According to our findings there was no statistical significant difference between three groups in the scores of frequency ($p = 0.369$), dysuria ($p = 0.85$) and nocturia ($p = 0.861$). A statistically significant difference between three groups was found in urgency score ($p = 0.037$). Only a significant correlation between urgency and the prostate volume was found ($p = 0.024$, $r = 0.291$). According to our findings in this work on relation between the non-obstructive symptoms and prostate volume in BPH patients we found that urgency was the only non-obstructive symptom that may be associated with prostate volume. Prospective studies are required in this regard to elucidate the symptom-related causes of LUTS in the patients with BPH.

Key words: Urinary tract, prostatic hyperplasia, nocturia, dysuria, urgency, symptoms

INTRODUCTION

Benign prostatic hyperplasia (BPH) is a chronic frequent disease in men and is often associated with troublesome Lower Urinary Tract Symptoms (LUTS) (Pinto *et al.*, 2009). BPH is the mainly common urological disease of elderly men, which has the presentation of obstruction in urinary flow with discomfort and pain. BPH is a complex disease from the etiological and pathogenesis point of view (Konwar *et al.*, 2008). The incidence of BPH has been increased and it is estimated that more than 50% of men by the age of 60 will have microscopic evidence of the disease and by the age of 85 years, as many as 90% of men will be affected (AUA Practice Guidelines Committee, 2003). The prevalence of BPH was 23.1% in Croatia (Galic and Simunovic, 2008). However, Mittal *et al.* (1989) reported that from 185 consecutive prostate specimens in India the predominant lesion noted was BPH with the rate of 92.97%.

LUTS associated with BPH are regarded as a common patients complaints managed by urologists. The

harshness of LUTS, fright of prostate cancer, meddling with normal and activities, complications of BPH and diminished quality of life result in referrals to urologists. Perez *et al.* (2009) revealed that Prevalence of moderate/severe LUTS was 16.6% among 1,804 men aged 40 or older who were living in Madrid and also proved that men aged 70 or older had a threefold increased frequency of serious symptoms compared to younger men (Perez *et al.*, 2009), however Li *et al.* (2008) showed that in 994 men aged 40-88 years from Singapore [details of symptoms of BPH were collected through the International Prostate Symptom Score (IPSS)] about 90% of the men had moderate-to-severe LUTS and the severity increased with age.

LUTS symptoms cannot discriminate obstructed from non-obstructed BPH cases, not all severely symptomatic BPH patients will have outlet obstruction, a significant percentage of mildly symptomatic BPH patients can have outlet obstruction and voiding dysfunctions in aged men, apart from of the etiology, make related symptoms (Yalla *et al.*, 1995). Eckhardt *et al.* (2001a) investigated

the associations of symptoms and prostate volume a large group of strictly selected men with LUTS suggestive of benign BPH and finally concluded that Prostate volume and obstruction grade were not associated with the symptom index (Eckhardt *et al.*, 2001b).

This study was aimed to evaluate the relation between sonographically measured volume of prostate and the severity of non-obstructive symptoms.

MATERIALS AND METHODS

This was an analytic-descriptive, cross-sectional and prospective study which was carried out on a sequential sample of 60 male patients that was conducted in one year period at Imam Khomeini and Sina Hospital in Tabriz since 2006 to 2008.

The patients were divided to three groups based on the volume of the prostate which measured based on trans-rectal ultrasonography:

- **Group 1:** Patients with prostate volume < 40 cc
- **Group 2:** Patients with 40 cc = prostate volume = 59 cc
- **Group 3:** Patients with prostate volume = 60 cc

Data selection: Interview and observation were the methods of data gathering from the patients. All the patients were referred to the centers because of BPH and were the candidates of open surgery or transurethral resection prostatectomy. The investigators recorded the non-obstructive symptoms of the patients.

From the 7 symptoms of American Urological Association (AUA), three of them (non-obstructive) were considered: frequency, urgency and nocturia. Dysuria was the fourth considered symptom. The scores of the considered symptoms were as below:

- **Zero score:** The symptom was not presented in the patient
- **One score:** The symptom was presented in less than 1/5th of the duration of the life of the patient
- **Two score:** The symptom was presented in less than half of the duration of the life of the patient
- **Three score:** The symptom was presented in about half of the duration of the life of the patient
- **Four score:** The symptom was presented in more than half of the duration of the life of the patient
- **Five score:** The symptom was presented almost in all time of the duration of the life of the patient

Finally, all the scores of non-obstructive symptoms were summarized. Due to the scoring system which was

selected in this work the score of each patient was between 0 and 20.

Statistical analysis: The data were subjected to statistical evaluation, using SPSS II, with descriptive statistics (mean, median, standard deviation [SD]) being determined for all variables. In our comparisons t-tests and chi-square tests were used for quantitative and qualitative variables. Correlations were assessed using Pearson correlation coefficients. p-values less than 0.05 were considered significant.

Medical ethics considerations: Trans-rectal ultrasonography is a necessary procedure in the approach of the patients with BPH. Each patient gave informed written consent to participate in the study, which was approved by Tabriz University of Medical Science Ethics Committee.

RESULTS

General characteristics of the patients: The mean age of the patients was 71.18±8.74 (Min: 52 Max: 86). The average of the volume of the prostates of the patients was 45.75±7.84 cc (Min: 31 cc Max: 78 cc) (Table 1).

The mean calculated scores of each non-obstructive symptoms of the patients for frequency, urgency, dysuria, nocturia, were: 3.78±1.22, 3.45±1.19, 3.06±1.19, 3.08±1.42, respectively. The total score of non-obstructive symptoms was 13.38±2.96 (Table 1).

Comparison of non-obstructive symptoms between three groups of the patients (group 1, 2 and 3): According to our findings there was no statistical significant difference between three groups in frequency score (F = 1.015, p = 0.369) (Fig. 1).

A statistically significant difference between three groups was found in urgency (F = 3.508, p = 0.037); this score was the lowest in group 1 and was the highest in group 3 (Fig. 2).

Based on the results there were no statistical significant difference between three groups in dysuria (F = 0.217, p = 0.85; Fig. 3) and nocturia (F = 0.150, p = 0.861; Fig. 4) score.

Table 1: General symptom characteristics of the patients

Characteristics (N = 60)	Values
The mean calculated scores of the non-obstructive symptoms of the patients	
Age (year)	71.18±8.74 (min: 52 max: 86)
Frequency	3.78±1.22 (min: 1 max: 5)
Urgency	3.45±1.19 (min: 1 max: 5)
Dysuria	3.06±1.19 (min: 1 max: 5)
Nocturia	3.08±1.42 (min: 1 max: 5)
The total score of non-obstructive symptoms	13.38±2.96

Values are expressed as Mean±SD

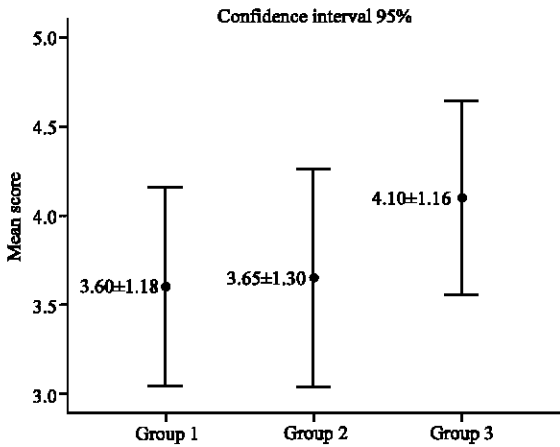


Fig. 1: The mean score of frequency symptom in three groups of patients with different volume of prostate. Group 1: Patients with prostate volume < 40 cc, Group 2: Patients with 40 cc = prostate volume = 59 cc, Group 3: Patients with prostate volume = 60 cc

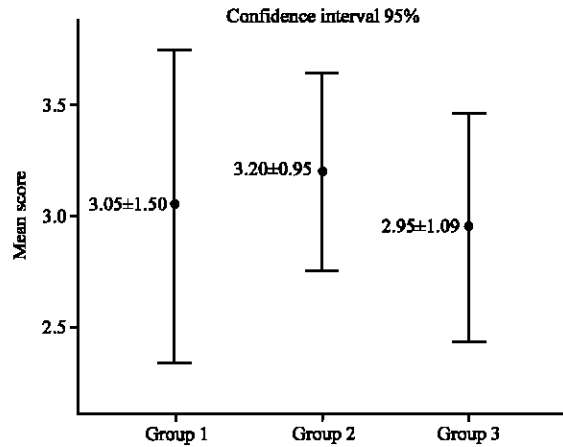


Fig. 3: The mean score of dysuria symptom in three groups of patients with different volume of prostate. Group 1: Patients with prostate volume < 40 cc, Group 2: Patients with 20 cc = prostate volume = 59 cc, Group 3: Patients with prostate volume = 60 cc

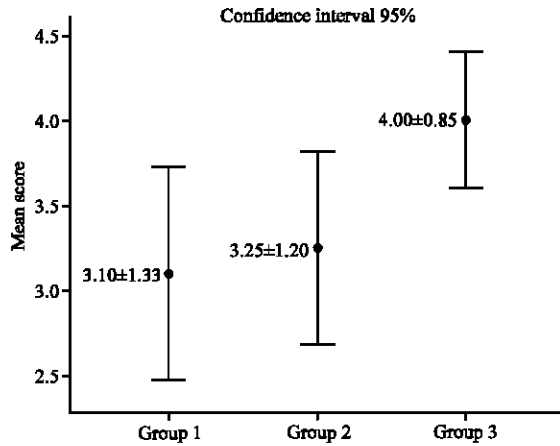


Fig. 2: The mean score of urgency symptom in three groups of patients with different volume of prostate. Group 1: Patients with prostate volume < 40 cc, Group 2: Patients with 40 cc = prostate volume = 59 cc, Group 3: Patients with prostate volume = 60 cc

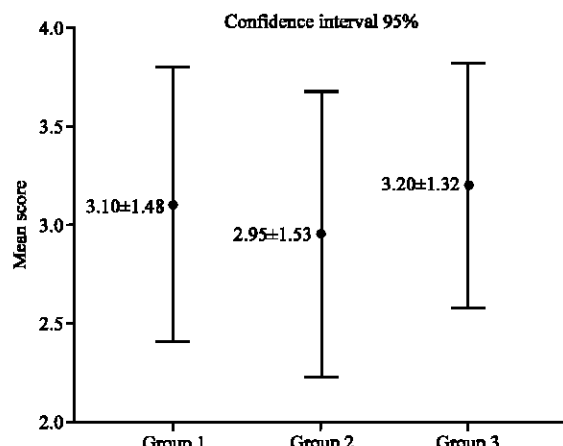


Fig. 4: The mean score of nocturia symptom in three groups of patients with different volume of prostate. Group 1: Patients with prostate volume < 40 cc, Group 2: Patients with 40 cc = prostate volume = 59 cc, Group 3: Patients with prostate volume = 60 cc

The total scores of the non-obstructive symptoms did not represent any significant difference between three groups ($F = 1.314$, $p = 0.227$) (Fig. 5).

$p = 0.711$, Fig. 2), dysuria ($t = -0.377$, $p = 0.708$, Fig. 3), nocturia ($t = 0.314$, $p = 0.755$, Fig. 4) and total score of non-obstructive symptoms ($t = -0.200$, $p = 0.843$, Fig. 5).

Comparison of non-obstructive symptoms between group 1 and 2: Upon to the results of this work no significant difference was found between group 1 and 2 in frequency score ($t = -0.127$, $p = 0.900$, Fig. 1), urgency ($t = 0.373$,

Comparison of non-obstructive symptoms between group 1 and 3: Upon the results of this work no significant difference was found between group 1 and 3 in frequency score ($t = -1.344$, $p = 0.187$, Fig. 1), dysuria ($t = -0.240$,

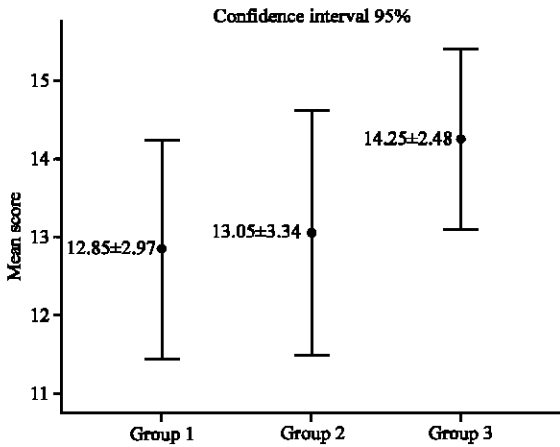


Fig. 5: The mean score of total non-obstructive symptoms in three groups of patients with different volume of prostate. Group 1: Patients with prostate volume <40 cc, Group 2: Patients with 40 cc = prostate volume = 59 cc, Group 3: Patients with prostate volume = 60 cc

Table 2: Correlations between non-obstructive symptoms and prostate volume

Variables	Prostate volume	
	r	p
Frequency	0.194	0.137
Urgency	0.291	0.024
Dysuria	0.065	0.620
Nocturia	0.010	0.938
The total score of non-obstructive symptoms	0.166	0.204

Correlations were assessed using Pearson correlation coefficients

p = 0.812, Fig. 3), nocturia (t = 0.225, p = 0.823, Fig. 4) and total score of non-obstructive symptoms (t = -1.619, p = 0.114, Fig. 5).

The scores of the patients in group 3 in urgency was significantly higher than group 1 (t = -2.538, p = 0.015, Fig. 2).

Comparison of non-obstructive symptoms between group 2 and 3: Upon the results of this work no significant difference was found between group 2 and 3 in frequency score (t = -1.148, p = 0.258, Fig. 1), dysuria (t = 0.769, p = 0.447, Fig. 3), nocturia (t = -0.585, p = 0.551, Fig. 4) and total score of non-obstructive symptoms (t = -1.290, p = 0.205, Fig. 5).

The scores of the patients in group 3 in urgency was significantly higher than group 2 (t = -2.263, p = 0.029, Fig. 2).

Correlations between non-obstructive symptoms and prostate volume: Table 2 shows the correlations between non-obstructive symptoms and prostate volumes

of the patients. Only there was a significant correlation between urgency and the prostate volume (p = 0.024, r = 0.291).

DISCUSSION

We found that urgency was the only non-obstructive LUTS that may be associated with prostate volume.

There is no association between other non-obstructive LUTS and prostate volume that is consistent with previous reports (Sirls *et al.*, 1996; Kojima *et al.*, 1997).

BPH is a hyperplastic enlargement of prostate resulting in growth of glandular-epithelial and stromal/muscle tissue in the prostate, leading to frequently quantifiable growth taking on different shapes and configurations which may impact symptoms and secondary results. It is imperative to recognize that BPH is a histological conditions, which is one but not the only cause of lower urinary tract symptoms and may or may not be associated with prostate enlargement and bladder outlet obstruction (Roehrborn, 2008). LUTS are the most common problem that affects BPH patients (Trueman *et al.*, 1999; Wu *et al.*, 2006). It is a general concern that LUTS that are associated with BPH to urinary obstruction caused by enlarged prostate, but there are some controversies in this regard (Bosch *et al.*, 2008). Several studies have indicated that there are correlations between urinary symptoms and prostate volume, peak flow rate or residual urine volume (Barry *et al.*, 1992; Madersbacher *et al.*, 1997). However, others have proved that prostate volume is not associated with LUTS and objective parameters cannot predict the severity of symptoms in BPH patients (Ezz el Din *et al.*, 1996; Eckhardt *et al.*, 2001a).

Tubaroa and Vecchia (2004) in an investigation of 802 patients reported that the association between LUTS and prostate volume remains questionable. Yalla *et al.* (1995) indicated that there is no correlation between the severity of obstruction and the AUA symptom index in the patients with BPH. Kok *et al.* (2009) in a study with follow up of 6.5 years in 1,688 men who were 50 to 78 years old from Netherlands clarified that 1 of 3 men without the risk factors of LUTS will still be diagnosed with lower urinary tract symptoms suggestive of BPH between ages 50 and 80 years. Loeb *et al.* (2009) from Baltimore study reported that changes in prostate size are highly variable among aging men. Although benign prostatic hyperplasia is common, a considerable proportion of aging men have a stable or decreasing prostate size. The volume of prostate is essential in medical approaches but it could not be

considered every time as an associated with LUTS. Patients who had a prostate volume ≥ 30 mL, a severe International Prostate Symptom Score and a Prostate Specific Antigen level ≥ 1.5 ng mL⁻¹ at baseline, were more likely to have surgical intervention during the follow-up period (Tsukamoto *et al.*, 2009).

The degree to which the patient is troubled is more significant than symptom score. More than a third of all elderly men have moderate or severe LUTS and not all of them should receive treatment (Jepsen and Bruskewitz, 1998). It is very important to assess the impact of BPH symptoms rather than the increase in prostate volume during the management of BPH (Liu *et al.*, 2004).

According to our findings there was an association between urgency and prostate volume that is not consistent with previous studies (Loh *et al.*, 2009; Zhang *et al.*, 2003). Yoshimura *et al.* (2003) investigated a total of 505 consecutively selected, newly diagnosed patients with symptomatic BPH and finally concluded that the frequency of nocturia in patients with BPH was higher than that in community-based studies and score of urgency and functional bladder capacity were each significantly associated with nocturia.

Generally it is imperative to point out that the symptoms of BPH are frequently attributed to simple mechanical obstruction of the prostatic urethra by an enlarged prostate gland, the pathophysiology of this common urologic disorder actually involves multiple factors that may include abnormalities of detrusor function, neuromuscular abnormalities of the prostatic urethra and sensory abnormalities of the bladder wall (Blaiivas, 1988). The diagnostic evaluation of patients with clinical prostatism must take these factors into account. It is of high importance to mention that a decreased urinary flow rate and/or increased post-void residual urine volume may be caused by either bladder outlet obstruction or impaired detrusor contractility.

CONCLUSION

Based on the results of this study it is concluded that urgency was the only non-obstructive LUTS that may be associated with prostate volume and there is no relation between the other non-obstructive LUTS and prostate volume in BPH patients. Further studies with multiple subjective and objective measurements are required in this regard to clarify the symptom-related causes of LUTS in the patients with BPH.

REFERENCES

- AUA Practice Guidelines Committee, 2003. AUA guideline on management of benign prostatic hyperplasia (2003). Chapter 1: Diagnosis and treatment recommendations. *J. Urol.*, 170: 530-547.
- Barry, M.J., F.J. Fowler, M.P. O'Leary and R.C. Bruskewitz *et al.*, 1992. The American urological association symptom index for benign prostatic hyperplasia. The measurement committee of the American Urological association. *J. Urol.*, 148: 1549-1557.
- Blaiivas, J.G., 1988. Pathophysiology and differential diagnosis of benign prostatic hypertrophy. *Urology*, 32: 5-11.
- Bosch, J.R., C.H. Bangma, F.P. Groeneveld and A.M. Bohnen, 2008. The long-term relationship between a real change in prostate volume and a significant change in lower urinary tract symptom severity in population-based men: The krimpen study. *Eur. Urol.*, 53: 819-827.
- Eckhardt, M.D., G.E. van Venrooij and T.A. Boon, 2001a. Interactions between prostate volume, filling cystometric estimated parameters, and data from pressure-flow studies in 565 men with lower urinary tract symptoms suggestive of benign prostatic hyperplasia. *Neurourol. Urodyn.*, 20: 579-590.
- Eckhardt, M.D., G.E. van Venrooij and T.A. Boon, 2001b. Symptoms and quality of life versus age, prostate volume, and urodynamic parameters in 565 strictly selected men with lower urinary tract symptoms suggestive of benign prostatic hyperplasia. *Urology*, 57: 695-700.
- Ezz el Din, K., L.A. Kiemeny, M.J. de Wildt, F.M. Debruyne and J.J. de la Rosette, 1996. Correlation between uroflowmetry, prostate volume, postvoid residue, and lower urinary tract symptoms as measured by the international prostate symptom score. *Urology*, 48: 393-397.
- Galic, J. and D. Simunovic, 2008. Prostate disease prevalence with epidemiological and hormonal analysis in randomly selected male population in Croatia. *Coll Antropol.*, 32: 1195-1202.
- Jepsen, J.V. and R.C. Bruskewitz, 1998. Comprehensive patient evaluation for benign prostatic hyperplasia. *Urology*, 51: 13-18.
- Kojima, M., Y. Naya, W. Inoue, O. Ukimura, M. Watanabe and M. Saitoh *et al.*, 1997. The American Urological association symptom index for benign prostatic hyperplasia as a function of age, volume and ultrasonic appearance of the prostate. *J. Urol.*, 157: 2160-2165.

- Kok, E.T., B.W. Schouten, A.M. Bohnen, F.P. Groeneveld, S. Thomas and J.L. Bosch, 2009. Risk factors for lower urinary tract symptoms suggestive of benign prostatic hyperplasia in a community based population of healthy aging men: The Krimpen study. *J. Urol.*, 181: 710-716.
- Konwar, R., N. Chattopadhyay and H.K. Bid, 2008. Genetic polymorphism and pathogenesis of benign prostatic hyperplasia. *BJU Int.*, 102: 536-544.
- Li, M.K., L. Garcia, N. Patron, L.C. Moh and M. Sundram *et al.*, 2008. An Asian multinational prospective observational registry of patients with benign prostatic hyperplasia, with a focus on comorbidities, lower urinary tract symptoms and sexual function. *BJU Int.*, 101: 197-202.
- Liu, C.C., C.J. Wang, S.P. Huang, Y.H. Chou, W.J. Wu and C.H. Huang, 2004. Relationships between American Urological association symptom index, prostate volume, and disease-specific quality of life question in patients with benign prostatic hyperplasia. *Kaohsiung J. Med. Sci.*, 20: 273-278.
- Loeb, S., A. Kettermann, H.B. Carter, L. Ferrucci, E.J. Metter and P.C. Walsh, 2009. Prostate volume changes over time: Results from the Baltimore longitudinal study of aging. *J. Urol.*, 182: 1458-1462.
- Loh, A.H., K.K. Ng and F.C. Ng, 2009. Presentation and progression of benign prostatic hyperplasia: A Singapore experience profiling ethnic differences in a multiracial study cohort. *Ann. Acad. Med. Singapore*, 38: 451-456.
- Madersbacher, S., H.C. Klingler, B. Djavan, T. Stulnig and G. Schatzl *et al.*, 1997. Is obstruction predictable by clinical evaluation in patients with lower urinary tract symptoms?. *Br. J. Urol.*, 80: 72-77.
- Mittal, B.V., M.B. Amin and S.G. Kinare, 1989. Spectrum of histological lesions in 185 consecutive prostatic specimens. *J. Postgrad Med.*, 35: 157-161.
- Perez, C.F., J.M. Sierra, S.C. Escudero, M.E.F. Ferrer, G.B. Fajardo and A.S. Moyano, 2009. Prevalence of lower urinary tract symptoms related with benign prostatic hyperplasia. Study of 1804 men aged 40 or older in Madrid. *Actas Urol. Esp.*, 33: 43-51.
- Pinto, F., M. Racioppi, E. Sacco, A. Totaro and A. Brescia *et al.*, 2009. Progression, risk factors and subsequent medical management of symptomatic benign prostatic hyperplasia. *Arch. Ital. Urol. Androl.*, 81: 1-8.
- Roehrborn, C.G., 2008. Pathology of benign prostatic hyperplasia. *Int. J. Impot. Res.*, 3: S11-8.
- Sirls, L.T., A.K. Kirkemo and J. Jay, 1996. Lack of correlation of the American Urological association symptom 7 Index with urodynamic bladder outlet obstruction. *Neurourol. Urodyn.*, 15: 447-456.
- Trueman, P., S.C. Hood, U.S.L. Nayak and M.F. Mrazek, 1999. Prevalence of lower urinary tract symptoms and self-reported diagnosed 'benign prostatic hyperplasia and their effect on quality of life in a community-based survey of men in the UK. *BJU Int.*, 83: 410-415.
- Tsukamoto, T., N. Masunori, H. Nakagawa, Y. Arai and A. Komiya *et al.*, 2009. Changes in prostate volume in Japanese patients with benign prostatic hyperplasia: Association with other urological measures and risk of surgical intervention. *Int. J. Urol.*, 16: 622-627.
- Tubaro, A. and C.A. Vecchia, 2004. The relation of lower urinary tract symptoms with life-style factors and objective measures of benign prostatic enlargement and obstruction: An Italian survey. *Eur. Urol.*, 45: 767-772.
- Wu, S.L., N.C. Li, Y.X. Xiao, J. Jin and S.P. Qiu *et al.*, 2006. Natural history of benign prostatic hyperplasia. *Chin Med. J.*, 119: 2085-2089.
- Yalla, S.V., M.P. Sullivan, H.S. Lecamwasam, C.E. DuBeau, M.A. Vickers and E.G. Cravalho, 1995. Correlation of American Urological association symptom index with obstructive and nonobstructive prostatism. *J. Urol.*, 153: 674-679.
- Yoshimura, K., H. Ohara, K. Ichioka, N. Terada and Y. Matsui *et al.*, 2003. Nocturia and benign prostatic hyperplasia. *Urology*, 61: 786-790.
- Zhang, P., Z.J. Wu and J.Z. Gao, 2003. Influence of bladder outlet obstruction and detrusor contractility on residue urine in patients with benign prostatic hyperplasia. *Chin Med. J.*, 116: 1508-1510.