

The correlation between several biochemical parameters and UTIs with progression of BPH

AlChalabi Rawaa^{1*}, Omer Dania¹, Khalid Basma¹ and AlAmery Hayder²

1. Department of Medical and Molecular Biotechnology, College of Biotechnology, Al-Nahrain University, IRAQ

2. Al-Yarmook Teaching Hospital, Urology Unit, IRAQ

*rawaaalchalabi_1984@yahoo.com; alola_1984@yahoo.com

Abstract

Benign prostatic hyperplasia (BPH) is a typical generous tumor of the prostate that is a typical condition as men get more established. This investigation was intended to reveal insight into the impacts of few biochemical parameters (urea, creatinine, Zn and PSA) and UTIs with seriousness and movement of BPH. Blood and pee tests were gathered from 97 subjects who went to the Urology Unit at Al-Yarmook Teaching Hospital and Al-Jaibachi Private Hospital in Baghdad at that point partitioned into two research bunches after clinical analysis and lab tests. The primary gathering made out of 66 (68%) patients had BPH while the second gathering comprised of 31 (32%) sound people. The principal bunch was subdivided into recently analyzed BPH patients 32(48.5%) and repeat BPH patients 34(51.5%).

*Results demonstrated that danger of BPH expanded with age and gathering \geq multi year had the most extreme rate (51.52%). Pee culture demonstrated that 60 (61.85%) of pee tests gave positive societies and 37 (38.15%) were negative. Bacteriological tests indicated 38 (63.34%) secludes distinguished as *Escherichia coli*. while all pee tests of sound people have an antagonistic culture. Biochemical tests demonstrated a huge contrast saw in the serum level of urea, creatinine and zinc of recently analyzed and intermittent BPH patients when contrasted and sound controls.*

Keywords: BPH, PSA, Zn, UTIs.

Introduction

BPH is because of the top development of both stromal and epithelial cells of the prostate which is normally analyzed sickness in old men and it extremely impacts the personal satisfaction. The observational examinations from Europe, the US and Asia have additionally shown more seasoned age to be a hazard factor for clinical BPH beginning and progression.¹⁸

A few parameters, for example, provocative middle people, hormones, dietary elements, incendiary qualities and oxidative pressure (OS) may assume an imperative job in the BPH improvement and may cause compensatory cell expansion with coming about hyperplastic development.^{22,25} Vital et al³⁰ have uncovered that irritation particularly adding

to the beginning of urinary tract contamination and BPH patients 7.7 times more than solid people. Aggravation grumbles symptomatic BPH actuated changes in the prostate condition to prompt different changes in qualities articulation, cytokines level and along these lines incessant conditions add to changes in the prostate structure and appearance of indications.²⁶

Prostate-particular antigen is a glycoprotein emitted by the epithelial cells of the prostate organ regularly raised within the sight of prostate growth or other prostate issue. PSA is certifiably not an exceptional marker of prostate tumor, yet may likewise identify prostatitis or BPH.^{12,24} Urea is the last corruption result of protein and amino corrosive digestion. In catabolism, the proteins are separated to amino acids and delaminated. The smelling salts shaped in this procedure are orchestrated to urea in the liver. The assurance of serum urea as of now is utilized for the assessment of kidney capacity and prostate state.^{1,13,20}

Creatinine is a breakdown result of creatine phosphate in muscle. Prostate issue, for example, BPH had a relationship with renal sickness along these lines. Latest examinations about BPH recorded a lifted serum level of creatinine and urea. Thus, expanded serum urea and additionally creatinine could be an early indication towards prostate sickness, for example, BPH or prostate disease and it is prescribed that guys \geq 40 years old ought to experience screening for serum PSA levels like clockwork.^{5,20}

Zinc is a fundamental micronutrient required for more than 300 distinctive cell forms like DNA blend, quality articulation, compound catalysis, neurotransmission and apoptosis.¹⁹ Zn is an imperative component in the structure of the prostate liquid and assumes a critical job in the immunology of the irresistible and neoplastic pathologies of the prostate. In this way zinc focuses in prostatic liquid or in the serum of patients with prostate pathologies vital as a symptomatic parameter.²⁸

Material and Methods

Samples Collection

- Urine Samples: Midstream urine samples were collected in sterile test tubes from patients of (Al-Yarmook teaching hospital and Al-Jabachi private hospital) and healthy individuals during the period from Sep. 1, 2017 to Feb. 28, 2018. The total of 97 samples were collected and transported to the laboratory during 1 hour by using a cool box because the low temperature serves to inhibit bacterial replication in the urine sample until processed

in the laboratory, because the number of bacteria in the urine sample is important in determining if there is clinically significant bacteriuria and if the sample is not properly stored, small number contaminating bacteria may multiply to large numbers and create a false impression of significant bacteriuria.

- **Blood Samples:** Whole blood samples (total 5 ml) were obtained by venipuncture from a peripheral vein into plain tubes, centrifuged for 15 minutes at approximately 5000 rpm to obtain serum for use in the biochemical tests.
- **Isolation of Bacteria:** One loopful of the undiluted urine sample was spread on each of blood agar and MacConkey agar plates. Then, the plates were incubated overnight at 37°C. This process was repeated several times for purity before use for further diagnosis steps.
- **Measurement of biochemical profile:** Kit estimates the level of creatinine in the sample which reacts with picrate in alkaline medium forming a coloured complex by using Jaffé method while a concentration of urea is hydrolyzed by urease into ammonia and carbon dioxide which is measured based on the intensity of the colour formed and is proportional to the concentration of urea in the samples. The ammonia generated reacts with alkaline hypochlorite and sodium salicylate in the presence of sodium nitroprusside as a coupling agent to yield a green chromophore.
- **Estimation of the serum zinc level:** Zinc is an essential micronutrient required for the different cellular process and the measurement procedure based on Zn in an alkaline medium reacting with Nitro-PAPS to a purple coloured complex directly formed proportionally to Zn concentration in the serum sample.
- **Estimation of Prostate Specific Antigen (PSA) in the Serum:** The assay principle of kit combines a two-step enzyme immunoassay sandwich method with Enzyme-Linked Fluorescence Assay (ELFA) (BioMerieux /France).

Results and Discussion

Ninety-seven Iraqi subjects have been incorporated into this investigation and isolated into two noteworthy gatherings. First gathering comprised of 66 (68%) BPH patients and second gathering comprised of 31(32%) healthy people. First gathering subdivided into recently analyzed BPH amass comprised of 48.5% patients and second gathering comprised of 51.5% subjects portrayed as intermittent BPH patients. The danger of BPH expanded with age; the mean age at the conclusion was 69.6 years extending between 48-85 years and the mean period of the solid gathering was 62.6 years.

Results in table 1 demonstrated that the age amass ≥ 70 years had the greatest occurrence (51.52%) of BPH patients pursued by age gathering (60-69) with (33.33 %) and (12.12%) of age gathering (50-59) while just 3.03% of the patients were recorded in the age gathering (40-49) year.

Such discoveries clarified that the older men were more defenseless to be influenced by favorable prostate hyperplasia. Proportion of BPH guess rises significantly with age and Bushman² expressed that commonness of BPH is multiplying after age 60 years.

After-effects of a few analysts concurred with the consequences of this investigation as appearing in the table. Goh et al⁸ recorded that age aggregate > 70 years was the most noteworthy unsafe gathering for BPH, Masu et al¹⁶ demonstrated that BPH is influencing 3% of men matured 40–49 years, ascending to $> 30\%$ in men matured ≥ 70 years. One reason for expanding commonness of BPH with maturing is that prostate volume changes with age. Notwithstanding that BPH occurrence was unequivocally identified with age; age-related change related with metabolic unsettling influences, changes in hormone balance and incessant aggravation may cause BPH improvement.^{6,14}

Ninety-seven urine tests have been gotten from BPH patients and healthy people at that point analyzed by social, morphological and bacteriological tests for distinguishing the nearness or non-attendance of UTIs. The consequences of urine culture demonstrated that 60 (61.85%) urine tests gave positive societies while 37 (38.15%) examples were negative. Positive pee societies were identified in 31 (91.18%) of intermittent BPH patients, 3(8.82%) urine tests were negative culture. 29 (90.62%) urine examples got from recently analyzed BPH patients gave positive culture and 3 (9.38%) gave negative societies while all urine tests of sound people gave an antagonistic culture as in figure 1.

The consequences of Gram staining and microscopically examination of all urine tests demonstrated that 2 (3.4 %) disconnects were distinguished as gram-positive microbes and 58 (96.6%) were gram-negative microorganisms as appearing in fig 2. Fadhil et al⁴ found that 8.9 % of the confines from midstream urine tests were named gram-positive, microscopic organisms and 91.1 % secludes as gram-negative microorganisms.

The culture outcomes demonstrated that all UTIs cases were caused by a solitary irresistible operator as pursues: 38 (63.34%) segregates distinguished as *Escherichia coli*, 9 (15%) confines were *Klebsiella sp.*, 8 (13.33%) *Proteus sp.*, 3(5%) were *Pseudomonas sp.* also, 2(3.33) were *Staphylococcus aureus* as appeared in table 2. As per such discoveries, individuals from Enterobacteriaceae family are viewed as the principal causative specialist of bacterial prostatitis, particularly *E. coli* which can cause UTI due to its appearance of a few destructiveness factors that are in charge of its pathogenicity.

The present outcomes were near outcomes announced by Schiller and Parikh²⁷ who reported that *E. coli* was the most ordinarily disengaged creature in intense and constant prostatitis, trailed by *Proteus* and *Klebsiella spp* as the second and third causative operators. Dickson³ found that often times recognized pathogen which tainted prostate

organ in Austrian populace was *E. coli* which is described by the high opposition and solid pathogenicity.

Gill and Shoskes⁷ detailed UTIs as a standout amongst the most usually analyzed contaminations in healing facilities and the microorganism causing UTI to fluctuate in their weakness to the antimicrobials from place to place and time to time. Naber et al²¹ recommended that the *E. coli* strains had been distinguished in ceaseless bacterial prostatitis and have more destructiveness factors and more prominent level of biofilm arrangement capacity than the strains recognized in uncomplicated urinary tract diseases.

BPH and kidney infection are fundamental maladies of maturing men. BPH has been portrayed as a typical clinical disorder in more established men described by bladder outlet deterrent, bring down urinary tract side effects and prostate organ amplification. BPH portrayed as a non-threatening abundance of prostatic tissue encompassing the urethra, eventually choking the urethral opening offering ascending to related lower urinary tracts indications in this way prompted increment of the serum level of urea and creatinine.¹¹

The present examination was expected to assess the serum levels of urea, creatinine and Zn in BPH patients. As appeared in table 3 the noteworthy contrast was seen in the serum level of urea, creatinine and Zinc of recently analyzed and intermittent BPH patients when compared with solid people. Exceedingly critical contrasts in the mean estimations of serum creatinine and urea were more set apart in intermittent BPH with mean level (3.47, 63.21) mg/dl than in recently determined clusters of prostate to have mean (1.81, 48.59) mg/dl when contrasted with solid people mean level (1.05,34.90) mg/dl. Likewise, significant contrasts in the serum level of Zn between recently analyzed, intermittent BPH patients and solid people were accounted for with mean level (77.53, 42.97 and 93.87) separately.

We concluded that patients with the prostate issue are probably going to advance renal brokenness and BPH is the most widely recognized sort of prostate issue in seniority and the zinc focus in serum might be an important file for the differential analysis and treatment of the prostate issue. Zinc is a fundamental follow component required for typical prostate capacity. Dysregulated zinc fixation i.e. either

overabundance or less can prompt distinctive prostatic sores like BHP.

Patients with prostate extension are probably going to advance renal brokenness with increment the serum level of urea and creatinin. Tahminur and Choudhury²⁸ announced that prostate zinc fixation had brought down in patients having a prostate tumour or BPH. Zinc applies its impact by different transporter proteins and fluctuation in transporter protein and can prompt BPH or a prostate tumour. Zinc can act both as a preventive segment in anticipating prostate injury or likewise can increase neoplastic expansion of prostate. The low Zn focuses acquired in patients with BPH and prostate malignancy, rather than the control gathering and drove us to think about prescribing zinc supplements as coadjuvant treatment in patients with prostate malady.⁹

Results in table 4 demonstrated that PSA levels of recently analyzed BPH patients ran (4.5-18.9 ng/ml) with a mean estimate of 7.89 and for intermittent BPH patients went (7.10-23.10 ng/ml) while the PSA levels for healthy men were extending (3-7ng/ml) with a mean estimation of 4.74. The measurable examination of results guaranteed a high noteworthy contrast (P<0.01) in the mean serum grouping of PSA between BPH patients and solid people.

Vicki et al²⁹ demonstrated that men who have the prostate disease may have a higher measure of PSA in their blood. A few elements, for example, prostate malignancy, BPH, prostatitis and prostate control including catheterization prompt an expansion in the serum PSA and the fundamental purpose behind raising the PSA in the serum of BPH patients might become back to the way that PSA is a tissue-particular biomarker of the prostate. Any interruption of the typical anatomic prostatic tissue may prompt expanding PSA level.²³

Conclusion

Urinary tracts infection caused by *E.coli* is strongly associated with BPH. Zinc is an essential trace element required for normal prostate function and its concentration in the serum may be a valuable index for the differential diagnosis and therapy of prostate disorder and abnormal PSA level either excess or less leading to different prostate lesions like BPH.

Table 1
Distribution of BPH patients and healthy men according to age groups.

Age group	Newly Diagnosed BPH patients		Recurrent BPH patients		Total		Healthy Individuals	
	No.	(%)	No.	%	No.	%	No.	(%)
40-49	2	6.25	0	0.00	2	3.03	5	16.13
50-59	8	25.00	0	0.00	8	12.12	12	38.71
60-69	16	50.00	6	17.65	22	33.33	10	32.26
≥ 70	6	18.75	28	82.35	34	51.52	4	12.90
Total	32	100	34	100	66	100	31	100

Table 2
Percentages of bacterial species have been isolated from urine samples of BPH patients

Isolate	patients				Total	
	Newly Diagnosed BPH		Recurrent BPH		No.	%
	No.	%	No.	%		
<i>Escherichia coli</i>	16	55.17	22	70.97	38	63.34
<i>Klebsiella sp.</i>	5	17.24	4	12.90	9	15.00
<i>Proteus sp.</i>	5	17.24	3	9.67	8	13.33
<i>Pseudomonas sp.</i>	2	6.90	1	3.23	3	5.00
<i>Staphylococcus aureus</i>	1	3.45	1	3.23	2	3.33
Total	29	100	31	100	60	100

Table 3
Serum levels of Creatinin, Urea and Zn among studied groups.

Parameters	BPH Patients		Healthy	Sig. between Groups	P. value
	Newly Diagnosed	Recurrent BPH			
	Mean ± S.E	Mean ± S.E	Mean ± S.E		
Creatinine (mg/dl)	1.81 ± 0.04 B	3.47 ± 1.64 A	1.05 ± 0.02 C	**	0.0001
Urea (mg/dl)	48.59 ± 1.14 B	63.21 ± 1.42 A	34.90 ± 1.31 C	**	0.0001
Zn(mg/dl)	77.53 ± 3.02 B	42.97 ± 1.97 C	93.87 ± 3.76 A	**	0.0001

** (P<0.01).

Table 4
Prostate specific antigen (PSA) of healthy, Recurrent and Newly diagnosed BPH patients

Group	No.	Range Min. – Max.	Mean ± S.E	P-value
Newly Diagnosed BPH	32	4.50-18.90	7.89 ± 0.54 B	0.0001 **
Recurrented BPH	34	7.10-23.10	15.35 ± 0.75 A	
Healthy	31	3.00-7.00	4.74 ± 0.19 C	

** (P<0.01).

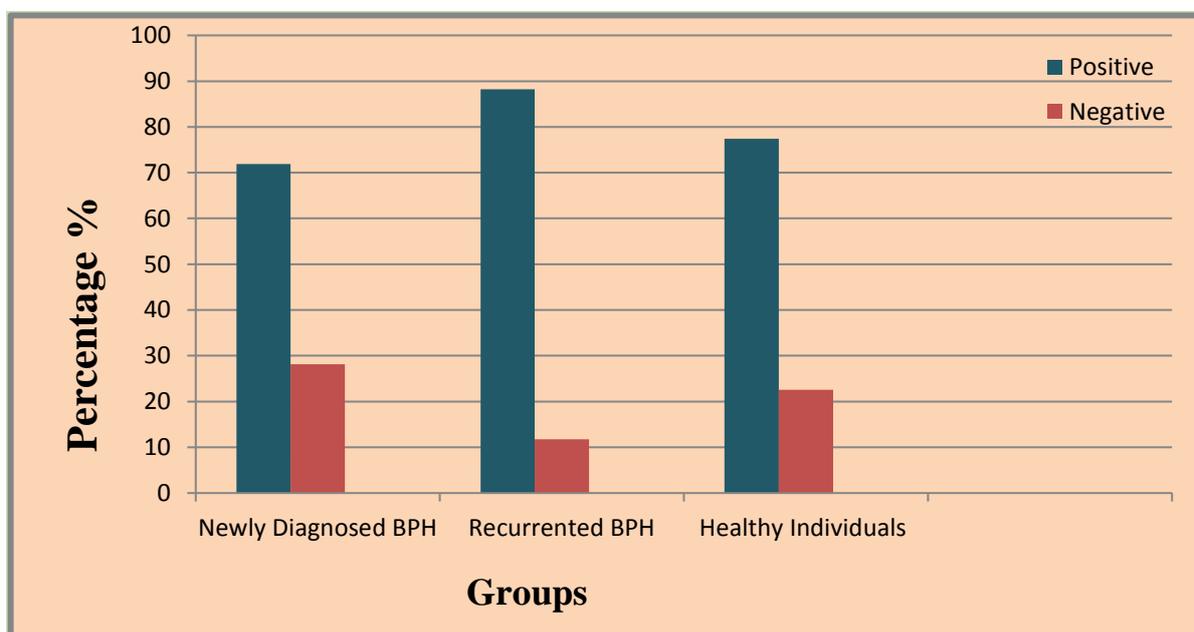


Figure 1: Prevalence of UTIs in BPH patients and healthy individuals.

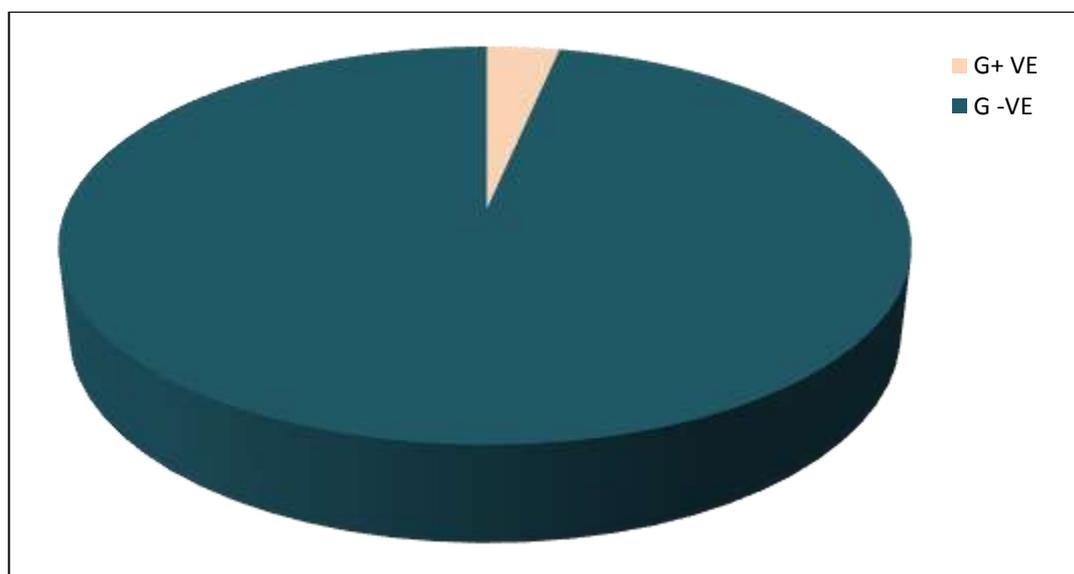


Figure 2: Percentage of G + VE and G-VE bacteria have been isolated from urine samples.

References

- Baum N., Lontyer M. and Steve K., Blood urea nitrogen and serum creatinine, *Urol*, **5(5)**, 583-88 (1975)
- Bushman W., Etiology, epidemiology and natural history of benign prostatic hyperplasia, *Urol. Clin. North Am*, **36**, 403-415 (2009)
- Dickson G., Prostatitis Diagnosis and treatment, *Australian Fam. Phy.*, **42(4)**, 75-81 (2013)
- Fadhil A., AlChalabi R. and AlAmery H., The Effect of Aqueous Extract of Aillum Sativum (Garlic) on Gram Negative Uropathogenic Bacteria Isolated from Hospitalized Children, *Journal of Cell & Plant Sciences*, **4(1)**, 1-5 (2013)
- Feletto E., Bang D., Cole-Clark V., Chalasani K., Rasiah P. and Smith D., An examination of prostate cancer trends in Australia, England, Canada and USA: Is the Australian death rate too high?, *World J Urol.*, **33(11)**, 1677-1687 (2014)
- Fukuta F., Masumori N., Mori M. and Tsukamoto T., Internal prostatic architecture on transrectal ultrasonography predicts future prostatic growth natural history of prostatic hyperplasia in a 15-year longitudinal community-based study, *Prostate*, **71**, 597-603 (2011)
- Gill B. and Shoskes D., Bacterial prostatitis, *Curr. Opin. Infect. Dis.*, **29(1)**, 86-91 (2016)
- Goh H., Kim S., Nam J., Choi B. and Moon H., Community-based research on the benign prostatic hyperplasia prevalence rate in Korean rural area, *Korean J. Urol.*, **56**, 68-75 (2015)
- Gómez Y., Arocha F., Espinoza F., Fernández D., Vásquez A. and Granadillo V., Zinc levels in prostatic fluid of patients with prostate pathologies, *Invest Clin.*, **48(3)**, 287-294 (2007)
- Harita N., Hayashi T. and Sato K., Lower serum creatinine is a new risk factor of type 2 diabetes: the Kansai healthcare study, *Diabetes Care*, **32(3)**, 424-426 (2009)
- Isaac P. et al, Assessment of Serum Prostate Specific Antigen, Some Renal Indices and Uric Acid Levels in Subjects with Benign Prostatic Hyperplasia at Lokoja, Nigeria, *Journal of Bioanalysis & Biomedicine*, **9(5)**, 256-262 (2017)
- Jung K., Bru B., Lein M., Rudolph B., Kristiansen G. and Hauptmann S., Molecular forms of prostate-specific antigen in malignant and benign prostatic tissue: biochemical and diagnostic implications, *Clin. Chem.*, **46(1)**, 47-54 (2000)
- Kalhan S., Protein metabolism in pregnancy, *Am J Clin Nutr*, **71(5)**, 1249S-1255S (2000)
- Kim E., Larson J. and Andriole G., Management of Benign Prostatic Hyperplasia, *Annual Review of Medicine Washington University School of Medicine*, **67**, 137-151 (2016)
- Kok B., Epidemiology of clinical benign prostatic hyperplasia, *Asian Journal of Urology*, **4(3)**, 148-151 (2017)
- Masu S., Mukadam P. and Mansuri A., A prevalence study of lower urinary tract symptoms (LUTS) in males, *Int. J. Med. Sci. Public Health*, **3(8)**, 927-930 (2014)
- McDonald T., Drescher J., Kristen M. and Annika W., Creatinine inhibits bacterial replication, *The Journal of Antibiotics*, **65(3)**, 153-156 (2012)
- McVary K., Roehrborn C., Avins A., Barry M., Bruskewitz R. and Donnell R., Update on AUA Guideline on the Management of Benign Prostatic Hyperplasia, *J Urol.*, **185**, 1793-1803 (2011)
- Meija J., Norby S. and Josiph L., Atomic weights of the elements 2013 (IUPAC Technical Report), *Pure and Applied Chemistry*, **88(3)**, 265-91 (2016)
- Mukund J., Suvarna P., Goyal K., Singh S., Rajesh P. and Singh J., Implications of serum urea and creatinine estimation in prostate cancer, *International Journal of Recent Trends in Science and Technology*, **13(2)**, 290-292 (2014)

21. Naber K., Wagenlehner F. and Weidner W., Acute bacterial prostatitis, In Shoskes D.A., ed., Current Clinical Urology Series, Chronic Prostatitis/Chronic Pelvic Pain Syndrome, Totowa N.J., Humana Press, 17–30 (2008)
22. Paola L., Antonino I., Navarra L., Gioacchino C. and Sebastiano G., Oxidative Stress in Benign Prostatic Hyperplasia: A Systematic Review, *Urol. Int.*, **10**, 115 (2014)
23. Payne H. and Cornford P., Prostate-specific antigen: an evolving role in diagnosis, monitoring and treatment evaluation in prostate cancer, *Urol. Oncol.*, **29**, 593–601 (2011)
24. Pejcić T., Tulic C., Lalic N., Glisic B., Ignjatovic S. and Markovic B., Urinary prostate-specific antigen: predictor of benign pro-static hyperplasia progression, *Can. J. Urol.*, **20**(2), 6707–13 (2013)
25. Raza I., Mukhtar S. and Kamran M., Benign prostate hyperplasia: Correlation of prostatic gland volume with age and /anthropometric parameters in patients, *Professional Med J.*, **24**(3), 445-452 (2017)
26. Rikiya T. and Yoshiyuki K., The Influence of asymptomatic inflammatory prostatitis on the onset and progression of lower urinary tract symptoms in men with histologic benign prostatic hyperplasia, *Asian Journal of Urology*, **7**, 158-167 (2017)
27. Schiller D. and Parikh A., Identification, pharmacologic considerations and management of prostatitis, *Am. J. Pharmacother.*, **9**, 37–48 (2011)
28. Tahminur R. and Choudhury M., Zinc and Benign Prostatic Hyperplasia (BPH) & Prostate Cancer (PCa) association, *Medical Research Archives*, **4**(7), 1-16 (2016)
29. Vicki M., Velonas I., Henry H., Cristobal G., Remedios P. and Stephen J., Current Status of Biomarkers for Prostate Cancer, *Int. J. Mol. Sci.*, **14**, 11034-11060 (2013)
30. Vital P., Castro P. and Itmann M., Oxidative stress promotes benign prostatic hyperplasia, *Prostate*, **76**, 58-67 (2016).