

Relationship between age, prostate size, and Prostate-Specific Antigen (PSA) role in patients with Benign Prostatic Hyperplasia (BPH)

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ABSTRACT

Background: Benign Prostatic Hyperplasia (BPH) is a chronic, progressive disease that affects many older men. It has been demonstrated that the prevalence of disease increase with age. Prostate Specific Antigen (PSA), Digital Rectal Examination (DRE), ultrasound diagnostic of the prostate gland with consideration to its volume and amount of residual urine is among the internationally validated tools used in the assessment of patients with BPH.

Aim: The study the relationship between age, prostate size, and PSA role in patients with BPH.

Materials and Methods: A total of 108 male participants aged 50 years or older in Prishtina (Kosovo) were enrolled for the study. The standard investigations of BPH for each patient were: blood tests, urinalysis, prostate specific antigen testing, ultrasound and post-void residual volume. The same patients were observed for twenty months in three time intervals (the average time per patient was 6 months-8 months) with the same clinical and laboratory measurements.

Results: The age range for the population studied was between 50 to 90 years, with a mean of 69.35 years \bar{A} (Age) \pm 9.35 SD (Standard Deviation). The obtained values showed a statistically significant comparing the first, second and third clinical measurements with sedimentation rate, Mean $\bar{A} \pm$ SD (28.46, 20.97, 15.82, $\bar{A} \pm$ 24.38, 20.91, 19.74) with $p < 0.001$, the number of PSA performed, Mean $\bar{A} \pm$ SD (1.04, 2.04, 3.00, $\bar{A} \pm$ 0.19, 0.23, 0.24) $p < 0.001$ and residual urine. Mean $\bar{A} \pm$ SD (119.94, 79.93, 73.23, $\bar{A} \pm$ 111.97, 66.79, 68.68) $p < 0.001$. Analyzing the relationship between BPH (dependent variable) and age, PSA level and weight in grams of the prostate, it was seen that there is a statistically significant relationship between BPH and age for every one-year increase in age, the odds increase by 9% to make BPH (OD (Omne in Die) = 1.085; CI (Confidence Interval): 1.012 and 1.162). For a BPH and PSA level, it can be said that for every unit increase in PSA, the likelihood of developing BPH increases by 18% (OD=1.176; CI: 95%: 1.070-1.292).

Conclusion: This study showed that the levels of prostate-specific antigen, prostate size grams and post-void residual urine volume significantly increased with age. Therefore, it is essential to create more public awareness, especially among men in their fourth decade of life and above, to visit an urologist whenever they have BPH symptoms.

Keywords: aging, post-void residual urine volume, prostate size grams, prostate-specific antigen

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INTRODUCTION

Benign Prostatic Hyperplasia (BPH) is nonmalignant adenomatous overgrowth of the periurethral prostate gland and is a common cause of lower urinary tract symptoms in men. Disease prevalence has been shown to increase with advancing age [1-3]. The prevalence and severity of Lower Urinary Tract Symptoms (LUTS) in aging males can be progressive and is an important diagnosis in the healthcare of patients and the welfare of society [4].

A total of 50% of 60 year-old men and 90% of 85 year-old have microscopic BPH, however only 50% of patients with this histological finding will have a macroscopic enlargement of the gland and about 50% of these will develop symptoms [1]. BPH prevalence and incidence rates increase with increasing age and vary by symptom severity [5]. Thus, with increasing age, there is a tendency to increase prostate size.

The assessment of patients with BPH is carried out through an internationally validated questionnaire-International Prostate Symptom Score/Quality Of Life (IPSS/QoL), Prostate Specific Antigen (PSA), Digital Rectal Examination (DRE), and ultrasound diagnostic of the prostate gland with consideration of its volume and the amount of residual urine [6, 7]. The prostate adenoma can be phenotype according to intravesical prostatic protrusion and prostate size. The BPH progresses slowly, and patients may adapt to it, not having symptoms even though they may have severe obstruction. Clinical BPH can be defined as prostate adenoma, irrespective of size, causing a varying degree of obstruction with or without symptoms [8].

The severity of the disease, clinical BPH, can be classified into stages from stage I to IV for further management.

Clinical BPH should be differentiated from other causes of male LUTS with non-invasive transabdominal ultrasound and uroflowmetry in the clinic. With intravesical prostatic protrusion, post-void residual urine, and IPSS/QoL, the disease can be classified according to severity for more cost-effective management [7, 9-12].

After assessment, further management can then be individualized. A low-grade or stage disease can generally be watched (active surveillance), while a high-grade or stage disease would need more invasive management with the option of surgery. Multiple studies have shown a good correlation between intravesical prostatic

protrusion and prostate size and benign prostatic obstruction, and therefore the progression of the disease [13-19].

Thus, the aim of this study was to investigate the relationship between age, prostate size and PSA level in Kosova men with histologically proven BPH.

Hypothesis of the study

There is an impact on age with increased prostate size, and PSA, in some cases, can be at normal values in patients with BPH.

METHODOLOGY

The methodology of this study was prospective and analytical and was carried out at the University Clinical Center of Kosovo in the Clinic of Urology in Prishtina. These involved 108 patients whose chief complaint was lower urinary tract symptoms or urinary retention who visited the Clinical Department of Urology from April 2022 to December 2023. The inclusion criteria were a minimum age of 50 years and a diagnosis of BPH (histopathologically proven).

Regarding the ethical consideration, of the study respondents gave their written agreement to the researcher after the University Clinical Center of Kosovo (UCCCK) and the Ethical Research Committee accepted it.

The standard investigations of BPH for each patient were: blood tests, urinalysis, prostate specific antigen testing, ultrasound and post-void residual volume. In some cases, there were indications for biopsy, including elevated PSA levels, abnormal DRE findings, or previous biopsy results showing abnormalities. The collected dataset included several variables, namely age, pre-biopsy PSA level, DRE findings and prostate volume.

Depending on the clinical and laboratory conditions, they were subjected to conservative treatment. The same patients were observed for twenty months in three time intervals (the average time per patient was 6 months-8 months) with the same clinical and laboratory measurements. Binary logistic regression analysis was used to assess the causal associations between the dependent variable and the independent variables, where the odds ratio was calculated for each variable (odds) and a 95% confidence interval. Statistical Package for Social Sciences (SPSS) version 25 was employed for statistical analyses.

RESULT

One hundred eight (108) patients were recruited for this study. The greatest proportions (58.3%) of the patients were between 61 years to 70 years. The age range for the population studied was between 50 years to 90 years, with a mean of 69.35 years ± 9.35 SD (Table 1).

Demographic Characteristics	Subgroup	f	%
Age group	50 years-60 years	16	14.8
	61 years-70 years	63	58.3
	71 years-80 years	15	13.9
	81 years-90 years	14	13
	Mean ± SD 69.35 ± 9.35		
	Min-Max 50 years-90 years		
Indwelling catheter	Yes	37	34.3
	No	71	65.7

f= Frequencies
 %= Percentage
 M= Mean of score
 S.D= Standard Deviation
 Min= Minimum
 Max= Maximum

Through the ANOVA analysis, it can be seen that there is a statistically significant difference comparing the first, second and third clinical measurement with SE, Mean ± SD (28.46, 20.97, 15.82 ± 24.38, 20.91, 19.74) with p<0.001, the number of PSA per-

formed Mean ± SD (1.04, 2.04, 3.00 ± 0.19, 0.23, 0.24) p<0.001 and residual urine Mean ± SD (119.94, 79.93, 73.23 ± 111.97, 66.79, 68.68) p<0.001 (Table 2). These results are illustrated in figures 1-3.

	Clinical measurement	No. of Patients	Mean	SD	CI 95%		Minimum	Maximum	p-value*
					Lower Bound	Upper Bound			
Sedimentation Rate (ESR)	I	108	28.46	24.38	23.81	33.11	4.4	94	<0.001
	II	108	20.97	20.91	16.98	24.96	0	98	
	III	108	15.82	19.74	12.06	19.59	0	106	

Leukocytes (WBC)	Clinical measurement I	108	9.75	5.32	8.74	10.77	3.4	46	0.972
	II clinical measurement	108	9.64	13.36	7.09	12.19	3.1	117	
	III clinical measurement	108	9.99	12.56	7.59	12.38	2.8	82	
CRP	Clinical measurement I	108	16.28	20.06	12.45	20.11	0	110	0.886
	II clinical measurement	108	13.78	37.93	6.55	21.02	0	382	
	III clinical measurement	108	14.92	48.62	5.64	24.19	0	393	
Glucose	Clinical measurement I	108	9.25	12.5	6.87	11.63	3	88	0.571
	II clinical measurement	108	8.85	15.58	5.87	11.82	2.98	120	
	III clinical measurement	108	7.47	10.25	5.51	9.42	3.3	74	
Urea	Clinical measurement I	108	10.98	14.18	8.28	13.69	2.9	98	0.342
	II clinical measurement	108	9.13	8.99	7.42	10.85	2.89	67	
	III clinical measurement	108	16.65	65.86	4.09	29.22	3	678	
Creatinine	Clinical measurement I	108	115.64	55.03	105.14	126.14	62	419.9	0.416
	II clinical measurement	108	131.89	142.75	104.66	159.12	67	873	
	III clinical measurement	108	114.74	104.24	94.86	134.63	65.5	879	
PSA levels	Clinical measurement I	108	9.27	14.37	6.53	12.01	0.28	93	0.506
	II clinical measurement	108	13.15	29.9	7.45	18.86	0.33	192	
	III clinical measurement	108	11.79	27.22	6.6	16.98	0.5	167	
Number of PSAs Performed	Clinical measurement I	108	1.04	0.19	1	1.07	1	2	<0.001
	II clinical measurement	108	2.04	0.23	1.99	2.08	1	3	
	III clinical measurement	108	3	0.24	2.95	3.05	1	4	
Prostate Size Grams	Clinical measurement I	108	78.87	32.96	72.58	85.16	31	170	0.79
	II clinical measurement	108	80.2	32.49	74.01	86.4	32	170	
	III clinical measurement	108	81.92	32.5	75.72	88.12	33	170	
Post-Void Residual Urine Volume	Clinical measurement I	108	119.94	111.97	98.58	141.29	0	700	<0.001
	II clinical measurement	108	79.93	66.79	67.19	92.67	0	300	
	III clinical measurement	108	73.23	68.68	60.13	86.33	0	400	

*One-way Analysis of Variance (ANOVA) test

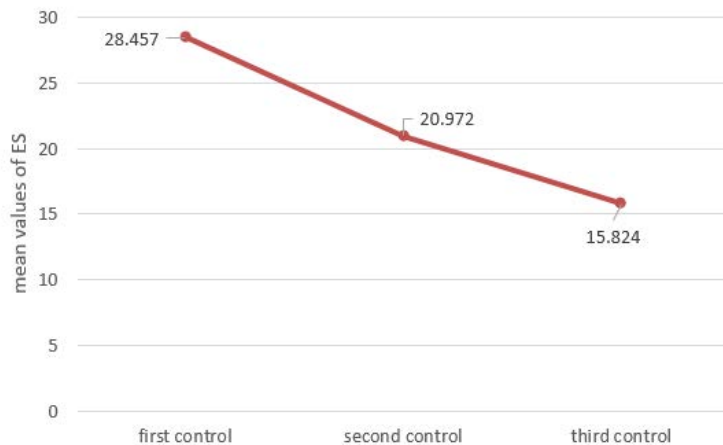


Fig. 1. The mean value of SE compared to the first, second and third controls

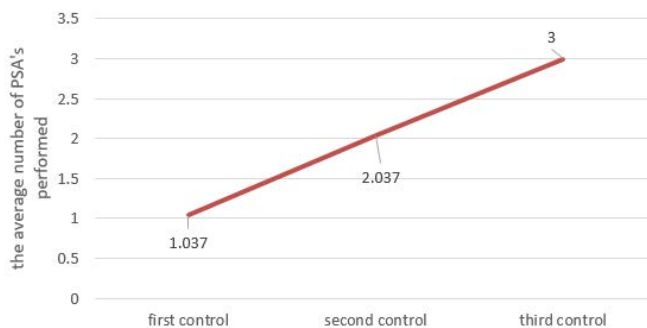


Fig. 2. The average numbers of PSA's performed compared to the first, second and third controls

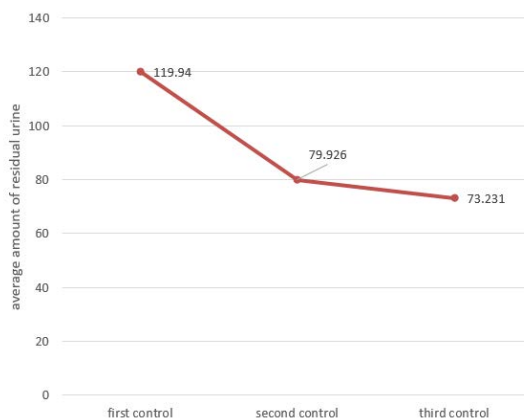


Fig. 3. The average amount of residual urine compared to the first, second and third controls

The results in table 3 showed that 54.6% of their treatment conservative treatment (Figure 4). in-volved surgical intervention, compared to 45.4% with

Treatment	Final Diagnosis			Total
	BPH	Ca-Prostate	Pre-Cancerous Lesions	
Conservative	43 48.30%	4 28.60%	2 40.00%	49 45.40%
Operation	46 51.70%	10 71.40%	3 60.00%	59 54.60%
Total	89 100.00%	14 100.00%	5 100.00%	108 100.00%

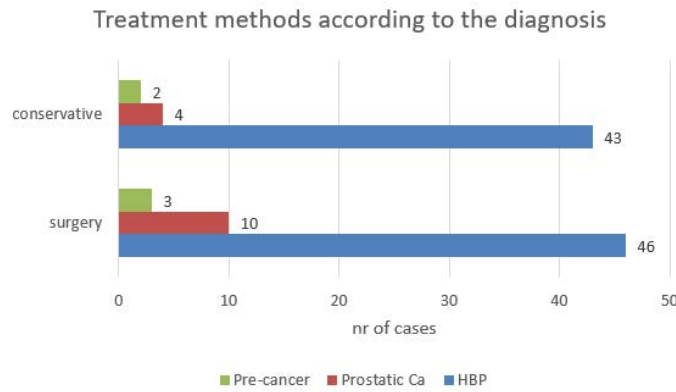


Fig. 4. The treatment methods according to the diagnosis

Analyzing the relationship between HBP (the dependent variable) and age, PSA level, and weight in grams of the prostate, it was seen that there is a statistically significant relationship between HBP and age; for every one-year increase in age, the odds increase by 9% to make HBP (OD=1.085; CI: 1.012-1.162). For a HBP and PSA level, it can be said that for every unit increase in PSA, the likelihood of developing HBP increases by 18% (OD=1.176; CI95%: 1.070-1.292) (Table 4).

Variable	Binary logistic regression: Univariate				Binary logistic regression: Multivariate			
	B	p-Value	OD	CI 95%	B	p-Value	OD	CI 95%
Age	0.059	0.033	1.06	1.005-1.119	0.081	0.021	1.085	1.012-1.162
PSA levels	0.137	0.001	1.147	1.056-1.246	0.162	0.001	1.176	1.070-1.292
Prostate size grams	-0.002	0.767	0.998	0.982-1.013	-0.011	0.311	0.99	0.970-1.010

The results in Table 5 showed the relationship between HBP (the dependent variable) and age, PSA level, and weight in grams of the prostate through interaction, it was seen that there is a statistically significant relationship between HBP in cases where an increase in PSA and an increase in weight are observed simultaneously in grams of prostate (Age=p<0.049 and prostate size grams by PSA levels=p<0.002).

Variable	Binary logistic regression: Multivariate				
	B	p-Value	OD	CI 95%	
Age	0.063	0.049	1.065	1	1.134
Prostate size grams *by PSA levels	0.001	0.002	1.001	1	1.002
Constant	-7.019	0.004	0.001	-	-

*Interaction

DISCUSSION

According to the study findings in Table 1, the greatest proportions (58.3%) of the patients were between 61 years to 70 years. The age range for the population studied was between 50 years to 90 years, with a mean of 69.35 years ± 9.35 SD. This suggests that the study population was predominantly older-aged, this finding was consistent with study conducted in Nigerian where the greatest proportions (67.5%) of the patients were between 60 years to 79 years, with a mean of 68 years ± 9 SD in Taiwan with a mean age of 67.3 years ± 9.1 SD, in Indonesia with (40.5%) of the patients were between 61 years-69 years [20-23].

The results of the first clinical measurement with laboratory analysis were done to excluded the inflammatory nature of the urinary tract, urinary bladder and prostate, while the focus in the second and third measurements after the exclusion of the inflammatory nature was the monitoring of PSA while trans-abdominal ultrasonography of the urotract conveyed the size of prostate in

grams and the measurement of residual urine. According to the recommendations of the European Association of Urology 2023 (EAU Guidelines), the commonest clinical presentation of BPH is LUTS characterized and patient’s management with LUTS is evaluated with history, physical examination, digital rectal examination, validated questionnaires like the International Prostate Symptoms Score (IPSS), trans-abdominal ultrasonography, uroflowmetry and laboratory studies [24].

The mean PVR in II clinical measurement and III clinical measurement with mean ± SD (79.93, 73.23 ± 66.79, 68.68) p<0.001 in this study is similar to the mean value of 79.5 ml ± 69.3 ml reported by Eze et al. and Elsaied et al. in Egypt, Sigdel et al. and Anyimba et al. in Nigeria with mean ± SD (77.70 ± 69.30), whereas in the other clinical measurements, we did not find any significant difference between the first, second and third measurements [23, 25-27].

According to the study findings in Table 3, there is no significant difference between conservative and surgical treatment of patients

with BPH. The treatment methods according to the diagnosis were based on the Guidelines of the European Association of Urology 2023 (EAU Guidelines) [24].

The results of the present study revealed that for every one-year increase in age, the odds increase by 9% to make BPH (OD=1.085; CI: 1.012–1.162). For a BPH and PSA level, it can be said that for every unit increase in PSA, the likelihood of developing BPH increases by 18% (OD=1.176; CI 95%: 1.070-1.292). Similar findings were reported in a study in China, where the mean value with a 95% CI for PSA level, PV, and PVR is 2.24 (95% CI: 2.16-2.32), 23.70 (95% CI: 23.37-24.04), and 4.97 (95% CI: 4.57-5.37) to increase with age [28]. Consistent with previous studies, BPH-related indicators were positively correlated with age in Germany, Korea and Russia [29-31].

According to the study findings in table 5, show the relationship between BPH (the dependent variable) and age, PSA level, and weight in grams of the prostate (the trans-abdominal ultrasonography used for prostate volume estimation). Through interaction, it was seen that there is a statistically significant relationship between BPH in cases where an increase in PSA and an increase in weight are observed simultaneously in grams of prostate (Age= $p < 0.049$ and prostate size grams by PSA levels= $p < 0.002$). Compared to the prostate volume documented by Awad Ali Alawad et al., this study found a relatively higher mean prostate volume in men with BPH [32]. The difference in prostate volume could be due to differences in the age groups used in his study, where trans-abdominal prostate volume estimation was done for

all the patients.

Consistent with the theory that aging is an etiologic factor of BPH; our results showed a trend of increasing median PSA level with advancing age and the weight in grams of the prostate. This result is consistent with studies in the Indonesian, Indian, and Chinese populations [22, 28, 33].

CONCLUSION

This study showed that there is a statistically significant relationship between HBP and age; for every one-year increase in age, the odds increase by 9% to make HBP, and it was found that for HBP and PSA level, it can be said that for every unit increase in PSA, the likelihood of developing HBP increases by 18%.

RECOMMENDATIONS

A recommendation for the Ministry of Health to provide all diagnostic measures and Benign prostatic hyperplasia-related medications free of charge for all patients to minimize the financial burden on patients and their families.

CONFLICT OF INTEREST

Members of the committee declare that they have no conflict with interest.

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