Evaluation of biochemical markers of renal dysfunction in prostate disorders and healthy controls

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Abstract

Aims & Objectives: Prostate disorders like prostatitis, Benign prostatic hyperplasia (BPH) and prostatitis are the most common disorders of the male population, the latter two being prevalent in the elderly men. PSA being the gold standard parameter to identify these diseases, is not of much importance in the differential diagnosis of prostate disorders. This study focuses on the blood levels of PSA, Urea, BUN, Creatinine BUN/creatinine ratio and eGFR in various disorders of prostate and healthy controls.

Methodology: Serum sample obtained from 25 patients each, diagnosed to have prostatitis, BPH and carcinoma prostate were analysed for the parameters mentioned above and compared with 75 age matched controls.

Results: The mean values for PSA as well as other markers of renal function included in the study were statistically significant between cases and controls. Further, significant values in the mean values of all the parameters were also observed in each of the prostate disorders as compared to controls.

Conclusion: On the basis of our findings, we conclude that patients with prostate disorders are likely to progress into renal dysfunction.

Keywords: BPH, Prostatitis, Prostate cancer, eGFR, BUN/Creatinine ratio

1. Introduction

The most commonly diagnosed diseases of the prostate include prostatitis, prostatic cancer and benign prostatic hypertrophy. Prostate gland doubles in size during puberty and grows thereafter at around the age of 25. Prostatitis which is classified as acute and chronic is an inflammatory condition caused due to bacterial infection which may even spread to the urinary bladder. Prostatic cancer which is the second leading cause of death in elderly men is a consequence of hypermethylation of GSTP1 gene promoter. Non malignant enlargement of the gland with age is referred to as benign prostatic hypertrophy (BPH). Obstruction of urethra is a common symptom in this condition. After the age of 60, 50% of the male populations are likely to develop symptoms of BPH. Conventionally used laboratory markers for the diagnosis of prostate disorders are acid phosphatase and PSA, a glycoprotein produced in the benign and malignant prostate cells. However the latter two being prevalent in the elderly men, are more prone to develop renal dysfunction.

2. Methodology

2.1. Study design
Case control study.

2.2. Sample size:
Patients with high PSA levels (above 4ng/ml), aged between 40-79 years, whose diseases were confirmed by biopsy report. The cases were further grouped as follows: Prostatitis (n=25), Benign prostatic hyperplasia(n=25) and Prostatic carcinoma(n=25).50 age matched controls were also enrolled for the study.

2.3. Exclusion Criteria
Patients with acute urinary tract infection, smokers, alcoholics, diabetics and kidney disorders. The study was approved by institutional ethics committee and informed consent was taken from all the subjects.

2.4. Methodology
5 ml venous blood was collected in a vacutainer and serum used for analysis. PSA was estimated by the method of ECLI using COBAS e411. Blood Urea was estimated by Urease/ GLDH Method. Serum Creatinine was estimated by Jaffé’s Method. Estimation of eGFR was based on the following formula:

\[
\text{eGFR} (\text{mL/min per 1.73 m}^2) = 1.86 \times (P_{\text{Cr}})^{-1.154} \times (\text{age})^{-0.203}
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Keywords: BPH, Prostatitis, Prostate cancer, eGFR, BUN/Creatinine ratio
3. Results

The mean values for PSA as well as other markers of renal function included in the study were statistically significant between cases and controls. (Table 1). Further, significant values in the mean values of all the parameters were also observed in each of the prostate disorders as compared to controls (Table 2).

### Table 1: Biochemical parameters in cases and controls (values are Mean± SD)

| Parameter                  | Controls (n=50) | Cases (n=75) |
|----------------------------|----------------|-------------|
| PSA (ng/mL)                | 1.51±1.09      | 37.30±34.42*|
| UREA (mg/dL)              | 25.54±8.91     | 78.93±36.68*|
| BUN (mg/dL)               | 11.93±4.16     | 48.82±16.15*|
| CREATININEMG/creatinine)   | 1.05±0.22      | 2.91±3.98*  |
| BUN:CREATININE RATIO       | 10.92±3.24     | 24.85±16.3* |
| eGFR (mL/min)             | 72.67±16.23    | 49.30±32.20**|

*p<0.0001 statistically significant between the groups  
**p<0.001 statistically significant between the groups

### Table 2: Biochemical parameters in various prostate disorders compared with controls (values are Mean± SD)

| Parameters             | Controls | Cancer Prostate | BPH | Prostateitis |
|------------------------|----------|-----------------|-----|--------------|
| PSA (ng/mL)            | 1.51±1.09| 8.68±3.09*      | 9.6±6.56* | 14.2±7.78*   |
| UREA (mg/dL)           | 25.54±8.91| 69.58±47.96*    | 74.27±68.77* | 96.94±58.84* |
| BUN (mg/dL)            | 11.93±4.16| 32.5±22.41*     | 34.7±32.13* | 45.3±27.49*  |
| CREATININE (mg/dL)     | 1.05±0.22 | 1.81±1.58      | 2.74±2.53* | 3.92±1.04*   |
| BUN:CREATININE         | 10.92±3.24| 20.78±8.76*    | 16.32±11.96* | 23.05±16.52*** |
| eGFR (mL/min)          | 72.67±16.23| 58.44±38.95*** | 50.09±30.33** | 42.3±33.07** |

*p<0.0001 statistically significant compared to controls  
**p<0.001 statistically significant compared to controls  
***p<0.05 statistically significant compared to controls

4. Discussion

PSA values were reported to be highest in Ca prostate in our study. Partin et al and Oesterling et al have shown that, serum PSA concentrations increase with increasing burden of malignancy in all untreated patients[12].

Benign prostatic hyperplasia which is a non malignant condition, is mostly prevalent in older men and is reported to be a major cause of lower urinary tract symptoms (LUTS)[2]. The doubling time of this non malignant tumor increases with age[11]. A tumor density of more than 0.15as determined by serial testing of PSA for 2 years, distinguished BPH from prostatic carcinoma[12].

Acute urinary retention is high in moderate to severe symptoms of lower urinary tract symptoms (LUTS)9. In moderate LUTS, eGFR was not proportionately decreased. These findings are conflicting considering the reports of Sampath Kumar et al[17].

Significant differences in the mean values of blood urea, BUN and BUN/creatinine ratio was more marked in prostate disorders compared to controls, and that, serum PSA was not proportionately decreased. This finding is in conformity with the opinion of Weinsten et al who have stated an association with chronic kidney disease and urinary bladder outlet obstruction which did not complement with prostatic enlargement[18].

Further, our study indicates that blood levels of urea, creatinine, BUN were highest in prostatitis suggesting maximal renal involvement in this condition, yet eGFR was not proportionately decreased. These findings are conflicting considering the reports of Sampath Kumar et al[17].

On the basis of our findings, we conclude that patients with prostate disorders are likely to progress into renal dysfunction. Also, based on the results of BUN/creatinine ratio, BPH and cancer of prostate, the most common types of prostatic disorders in old age, are more prone to develop renal dysfunction.

References

1. Cairns P, Esteller M, Herman JG, Schoeneng M. Molecular detection of prostate cancer in urine by GSTP1 hypermethylation. *Clin Cancer Res*, 2001; 7(9):2727-30.
2. Partin AW, Oesterling JE, Epstein JI, Horton R, Walsh PC. Influence of age and endocrine factors on the volume of BPH. *J Urology*, 1991; 145(2):405-409.
3. Weinstein SI, Mackrinn K, Virtamo J, Albanes D, et al. Serum creatinine and prostrate cancer risk in a prospective study. *Cancer Epidemiol Biomarkers Prev* 2009; 18(10):2643-9.
4. Miele ME. Percent free PSA as an additional measure in a prostate cancer screen. *Clin Lab Sci*, 2001; 14 (2):102-107.
5. Jacobson DJ, Robert RO. The association between Benign Prostatic hyperplasia and chronic kidney disease in community dwelling men. *Kidney Int* 2005; 67(6):2376-82.
6. Stephen J, McPhee, Maxine A. Papadakis. Urology. Lowrence M. Tierney, JR.(eds). In: Current Medical Diagnosis and Treatment.46th ed. USA, McGrawHill; 2007.
7. Wada Y, Nakanishi J, Takahashi W, Kai N, Nakayama Y, Yamashita Y, Honda J, Ueda S. Mass screening for prostate cancer in patients with end-stage renal disease: a comparative study. BJU Int 2006; 98(4):794-797.
8. Roddam AW, Rimmer J, Nickerson C, Ward AM. Prostate specific antigen: bias and molarity of commercial assays for PSA in use in England. Ann Clin Biochem 2006; 43: 35-48.
9. Burtis CA, Ashwood ER (editors). Renal function and nitrogen metabolites. In: Teitz textbook of clinical chemistry. 3rd edition. Philadelphia: WB Saunders Company 1999; p1838.
10. Newman DJ, Price CP. Renal function and nitrogen metabolites. In: Burtis CA, Ashwood ER (editors). In: Teitz textbook of clinical chemistry. 3rd edition. Philadelphia: WB Saunders Company 1999; p1204.
11. Levey AS, Stevens LA, Schmid CH, Zhang YL, Castro AF, 3rd, Feldman HI, et al. A new equation to estimate glomerular filtration rate. Ann Intern Med 2009; 150(9):604-12.
12. Thomas J, Polascik, Joseph e. Oesterlingalan, W Partin. Prostate specific antigen: a decade of discovery—what we have learned and where we are going? J of Urology 1999; 162(2):293-306.
13. Yeon Won Park, Seung Ki Min, Jun Hankin. Relationship between lower urinary tract symptoms/benign prostatic hyperplasia and metabolic syndrome in Korean men. World J Mens Health 2012; 30(3):183-188.
14. Berry SS, Coffey DS, Walsh PC, Euring L L. The development of human benign prostatic hyperplasia with age. J. Urol 1984; 132(2):293-306.
15. Herbert Lepor. Pathology, Epidemiology and Natural History of Benign Prostatic Hyperplasia. Rev Urol 2004; 9:S3-S10.
16. Rule AD, Jacques Iran, Laurent Salomon, Michel Soulié, Alexandre Ziotta, Alexandre de la Taille, Bertrand Doré, Christine Mill et. Urinary/serum PSA: comparison with free/total PSA ratio in improving prostate cancer detection. Urology 2005; 65(3):533-537.
17. Bhaigya Lakshmi A, Sampath Kumar V, Rama Devi, Rama Rao J, Harini. Comparative study of biochemical markers in prostatitis, benign prostate hypertrophy and carcinoma of prostate with and without metastasis. International J Pharma Biosciences 2012; 2(2):117-122.
18. Andrew DR, Debra JJ, Rosebud OR, Cynthia JG, Michaela EM, Steven JC. The association between benign prostatic hyperplasia and chronic kidney disease in community dwelling man. Kidney International, 67:2576-2382, (2005).
19. Hung SC, Lai SW, Tsai PY, Chen PC, Wu HC, Lin WH, Sung FC. Synergistic interaction of benign prostatic hyperplasia and prostatitis on prostate cancer risk. Br J cancer 2013; 108(9):1778-83.
20. Agrawal M, Swartz R. Acute renal failure. Am Fam Physician 2000; 61:2077-2088.
21. Shigahiko Uchino, Rinaldo Bellomo and Donna Goldsmith. The meaning of blood urea nitrogen/creatinine ratio in acute kidney injury. Clin Kidney J 2012; 5(2):187-191.