

Research Article

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 prostatic cancer 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. 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.

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 promoter¹. 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 BPH². 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 has replaced the former with regard to sensitivity and specificity. It was earlier reported that serum creatinine is associated with a high risk of prostate cancer; more so in advanced cases where the chances of survival were low³. Some of the biochemical parameters that were reported to be useful in the diagnosis of prostate cancer include free PSA to total PSA ratio^{4,5} and serum to urinary PSA ratio⁶. It is evident in the current scenario, that there is a dearth of biochemical parameters for differential diagnosis of prostate disorders, paving way for the identification of newer ones. Since prostate disorders have an association with end stage renal disorders(ESRD) and is also age related⁷, this study focuses on the utility of blood levels of urea, creatinine, BUN, BUN/Creatinine ratio (BCR) and eGFR as a possible aid in the diagnosis of prostate disorders and association of these disorders with renal dysfunction.

2. Methodology

2.1. Study design

Case control study.

2.2. Sample size:

75 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 ECLIA using COBAS e411⁸. Blood Urea was estimated by Urease/ GLDH Method⁹ Serum Creatinine was estimated by Jaffe's Method¹⁰. Estimation of eGFR was based on the following formula¹¹

$$\text{Equation from the Modification of Diet in Renal Disease study(MDRD formula)} \\ \text{Estimated GFR (mL/min per 1.73 m}^2\text{)} = 1.86 \times (\text{P}_{\text{Cr}})^{-1.154} \times (\text{age})^{-0.203}$$

Statistical Analysis was done using Mann Whitney U test, $p < 0.05$ was considered to be significant

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 \pm SD)

Parameter	Controls (n=50)	Cases (n=75)
PSA(ng/mL)	1.51 \pm 1.09	37.30 \pm 34.42*
UREA (mg/dL)	25.54 \pm 8.91	78.93 \pm 36.68*
BUN (mg/dL)	11.93 \pm 4.16	48.82 \pm 36.15*
CREATININE (mg/dL)	1.05 \pm 0.22	2.91 \pm 3.98*
BUN:CREATININE RATIO	10.92 \pm 3.24	24.85 \pm 16.3*
eGFR (mL/min)	72.67 \pm 16.23	49.30 \pm 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 \pm SD)

Parameters	Controls	Cancer Prostate	BPH	Prostatitis
PSA(ng/mL)	1.51 \pm 1.09	86.85 \pm 3.09*	9.67 \pm 6.56*	14.24 \pm 7.78*
UREA(mg/dL)	25.54 \pm 8.91	69.58 \pm 47.96*	74.27 \pm 68.77*	96.94 \pm 58.84*
BUN(mg/dL)	11.93 \pm 4.16	32.51 \pm 22.41*	34.70 \pm 32.13*	45.30 \pm 27.49*
CREATININE(mg/dL)	1.05 \pm 0.22	1.81 \pm 1.58	2.74 \pm 2.53*	3.92 \pm 1.04*
BUN:CREATININE	10.92 \pm 3.24	20.78 \pm 8.76*	16.32 \pm 11.96*	23.05 \pm 16.52***
eGFR(mL/min)	72.67 \pm 16.23	58.44 \pm 38.95***	50.09 \pm 30.33**	42.39 \pm 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 patients¹²

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)¹³. The doubling time of this non malignant tumor increases with age¹⁴. A tumor density of more than 0.15as determined by serial testing of PSA for 2 years, distinguished BPH from prostatic carcinoma¹².

Acute urinary retention is high in moderate prostate enlargement which can be predicted from the baseline serum PSA levels. It has also been reported that there is a strong correlation between prostate volume and PSA levels and therefore acute urinary retention¹⁵. However blood urea and creatinine, the markers of acute urinary retention, reported in cases with prostatic carcinoma in our study, which had significantly higher PSA values as compared to other disorders of prostate, did not correlate. This finding is in conformity with the opinion of Weinstein *et al* who have stated an association with chronic kidney disease and urinary bladder outlet obstruction which did not complement with prostatic enlargement¹⁶.

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.

Significant differences in the mean values of blood urea, BUN and BUN/creatinine ratio was more marked in prostate disorders in general, compared to controls. BUN/creatinine ratio was highly significant in cancer of prostate and BPH in particular, amongst the various disorders of prostate, when compared to controls. In support to this observation, it has been stated earlier that many patients with kidney disease responded to surgical treatment of BPH¹⁸.

It has also been reported in earlier studies, that BPH can progress into prostatic cancer¹⁹.

A BUN/creatinine ratio of >20 was reported to be useful in differentiating pre renal azotemia(PRA) from acute tubular necrosis²⁰, but was disagreed later on by Shigehicko *et al*²¹.

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.

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