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ASSOCIATION OF PROSTATE DISORDERS WITH RENAL DYSFUNCTION: ROLE OF BIOCHEMICAL MARKERS

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ABSTRACT

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 of blood levels of PSA, Urea, BUN, Creatinine BUN/creatinine ratio and eGFR and the correlations between these parameters and note the association of various disorders of prostate with renal dysfunction. Serum sample obtained from 25 patients each ,diagnosed to have prostatitis,BPH and carcinoma prostate were analysed for the parameters mentioned above. Results indicated that there was a significant negative correlation of eGFR with PSA and a significant positive correlation of eGFR with BUN/creatinine ratio in patients diagnosed with BPH. No other parameters correlated in other disorders were found to be significant. Based on our results we conclude that patients with BPH are most likely to progress into kidney dysfunction and also that eGFR may be a better marker as compared to BUN/creatinine ratio in the assessment of kidney damage consequent to prostate hypertrophy.

KEY WORDS : BPH, Prostatitis, Prostate cancer, eGFR, BUN/Creatinine ratio

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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[1].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 population are likely to develop symptoms of BPH[2].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 low[3]. 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 ratio[6]. 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 related[7], this study focusses on the utility of blood levels of urea,creatinine,BUN, BUN/Creatinine ratio (BCR)andeGFR as a possible aid in the diagnosis of prostate disorders and association of these disorders with renal dysfunction.

METHODOLOGY

Inclusion Criteria

75Patients 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 followsProstatitis(n=25), Benign prostatic hyperplasia(n=25) and Prostatic carcinoma(n=25).

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. 5 ml venous blood was collected in a vacutainer and serum used for analysis. PSA was estimated by the method of ECLIA using COBAS e411[8]. Blood Urea was estimated by Urease/ GLDH Method[9] Serum Creatinine was estimated by Jaffe's Method[10].Estimation of eGFR was based on the following formula[11]

Equation from the Modification of Diet in Renal Disease study(MDRD formula)

Estimated GFR (mL/min per 1.73 m^2) = 1.86 x $(P_{Cr})^{-1.154}$ x $(age)^{-0.203}$

Statistical Analysis was done using Kruskalwallis test and Spearman's rank correlation, Post Hoc comparison was done using Tukey HSD test

RESULTS

There was significant change [$p<0.01$] in the PSA value between 3 groups-Prostate Cancer, BPH & Prostatitis.(Table 1). The mean score for PSA value of Prostate Cancer (86.85±83.09) was significantly [$p=0.002$] higher compared to BPH (11.49±12.31) as well as Prostatitis (14.24±7.78; $p=0.010$]. There was no significant difference in the PSA values between BPH and Prostatitis group. Further, there were no significant changes in the mean blood values of urea, creatinine, BUN/Creatinine ratio or eGFR between the different diseases of prostate. But highest mean values for blood levels of urea ,creatinine,BUN and BUN /creatinine ratio was observed in patients with prostatitis.

While eGFR was observed to be least in benign prostatic hypertrophy (Table 1) . PSA was found to be significantly elevated in patients with prostate cancer in the age group 60-79yrs,while it was markedly elevated in patients with BPH in the age group70-79yrs **.** The onset of BPH takes place at an earlier age as compared to prostate cancer (Table 2).No significant correlations were observed between PSA and BUN/creatinine ratio or PSA and eGFR in cancer and prostatitis. However there was a positive correlation between BUN/creatinine ratio and PSA which was not significant in prostate disorders (Table 3). PSA and eGFR negatively correlated (r=-0.360) in patients with BPH and it was significant at $p<0.05$. eGFR and BUN/creatinine was positively correlated (r = 0.416) in patients with BPH and it was significant at $p<0.05$. not significant in cases (Table 4).

Table 1

Biochemical parameters in various prostate disorders: Values are Mean± SD

	Prostate cancer	BPH	Prostatitis
PSA(ng/ml)	86.8542 ± 83.0948*	9.6743 ± 6.5663	14.2481 ± 7.7803
UREA(mg/dl)	69.5857 ± 47.9611	74.271 ± 68.7777	96.9454 ± 58.8406
BUN(mg/dl)	32.5166 ± 22.4117	34.7061 ± 32.1391	45.3016 ± 27.495
Creatinine (mg/dl)	1.8196 ± 1.5827	2.7477 ± 2.53	3.9267 ± 1.044
BUN:Creatinine	20.7802 ± 8.7615	16.3279 ± 11.9684	23.0508 ± 16.5218
eGFR(ml/min)	61.6285 ± 36.9047	45.9545 ± 28.9602	46.5818 ± 34.7199

Values are significant between the three groups (p<0.01)

Table 2

PSA (ng/ml) levels in prostate disorders based on age groups: Values are Mean± SD

Age (yrs)	Prostate cancer	BPH	Prostatitis
<50	nil (n = 0)	Nil (n = 0)	12.25±1.56 (n=15)
50-59	Nil (n= 0)	8.173±2.58 (n=7)	26.19±8.06 (n=5)
60-69	94.68±106.63 (n=12)	7.86±2.88 (n=9)	12.54±7.46 (n=4)
70-79	98.75±85.37 (n=13)	16.74±18.5 (n=9)	7.55 (n=1)

n=number of patients

Table3

Correlation of PSA with other parameters in prostate disorders

	"r"	p value
PSA v/s BUN:Creatinine Ratio	0.142	0.314
PSA v/s eGFR	-0.204	0.147
BUN:Creatinine Ratio v/s eGFR	0.416	0.002*
PSA v/s Age	0.265	0.050*

**** Statistically significant***

Table 4

Correlation between PSA and other parameters-Spearmanns Correlation based on Diagnosis

	Prostate cancer		BPH		Prostatitis	
	R	p	r	p	r	P
PSA vs eGFR	-0.524	0.183	-0.360	0.040*	0.400	0.223
PSA vs BUN/Creatinine ratio	0.120	0.778	0.005	0.979	0.173	0.611
eGFR vs BUN/creatinine ratio	0.563	0.146	0.416	0.016*	0.369	0.264

****Statistically significant***

DISCUSSION

All patients enrolled in our study, showed a significant increase in PSA values with age irrespective of the type of prostate disorder, which is in agreement with earlier reports[12] PSA values are the highest in Ca prostate.Partin et al and Oesterling et al have shown that,serum PSA concentrations increase with increasing burden of malignancy in all untreated patients[13] 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) [14].The doubling time of this non malignant tumor increases with age [15].A tumor density of more than 0.15as determined by serial testing of PSA for 2 years, distinguishes BPH from prostatic carcinoma [13]. 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 retention[16].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 Weisteinetal who have stated an association with chronic kidney disease and urinary bladder outlet obstruction which did not complement with prostatic enlargement [17]. Further,our study indicates that blood levels of urea, creatinine, BUN were highest in prostatitis suggesting maximal renal involvement in this condition,yeteGFR was not proportionately decreased.These findings are conflicting considering the reports of Sampath Kumar etal[18]. However our results suggest a negative correlation between PSA and eGFR in BPH. Since PSA levels in the blood is an index of tumor size and volume[6] and eGFR is a marker of kidney function, a negative correlation between the two parameters indicates a marked association of symptoms ofrenal dysfunctionin BPH, which is not observed in cancer of prostate or prostatitis. In support to this observation,it has been stated earlier that many patients with kidney disease responded to surgical treatment of BPH [19]. A positive correlation between eGFR and BUN/Creatinine ratio in BPH is suggestive of the progression of BPH to kidney dysfunction .Similar correlations are not observed in either prostatitis or prostatic carcinoma.Ithas also been reported in earlier studies, that BPH can progress into prostatic cancer[20]. On the basis of our findings, we conclude that patients with BPH, the most common type of prostatic disorder in oldage, are more prone to develop renal dysfunction as compared to prostatitis or prostatic carcinoma. eGFR is a relatively better marker in this regard, although BUN /Creatinine ratio does not seem to be of much significance either in the differential diagnosis of prostatic disorders or in suggesting the type of prostate disorder that may lead to kidney dysfunction in future.

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