Original Article

PSA Levels

Histological Prostatitis and its Correlation with Prostate Specific Antigen Levels

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ABSTRACT

Objectives: The aim of the study was to find a relationship between Prostate Specific Antigen levels and histological prostatitis in people belonging to our part of the world mainly Khyber Pakhtunkhwa and adjoining areas of Afghanistan.

Study Design: Analytical / cross sectional study

Place and Duration of Study: The study was conducted at the North West Hospital, Peshawar for a period of six months.

Materials and Methods: A total of 200 patients who underwent surgical treatments for Benign prostatic hyperplasia due to obstructive or irritative symptoms were prospectively studied.Patients who complained of chronic pelvic pain or had a history of laboratory exam suggesting acute prostatitis were excluded.Results were analysed using Mann-Whitney rank sum test or Pearson product moment correlation (for Prostate specific antigen vs inflammation) at 95%CI.

Results: In my study of the 200 cases, 98 cases with histological prostatitis had normal PSA levels and 102 cases with histological prostatitis had raised PSA levels. Of the cases with raised PSA levels , most cases were of grade I inflammation with multiple spread and their location was glandular, peri- glandular plus stromal.

Conclusion: It is shown in numerous studies that there is a relationship between PSA levels and Histological Prostatitis .My study revealed that a relationship doesexist between PSAlevels and Prostatitis but it is a weak one.PSA levels can be raised in conditions other than prostatitis.

Key Words: Prostate specific antigen, benign prostatic hyperplasia, Prostatitis

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INTRODUCTION

The prostate gland is derived from the Greek word προστάτης – prostates, which means one who stands before, protector or guardian. (Ayala et al. 1989)[1]. Prostate is an exocrine gland of the compound tubuloalveolar variety (Baade et al. 2009)[2]. Herophilus of Alexandria first used the word prostatitis in 335B.C. to describe an organ present in front of the bladder.(Bennet and Harrison, 1969)[3]. The prostate surrounds the first part of the urethra, the prostatic urethra, and is considered the largest accessory reproductive gland in the males (Bankhoff and Remberger, 1998)[4]. The prostatic part of the urethra surrounds the prostate gland anteriorly It is divided into proximal and distal portions by an angulation of 30degrees in its mid portion. The posterior wall of the gland has a ridge , distal to this angulation, Verumo-ntanum(crista urethralis)[5].

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The ejaculatory ducts that receive about 90% of the ducts of the prostate gland also open in the distal segment of the urethra(Brendler et al., 1992)[6]. The differentiation and the growth of the prostate depends on the androgenic hormones which are synthesized in the testis[7].

The most common benign diseases of the prostate gland include BPH and prostatitis and affect a large majority of men over a period of time. Prostatitis is defined as the presence of pathological infiltration of the prostate by inflammatory cells.

Prostatitis was considered to be the disease of the young men, but now it is proven that it is as common in older men[8]. Compared to men aged 51 and higher the odds of a documented prostatitis diagnosis is only 2-fold greater in younger men[9]. Approximately 8% of men over 50 years of age report atleast some mild prostatitis like symptoms compared to 11% of younger men.

In 1992, 31,681 United States health professional without prostate cancer showed a relationship between the diagnosis of urological diseases and the symptoms of the lower urinary tract. 57.2% of the 5,053 with prostatitis also had a history of BPH and 38.7% of the 7,465 men who had a diagnosis of BPH also had a history of prostatitis[10].

There is a tendency to correlate inflammatory prostatitis with an elevation of PSA.(Irani et al.,2014) studied the

effect of inflammation of prostate on the serum PSA concentration in patients with BPH tissue on prostate biopsies. Inflammatory infiltrate were given the following grades: Grade 0(no inflammatory cells), 1 (inflammatory cells are scattered in the stroma but with absent lymphoid nodules), 2 (non-confluent lymphoid nodules) and 3 (large areas of inflammation with confluence of infiltrate)[11].

It was reported that the inflammation seen in the biopsies of the prostate were not associated with the raised serum PSA levels unless the glandular epithelium isdisrupted[12]. Another research showed that the inflammation of the prostate is an important factor contributing to elevation of serum PSA levels in men with no prostate cancer[13].

Inflammation in the prostate was divided as acute (polymorphonuclear leukocytes with glandular or ductal lumina, their epithelium and/or adjacent stroma) and chronic (mononuclear cell infiltrate in the stroma around prostatic glands) and was graded on a 3-point scale of 0(none), 1(low grade), 2 (high grade). When prostatic inflammation is seen on a biopsy sample of patient with elevated PSA levels, the rise in PSA is attributed to presence of prostatitis[14].

In this study a total of 200 patients who underwent surgical treatments for Benign prostatic hyperplasia due to obstructive or irritative symptoms were prospectively studied.Patients who complained of chronic pelvic pain or had a history of laboratory exam suggesting acute prostatitis were excluded.Results were analysed using Mann-Whitney rank sum test or Pearson product moment correlation (for Prostate specific antigen vs inflammation) at 95%CI.

MATERIALS AND METHODS

A total of 200 patients who underwent surgical treatments for Benign prostatic hyperplasia due to obstructive or irritative symptoms were prospectively studied.Patients who complained of chronic pelvic pain or had a history of laboratory exam suggesting acute prostatitis were excluded.Results were analysed using Mann-Whitney rank sum test or Pearson product moment correlation (for Prostate specific antigen vs inflammation)at 95%CI.All patients underwent a digital rectal examination ,serum prostate specific antigen .Prostate tissue from each case was examined microscopically. For each focus of inflammation the pattern was categorized as glandular, periglandular, stromal and periurethral ,the surface area measured and the intensity of inflammation graded from 1 to 3. Total prostate specific antigen was assayed before transurethral resection procedure using the Bayer Immunolk automated system. Patients with unsuspected prostate cancer on pathological examination were excluded from this analysis.

RESULTS

Results was analysed using the Mann- Whitney rank sum test or Pearson product moment correlation (for Prostate specific antigen vs inflammation)at 95% CI.

Table No.1: Incidence of Prostatitis

Statistics		
Age		
N	Valid	200
	Missing	0
Mean		69.16
Median		70.00
Mode		70
Std. Deviation		9.446
Minimum		40
Maximum		98

Table No.2: Relationship of degree of inflammation and PSA Level

Count		**PSA**				
		Normal (<4 ng/ml)	Mild (4-8 ng/ml)	Moderate (9-12 ng/ml)	Severe (>12 ng/ml)	
inflammation	Acute	1	0	0	1	2
	Chronic	59	28	25	20	132
	Acute + Chronic	37	6	13	9	65
	No Infla	1	0	0	0	1
Total		98	34	38	30	200

Table No.3: Chi Square values of relationship between degree of inflammation and PSA levels

Chi-Square Tests

	Value	df	Asymp. Sig. (2-sided)
Pearson Chi-Square	8.506[a]	9	.484
Likelihood Ratio	9.323	9	.408
N of Valid Cases	200		

8 cells (50.0%) have expected count less than 5. The minimum expected count is .15.

In my research of 200 cases, 199 cases had inflammation of which 2 cases (1%) had acute inflammation. In 132 cases (66%) the patient had chronic inflammation and in 65 cases(32.5%) the patient had acute and chronic inflammation. In 1 case (0.5%) the patient had no inflammation. In patients with acute inflammation one case had severely raised PSA

levels i-e more than 12ng/ml. In patients with chronic inflammation 20 cases had severely raised PSA levels, 25 cases had moderately raised PSA levels and 28 cases had mildly raised PSA levels that is less than 4ng/ml. In 59 cases (44.7%) with chronic inflammation the PSA levels were normal. In patients with acute and chronic inflammation 9 cases (13.8%) had severly raised PSA level, 13 cases (20%) had moderately raised PSA levels and 6 cases(9.2%) had mildly raised PSA levels. In 37 cases (56.9%) with acute and chronic inflammation the PSA levels were normal. In 1 patient (100%) with no inflammation the PSA levels were normal. Thus of the total cases 98 cases (49%) had normal PSA levels. 34 cases (17%) had mildly raised PSA levels. In 38 cases (19%) the PSA levels were moderately raised and in 30 cases (15%) the PSA levels were severely raised.

DISCUSSION

Prostate specific antigen (PSA) a "glycoprotein serine protease" was first identified by Wang *et al* in 1979[15]. Although it was first designed as a serum marker for detecting and monitoring patients with prostate cancer it is now proven that it can be raised in other conditions such as prostatitis, BPH and diagnostic and surgical procedures(Pollack, 1991)[16]. PSA which is secreted entirely by the epithelial cells lining the prostatic acini and ducts of prostatic tissue is non specific for prostatic cancer and specific for prostatic tissues (Price H et al. 1990)[17]. Many researches have been carried out all over the world which has proven this fact (Shapiro et al., 1992)[18]. Immunoreactive PSA exist in two forms ((Siegel, 2011)[19]. Major fraction is bound to serum (<PSA) and 10-30% is free (fPSA). Many reports indicate that serum PSA level is elevated in patients with clinical acute prostatitis[20]. The exact reason for the elevation in PSA with inflammation is poorly understood, however there are many theories (Smith MJ, 2006)[21]. One theory is that the inflammatory process may trigger the release of unknown substances that in turn cause the release of PSA from the epithelial cells surrounding the affected area(Stamey et al., 2004)[22]. On the other hand Hasui et al proposed that elevated PSA levels is caused by the leakage of stored PSA in epithelial cells into the stromal tissue and blood circulating after epithelial cell death (Van der Cruijsen-Koeter et al., 2005)[23].

The correlation of histological prostatitis with elevated PSA levels remain controversial. Some researchers support the theory while some studies were unable to establish a correlation between PSA levels and histological prostatitis(Van de Voorde et al., 1995)[24].

One study carried out by Affonso et al in 2006 revealed that abnormal PSA level could not be attributed to the inflammatory process[25]. Of the 183 patients 145 had histological prostatitis and 38 cases had no prostatitis (Venkateswaran and Klotz, 2010)[26]. Similarly another study carried out by Lakhey et al from January 2008 to December 2009 revealed that serum PSA was marginally elevated in patients with BPH without inflammation and active inflammation and high grade lesions were associated with PSA levels more than 5ng/ml[27]. In asymptomatic men the histological evidence of prostatitis is very common(Wasson *et al*., 1995)[28]. There was 98% incidence of prostatitis in 168 asymptommatic patients in a study carried out by Khoen et al[29]. Similarly Nickel et al reported that the material obtained from patients undergoing TURP, there was inflammation in all 80 specimens (Zeegers,2003)[30]. In my research 200 patients who were to undergo surgical treatment were studied. They were categorized as glandular, peri-glandular, stromal and peri-urethral. The intensity of inflammation was graded from 1-3. Total PSA levels were assayed before TURP using the Bayer Immunolk automated system . Those cases were excluded who had preoperative diagnosis of prostatitis, prostatic cancer, previos prostatic surgery or documented UTI. It was found that of the 200 cases undergoing TURP, 2 cases had acute inflammation, 132 cases had chronic prostatitis and 65 cases had both acute and chronic prostatitis. Only one case had no inflammation, signifying that a total of 199 cases who were previously undiagnosed had prostatitis, of these 98 cases had PSA levels in the normal range, that is less than 4ng/ml. 102 cases had PSA levels that were raised, of these 102 cases, 34 cases had PSA levels in the mild range that is between 4-8ng/ml, 38 cases had PSA levels in the moderate range, that is between 9-12ng/ml and 30 cases had PSA levels in the severe range, that is more than 12ng/ml. The extent of inflammation was focal in 43 cases, multiple in 126 cases and diffuse in 28 cases. Of the focal cases 13 cases had PSA levels in the normal range and 30 cases had raised PSA levels. When the extent of inflammation was multiple, 70 cases had PSA levels in the normal range and 56 cases had raised PSA levels. In cases of diffuse inflammation, the PSA levels were normal in 15 cases and 13 cases had raised PSA levels. So when the extent of inflammation is multiple the PSA levels are most raised. In cases of grade I inflammation, of the 140 cases , 68 cases had normal PSA levels and 72 cases had raised PSA levels. In contrast of the 51 cases with grade II inflammation, 26 cases had PSA levels in the normal range and 25 cases had raised PSA levels. Similarly of the 9 cases with grade III inflammation 4 cases had normal PSA levels and 5 cases had raised PSA levels. So of the 200 cases PSA levels were most raised with grade I inflammation. Hence my study revealed that although a relationship does exist between prostatitis and PSA levels ,it is a very weak one and it should not be used as a diagnostic criteria for histological prostatitis. With histologically proven prostatitis, 98 cases had normal PSA levels and in comparison 102 cases had raised PSA levels which is not a significant difference. This data suggests that

incidental finding of histological prostatitis is very common and is not necessarily related with an increased PSA value. It can exist without raised PSA level and PSA levels can be raised in other conditions such as prostatic cancer, BPH or previous surgical intervention.

CONCLUSION

It is shown in numerous studies that there is a relationship between PSA levels and Histological Prostatitis. My study revealed that a relationship does exit between PSA levels and Prostatitis but it is a weak one.PSA levels can be raised in conditions other than prostatitis.

Author's Contribution:

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Conflict of Interest: The study has no conflict of interest to declare by any author.

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