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Role of PSA in Diagnosis of Chronic Prostatitis

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Abstract

Background: Prostatitis is the poor cousin of prostatic cancer and Benign hyperplasia. The prevalence of prostatitis in general population was estimated to be 0.5 to 14.2% in developed countries. Publishing in Iraq was concern mainly with treatment of prostatitis.

Objective: This work was carried out to comment on the concept of prostatitis in clinical practice.

Method: A total of 275 males was included in this study. They were complaining of urinary symptoms (frequency, urgency, hesitancy, straining, difficulty in initiation urinary stream).All cases were confirmed to have chronic prostatic after excluding prostatic carcinoma by abdominal ultrasound, free to total PSA and urinary Prostatic carcino-antigen-3. Their age was 45.6 ± 9.6 year. Urine samples were proceeded immediately after collection. Centrifuged and non-centrifuged specimen were examined.

Results: PSA was affected significantly by age (p = 0.002). A significant high level was observed among those complaining of pain during ejaculation (p = 0.0001).Those showed epithelial cells in urine had significant high level of PSA (p = 0.0001). Uric acid in urine was associated with significant high level of PSA (p = 0,03).

Conclusion: The diagnosis of CP / CPPS might be outside the traditional urologic practice and might consider PSA level too.

Key words: *Prostatitis, PSA, urinary symptoms, chronic pelvic pain syndrome, Iraq.*

Introduction

Prostatitis is a microscopic inflammation of the prostate gland that covers a wide range of clinical conditions in relation.[1]

Prostatitis is the "poor cousin" of prostate cancer and benign prostate hyperplasia (BPH) which is the most common urologic diagnosis in younger than 50 years, and the 3rd most common diagnosis in men older than 50 years.[2]Factors identifiable with prostatitis are microorganism, urine reflux and high voiding pressure, immunological status and mental stress.[3-6]

Prostatitis was classified by National Institute of Health (NIH) into four categories, I, II, III, and IV, representing acute prostatitis (CP), chronic prostatitis/ chronic pelvic pain syndrome (inflammatory and non-inflammatory) (CPPS) and asymptomatic inflammatory prostatitis, respectively.[7]

Acute prostatitis is mostly caused by several different types of bacterial infections and represented as a medical emergency. 5% of patients might end up with chronic bacterial prostatitis, which is mostly caused by *E. coli* and other gram negative Enterobacteriaceae.

Chronic nonbacterial prostatitis, also known as chronic prostatitis/chronic pelvic pain syndrome (CP/ CPPS), is long term pelvic pain and symptoms with urination without evidence of a bacterial infection.[1]

Asymptomatic inflammatory prostatitis is a painless inflammation of the prostate gland where there is no evidence of infection.[1]

PSA was first identified in human prostatic tissue extracts in 1970, purified and characterized by Wang and associates in 1979 , and detected in human serum by Papsidero and associates in 1980.[8]

PSA is a single chain, 240–amino acid glycoprotein

with a molecular weight of 33 kDa. The human PSA gene is located on chromosome 19 (544). The mRNA of PSA, like other cytoplasmic serine proteases, is translated as an inactive pre-PSA/pro-PSA precursor. Following passage through the intracellular secretory pathway, the signal peptide is cleaved, yielding the proform of the protein. Evidence suggests the conversion of pro-PSA to the mature enzymatically active PSA requires the action of human kallikrein 2 (hK2) [9].

PSA shares sequence homology with the human kallikreinsand in fact, a 78% homology with hK2. PSA possesses chymotrypsin-like activity and has a weak interaction with the plasma inhibitor,aprotinin. PSA also has modest overlapping homology with urokinase-like plasminogen activator and is capable of facilitating the degradation of the extracellular matrix. PSA is primarily produced by adluminal or secretory cells of the prostate and the epithelial lining of the periurethral glands [10].

The basal cells of the prostate do not express this protein. It is androgen regulated and one of the most abundant serine proteases in the seminal plasma (1,000,000 ng/mL). Its major physiologic role is to promote the liquefaction of seminal clot. Seminal clotting is due to the presence of semenogelin 1 and semenogelin 2 and fibronectin. PSA targets the semenogelincomponent, thus liquefying the seminal clot, which in turn facilitates sperm motility. The half-life of PSA is 2.2 to 3.2 days [11].

Low levels of PSA and/or PSA-gene expression have been detected in various tissues, particularly those that have constitutive expression of the steroid receptor superfamily, including the uterine endometrium and amniotic fluid, normal/lactating breast tissue and the milk of lactating women, breast cancer; perianal/ periurethralglands, salivary glands, adrenal/renal neoplasms, and various other malignant tumors [10].

The prevalence of prostatitis in general population was estimated to be 5.0 to 14.2%.[12] The figure was for developed countries (America and Europe). No publish figure on prevalence of prostatitis in Iraq which is might be endemic like other endemic diseases in Iraq like hydatid cyst[22] and brucellosis[23], and publishing were mainly concerned with treatment with antibiotics.[13]

The aim of this study is to comment on the role of PSA in chronic prostatitis in clinical practice.

Materials and Method

During the study period July 2016 to April 2018, a total of 275 males referred to Lagash laboratory for general urinalysis because pain and urinary symptoms (frequency, urgency, hesitancy, straining, difficulty in initiation of urinary stream and incomplete bladder emptying).After excluding prostatic carcinoma by abdominal ultrasound, free to total PSA values, and estimating the level of Prostatic carcinoantigen-3 in urine by ElISA method (PCA-3),the diagnosis of CP / CPPS was according to NIH criteria.[7]Their age was 45.6 ± 9.6 year.

Urine samples were processed immediately after collection. The centrifuged and the non-centrifuged specimen were examined under 10x and 40x of bright field microscope to find out the presence of pus cells, RBCs, casts, crystals and bacterial cells. Blood samples to obtain serum PSA levels and was processed by Snibe Maglumi 800 Immunoassay Analyzer chemiluminiscence immunoassay system.

Data was dichotomized for age (≤ 50 and > 50 year), pain on ejaculation (yes and no), epithelial cell in urine (present and not present), pus cells in urine (present or not present), bacteria in the urine (high density or low density), uric acid (present or not), seminal fluid pus cells (present or not present), seminal fluid uric acid (present or not present) and history of smoking (positive or negative)

Student's t test was carried out to examine the differences in means of PSA between the dichotomized variables. P value < 0.05 was considered significant.

Results

PSA among those aged ≤ 50 and > 50 year, were 1.6 ± 0.1 and 1.4 ± o.1, respectively. A significant difference in PSA between the two groups (t = 3.1, d.f.= 273, p = 0.002). (Table 1). PSA was increasing with age (Fig.1).

Men complaining of pain on ejaculation had significantly higher PSA (6.6 ± 1.5) than those with no pain on ejaculation (5.1 ± 1.2) (t = 6.6, d.f. =273, p = 0.0001).

Those men showed epithelial cells on urinalysis had a significant higher PSA (9.2 ± 1.7) than those showed no epithelial cells on urinalysis (6.2 ± 1.5) (t = 5.1, d.f. = 273, p = 0.0001).

Pus cells in urine was significantly associated with higher PSA (6.4 ± 1.5) than those without pus cells in urine (4.7 ± 1.1) (t = 3.8, d.f.= 273, p = 0.0001).

Men showed bacteria in urine with a significant higher PSA (6.7 ± 1.7) than those without bacteria in urine (6.2 ± 1.4). There was a significant difference in PSA between the two groups (t = 2.6, d.f. = 273, p = 0.006).

Men with uric acid in urine showed higher PSA (6.6 ± 1.8) than those without uric acid in urine (6.2 ± 1.4). A significant difference was observed between the two groups (t = 2.1, d.f. = 273, p = 0.03).

Smokers showed a level of PSA (6.4 ± 1.6) and non-smokers showed (6.3 ± 1.6). No significant difference in PSA due smoking was noticed (t = 0.7, d.f.= 273, p = 0.4).

Table 1. PSA distribution among patients according to studied factors

Variable			**PSA**	
No.		**mean**	**SD**	
Age (year)				
	≤ 50	194	1.6	0.1
	> 50	81	1.4	0.1
	t = 3.1, d.f.= 273, p = 0.002			
Pain on ejaculation				
	Yes	225	6.6	1.5
	No	50	5.1	1.2
		t = 6.6, d.f.= 273, p = 0.0001		
Epithelial cells				
	Yes	7	9.2	1.7
	No	268	6.2	1.5
		t = 5.1, d.f.= 273, p = 0.0001		
Pus cells (urine)				
	++	262	6.4	1.5
	+	13	4.7	1.1
		t = 3.8, d.f.= 273, p = 0.0001		
Bacteria (urine)				
	++	98	6.7	1.7
	+	166	6.2	1.4
		t = 2.6, d.f.= 273, p = 0.006		
Uric acid				
	++	101	6.6	1.8
	+	174	6.2	1.4
		t = 2.1, d.f.= 273, p = 0.031		
Seminal fluid pus cells				
	++	262	6.4	1.5
	+	13	4.7	1.1
		t = 3.8, d.f.= 273, p = 0.0001		
Seminal fluid uric acid				
	++	275	6.3	1.6
History of smoking				
	Yes	72	6.4	1.6
	No	203	6.3	1.6
		t = 0.7, d.f.= 273, p = 0.4		

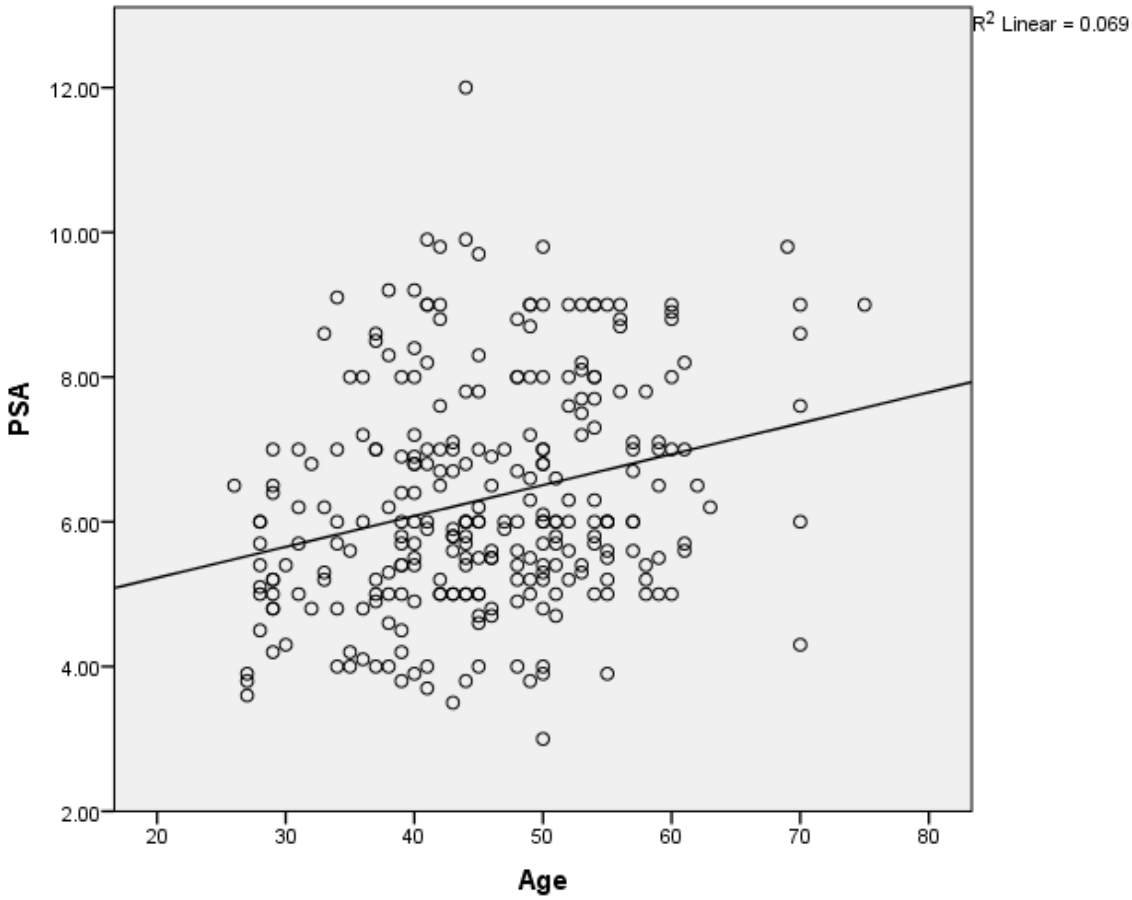

Fig.1Regression line showing the impact of age on PSA

Discussion

Prostatitis refers to a fascinating urologic diagnosis with spectrum of etiologies and varying natural histories. The term Chronic prostatitis (CP) / chronic pelvic pain syndrome (CPPS) were usually usedas (CP/CPPS).

PSA was not mentioned in diagnosis of CP/CPPS in the recent published data.[14] This report was done to comment on the role of PSA in diagnosis of the CP/CPPS.

This study revealed that PSA was significantly elevated in men with CD/CPPS. This finding is in agreement with that reported recently.[15] This finding is intriguing in the light of general practice in Iraq. However, recently a postulation that genetic variations in the promotor of gene of PSA might contribute to the individual variations in the serum PSA levels in men without prostatic diseases.[16]

The study revealed that PSA was significantly higher among those ≤ 50 years than among those > 50 years old (p=0.002). This finding is similar to that reported in Jordan.[17]

In the line with that in literature,[18] PSA was showing a positive significant association with age in the above normal levels. Recently, it was reported that ageing is usually characterized by a mild chronic pro-inflammatory state. This phenomenon is called inflammageing.[18] Therefore, the finding that PSA level was associated with age might be attributed to inflammatory process.

The study showed that markers of inflammation (epithelial cells, pus cells and bacteria cells) in urinalysis were associated significantly with elevated PSA level than that showing no inflammatory markers (p = 0.0001 for each marker) which could indicate that PSA is part of the pathophysiological inflammatory reaction.

Presence of pus cells in seminal fluid was significantly associated with higher PSA level than that in patients with no pus cells in their seminal fluid (p =

0.0001). Literature documented that chronic bacterial infection of prostate has been identifiable with virulent microorganism in prostatic secretion.[18] The finding shows the PSA as a reflection to the inflammatory state of prostate.

It was stated that painful ejaculation in men address prostatitis and.[19-21] This study showed that painful ejaculation was associated with elevated level of PSA which is it non malignant[24] than that not complaining of painful ejaculation (p = 0.0001). The finding might be suggesting that PSA reflects prostatitis again.

Conclusion

The diagnosis of CP / CPPS might be outside the traditional urologic practice and might consider PSA level too as an acute reactant protein. PSA increase in Chronic prostatitis indicates it's an inflammatory marker not only a tumor marker.

Limitation of detection:

Free PSA was not included.

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