8-Hydroxydeoxyquanosine as apotential tumer marker for diagnosis of prostate cancer and its association with Prostatic Specific Antigen

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Abstract

Background

Prostate cancer(PCa) is one of the malignancies that affects men and significantly contributes to increased mortality rates in men globally.8-Hydroxydeoxyquanosine(8OHdG) is one of the predominant forms of free radical-induced oxidative lesions, and has therefore been widely used as a biomarker for oxidative stress and carcinogenesis. Prostate Specific Antigen (PSA) is a tumor marker for prostate cancer.PSA is an enzyme produced by the prostate gland and is detected in the blood under normal conditions .Objective Evaluation of serum 8OHdG as tumer marker of prostate cancer and its relationship with PSA.Method This case- control study was carried out at Department of Biochemistry, College of Medicine, University of Baghdad and at Urology department, Ghazi Al-Hariri Hospital for surgical speciality during the period from March 2022 to May 2023. It included 120 men patients, 60 men patients who diagnosed to have prostate cancer ,and 60 men were apparently healthy men. Investigations included serum measurements of 8OHdG by using enzyme linked immunosorbent assay (ELISA) technique and also measurement of serum PSA. Results The results of the present study showed that there was a significant differences in 8OHdG in prostate cancer patients as compared with the control group. The results also showed that the S.PSA were higher in the patients group compared to the controls group with significant statistical difference. Conclusion According to the results obtained we can be concluded that higher levels of 8OHdG and PSA may be associated with risk of prostate cancer.

Keywords: *prostate cancer, 8-Hydroxydeoxyquanosine, Prostate Specific Antigen*

INTRODUCTION

Prostate Cancer (PCa) is the second most diagnosed solid cancer in adult males, surpassed only by non-melanoma skin cancer. It is the second leading cause of male cancer death worldwide.(1) In the United States alone, 10 billion dollars is spent annually treating prostate cancer.(2) This figure has been increasing over the past 20 years, proportionately to the increase in prostate cancer diagnosis, likely due to the aging population and improved detection utilizing serum prostate-specific antigen (PSA).(3)

PCa screening is a medical diagnostic practice based on prostate-specific antigen (PSA) testing. PSA is an enzyme produced by the prostate that degrades a gelatinous semen protein, thereby releasing motile sperm (4, 5). When prostate epithelial cells are destroyed by tumors, large amounts of PSA are released into the bloodstream (5). PSA levels are also elevated when the prostate is inflamed, infected, or benign prostate hyperplasia (6, 7). As a result, Elevated PSA is not enough to make a definitive diagnosis of prostate cancer (8). However, PSA can screen out potential PCa patients from the

population who need further diagnosis (9). PSA testing is commonly used in middle-aged and older men with lower urinary tract symptoms (LUTS) and in asymptomatic men at risk for PCa (10). Patients with elevated PSA often require prostate magnetic resonance imaging (MRI) and/or prostate biopsy for further diagnosis (11).

8-Hydroxy-deoxyguanosine (8-OHdG) is the most widely used oxidative stress marker that mismatches with adenine residues, leading to a G:C to T:A transversion mutation.(12) An elevated 8-OHdG content in DNA has been shown to promote malignant abilities. Recent studies have shown that 8-OHdG, as a ROS-related factor, plays a crucial role in the aggregate of malignant capacities.(13,14) 8-OHdG is removed from DNA primarily by the base excision repair using 8-OHdG DNA glycosylase (OGG1).(15)

Changes in the levels of 8-OHdG are associated with PCa onset and progression (16).

Increased 8-OHdG levels have been observed in target tissues of several animal cancer models and in human leukocytes from patients with various diseases associated with oxidative stress . Decreased 8-OHdG levels have also been reported in human leukocytes from patients receiving foods high in antioxidants (17).

MATERIALS AND METHODS

*This case- control study was carried out at Department of Biochemistry, College of Medicine, University of Baghdad and at Urology department, Ghazi Al-Hariri Hospital for surgical speciality during the period from March 2022 to May 2023. It included 120 men patients and divided into two groups. *Group 1: 60 patients who newly diagnosed to have primary prostate cancer (Pca) of different stage and grade depending on clinical and ultrasound examination and biopsy prostate, also by laboratory measurement such as prostatic specific Antigen (PSA) .*Group 2: 60 healthy men served as control group who have had no history or clinical evidence of prostate diseases.*

Inclusion criteria of men with Pca included patients with high PSA and patients with hard nodule in prostate

Exclusion criteria included prostatitis and recent urethral instrumentation. serum were tested along with patients and normal control for measurement of 8 Hydroxy-deoxyguanosine which measure by ELISA technique , ,and also for measurement of S.PSA.

RESULTS

The results of the present study showed that Table (1) reveals the difference in the mean and (±SD) values of PSA , 8-OHdG between the patient and control groups. Were the mean and (±SD) values of this parameter were higher in the patients group compere to the controls group with significant statistical difference (p< 0.001). as shown in (figure1),(figure 2)and (table1):

Table 1. Distribution of study sample according to (PAS, 8-OHdG,) means and (±SD) values

Parameters	Patients Mean (n=60)	Patients Std. Deviation	Controls (n=60)	Controls Std. Deviation	P- value
PSA (ng/ml)	24.620	26.795	2.099	0.955	< 0.001
8-OHdG (pg/ml)	1625.27	578.11	782.80	180.22	< 0.001

**p-value ≤ 0.05* *Independent t-test*

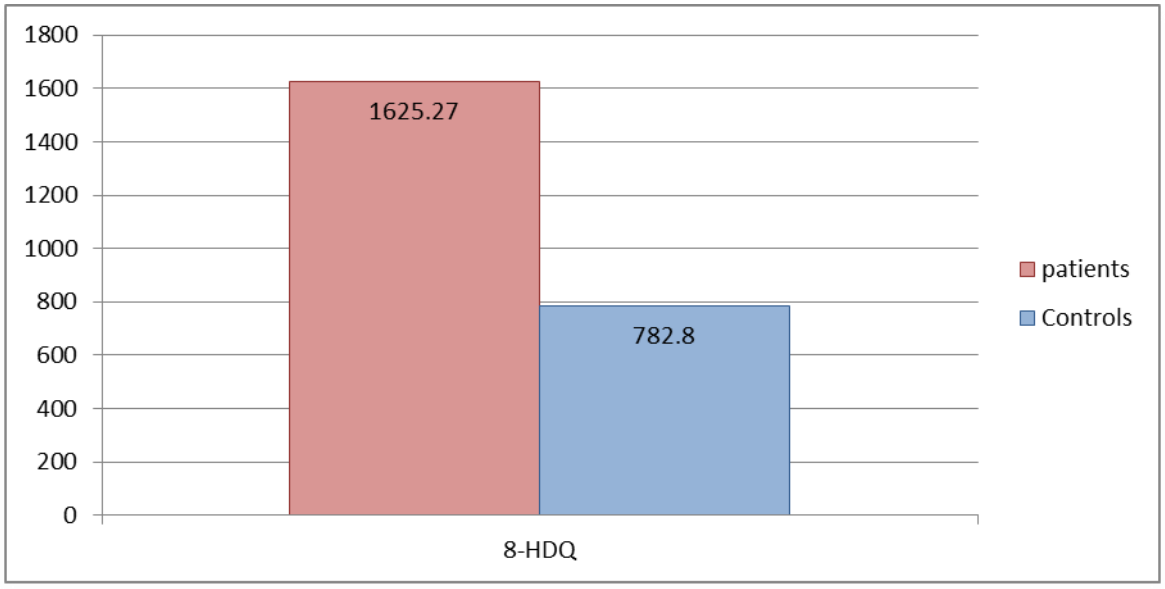

Figure 1. Distribution of study sample according to groups with 8-OHdG

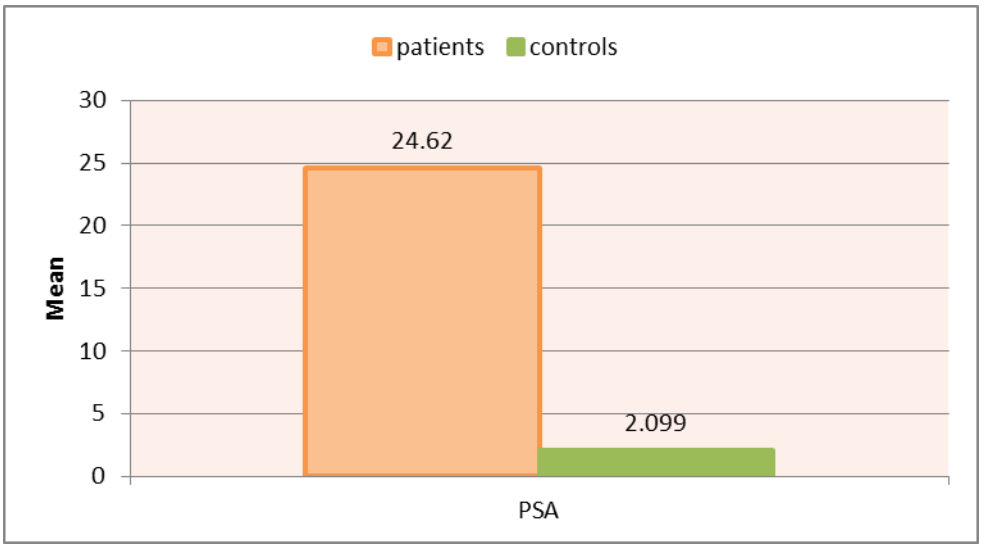

Figure 2. Distribution of study sample according to PSA mean.

Regarding the biopsy, ***Table (2)*** *reveals the highest positive results among the patients group which is (75%) for 45 patients while the highest negative results among the controls group which is (55%) for 33 healthy individuals. Both results were with significant statistical difference (p = 0.01).*

Table 2. Distribution and percentage of study groups with biopsy results.

Biopsy	*Patients*	*Controls*	*Total*	*P- Value*
Positive	*45*	*7*	*52*	
	75%	*11.7%*	*43.4%*	
Negative	*2*	*33*	*35*	
	3.3%	*55%*	*29.1%*	
False positive	*5*	*12*	*17*	*0.01**
	8.4%	*20.0%*	*28.4%*	
False negative	*8*	*8*	*8*	
	13.4 %	*13.4 %*	*20%*	

**p-value ≤ 0.05*

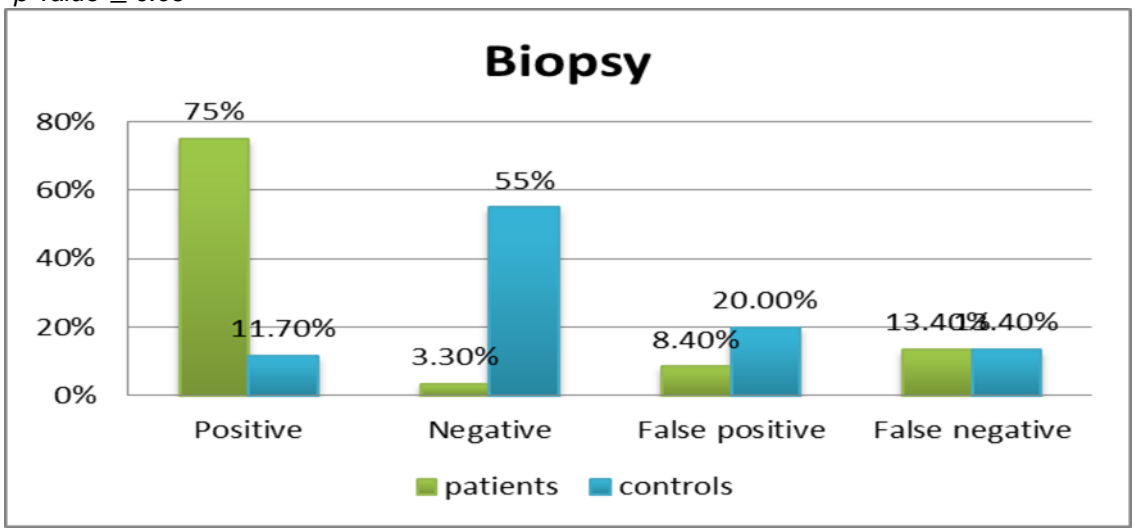

Figure 3. Distribution and percentage of study groups with biopsy.

The receiver operator characteristic (ROC) curve is a graphical representation of the relationship between clinical Specificity and Sensitivity for each cut-off for a test. Which demonstrated that the levels of serum 8-OHdG could distinguish disease patients from healthy controls. The optimum cutoff values for the diagnosis of disease patients, (AUC), specificity, and sensitivity for each biomarker are tabulated in ***Table (3)*** *and* ***Figure (4).***

Table 3. Sensitivity and Specificity, area under curve (AUC) and Cut-off value for 8-OHdG in prostate cancer patients.

Parameters	*Sensitivity*	*Specificity*	*AUC*	*Cut-off value*
S.8-OHdG	*86%*	*85%*	*0.905*	*1525.45*

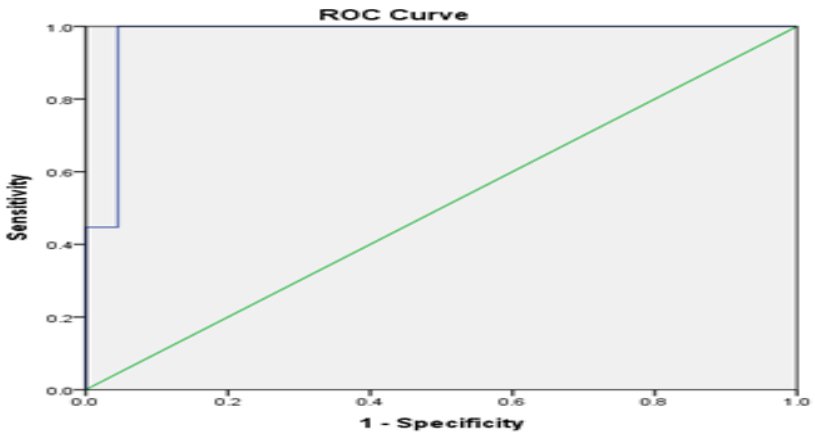

Figure 4. ROC curves for serum 8-OHdG

DISCUSSION

At present, prostate cancer (PCa) ranks as the second leading factor for male cancer fatalities exceeded only by lung cancer (18). By the year 2020, it is estimated that there will be around 1.4 million fresh instances and 375,000 fatalities globally. Furthermore, PCa stands as the prevailing form of cancer among males in over half of the nations across the globe (19). Over the past few years, one

*study reported that PCa screening can reduce the death rate of prostate cancer by 20% (**20**). Therefore, PSA screening has made great progress in the diagnosis of PCa because of its importance. Prostate-specific antigen (PSA) is avaluable tumor marker used for diagnosis and management of prostate cancer. (21). PSA testing is usually performed for one of two reasons: assessing a patient suffering from lower urinary tract symptoms (LUTS) (22) or screening for a patient who is asymptomatic but concerned about their risk of prostate cancer (23, 24). Patients with an elevated PSA are usually referred to a urologist for diagnostic testing, which may include magnetic resonance imaging (MRI) of the prostate and/or a prostate biopsy (25). Oxidative stress arises from a state of disequilibrium between the endogenous generation of oxidative stress, antioxidant defenses, and reactive oxygen species (26).*

Oxidative stress affects the development and progression of PCa (27), while accumulated DNA damage increases the risk of prostate cancer (28). 8-OHdG is largely used to measure oxidative DNA damage (29). As many as 42% of men aged 55–80 years exhibit prostate DNA damage, as assessed by 8-OHdG levels in tissue and urine samples (30)

Depending on our results, we can recognize that the levels of 8-OHdG were the highest among the prostate cancer patients group with a statistically significant association (p< 0.001). With a sensitivity of 86% and a specificity of 85% and these results are in agreement with the results of other studies such as Miyake et al showed that prostate cancer patients had significantly higher levels of urine 8-OHdG/Cre than those without cancer (31). Similar to the results regarding prostate cancer in the present study, Chiou et al. found an increase in 8-OHdG and its analogs in patients with prostate cancer when compared with that of healthy individuals.They concluded that the competitive ELISA for 8-OHdG and its analogs appears to be a simple method for quantifying the extent of oxidative stress and may have potential for identifying cancer risk (32).

In contrast to our study, there is a study conducted by Sayal et al who reported that there is no significant change was found in plasma 8-OHdG concentration in the prostate cancer and benign prostatic hyperplasia and control subjects(33) .

therefore the results their of study indicate that evaluation of the 8-OhdG in the plasma of prostate cancer and BPH patients may not be used as a biomarker to discriminate between these diseases.

The result of present study revealed that the levels of PSA of Pca patients were significantly higher compared to healthy controls with a statistically significant association (p< 0.001). these results confirmed the results of previous studies such as Al-Kafaji et al who reported that the mean serum PSA level was significantly higher in patients with PCa than in controls group (P<0.05) (34).

Similary to our study Al-Dahy et al found that the levels of PSA were higher in the PCa group than that of the controls group (35).

Richie et al found that higher PSA levels and increasing age were associated with a higher risk of prostate cancer (36) .

CONCLUSION

The present study showed that the levels of 8Hydroxydeoxyquanosine and PSA were significantly raised in prostate cancer patients and associated with risk of prostate cancer.

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