The Role of Serum Level of Indoleamine 2,3–dioxygenase 1 (IDO1) in Patients with Prostate Cancer

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Abstract

Prostate cancer or carcinoma of prostate is the development of cancer in the prostate a gland in the male reproductive system. This is a cross sectional, hospital based study. This study was carried out at the Oncology Center in Kirkuk City- Iraq from the 1st of February 2020 to the end of June 2020. A verbal consent was taken from each Men included in this study whether considered as a case or control. Sixty _ Seven men with prostatic cancer were screened to participate in the present study. Men with prostatic cancer attended to Oncology Center were enrolled in this study. The diagnosis of prostate cancer was made by the patient's file contain information about his state after take agreement from each Men included in this study, that is mean that the diagnosis of prostate cancer was according to discussion of the oncologist . Men ages were between 52 to 89 years, and they were from the center and periphery of Kirkuk City. Forty-Seven Men with prostatic cancer were considered as a study group, three Men did not meeting the inclusion criteria and 17 Men refuse to participate in this study due to the personal reasons. Forty apparently healthy Men without prostatic cancer and with negative family history. Each Men with benign tumor, benign prostatic hyperplasia or prostatitis diseases were excluded from this study. By using a sterile disposable syringe, 5 ml of venous blood sample was drawn from the vein of each Men at morning and was kept into disposable gel tube and allowed to clot for(2hour) at room temperature, then each sample was centrifuged at 6000 rpm for 10 minutes to obtain serum. The serum was aspirated by mechanical micropipette and transferred into clean Eppendorf tubes which labeled with number, then put this Eppendorf tubes in urine cups for safety and addition more information like name, date, number and stored at - 20 ^{0}C until the time of estimation. Serum of the patients and controls had assay for: Human IDO1 (Indoleamine 2,3-dioxygenase 1) and Human acid phosphatase/prostate by ELISA. The study demonstrated that, the rate of prostate cancer occurrence was increased with age and majority of patients were belonged to the age group (70-79 years). The study also showed non-significant difference between patients and control regarding their BMI mean (27.36±5.16 vs. 27.24±3.34kg\m²) respectively**.** The study showed that, serum level of IDO1 enzyme was elevated significantly (P<0.01) in prostate cancer patients (11.74±0.28 pg/ml) as compared with healthy control group (4.78±0.15 pg/ml). The study showed that, the highest mean of PAP enzyme was recorded in prostate cancer patients (0.111±0.075 pg/ml) as compared with healthy control group (0.069±0.024 pg/ml). The difference was highly significant (P<0.01), Table 3. The study showed positive correlation between PAP enzyme and stage of prostate cancer (r: 0.34). The study showed positive correlation between IDO1 level and stage of prostate cancer (r: 0.62). The study showed negative correlation between IDO1 level and PAP level in prostate cancer patients (r: -0.22).

Keywords: *Indoleamine 2,3–dioxygenase 1; Prostate cancer; PAP; Kirkuk.*

Introduction

Prostate cancer (PCa) or carcinoma of prostate is the development of cancer in the prostate a gland in the male reproductive system(1). PC is a significant public health burden and a major cause of morbidity and mortality among men worldwide(2). Prostatic intraepithelial neoplasia (PIN) is the possible precursor of prostatic carcinoma. It is responsible for the abnormal growth of epithelial cells that line the prostate gland. PCa is the most common cancer in men, with approximately one

in nine men developing the disease in their lifetime[3]. Informed decision making is recommended when it comes to screening among those 55 to 69 years old [4]. PCa is one of the heritable malignancies and (10 %–20 %) of PCa patients have a family history of cancer that is associated with elevated risk of lethal disease [5]. The IDO1 is an intracellular enzyme that catalyses the first, rate –limiting step in the kynurenine pathway of tryptophan catabolism [6]. The ability of IDO1 to modulate the immune response was first discovered in 1998, and most commonly studied in the context of immune regulation and as a host response to infection[7]. Is widely expressed in the body tissue and cell type either constitutively or upon stimulation by relevant inflammatory and immune stimuli. IDO1 has been described as a novel therapeutic immune target in recent years[8]. The aim of this study was to evaluate the levels of IDO1 (Indoleamine2,3 dioxygenase 1) in the sera of patients with prostate cancer in different stages.

Materials and Method

This is a cross sectional, hospital based study. This study was carried out at the Oncology Center in Kirkuk City- Iraq from the 1st of February 2020 to the end of June 2020. A verbal consent was taken from each Men included in this study whether considered as a case or control. Sixty _ Seven men with prostatic cancer were screened to participate in the present study. Men with prostatic cancer attended to Oncology Center were enrolled in this study. The diagnosis of prostate cancer was made by the patient's file contain information about his state after take agreement from each Men included in this study, that is mean that the diagnosis of prostate cancer was according to discussion of the oncologist . Men ages were between 52 to 89 years, and they were from the center and periphery of Kirkuk City. Forty-Seven Men with prostatic cancer were considered as a study group, three Men did not meeting the inclusion criteria and 17 Men refuse to participate in this study due to the personal reasons. Forty apparently healthy Men without prostatic cancer and with negative family history. Each Men with benign tumor, benign prostatic hyperplasia or prostatitis diseases were excluded from this study.

By using a sterile disposable syringe, 5 ml of venous blood sample was drawn from the vein of each Men at morning and was kept into disposable gel tube and allowed to clot for (2 hour) at room temperature, then each sample was centrifuged at 6000 rpm for 10 minutes to obtain serum. The serum was aspirated by mechanical micropipette and transferred into clean Eppendorf tubes which labeled with number, then put this Eppendorf tubes in urine cups for safety and addition more information like name, date, number and stored at - 20 ^{0}C until the time of estimation. Serum of the patients and controls had assay for: Human IDO1 (Indoleamine 2,3-dioxygenase 1) and Human acid phosphatase/ prostate by ELISA.

Statistical Analysis: Computerized statistically analysis was performed using Minitab version 23 statistic program. Comparison was carried out using Chi-square (X^2) and T-Test probability. The P value>0.05 was considered statistically significant, while for those which its P value was greater than 0.05 considered non-significant statistically.

Results

The study demonstrated that, the rate of prostate cancer occurrence was increased with age and majority of patients were belonged to the age group (70-79 years). The study also showed non-significant difference between patients and control regarding their BMI mean (27.36±5.16 vs. 27.24±3.34kg\m²) respectively**,** Table 1.

Table 1: Distribution of patients with prostate cancer and the control group according to age.

Age groups	Patients with prostate cancer		Control group		P. value
	No.	%	No.	%	
50-59	11	23.40	19	47.5	0.008
60-69	12	25.53	13	32.5	
70-79	18	38.30	8	20	
>79	6	12.77	0	0	
Total	47	100	40	100	
Mean±SD	68.32±8.89		60.81±7.81		0.001
BMI(kg\m²)	27.36±5.16		27.24±3.34		0.91

P<0.01: Highly Significant, P. value >0.05 : Non-significant (NS)

The study showed that, serum level of IDO1 enzyme was elevated significantly (P<0.01) in prostate cancer patients (11.74±0.28 pg/ml) as compared with healthy control group (4.78±0.15 pg/ml), Table 2.

Table 2: Relation of Indoleamine 2,3-dioxygenase 1 (IDO1) with prostate cancer.

IDO1 (ng/ml)	Patients with prostate cancer (n:47)	Control group (n:40)
Mean±SD	11.74±0.28	4.78±0.15
Minimum	5.34	5.39
Maximum	30.1	9.85
T. Test: 2.18 P. value: 0.001		

P<0.05: Significant

The study showed that, the highest mean of PAP enzyme was recorded in prostate cancer patients (0.111±0.075 pg/ml) as compared with healthy control group (0.069±0.024 pg/ml). The difference was highly significant (P<0.01), Table 3.

Table 3: Relation of Prostate acid phosphatase (PAP) with prostate cancer.

PAP enzyme (pg/ml)	Patients with prostate cancer (n:47)	Control group (n:40)
Mean±SD	0.111±0.075	0.069±0.024
Minimum	0.056	0.045
Maximum	0.33	0.15
T. Test: 3.62 P. value: 0.001		

The study showed positive correlation between PAP enzyme and stage of prostate cancer (r: 0.34), Figure 1.

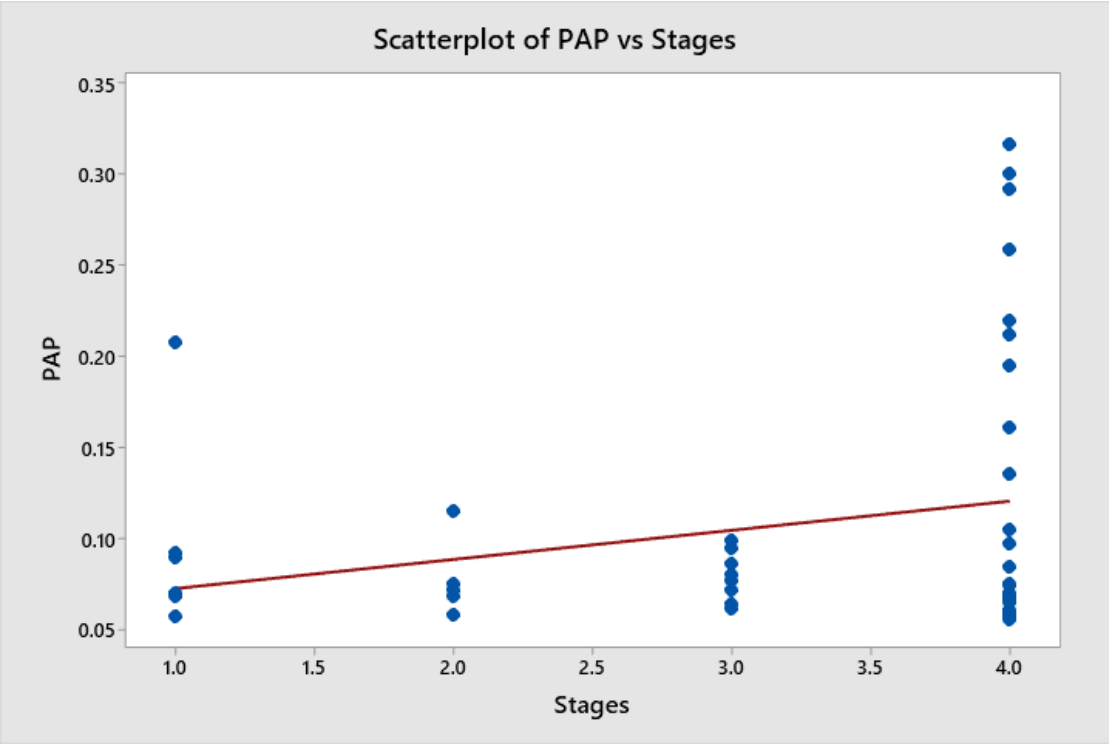

Figure 2: Correlation of PAP enzyme level with stage of prostate cancer

The study showed positive correlation between IDO1 level and stage of prostate cancer (r: 0.62), Figure 3.

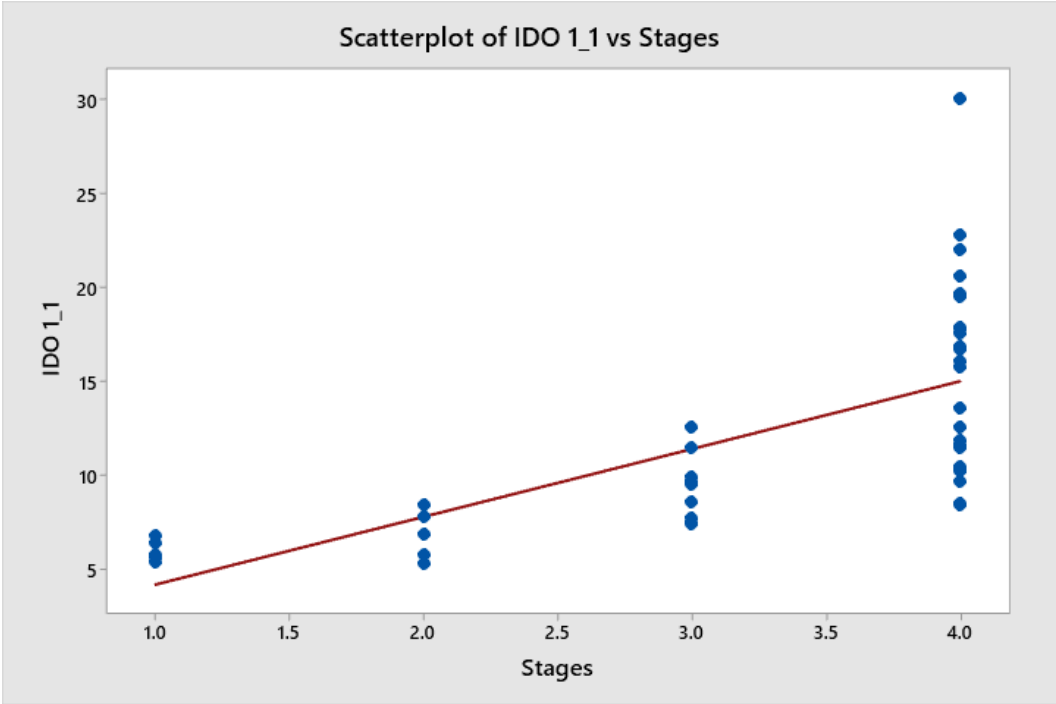

Figure 3: Correlation of IDO1 enzyme with stage of prostate cancer

The study showed negative correlation between IDO1 level and PAP level in prostate cancer patients (r: -0.22), Figure 4.

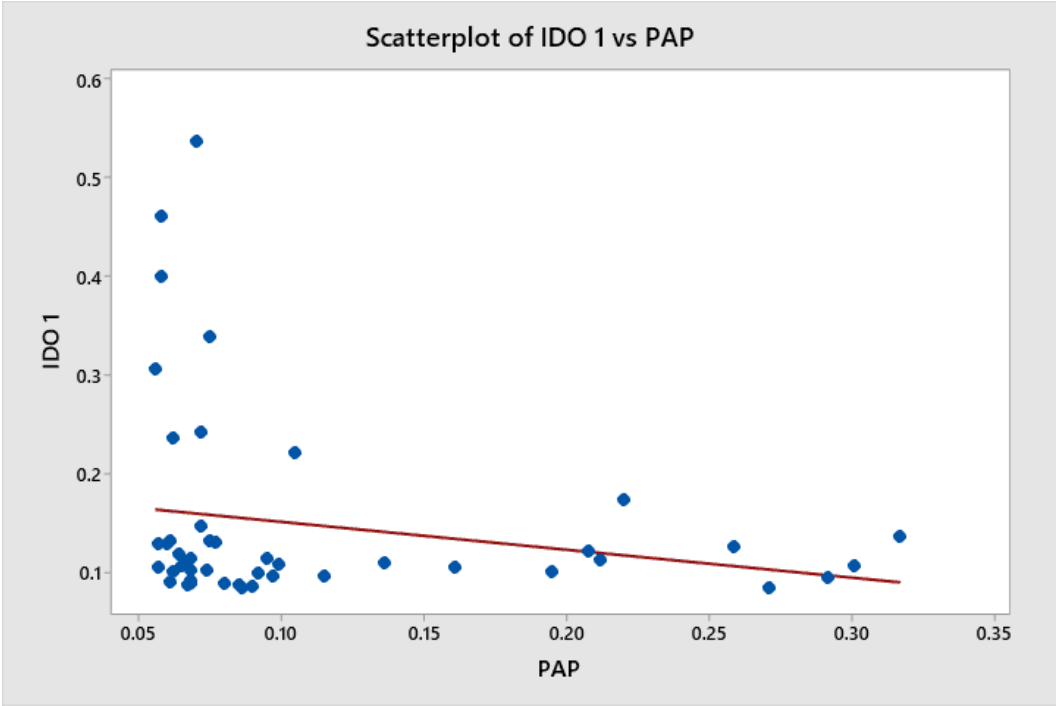

Figure 4: Correlation between IDO1 and PAP in prostate cancer patients

Discussion

The study demonstrated that, the rate of prostate cancer occurrence was increased with age and majority of patients were belonged to the age group (70-79 years). The study also showed non-significant difference between patients and control regarding their BMI mean

(27.36±5.16 vs. 27.24±3.34kg\m²) respectively**.** In agreement with these finding, Al-Tmemi [9] reported that, the number of prostate cancer patients was maximally recorded in age group (60-69) years (43.75%), and followed age group (≥ 70) years. this gives clear idea that there are a relationship between the disease and age, This confirmed by present study and by other previous studies of several authors; Ke Zhou *et al*[2], who found that in united states more than (65%) of all prostate cancer are diagnosed in age men over the age of 65 and the average age diagnosis of prostate cancer is 69 years, after that age, the chance of developing prostate cancer becomes more common than any other cancer in men. The result of the current study was in agreement with Ferreira *et al*[10] study, who found a significant elevation in IDO1 levels in prostate cancer patients as compared with healthy control group. Banzola *et al*[11] found that IDO1 was elevated significantly (P<0.01) in prostate cancer patients. Moreover, IDO1 was also expressed in tumor cells as well as in various non-tumor cells in the tumor microenvironment, such as fibroblasts, endothelial cells, eosinophils, dendritic cells, and macrophages [12,13]. In addition, the expression of IDO by tumor cells can result in a decrease in the number of tumor-infiltrating lymphocytes in various tumors [14,15].

The study also in agreement with that found by Junk Quiroz-Munoz *et al*[16] who found that increasing of serum PAP enzyme were positively correlated with stage of prostate cancer. Previous studies have shown that PAP can serve as a prostate cancer marker by proportionally increasing secretory PAP expression as prostate cancer progresses [17,18]. High levels of PAP expression were detected by Jia *et al*[19] in patients with prostate cancers at advanced stage, as determined by immunohistochemistry . Van Der Toom *et al*[20] also reported that, PAP enzyme levels has significantly higher correlation with prostate cancer progression . Banzola *et al*[11] study, showed that, when PAP concentration is correlated positively with the progression of prostate cancer. PAP appears to be particularly valuable in predicting distant failure in higher-risk patients for whom high levels of local control are achieved with aggressive initial local treatment. Many studies subsequently demonstrated that the expression of IDO1 in tumors was associated with patients' clinical outcome [21,22]. Several other studies indicated that, IDO1 predicted a poor clinical outcome in many tumors, such as ovarian adenocarcinomas, colorectal adenocarcinomas, and endometrial and esophageal cancer[23,24].

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Conflict of Interest: None to declare.

Ethical Clearance: All experimental protocols were approved under the Kirkuk Health Directorate and all experiments were carried out in accordance with approved guidelines.

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