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Hyper Alkaline Phosphatasemia in Patients with Prostatic Cancer, Central Sudan

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Article History: | Received: 12.06.2022 | Accepted: 25.07.2022 | Published: 29.07.2022 |

Abstract: Background: Aim: Estimation of alkaline phosphatase levels in prostate cancer patients attending the National Cancer Institute of Gezira University to determine the association between elevated alkaline phosphatase levels and metastases in prostatic cancer patients. **Methods:** This is a descriptive cross-sectional hospital-based study to estimate alkaline phosphatase enzyme levels in patients with prostatic cancer who attended National Cancer Institute, Gezira University's between September and December 2018. A structured questionnaire was developed and prescribed to 100 subjects, which included personal and medically important information. The level of alkaline phosphatase was determined, and a biopsy was performed, with the results interpreted by a histopathologist. SPSS-23 was used to analyze the data. **Results:** Patients with metastatic prostatic cancer accounted for 50% of the patients in the research, and 51% of them had an alkaline phosphatase level greater than (124U/L). Bone metastasis was the most prevalent site of metastasis, accounting for 50% of all cases, whereas liver metastasis accounted for 12% of all cases. Radiation prostatectomy plus radiotherapy was the most prevalent treatment for prostatic cancer, accounting for 86 % of cases. In comparison to individuals with non-metastatic prostate cancer, the majority of patients with metastatic prostatic cancer had an elevated alkaline phosphatase. **Conclusion:** Finally, we discovered that the level of alkaline phosphatase is significantly raised in patients with metastatic prostate cancer. Early detection and treatment will limit the impact of this serious condition.

Keywords: Alkaline Phosphatase, Prostatic Cancer, Gezira State, Sudan

Abrivations: NCI=National cancer institute; PSA=Prostate surface antigen; ALP=Alkaline phosphatase; DRE=Digital rectal examination.

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INTRODUCTION

In 2014, there were an estimated 233,000 new cases and 29,480 deaths (American Cancer Society, 2014). Prostate cancer is the fifth most common cancer-related death in men (6.6 percent of the total men deaths). The incidence of prostate cancer varies more than 25-fold around the world (David M, et al., 1974); the greatest rates are found in Australia/New Zealand

and Northern America (ASR 111.6 and 97.2 per 100,000, respectively), as well as Western and Northern Europe. Incidence rates are particularly high in some less developed locations, such as the Caribbean (79.8%), Southern Africa (61.8%), and South America (60.1%), but remain low in Asian populations, with estimated rates of 10.5 and 4.5 in Eastern and South-Central Asia, respectively (Baade P D *et al*, 2013).

Citation: Abderrhman Ahmed Mohamed Ismaeil *et al* (2022). Hyper Alkaline Phosphatasemia in Patients with Prostatic Cancer, Central Sudan. *SAR J Pathol Microbiol*, 3(4), 54-58.

A healthy human male prostate is traditionally described as being slightly larger than a walnut. In adult males, the typical prostate weighs about 11 grams on average, ranging between 7 and 16 grams. The prostate can be divided into two types: zones and lobes. It is surrounded by an integrated fibromuscular band rather than a capsule. It's encased in the pelvic floor muscles, which contract during the ejaculatory process (Hsing AW and Chokkalingam AP, 2006). Prostate cancer is detected using Prostate-Specific Antigen (PSA). Test results of 4 to 10 ng/mL are considered suspiciously abnormal. PSA levels of 4 ng/mL (mean 1.85 ng/mL total) were seen in both patients with prostatic adenocarcinoma (13.1%) and benign hyperplasia (10.1%). (86.7 percent). As a result, the total PSA cutoff value for screening was lowered to 0.2–2.1 ng/mL (free PSA to total PSA ratio of 11–20%). During the years 2008–2010, patients with no recent urinary tract infection (n = 1051) and ages 40–90 years old had a mean PSA of 1.48 ng/mL in the Central Laboratory Services of Soba University Hospital in Khartoum, Sudan. Prostate cancer detection rates were higher when DRE and PSA were used together than when PSA was used alone. After the introduction of Tran's rectal ultrasound, the detection of new instances of prostate cancer per year at the NCI-Gezira University increased considerably from 8.1 percent of all cancers in 2002 to 17.2 percent in 2007, as well as in metastasized cancer (Bashir M N *et al*, 2015).

Alkaline phosphatase is a homodimeric enzyme that catalyzes the hydrolysis of monoesters in phosphoric acid and can also catalyze a Tran's phosphorylation process with high phosphate acceptor concentrations. Mammalian alkaline phosphatase has a lower affinity, more alkaline pH optimum, and weaker heat stability, and is generally membrane bound and inhibited by l-amino acids and peptides via an uncompetitive mechanism. These properties change noticeably between mammalian alkaline phosphatase isozymes, indicating a variance in in vivo roles (Ferlay J *et al*, 2015). Alkaline phosphatase is found in many tissues, but is especially abundant in the liver, bone, bile duct, kidney, intestinal mucosa, and placenta. Skeletal and hepatic alkaline phosphatase isozymes predominate in serum. The majority of alkaline phosphatase in children comes from the skeleton (David M *et al*, 1974).

Early diagnosis of metastasis can be aided by establishing a link between alkaline phosphates and prostate cancer metastasis. Despite the fact that prostate cancer is the most common cancer among Sudanese men, little studies have been published on the disease's epidemiology and pathology. Age, history of cigarette and alcohol intake, and family history of the disease were the most prevalent possible risk factors for prostate cancer among patients referred to NCI, central Sudan, between 2006 and 2009. Farming was the most common profession risk factor (Askari F *et al*, 2014).

During the treatment of prostate cancer, it is critical to closely monitor non-metastatic patients in order to detect any early metastasis. There are a variety of investigations available to flow up the patients, the majority of which are imaging- based, such as a bone scan. The advantages of these investigations are that they are sensitive and specific detection, but the disadvantages are that they are often unaffordable and not always available in the Sudan context. Until now, finding a delicate and trustworthy investigation to flow up the patients has been a challenge.

MATERIALS & METHODS

Study Design and Area

A retrospective case control study which was conducted between September and December 2018 in national cancer institute- Gezira University, Wad Madani, Gezira state, Sudan.

Sample Size and Population

The patients were diagnosed with prostate cancer and were admitted to Gezira University's national cancer institute. A total of 100 patients with prostatic cancer were included in the study. The first 50 had non-metastatic prostate cancer, while the remaining 50 had metastatic prostate cancer. All patients with prostate cancer who visit the center will be included.

Data Collection Tool

A structural questionnaire covered the most personal data of the patient and other medically significant aspects, filled from the admission file, which was verified to ensure that it met the inclusion criteria. The alkaline phosphatase level was then determined, and a biopsy was obtained, with the results being analyzed by a histopathologist.

Data Analysis

The Data was computerized through the statistical package for social sciences (SPSS version 23).

Ethical Consideration

After the research committee of Gezira University's college of medicine, department of physiology, and the research commission of the Gezira state ministry of health, as well as the national cancer institute at Gezira University, gave their approval; the study was carried out and authorized. A formal consent form was signed by each participant.

RESULTS

Table 1 show that 69 % were between the ages of 70 and 89. Around Wad Madani, 76 % of the population resided in rural regions. Ninety-two percent were married, while 7 % were widowed. The participants in the study had a median educational level of 37 %, with the majority of them being in basic school. Only 34% were ignorant, while the rest completed school and university education. In terms of

symptoms, 33 % reported hematuria, 32 % back discomfort, 86 % urine retention, and % reported other symptoms (i.e. dysuria, nocturia and increased urinary

frequency). 86 % of the patients had PSA values more than 10 IU\L.

Table 1: Demographic Background

Variable	Characteristics	Frequency	Percent
Age\Yrs.	Less than 50	0	0
	50-69	30	30
	70-89	69	69
	90 or more	1	1
Residence	Rural	76	76
	Urban	24	24
Marital status	Married	92	92
	Single	1	1
	Divorced	0	0
	Widowed	7	7
Level of education	Primary	37	37
	Secondary	9	9
	University	20	20
	Uneducated	34	34
Symptom	Hematuria	33	67
	Urinary Retention	86	14
	Back pain	32	32
	Other presentation	44	44
PSA	<5	8	8
	5-10	6	6
	>10	86	86
	Total	100	100

PSA=Prostate surface antigen

Table 2 shows that 90% of them were diagnosed in 2016, while the remaining 9% and 1% were diagnosed in 2015 and 2017, respectively.

Table 2: Distribution of study sample according to with Prostatic cancer

Variable	Characteristics	Frequency	Percent
Time of diagnosis	2015	9	9.0
	2016	90	90.0
	2017	1	1.0

Bone metastasis affected 50% of those with metastasis, 2% of those with brain metastasis, and 12% of those with liver metastasis. Chemotherapy was given to 38% of patients, whereas radiotherapy was given to 96% of patients, and surgical excision was given to

94% of patients. According to the table above, 53 percent of patients used cigarettes, while only 47 percent did not. Table 3 demonstrates that 21% of patients drank alcohol, whereas the remaining 79% did not.

Table 3: Distribution of study sample according to study variables and Prostatic cancer

Variable	Characteristics	No	Yes
Distance metastasis	Bone	50(50.0%)	50 (50.0%)
	Brain	98 (98.0%)	2(2.0%)
	Liver	88(88.0%)	12(12.0%)
Distribution according to treatment	Chemotherapy	62(62.0%)	38(38.0%)
	Radiotherapy	4(4.0%)	96(96.0%)
	Surgical excision	6(6.0%)	94(94.0%)
Habits	Bad habits	47(47.0%)	53(53.0%)
	Tobacco use	47(47.7%)	53(53.0%)
	Alcohol use	79(70.0%)	21(21.0%)

The average ALP concentration was 144.7 IU/L. High alkaline phosphatase (> 124 IUL) was found in 51% of the participants, while normal alkaline

phosphatase was found in 49% (value below 124 IU\L). In the 50-69 age groups, 15% had elevated ALP levels,

and in the 70-89 age groups, 36% had raised ALP levels.

Table 4: The following table shows the estimated levels of ALP in different age groups

Characteristics	Frequency	50-69	70-89	90 or more	Mean of the overall ALP	Total
Not elevated	49(49.0%)	15%	33%	1%	144.7 IU\L	49%
Elevated	51(51.0%)	15%	36%	0%		51%
Total	100(100%)	30%	69%	1%		100%

IU\L=International Unit\Liter; ALP=Alkaline Phosphatase

DISCUSSION

Prostate cancer is a condition that affects elderly men, as seen by the participants' average age of 60 years. Almost six out of ten instances are discovered after the age of 65. It is uncommon before the age of 40, but the risk of prostate cancer increases dramatically beyond the age of 50, and was found to be positively associated with the risk of prostate cancer. At the time of diagnosis, the average age is nearly 66 years (American Cancer Society, 2015; Bashir MN *et al*, 2014). According to Howlader *et al*, 2014, between 2007 and 2011, approximately 0.6 % of prostate cancer cases were diagnosed in men aged 35 to 44, 9.7% in men aged 45 to 54, 32.7 % in men aged 55 to 64, 36.3 % in men aged 65 to 74, 16.8% in men aged 75 to 84, and 3.8 % in men aged 85 and up. When compared to those under the age of 55, those aged 55 and up had a nearly 17-fold increased risk of prostate cancer (Bashir M N *et al*, 2014).

Several studies have found family aggregation of prostate cancer risk, with a 2 to 3 fold greater risk of prostate cancer among males with a first-degree relative (father, son, brother) who has a positive history of prostate cancer, similar to our findings (Janet L *et al*, 2001; Nemesure *et al*, 2012 ; Bashir M N *et al*, 2014). In a meta-analysis based on 33 epidemiologic studies, (Seeger *et al*, 2003) discovered that males with affected brothers and fathers of prostate cancer had a nearly threefold increased risk of having prostate cancer. In this meta-analysis, males with affected brothers were found to be at higher risk than men with affected fathers. The reason for this disparity in risk is unknown. Furthermore, risk was increased with increasing number of affected first-degree relative (FDR) (Bashir M N *et al*, 2014).

The study showed that 21% of the patients had different bad habits and 53% included in tobacco smoking and 21% where alcoholic. These findings were in agreement with that of (hubcharek *et al*, 2010) who reported a significant increase in prostate cancer risk for heavy smokers. In contrast to our study current and past smokers had higher risk for prostate cancer, but the association was statistically significant only in case of past smokers (Tyagi *et al*, 2010). Furthermore, smoking is positively associated with prostate cancer mortality. Smokers have 14% more risk of dying from prostate cancer as compared to nonsmokers (Huncharek *et al*, 2010).

Patients from rural areas made up roughly 76 % of the patients in the current study. This could be related to their occupation as farmers, which increases the risk of prostatic cancer significantly. This is in line with a meta-analysis conducted by Ragin in 2012, which looked into the effects of farming, pesticides, and occupation on prostate cancer. 3978 men with prostate cancer were included in the trial, with 7393 serving as controls. Farmers were shown to have a four-fold higher incidence of prostate cancer than non-farmers. (Meyer *et al*, 2007) discovered that farmers who used pesticides had a nearly two-fold increased incidence of prostate cancer. Furthermore, farmers who were exposed to diesel engine emissions had a nearly six-fold increased risk of contracting the disease (Leitzmann M F *et al*, 2012).

The prevalence of prostate cancer among married men was found to be 92 % in this study, indicating that the chance of acquiring prostatic cancer rises with marriage. This is in line with a study published in 2002 by Dennis and Dawson 2002, who found a link between increasing sexual frequency and an increased risk of prostate cancer. Prostatitis history was found to be positively linked with prostate cancer risk (Hosseini *et al*, 2010). This could be explained by a number of studies that found a link between prostate cancer risk and a history of sexually transmitted diseases (gonorrhoea and syphilis). The frequency of sexual activity has been demonstrated to have a direct association with the development of prostate cancer in many studies (Dennis *et al*, 2002). In their study, (Pourmand *et al*, 2007) discovered that having two or more sexual encounters each week increased the risk of prostate cancer. Many prospective investigations, on the other hand, have found no substantial link between gonorrhoea or syphilis and prostate cancer (Huang *et al*, 2008; Sutcliffe *et al*, 2006).

In addition, we discovered that individuals with metastatic prostate cancer had a high alkaline phosphatase level of 51%, which agrees with a study done by Wei RJ in 2015, in which 83 prostate cancer patients were included, with 42 in the bone metastases group and 41 in the non-bone metastases group. The bone metastases group had the highest serum levels of ALP, followed by the non-bone metastases group, hyperplasia group, and finally the control group. Another study included healthy and benign controls as well as 62 confirmed instances of prostate cancer at various stages of development. When compared group I

to group III, the mean value of group III had extremely significant increased PSA levels (Gadre S G, 2000). High ALP levels can occur if the bile ducts are obstructed. Also, if there is active bone formation occurring (as in the case in Paget's disease of bone), untreated coeliac disease and was found in 60% of patients with untreated prostatic cancer and in only 6% of patients free of prostatic cancer (Jemal *et al*, 2011; Lange *et al*, 2012; David M *et al*, 1974).

CONCLUSION

In conclusion we identified that alkaline phosphatase level is generally elevated in patients with metastatic prostatic cancer. Early screening will reduce the burden of this decapitating health condition. Further researches should be done to decrease and improve the mortality and morbidity of prostatic cancer

RECOMMENDATIONS

Before deciding whether to be screened, men should have an opportunity to discuss the potential benefits and harms of screening with their clinician and to incorporate their values and preferences in the decision. Increased public awareness early detection and aggressive treatment at early diagnosis remain gold standard management for prostatic cancer.

DECLARATION

We declare that none of the work referred to in this research has been submitted in support of application for another degree or qualification at this or any other university or institution and it has been done in the department of physiology, faculty of medicine Gezira University

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