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STUDIES ON UREA, CREATININE, WHITE BLOOD CELL AND DIFFERENTIAL WHITE CELL COUNTS IN PROSTATE CANCER PATIENTS ON TREATMENT ATTENDING IMO STATE SPECIALIST HOSPITAL UMUGUMA, OWERRI, NIGERIA

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Abstract: Prostate cancer is the uncontrolled growth of cells in the prostate gland in males. It represents the second most common cancer in men and the fifth most common cause of cancer death in men. This study was aimed at evaluating the levels of some haematological parameters, creatinine and urea in patients with prostate cancer on a three month treatment. It was a cross-sectional study carried out from the month of June to August, 2023. All eligible subjects who filled the questionnaire and gave a written informed consent for the study were enrolled. The study population consisted of 30 male patients with prostate cancer who were on treatment, and an equivalent number of age-matched apparently healthy subjects who served as the controls. 7ml of venous blood sample was collected at the ante-cubital vein aseptically. 2ml was dispensed into ethylenediaminetetraacetic acid containers for WBC and differential white cell counts, while 5ml was dispensed into plain containers for urea and creatinine estimations. The EDTA and plain containers were properly labeled with the subjects' names, sample number and date of collection. The blood dispensed into the EDTA containers were stored in a refrigerator at 40C, while the serum was stored in a freezer at -200C prior to use. The procedure was carried out at the Specialist Hospital, Umuguma, Owerri. WBC and differential counts were determined using haematology autoanalyzer, urea was determined using the diacetyl monoxime method, while creatinine was determined using the alkaline picrate method. The results of the tests were analyzed using SPSS version 21. The mean values of WBC (8300.00±2419.03)cells/µl, Neutrophils (55.27±17.76)%, and Monocytes (11.87±4.38)% were significantly increased in prostate cancer patients when compared to controls (4943.33±1208.21)cells/µl, (40.10±7.04) and (4.38±3.19)% (p=0.000). There were no significant difference in the mean values of lymphocytes (44.80±10.93)% and eosinophils (2.03±1.75)% in prostate cancer patients when compared to controls (44.83±64.93)% and (2.10±2.12)% (p=0.998 and 0.895). The mean values of serum creatinine (1.63±0.79)mg/dl and urea (40.90±28.43)mg/dl were significantly increased in prostate cancer patients when compared to controls (19.43±6.60)mg/dl and (0.72±0.34)mg/dl (p=0.000). There was no significant difference in the mean values of WBC, neutrophils, lymphocytes, monocytes, eosinophils, urea and creatinine in prostate cancer patients when compared based on age (p=0.476, p=0.624, p=0.621, p=0.471, p=0.228, p=0.358 and p=0.265). There was a non- significant positive correlation of WBC with urea and creatinine in prostate cancer patients (r=0.15, p=0.435 and r=0.14, p=0.439). Prostate cancer is associated with significant increase in the mean values of urea and creatinine. There were also alterations in the levels of total white blood cell, neutrophils and monocytes in prostate cancer patients. Therefore haematological parameters, urea and creatinine should be included into the panel of test for screening of a prostate cancer patients.
Keywords: Urea; Creatinine; White blood cell; Differential white cell; Prostate cancer

1 INTRODUCTION

Prostate cancer (PCa) is the second most common cancer in men worldwide, with an estimated incidence of 1.1 million new cases in 2012 and the sixth most important cancer in the world, and its incidence in blacks has been on the increase in men of 50 years and above [1].

The prostate gland is a major secondary endocrine organ of males whose development and growth depends on androgen stimulation especially by dihydrotestosterone (DHT), an active metabolic product from the conversion of testosterone by steroid 5 "-reductase [2].

Prostate specific antigen (PSA) is a serine protease that is immunologically specific for prostate tissue as opined by Heller. The initiation, development, invasion, and metastasis of a tumor are always accompanied by inflammation and immune response, which have a complex interaction with the tumor microenvironment [1].

In developed countries, carcinoma of the prostate gland is more prevalent in the elderly male population compared with younger men. Around 15% of men diagnosed to have cancer of the prostate in the developed world when compared to only about 4% of men in emerging nations [3]. While, many men present with localized and potentially curable disease, a large number of deaths from prostate cancer is due to the development of metastatic disease. Therefore, more accurate prognosis and predictive markers should be applied for prostate cancer to guide therapy and monitor disease progress in individual patients [2].

Haematological parameters measures the variability in the and count of circulating blood cells. It is routinely reported to physicians in clinical practice as part of the automated complete blood count and is currently mainly used as an index in the differential diagnosis of anemia [4]. Recently, studies have demonstrated that haematological parameters might provide useful information for the prognosis of patients with cardiovascular diseases, heart failure, coronary artery diseases, and chronic heart disease. Although the underlying biological mechanisms remain understand. Haematological parameters have being recognized as a global marker of chronic inflammation and oxidative stress. Various studies have reported that cancer affects haematological parameters such as a reduction in mean haemoglobin (Hb), mean corpuscular volume (MCV), mean cell haemoglobin (MCH), and mean corpuscular haemoglobin concentration (MCHC) and an increase in red cell distribution width (RCDW) [5].

Creatinine is a waste product produced by muscles from the breakdown of a compound called creatine [6]. Creatinine is removed from the body by the kidneys, which filter almost all of it from the blood and release it into the urine.

Urea is major nitrogenous end product of protein and amino acid catabolism, produced by liver and distributed throughout intracellular and extracellular fluid. In kidneys urea is filtered out of blood by glomerulli and is partially being reabsorbed with water [7].

Conventionally used laboratory markers for the diagnosis of prostate disorders are acid phosphatase and PSA, a glycoprotein produced in the benign and malignant prostate cells. However, the latter has replaced the former with regard to sensitivity and specificity. It was earlier reported that serum creatinine and urea is associated with a high risk of prostate cancer, more so in advanced cases where the chances of survival were low [8].

2 MATERIALS AND METHODS

2.1 Study Area

The study was conducted at Imo Specialist Hospital Umuguma, Owerri, Imo state, Nigeria.

2.2 Study Design

A cross-sectional study was carried out from the month of June to August, 2023. All eligible subjects who filled the questionnaire and gave a written informed consent for the study period were enrolled. The study population consisted of 30 male patients with prostate cancer who were on treatment and an equivalent number of age-matched apparently healthy subjects who served as the controls. The procedure was carried out at the Specialist Hospital, Umuguma, Owerri. The results of the tests were compared with controls and analyzed using SPSS version 21.

7ml of venous blood sample was collected at the ante-cubital vein aseptically, 2ml was dispensed into ethylenediaminetetraacetic acid containers for WBC and differential white cell counts, while 5ml was dispensed into plain containers for urea and creatinine estimations. The EDTA and plain containers were properly labeled with the subject's name, sample number and date of collection. The blood dispensed into the EDTA container was stored in a refrigerator at 40C while the serum was stored in a freezer at -200C prior to use.

2.3 Ethical Consideration

The study was approved by the ethics committee of Imo State specialist Hospital, Umuguma, Owerri, and all eligible subjects who gave their written informed consent were enrolled for the study.

2.4 Laboratory Methods

The white blood cell (WBC) and differential white cell counts were performed using the haematology autoanalyzer. Urea estimation was done using the diacetly monoxime method, while creatinine was estimated using the alkaline picrate method.

2.5 Statistical Analysis

Statistical analysis was performed using software package for social sciences (SPSS), version 21. Mean, standard deviation, t-test and Pearson correlation were determined. The level of significance was set at $p < 0.05$.

3 RESULTS

The mean values of WBC (8300.00±2419.03)cells/µl, neutrophils (55.27±17.76)%, and monocytes (11.87±4.38)% was significantly increased in prostate cancer patients when compared to controls (4943.33±1208.21)cells/µl and (40.10±7.04) and (4.38±3.19)% (t=6.79, p=0.000; t=4.35, p=0.000; and t=9.0, p=0.000)
There were no significant differences in the mean values of lymphocytes (44.80±10.93)% and eosinophils (2.03±1.75)% in prostate cancer patients when compared to controls (44.83±64.93)% and (2.10±2.12)% (t=0.01, p=0.998 and t=0.13, 0.895).
The mean values of serum creatinine (1.63±0.79)mg/dl and urea (40.90±28.43)mg/dl were significantly increased in prostate cancer patients when compared to controls (19.43±6.60)mg/dl and (0.72±0.34)mg/dl (t=4.03, p=0.000 and t=5.78, p=0.000) (Table 1).

Table 1 Mean Values of WBC, Neutrophils, Lymphocytes, Monocytes, Eosinophils, Urea and Creatinine in Prostate Cancer Versus Controls

Parameter	Test	Control	t-value	p-value
WBC cells/µl	8300.00±2419.03	4943.33±1208.21	6.79	0.000
Neutrophils (%)	55.27±17.76	40.10±7.04	4.35	0.000
Lymphocytes (%)	44.80±10.93	44.83±64.93	0.01	0.998
Monocytes (%)	11.87±4.38	4.38±3.19	9.00	0.000
Eosinophils (%)	2.03±1.75	2.10±2.12	0.13	0.895
Urea (mg/dl)	40.90±28.43	19.43±6.60	4.03	0.000
Creatinine (mg/dl)	1.63±0.79	0.72±0.34	5.78	0.000

There were no significant differences in the mean values of WBC (4818.75±942.49) cells/µl, neutrophils (40.19±6.79)%, lymphocytes (46.44±7.19)%, monocytes (11.00±3.16)%, eosinophils (2.38±1.89)%, urea (33.31±12.72)mg/dl and creatinine (1.43±0.43)mg/dl in Prostate Cancer patients of age (50-60)years when compared to prostate cancer patients of age >60 years (4536.36±1074.49) cells/µl, (41.45±6.07)%,(45.09±6.36)%,(10.18±2.32)%, (10.18±2.32)%, (41.00±29.26)mg/dl and (1.71±0.86)mg/dl (t=0.72, p=0.476, t-0.49, p=0.624; t=0.73, p=0.621; t=0.73 p=0.471; t=1.24, p=0.228; t=0.94, p=0.358 and t=1.14, p=0.265) (Table 2).

Table 2 Comparison of the Mean Values of WBC, Neutrophils, Lymphocytes, Monocytes, Eosinophils, Urea and Creatinine in Prostate Cancer Patients Based on Age

Parameter	50-60	>60	t-value	p-value
WBC cells/µl	4818.75±942.49	4536.36±1074.49	0.72	0.476
Neutrophil (%)	40.19±6.79	41.45±6.07	0.49	0.624
Lymphocytes (%)	46.44±7.19	45.09±6.36	0.50	0.621
Monocytes (%)	11.00±3.16	10.18±2.32	0.73	0.471
Eosinophils (%)	2.38±1.89	3.27±1.79	1.24	0.228
Urea (mg/dl)	33.31±12.72	41.00±29.26	0.94	0.358
Creatinine (mg/dl)	1.43±0.43	1.71±0.86	1.14	0.265

There was a non - significant positive correlation of WBC with urea and creatinine, lymphocytes, eosinophils, in Prostate Cancer Patients (r=0.15, p=0.435, r=0.14, p=0.439; r=0.12, p=0.077 and r=0.34, p=0.112).
There was a significant positive correlation of WBC with neutrophils and monocytes (t=3.67, p=0.000 and t=2.76, p=0.026) (Table 3).

Table 3 Correlation of WBC with Differential White Cell Count, Urea and Creatinine in Prostate Cancer Patients

Variable	n	r	p-value
Urea	30	0.15	0.435
Creatinine	30	0.14	0.439
Neutrophils	30	3.67	0.000
Eosinophils	30	0.12	0.077
Lymphocytes	30	0.34	0.112
Monocytes	30	2.76	0.026

4 DISCUSSION

Prostate cancer is increasing at alarming rate especially with aging men in Nigeria and the world at large. Prostate cancer is the sixth most important cancer in the world, and its incidence in blacks has been on the increase in men of 50 years and above [9].
The current study revealed that the mean values of WBC, neutrophils and monocytes were significantly increased in prostate cancer patients when compared to controls. The result of the study is in consistent with the study carried out by Mansour et al., (2017) [10]. An increased number of WBC, neutrophils and monocytes occur abnormally as a result of an

infection, cancer, or toxic chemical [10]. There have been reports that inflammation is a cause of prostatic enlargement [11]. A possible explanation by Fukami et al., (2016) is that asymptomatic inflammation of the prostate may increase the WBC and the neutrophils count [12]. The mechanism at which inflammation of the prostate leads to an increase in white blood cells is not fully known.

There was no significant difference in the mean values of lymphocytes and eosinophils in prostate cancer patients when compared to controls. A report by Ogunbiyi, (2015) reported reduced lymphocytes in prostate cancer patients. They stated that the immune system is been compromised when a person gets prostate cancer [13]. This result agrees with previous study that prostate cancer may disrupt the body's immune and adaptive responses. Duzlu et al., (2018) and Grimm et al., (2016) also found a significant decrease in lymphocyte count in prostate cancer patients when compared to their respective controls [14-15]. Factors such as sample size and the treatment regimen might have influenced the result.

The mean value of urea was significantly increased in prostate cancer patients when compared to controls. Urea is a bio-product of protein metabolism and act a diagnostic parameter in ascertaining renal function. This result agrees with the study carried out by Abelev and Eraiser, (2015), who reported a high level of serum urea in prostate cancer patients when compared to controls [16]. They stated that the elevated levels of urea may also be due to the drugs used in the treatment of cancer prostate.

The mean value of serum creatinine was significantly increased in prostate cancer patient when compared to controls. Creatinine is a bio-product of creatine metabolism. Creatine is abundant in the muscles, raised level of serum creatinine is a clear indication of renal dysfunction and is therefore used as a marker in ascertaining renal function. Merseburger et al., (2017) agrees with the result of the current study [17]. They reported that the elevated levels of creatinine may also be due to the drugs used in the treatment of cancer prostate.

From the result of the current study, there was no significant difference in the mean values of WBC, neutrophils, lymphocytes, monocytes eosinophils, urea and creatinine in prostate cancer when compared based on age. This clearly indicates that age is not a predisposing factor. The result is in consistent with the study carried out by Merseburger et al., (2017) [17].

The present study reveals a non - significant positive correlation of WBC with urea and creatinine. Elevated levels of WBC can be frequently detected in patients with impaired kidney function due to an infection. The non-significant positive correlation may indicate that there is no relationship between WBC and renal dysfunction.

5 CONCLUSION

Prostate cancer is associated with significant increase in the mean values of urea, creatinine, WBC, neutrophils, and monocytes, but no significant effect on lymphocytes and eosinophils.

COMPETING INTERESTS

The authors have no relevant financial or non-financial interests to disclose.

REFERENCES

[1] Aligbe JU. Morphological characterization of prostate diseases in adult males, a retrospective survey from UBTH: A dissertation submitted to the National Postgraduate Medical College of Nigeria. ResearchGate, 2015, 43(9): 73-90.

[2] McArdle PA, Mir K, Almushatat AS, et al. Systemic inflammatory response, prostate- specific antigen and survival in patients with metastatic prostate cancer. Urology Journal, 2016, 77: 127–129.

[3] Hoffman RM, Gilliland FD, Eley JW, et al. Racial and ethnic differences in advanced-stage prostate cancer: the Prostate Cancer Outcomes Study. Journal of National Cancer Institute, 2018, 93(5): 388–395.

[4] Montagnana M, Cervellin G, Meschi T et al. The role of haematological indices in cardiovascular and thrombotic disorders. Clinical Chemistry and Laboratory Medicine, 2016, 50: 635-641.

[5] Kautz L, Nemeth E. Molecular liaisons between erythropoiesis and iron metabolism. Blood, 2014, 124(4): 479–482.

[6] Baxmann AC, Ahmed MS, Marques NC. Influence of muscle mass physical activity on serum urinary creatinine serum cystatin. Clinical Journal of American Nephrology, 2018, 23: 348–354.

[7] Corbett S. Urinary beta 2-microglobulin and N-acetyl-beta-D-glucosaminidase (NAG) as early markers of renal tubular dysfunction in sick neonates. Journal of Formos Medical Association, 2018, 90(2): 132–137

[8] Lalitha K, Suman G, Pruthvish S, et al. Estimation of time trends of incidence of prostate cancer-an Indian scenario. Asian Pacific Journal of Cancer Preview, 2016, 13(12): 6245-6250.

[9] Rodrigues A, George W, Padraig T, et al. Pre-treatment risk stratification of prostate cancer patients. Canadian Urological Association Journal, 2016, 6(2): 121-127.

[10] Mansour SA, Mossa AH, Heikal TM. Haematoxicity of a new natural insecticide Spinosad on male Albino rats. International Journal of Agricultural Biology, 2017, 9: 342-346.

[11] De Nunzio C, Kramer G, Marberger M, et al.; The controversial relationship between benign prostatic hyperplasia and prostate cancer: the role of inflammation. Eur Urol, 2011, 60: 106-117.
[12] Fukami A, Yamagishi S, Adachi H. High white blood cell count and low estimated glomerular filtration rate are independently associated with serum level of monocyte chemo-attractant pbrotein-1 in a general population. Clinical Cardiology, 2017, 34(3): 189-194.
[13] Ogunbiyi OJ. Impact of health system challenges on prostate cancer control: health care experiences in Nigeria. Infectious Agent Cancer, 2015, 12(3): 12-14.
[14] Düzlü M, Karamert R, Tutar H. Diagnostic role of neutrophil-lymphocyte ratio in oral cavity cancers. Journal of Clinical Practic, 2018, 21(1): 49-53.
[15] Feng Li, Haio Hu, Shuo Gu, et al. Platelet to lymphocyte ratio plays an important role in prostate cancers diagnosis and prognosis. International Journal of Clinical and Experimental Medicine, 2015, 8(7): 11746 – 117551.
[16] Abelev GI, Eraiser TL. Cellular aspects of alpha-fetoprotein expression in tumors. Seminar Cancer Biology, 2015, 9: 95-107.
[17] Merseburger AS, Connelly RR, Sun L, et al. Use of serum creatinine to predict pathologic stage and recurrence among radical prostatectomy patients. Urology, 2017, 58:729–34.