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Anaemia in Nigerian Men with Prostate Cancer

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Abstract

Background: *Prostate cancer causes significant morbidity and mortality among African men. Anaemia is a known association of cancer patients.*

Aim: *To determine the prevalence and risk factors for anaemia in prostate cancer (CaP) patients in Nigeria.*

Method: *A prospective study of prostate cancer patients and matched healthy controls, clinical data were obtained and samples were taken for Haemoglobin estimation. Data analysed using EPI Info, version 6.0 .*

Result: *A total of 128 men were recruited for the study, 88 men with histologically proven prostate cancer and 40 otherwise healthy male controls. The mean haemoglobin for the cancer patients' population was 10.79 ± 2.20g/dl and 13.59± 2.02g/dl in controls (p=0.001). Thirty four patients (38.64%) had anaemia.*
There was a statistically significant reduction in the haemoglobin levels of the patients with metastasis, compared with those with localized disease, (p=0.001). Increased number of co-morbidities in the patients significantly affected the haemoglobin level (p=0.001). A significant negative linear correlation was found between the haemoglobin and performance status of the cases using Pearson's 2-tailed correlation (r = -0.427, p= 0.001). There was also a negative linear correlation between the haemoglobin level at time of entry and the PSA level at first presentation (r = – 0.404, p= 0.001). Haemoglobin was significantly lower in hospitalized patients (p=0.001) and those with castration resistant prostate cancer (CRCP) who were on Docetaxel (p=0.01].

Conclusion: *A significant proportion of CaP patients in this study were anaemic. Anaemia was worse in patient with other co-morbidities, castration-resistant CaP and metastatic disease. It is necessary to investigate for, prevent and treat causes of anaemia in CaP.*

Keywords: *Anaemia, prostate cancer, androgen-deprivation therapy.*

I. Introduction

Anaemia is a common complication of malignancies and the mechanism of its occurrence in cancer differs with the biology of the malignancy and modalities of treatment used to control the disease. Prostate cancer is the commonest hormone dependent malignancy in men and the hormones that drive its growth or progression, such as androgens stimulate haemopoiesis by increasing erythropoietin release amongst other mechanisms. Erythropoietin is the central hormone in erythropoiesis.

Men with prostate cancer have several episodes of haematuria in the course of the disease, leading to gradual depletion of iron from the system. Androgen Deprivation Therapy (ADT), poor nutrition and a chronic inflammatory state also play an important role in anaemia in this group of patients [1]. Advanced disease may have a greater risk of developing anaemia. Many patients in developing countries present to hospital with advances stages of the disease and so may have a high risk of developing anaemia. Advanced disease can also be accompanied with renal complications which will further increase the risk of anaemia.

The use of surgical and/or pharmacological (ADT) is the cornerstone for the treatment of advanced prostate cancer today. This is also associated with the exacerbation of anaemia by indirectly inhibiting erythropoiesis [2].

Anaemia is a well-established, independent prognostic marker of poor outcome in men with prostate cancer, increasing the relative risk of death by 47% (21%–78%) [3] thus the need for its evaluation in this population in Nigeria. Previous studies in Nigeria have shown that anaemia is present in 40 – 69.8% of prostate cancer patients [4][5][6]; however the risk factors for anaemia have not been documented. This study aims to determine the prevalence of anaemia in prostate cancer patients in the study population and also delineate possible risk factors associated with it.

II. Subjects And Methods

The study was carried out in the University of Port Harcourt Teaching Hospital, between February and July 2013. Written consent was obtained from patients. Patients with histologically confirmed CaP within the study period were recruited. Data obtained with the aid of a proforma included; time of diagnosis, duration of symptoms, stage of disease, the modality of treatment received, and their ECOG performance status. Three mililiters of venous blood was drawn into plasma vacutainer bottles (Sarstedt monovette®) containing potassium EDTA-K by sterile, atraumatic venipuncture at the study entry. The full blood count and red cell indices was done for all the samples within 30 minutes of collection using Sysmex KX-21^{TM} Hematoanalyzer, a 3-part auto analyzer and the results were documented. Statistical analysis was done by EPI info version 6.04 and results presented in tables.

III. Results

A total of 128 men were recruited for the study, 88 men with histologically proven prostate cancer and 40 otherwise healthy male controls. The mean age of the patients was 64.66 ± 8.89 years. The mean duration of symptoms of the disease before the patients presented to the hospital for medical care was 7.94 ± 18.04 months, 22(25%) of the cases entered this study within 3 months of diagnosis. 26 (29.5%) had metastatic disease at entry. The commonest presenting complaints were symptoms of lower urinary tract obstruction 71(80.7%), low back pain in 9 (10.2%), haematuria in 8(9.1%), inability to walk in 5 (5.68%). Fifty nine (67.1%) of the patients had other medical co-morbidities, hypertension was reported in 47(52.2%), diabetes in 20 (22%) and chronic kidney disease in 4(4.4%) of the cases.

Seventy six (86.3%) patients had received different forms of treatment such as radical prostatectomy, Bilateral Subcapsular Orchidectomy and pharmacological ADT, 12 (13.6%) were treatment naïve at study entry. See Table 1. The mean haemoglobin for the cancer patients' population was 10.79 ± 2.20g/dl compared to controls 13.59 ± 2.02g/dl (p=0.001). Thirty four patients (38.64%) had anaemia with haemoglobin levels less than 10g/dl (mean 8.52± 1.16g/dl).

There was a statistically significant reduction in the haemoglobin levels of the patients with metastasis, compared with those with localized disease, (p=0.001). Increased number of co-morbidities in the patients significantly affected the haemoglobin level (p=0.001). Table 2.

In this study, a significant coefficient of correlation was found between the haemoglobin and performance status of the cases using Pearson's 2-tailed correlation (r = -0.427, p= 0.001); this correlation was negatively linear. There was also a negative linear correlation between the haemoglobin level at time of entry and the PSA level at first presentation (r = – 0.404, p= 0.001). Haemoglobin was significantly lower in hospitalized patients (p=0.001) and those with ADT-resistant CaP who were on Docetaxel; (p=0.01).

There was no significant statistical difference between the red cell indices of the patients and the controls; they were all within normal ranges. Table 3.

Table 1: Characteristics of the Prostate Cancer patients

Variables	**Case, n = 88**
AGE	64.66 ± 8.89
DURATION OF ILLNESS (MONTHS)	7.94 ± 18.04
PERFORMANCE STATUS (ECOG) n (%)	
0 – 1	52 (59.09)
2 – 4	36 (40.91)
CLASSIFICATION OF TUMOR n (%)	
Localized	62 (70.5)
Metastatic	26 (29.5)
NUMBER OF CO-MORBIDITIES - n (%)	1.40 ± 0.73
0	29 (33.0)
1	35 (39.8)
2	19 (21.6)
3	3 (3.4)
4	2 (2.3)
PAST MEDICAL HISTORY - n (%)	
Hypertension	47 (52.2)
Diabetes	20 (22.2)
HBSS	1 (1.1)
Lipidosis	8 (8.9)
CCF	1 (1.1)
CKD	4 (4.4)
CVD	4 (4.4)
Other malignancies	4 (4.4)
TREATMENT MODALITIES USED, n (%) (Surgery –Radical Prostatectomy, orchidectomy)	
Surgery only	3 (3.4)
Surgery and hormone only	18 (20.45)
Surgery, Chemotherapy, Hormone	9 (10.2)
Hormone and chemotherapy only	0 (0.0)
Hormone only	46 (52.3)
Treatment Naïve	12 (13.6)
PSA ng/dl	65.95 ± 49.04

HBSS- Haemoglobin SS, CCF – congestive cardiac failure, CKD – Chronic Kidney Disease, CVD – Cardiovascular Disease.

Table 2: Effect of Age, Stage, co-morbidity, Gleason's score, Hospitalization and chemotherapy on Haemoglobin level.

	Mean Haemoglobin (g/dl)
AGE CATEGORY	
≤ 45 (n=4)	8.53 ± 2.45
46 – 55 (n=9)	12.21 ± 1.55
56 – 65 (n=33)	11.33 ± 2.07
66 – 75 (n=36)	10.34 ± 2.30
>75 (n=6)	9.58 ± 0.47
ANOVA	3.70*
STAGE	
Metastasis(n=26)	9.10 ± 1.73
Localized(n=62)	11.52 ± 1.98
Student-T test	5.29*
Co-morbidities	
0 (n=29)	8.80 ± 1.09
1 (n=35)	10.70 ± 2.15
2 (n=19)	11.69 ± 2.03
3 (n=3)	7.38 ± 1.24
ANOVA	6.25*
GLEASON'S	
Unspecified (n=35)	10.61 ± 2.49
2 – 6 (n=15)	11.03 ± 1.70
7 (n=10)	10.62 ± 1.85
8 – 10 (n=28)	11.00 ± 2.21
ANOVA	0.22
Hospitalized	
Yes (n=36)	9.73± 2.24
No (n=52)	11.57± 1.84
Student T-Test	4.11
p-value	0.001*
Chemotherapy	
Yes (n=11)	9.16± 1.71
No (n=66)	11.02±2.18
Student T-Test	2.58
p-value	0.01*

*Significant p-value

Table 3: Full Blood Count of prostate cancer patients and healthy controls

	Case, N = 88	**Control = 40**	**P-value**
Haemoglobin	10.79 ± 2.20	13.59 ± 2.02	0.001*
PCV	35.36 ± 9.84	40.43 ± 3.60	0.02*
WBC	7.07 ± 4.64	5.57 ± 1.26	0.05*
Platelet	243.14 ± 150.85	226.80 ± 53.83	0.508
RBCC	4.12 ± 0.68	5.08 ± 0.47	0.02*
MCV	81.28 ± 6.59	79.61 ± 4.61	0.152
MCH	26.11 ± 3.08	26.20 ± 2.15	0.861
MCHC	32.31 ± 4.22	32.65 ± 1.96	0.629

PCV – Packed Cell Volume, WBC – Total Whit Cell Count, RBCC – Red Cell Count, MCV – Mean corpuscular volume, MCH – mean corpuscular haemoglobin, MCHC- Mean corpuscular haemoglobin concentration

IV. Discussion

The most common cancer among African-American men in the past few years is prostate cancer. It is also now the second most common cause of cancer death in the Western world [7]. The incidence of prostate cancer in Nigeria is unknown, but hospital prevalence has been stated to be 114-127/100,000 [8].

In our study, the mean duration of symptoms before presentation was 7.94 ± 18.04 months (range of 1 – 36 months). The reasons for late presentation include poverty, ignorance and superstition [7]. This delay may contribute to the metastasis of the disease before it is diagnosed. Other studies in Nigeria have shown that many patients present late [5][9][10]and this may contribute to poor prognosis.

Anaemia in prostate cancer is associated with advanced disease and the modality of treatment. ADT is the mainstay of advanced CaP treatment today and there are many forms of ADT. In a study by Asbell et al 75% patients on

combined androgen blockade for up to two months were anaemic [11]. All forms of ADT are known to cause progressive reduction in haemoglobin levels of patients.

In this study the haemoglobin of the cancer patients was significantly lower than the controls (p=0.001). This suggests that anaemia is more common in cancer patients. 34 (38.64%) patients had anaemia with Hb <10g/dl and 5(5.68%) had severe anaemia with Hb <7g/dl. The red cell indices for the cases and controls were comparable and within normal ranges. Other studies in Nigeria have confirmed this observation [4][5][6]. This could well be due to late presentation and advanced disease.

Anaemia in CaP patients has been reported to be normochromic normocytic in nature [12] and usually mild but may have clinical consequences in a minority of patients [7], especially those on combined androgen blocked, metastatic disease and those on ADT for a long time.

In this study patients with metastatic disease had significantly lower haemoglobin levels (p=0.001). Approximately 30% of patients with metastasis to the bone have anaemia at diagnosis [1]; prostatic Cancer rapidly metastases to the bone marrow and may have influence on erythropoiesis. The production of inflammatory cytokines by prostate cancer cells may also cause a decrease in erythropoietin production, leading to the anemia of chronic disease [13]. This myelosuppressive effect on red blood cell supply is believed to be mediated by moieties such as integrins, collagens, laminin, and other bone-derived proteins [3]. Prostate cancer rapidly metastases to the bone marrow and some patients may present with metastatic disease at diagnosis. In a study by Shamdas et al. 28.6% of men with metastatic prostate cancer had leucoerythroblastic anaemia [14]. In our study, 26 (29.5%) of patients had advanced disease, see Table 1.

Anaemia has significant impact on the quality of life of cancer patients. In this study, older patients were more likely to be hospitalized, they had significantly poor performance status(ECOG 3-4) and significantly lower haemoglobin(p = 0.01). Low haemoglobin levels are strongly associated with disease-related fatigue and reduced quality of life, anaemia also correlates with poor clinical outcome in cancer patients [6].

Anaemia may lead to therapy resistance either directly or by association. Anaemia- related tumor hypoxia may contribute to treatment resistance. Tumor hypoxia has been implicated in prostate cancer resistance to apoptosis [15]. The baseline haemoglobin level of patients should be determined before commencement of ADT and checked periodically. Other possible causes of anaemia such as Malaria, helminthiasis, poor nutrition and avitaminosis can be treated in this group of patients.

Patients who are found to have significant anaemia should be treated. Blood transfusion may be the most useful form of treatment in those with metastatic disease with reduced bone marrow reserves. Erythropoietin stimulating agents (ESA) may be used, but the benefits must be weighed against the risk of its use in cancer patients. Pharmacotherapy with erythropoietin or other ESAs has been demonstrated to improve ADT-associated anemia [16].

V. Conclusion

There was high prevalence of anaemia in Nigerian patients with prostate cancer. The risk factors for anaemia in the study group were advanced disease, ADT, chemotherapy and presence of co-morbidities. Anaemia negatively impacted on the QOL of our patients. In view of the impact of anaemia on the QOL and treatment outcome of patients with CaP, it is necessary to investigate for, prevent and treat causes of anaemia in CaP patients in our population.

Additional studies will be necessary in this population to determine the efficacy of prevention and treatment modalities of anaemia in prostate cancer patients in this population.

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