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Anaemia prevalence and factors associated with haemoglobin change following radiotherapy in individuals with cancers at the Ocean Road Cancer Institute in Tanzania

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Abstract
Background: Despite the fact that anaemia is common worldwide, limited studies have been done in most developing countries to estimate its prevalence and factors associated with haemoglobin change in patients with cancers receiving radiotherapy.
Methods: This was a descriptive cross-sectional study conducted at the Ocean Road Cancer Institute in Dar es salaam, Tanzania. All individuals with cancers who were admitted in the wards for radiation treatment from August to December 2013 were included. Information on social-clinical characteristics, cancer type and associated factors as well as haemoglobin level before and after radiation were obtained. The prevalence of anaemia was determined as a proportion and linear regression was used to determine factors associated with haemoglobin change.
Results: A total of 230 study subjects were available for analysis, of whom 82% were females. The overall mean age was 50±14 years. Most of the subjects (44%) were residing in the coastal regions, 50% had never attended school and 77% had no formal employment. The overall prevalence of anaemia was 77% before and 82% after radiotherapy. Multivariate linear regression analysis revealed that history of blood transfusion (beta-coefficient= 1.193; p=0.004) was the only factor associated with absolute change in haemoglobin.
Conclusion: The prevalence of anaemia was high, regardless of the cancer type. Blood transfusion appeared to have a positive change in haemoglobin following radiotherapy. Awareness should be increased to provide early detection of the condition with appropriate corrective measures.

Keywords: cancer, anaemia, haemoglobin, radiotherapy, Tanzania

Introduction

Anaemia is a common and significant public health problem worldwide and its magnitude has been extensively studied in developed countries. It has been identified in 9% to 90% of patients who have been diagnosed to have cancer, depending on the type of cancer (Balducci, 2003; Knight *et al.,* 2004). In Sub-Saharan Africa (SSA), the burden of anaemia in this unique population is less well known. Anaemia results in poorer survival and slow local tumour regression (Obralić *et al.,* 1990) The most serious complication of anaemia arise from tissue hypoxia which is associated with poor treatment outcome after radiotherapy (Glaspy & Cavill, 1999)

Association between anaemia and radiotherapy in patients with cancers has been well established in developed countries (Harrison *et al*., 2000, 2002; Serkies *et al*., 2006). In a series of studies, Harrison *et al.* (2000, 2002) found the prevalence of anaemia in patients with cancers to be 9-55% before radiotherapy and 57-82% after radiotherapy. Awareness of this burden in developed countries has helped to reduce the incidence and treatment burden in their settings, resulting into significantly low morbidity and mortality related to cancer (Harrison et al., 2000; Shasha & Harrison, 2001; Knight *et al.*, 2004). Limited statistics of anaemia compounded with few medical facilities might result in poor management and outcome of these patients in Tanzania.

Factors associated with negative or positive haemoglobin changes following radiotherapy, are not clearly known, a better understanding of which might draw attention to the public health authorities on the need to re-evaluate current strategies to control anaemia by making sure that the contributing factors are identified and addressed properly. Thus the current study aimed to

determine the prevalence of anaemia and factors associated with haemoglobin change following radiotherapy in individuals with cancers at Ocean Road Cancer Institute in Tanzania.

Materials and Methods

Study design and setting

This was a descriptive cross sectional study of individuals with cancers who were admitted at Ocean Road Cancer Institute (ORCI) for radiation therapy from August to December 2013. Ocean Road Cancer Institute is the only health institution for cancer treatment in Tanzania in Dar es Salaam. It offers laboratory services, diagnostic imaging, chemotherapy, radiotherapy and palliative care services. The institute has a total of 257 beds, and approximately 30 patients are admitted per day.

Data collection

All consecutive patients aged ≥18 years, diagnosed with cancer and admitted for radiotherapy were included in this study. Those who did not provide consent for participation into the study were excluded. Patient's demographic data (age sex, residence, education and occupation), medical history on when the disease was diagnosed, full blood picture results, radiation history on the dose of radiation received, history of chemotherapy, blood transfusion, and use of haematinic during radiation therapy were obtained from hospital medical records. Residence was grouped into zones: Coastal Zone (Tanga, Morogoro, Dar es Salaam, and Zanzibar); Northern Highlands (Arusha and Kilimanjaro); Lake Zone (Tabora, Kigoma, Shinyanga, Kagera, Mwanza and Mara); Central Zone (Dodoma and Singida); Southern Zone (Iringa, Mbeya, Rukwa, Lindi, Mtwara and Ruvuma). This information was recorded in the checklist prepared and later analysed.

Blood sample analysis

Blood samples were used to generate full blood count measures (including haemoglobin) from each admitted patient. Venous blood sample was obtained in a closed blood collection system (Monovette) with EDTA, and later processed at the central laboratory of OCRI. Full blood pictures were obtained by means of a haematology analyser (Beckman Coulter ACT5 DIFF) and were collected within one week, before and after radiotherapy.

Data analysis

Data was entered into a computer and cleared using SPSS package software version 20. The prevalence of anaemia before and after radiation was determined as a percentage among all admitted cancer patients whose haemoglobin level were below the WHO cut-offs based on sex. Anaemia being the primary outcome was defined by WHO as reduced concentration of haemoglobin in blood below 13.0 g/ dl for males and 12 g/dl for females. The secondary outcome was haemoglobin change (in g/dl) calculated as a difference between haemoglobin levels before and after radiotherapy. Linear regression was used to determine factors associated with haemoglobin change following radiotherapy. All analysis was conducted with SPSS version 20, and the test of significance was evaluated with a probability cut-off value of 0.05.

Ethical considerations

The study and consent procedures were approved by the Muhimbili University of Health and Allied Sciences Ethical Review Board. Permission to conduct the study was obtained from the Hospital in-charge of Ocean Road Cancer Institute. Prior informed written consent (in the local language (Kiswahili) was sought from all patients who had to agree or disagree with study participation and provided a documented signature. Patients who were diagnosed to have anaemia were treated accordingly either by haematinics or blood transfusion depending on the severity of the problem.

Results

Characteristics of study patients

A total of 275 patients were recruited in the study of whom 45 were excluded because their data were incomplete or died during the study period (Figure 1).

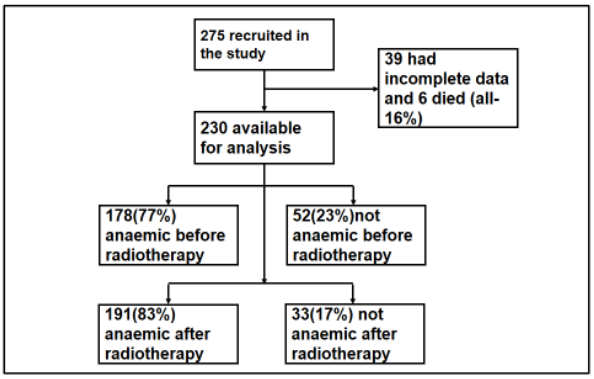

Figure 1. Flow chat for patients included for analysis

Table 1: Socio-demographic and clinical characteristics of patients with cancers by sex

Variable	Response	All		Male		Female	
		N	%	N	%	N	%
Age group (years)	< 35	30	13	14	33.3	16	8.5
	36 – 50	110	47.8	21	50	89	47.3
	>51	90	39.1	7	16.7	83	44.1
Residence	Northern Highlands	17	7.4	5	11.9	12	6.4
	Coastal Zone	100	43.5	18	42.9	82	43.6
	Lake Zone	31	13.5	3	7.1	28	14.9
	Southern Highlands	39	17	8	19	31	16.5
	Central Zone	43	18.7	8	19	35	18.6
Education	None	115	50	16	38.1	99	52.7
	Primary	105	45.7	23	54.8	82	43.6
	Secondary	8	3.5	1	2.4	7	3.7
	College	2	0.9	2	4.8	0	0
Occupation	Unemployment	45	19.6	3	7.1	42	22.3
	Informal	178	77.4	37	88.1	141	75
	Formal	7	3	2	4.8	5	2.7
Cancer type	Cervix					139	73.9
	Breast					11	5.9
	Oesophagus	9	3.9	6	14.3	2	1.1
	Colorectal	6	2.6	2	4.8	4	2.1
	Kaposi	8	3.6	8	19	0	0
	Prostate	1	0.4	1	2.4.		
	Others	56	24.4	26	61.9	30	16
Other clinical parameters	Blood transfusion history	49	21.3	3	7.1	46	24.5
	Prior chemotherapy use	72	31.4	19	45.2	53	28.2
	Post chemotherapy use	98	42.6	18	42.9	80	42.6
	Hematinic use	18	7.9	0	0	18	9.6

A total of 230 cancer treated patients met the criteria to be included in the study. The study subjects were aged 15 to 92 years with overall mean age of 50±14 years (Table 1). Majority of the study subjects (48%) were in the age group 36-50 years, were females (82%) and had no formal employment (77%). Likewise, majority of the patients had cervical cancer (60%) followed by breast

(5%), oesophageal (4%), Kaposi Sarcoma (4%), Colorectal (3%) and Prostate (0.4%) cancers. Other types of cancer contributed to 25% of the patients admitted (Table 1).

Prevalence of anaemia in individuals with cancers

Among all patients who were in the wards during the study period 77% were anaemic on admission. After (within one week) treatment with the single dose of radiation there was increase to 83%. In males, the prevalence of anaemia before radiation was 81% and after radiation was 86%, while in females the prevalence before radiation was 77% and 85 % after radiation (Figure 2). Anaemia in patients with cervical cancer was 78% before radiation and 87% after radiation, in breast cancer was 58% before and 92% after, in oesophageal cancer was 0.9% and later dropped to 0.7% and in colorectal cancer was 100% and dropped to 50% after radiotherapy (Table 2).

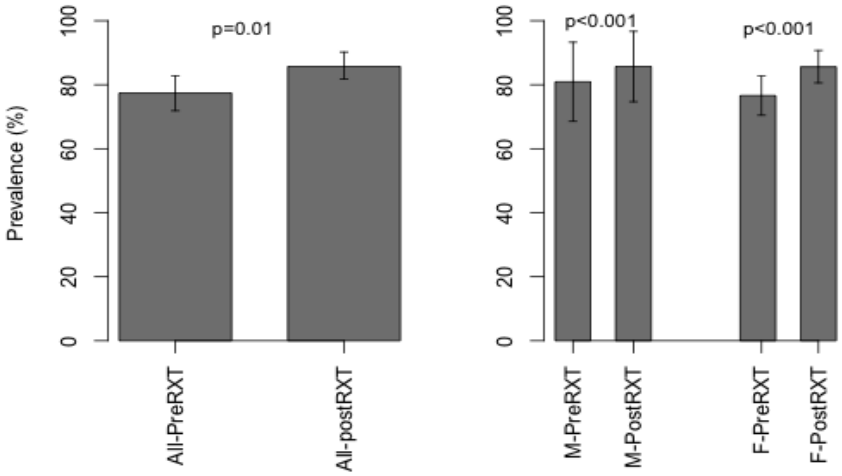

Figure 2: Prevalence of anaemia pre- and post-radiation-therapy in patients with cancers

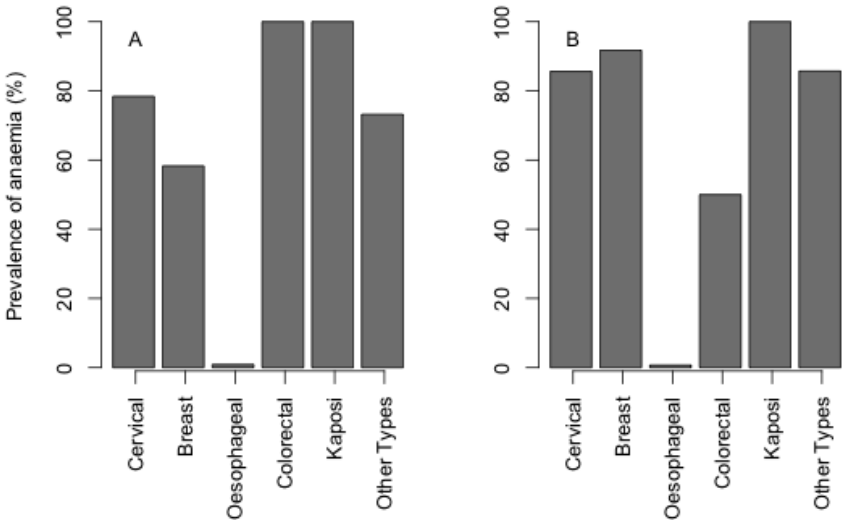

Figure 3: Prevalence of anaemia in various cancer types, before (A) and after (B) radiotherapy

The factors associated with haemoglobin change

Multivariate linear regression analysis (Figure 2) revealed only one factor associated with absolute change in haemoglobin; history of blood transfusion (beta-coefficient= 1.193; p=0.004). The mean haemoglobin change among patients who received blood transfusion was 1.2g/dl higher than those patients who did not receive. Both in univariate and multivariate linear regression analyses,

the association between haemoglobin change and age, sex, cancer stage, use of haematinics and use of chemotherapy, did not reach statistical significance.

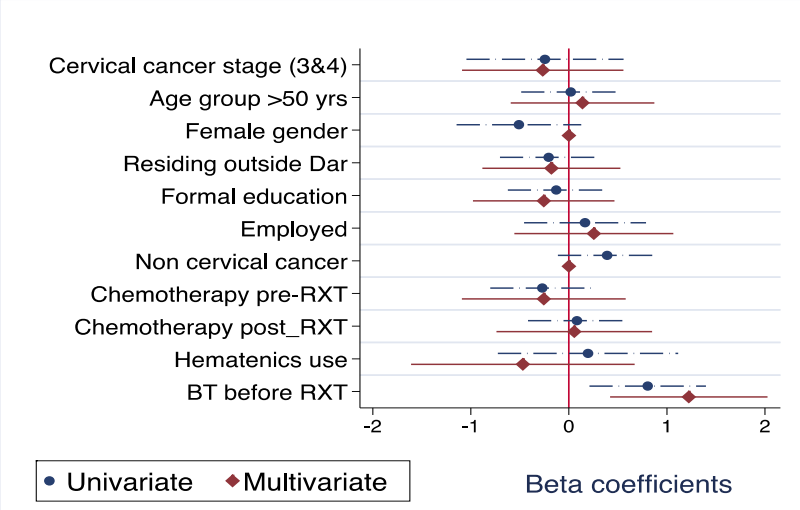

Figure 4: Factors associated with haemoglobin change following radiotherapy in patients with cancers.

Discussion

This study represents a unique population of individuals with cancers who are able to access radiation therapy in Tanzania. Anaemia was found to be common in this population and increased with exposure to radiotherapy suggesting intervention for improved prognosis. Blood transfusion given before radiation was associated with a positive haemoglobin change. Many observational studies have focused on impact of anaemia on prognosis rather than its prevalence among patients undergoing radiotherapy (Harrison *et al.*, 2000, 2002; Shasha & Harrison, 2001). Little attention is paid to the dynamics of anaemia prevalence before or after radiotherapy. In the current study, the prevalence of anaemia study was high both before and after radiotherapy but is closely comparable to the findings reported by Harrison *et al.* (2002) in which the prevalence rose from 78% before radiation to 86% after radiation therapy. This implies that within this short duration the level of haemoglobin decreases significantly, restoration of which has the potential to improve local tumour control and survival and produce improvement in quality of life (Harrison *et al.*, 2000). Thus, in Tanzania where anaemia is already prevalent in the general population(Kitange *et al.*, 1993; Makubi *et al.*, 2013), early detection and intervention at this stage is of clinical relevancy.

Interesting, in our study, all patients with colorectal cancer were anaemic before radiation therapy and later after radiation treatment the prevalence dropped by half. This differs from a study by Harrison *et al.* (2002) which found that 44% patients with colorectal cancer had anaemia before radiation therapy, and the prevalence rose to 63% afterward. This difference can be explained by the fact that the number of study subjects with colorectal carcinoma was small (two patients) and also among them one patient received blood transfusion during radiation therapy thus restoring the anaemic status.

Since cancer or treatment-related anaemia is present in up to 90% of patients, our finding has considerable significance at the population level. Moreover, because haemoglobin level is frequently measured in the routinely tested complete blood count panel, haemoglobin change may be a potentially important variable that can be incorporated with other host and clinical factors to build cancer prognosis assessment models.

The mechanism of anaemia during radiotherapy might be related the direct toxicity to any cells in the body that divide rapidly, which include blood cells and bone marrow cells that make the blood cells. Inflammation caused by irradiation exposure might be another explanation(Grellier *et al.*, 2015). However, the present data do not permit further elaboration on this issue.

The present findings of association between blood transfusion and positive haemoglobin change have important prognostic and policy implications. Low haemoglobin during radiotherapy leads to tissue hypoxia and has been associated with poor treatment outcome afterwards (Obralić *et al.*, 1990; Glaspy & Cavill, 1999; Harrison *et al*., 2002; Wan *et al*., 2013). A few studies have reported maintaining patient haemoglobin levels > 12.5 g/L significantly improves local tumour control rates compared with the rates in patients with lower haemoglobin levels in patients with cervical cancer (Bergsjo, 1965; Bush *et al.,* 1978). Thus blood transfusion centres should provide adequate blood to patients with cancers before and after radiotherapy to counteract the effect of haemoglobin reduction and hence improve the survival of these patients.

Our study has some limitations. The sample size was small and the study was conducted in a very specialized facility and thus might not represent the cancer population in Tanzania. This might have also resulted in lack of statistical power for detection of some associations. Even with these limitations, this study serves as a reference for future recommendations to improve care of patients with cancers by active screening and correction of anaemia during radiotherapy.

In conclusion, we have observed a high prevalence of anaemia in individuals with cancer receiving radiotherapy and only blood transfusion might have a positive effect on haemoglobin dynamics. Therefore, there should be an increase in awareness of this problem to provide early detection of the disease and improve the outcome and quality of life of the patients.

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Author contributions

All authors have made significant contributions to the design, execution, analysis and writing of this study

Competing interests

None

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