ORIGINAL ARTICLE

CANCER PATIENTS AND BLOOD TRANSFUSION DEMAND IN A RESOURCE-CONSTRAINED SETTING: A RETROSPECTIVE STUDY

Oiza T. Ahmadu[1], Shehu S. Umar[2], Sani Awwalu[3], Albert M. Alfred[4], Aminu B. Liman[2], Gaddafi Yusuf[5], Mustapha I. Aliyu[5], Muhammad Salihu[2], Munir Sani[2], Arinze A. Mbanusi[4], Tajudeen A. Olasinde[2]

1. Department of Radiotherapy and Oncology, Federal Medical Centre, Abuja, FCT, Nigeria.
2. Department of Radiation and Clinical Oncology, Ahmadu Bello University Teaching Hospital Zaria, Kaduna State, Nigeria.
3. Department of Haematology, Ahmadu Bello University Teaching Hospital Zaria, Kaduna State, Nigeria.
4. Southwest Wales Cancer Center, Singleton Hospital, Swansea, United Kingdom
5. Department of Radiation and Clinical Oncology, Federal Teaching Hospital Katsina, Katsina State, Nigeria.

Corresponding Author:
Dr. Oiza Tessy Ahmadu, Department of Radiotherapy and Oncology, Federal Medical Centre, Abuja, FCT, Nigeria, tessyoiza@yahoo.com

ABSTRACT

Background: Cancer patients on treatment have anaemia as a common complication resulting from deceased red blood cell production, increased destruction of circulating red blood cells or bleeding from cancer. Blood transfusion in cancer patients is quite frequent as a hospital-based study demonstrated that 34% of blood donated in a health facility were transfused to cancer patients.

Objective: This study aims to assess the indications for, pattern of, and frequency of blood transfusion in cancer patients who received chemotherapy in an oncology specialist center in a low-resource setting.

Methods: The study was a retrospective study carried out on cancer patients who received chemotherapy at the Department of Radiotherapy and Oncology, Ahmadu Bello University Teaching Hospital Zaria over three and a half years period from September 2016 to March 2020.

Results: The mean age of patients was 46.1 ± 14.8 years with half 78(50.3%) of the participants within the 41-60 years age group and majority 116(74.5%) were females. The average baseline haemoglobin level of the patients was 9.88 ±2.15 g/dl and the average drop in haemoglobin from baseline to first transfusion was 1.25g/dl. There was an average of 3.92 units of blood transfused, with an average of 2.13 transfusion events. The average units of blood transfused per transfusion event was 1.84 while the Transfusion Severity Index (TSI) was 4.88.

Conclusion: The study found a high incidence of baseline and chemotherapy induced anaemia in cancer patients. The patients received frequent blood transfusion due to anaemia as indicated by a high transfusion severity index of 4.88. There is need for use of guidelines to streamline transfusion needs and increase the use of alternatives to blood transfusion so as to reduce the demand on blood transfusion and the accompanying adverse effects in cancer patients receiving chemotherapy.

Keywords: Cancer, patients, blood transfusion, low resource

INTRODUCTION
Causes of Anaemia in Cancer Patients

Cancer constitutes one of the leading non-communicable diseases globally accounting for nearly 20 million new cases and 9.7 million deaths in 2022.[1] The treatment of cancer is multi-modal and includes surgery, radiotherapy, systemic therapy and palliative care.[2] Cancer progression, spread, high turnover and bone marrow metastases may lead to anaemia. Additionally, a sizeable number of cancer patients will develop anaemia as a result of any or a combination of malnutrition, adjuvant or neoadjuvant chemotherapy, radiotherapy, concurrent systemic infections, spontaneous tumour bleeding, or surgical blood loss.[3] Cancer patients on treatment have anaemia as a common complication resulting from deceased red blood cell production, increased destruction of circulating red blood cells or bleeding from cancer.[4] Patients with metastases could also develop cytopenia such as leucopenia, thrombocytopenia with or without anaemia. These could lead to administration of blood or blood products to correct the derangements while on treatment, or use of newer agents such as the administration of recombinant growth factors.[5-8]

Challenges of Blood Transfusion

Blood transfusion is an important part of cancer treatment, commonly applied in management of tissue hypoxia, acute anaemia from blood loss, chemotherapy induced anaemia or cardiovascular decompensation from anaemia.[9] Red blood cells (RBCs) may be needed because of myelosuppression from chemotherapy or anemia in the setting of chronic disease.[9] Platelets are often part of the continuum of care for patients with cancer due to myelosuppression and plasma is needed in situations in which coagulation factor replacement is needed while granulocyte transfusions may be considered for recalcitrant infections in patients with severe neutropenia.[9]

Blood transfusion in cancer patients is quite frequent as a hospital-based study demonstrated that 34% of blood donated in a health facility were transfused to cancer patients.[10] While another study asserted that 15.1% of all blood donated in the United States were utilized by cancer patients.[11]

A study on transfusion challenges in patients with haematological malignancies in Sub-Saharan Africa found that anaemia of Hb ≤ 10g/dl occurred in over 90% of these patients while 62% of them received at least one blood transfusion during the course of their treatment. Similarly, thrombocytopenia occurred at least once in 58% of these patients during the course of their treatment and 39% of them received platelet transfusion as treatment.[12] This point was further buttressed by a systemic review on patients with advanced cancers which found anaemia in 68% to 77% with only a few receiving blood transfusions due to unclear reasons.[4]

No single criterion can be used as an indication for RBC transfusion. Therefore, patients' clinical conditions along with treatments received or proposed treatments are usually considered by the clinician with clear target hemoglobin or platelet concentration set before transfusion. Adhering to these usually lead to improvement in these indices. Therefore, the decision to transfuse should not only be driven by hemoglobin concentration alone.[13] Though no structured studies have determined the optimal hemoglobin levels for patients with

advanced cancer, but there are also suggestions that hemoglobin levels of 7 g/dL in cancer patients may be adequate for wellbeing and stamina without the need of blood transfusion.[9]

Despite its importance in the correction of physiological abnormalities associated with anaemia, blood transfusion has long been demonstrated to have detrimental effects on some patients. These include transfusion-associated immunomodulation, infections, graft versus host reaction, allo-immunization, iron overload and thromboembolism, amongst others. The advantages and potential harms of blood transfusion, therefore, have to be balanced against the recognition of blood as a scarce, lifesaving resource especially in developing settings.

In Nigeria, the present donation rate is 0.2 donations/1000 population, and an estimated 1.5 million units of blood is required annually, Therefore the demand for blood transfusion cannot be adequately met, which implies a more judicious use of that available blood to avoid wastage.[14,15]

Therefore, there is need to judiciously utilize blood transfusion in order to minimize its complications through unnecessary transfusions by following standard guidelines in managing cancer patients.[16–20]

This study aims to assess the indications for, pattern of, and frequency of blood transfusion in cancer patients who received chemotherapy in an oncology specialist center in a low-resource setting.

MATERIALS AND METHODS

The study was a retrospective study carried out on cancer patients who received chemotherapy at the Department of Radiotherapy and Oncology, Ahmadu Bello University Teaching Hospital Zaria over three and a half years period from September 2016 to March 2020. Records of patients who received chemotherapy within this period were scrutinized and case folders of those who received blood transfusions during chemotherapy were retrieved and information recorded in standard proforma questionnaire.

The case notes of patients with a record of at least four courses of chemotherapy and at least one unit of blood transfused within the study period were used for this study.

Patients with incomplete data of their chemotherapy schedule and those who were lost to follow up before receiving 4 courses of chemotherapy were excluded from the study (Plate 1).

Information obtained from patients' records included their biodata, histologic diagnosis, stage of disease, presence of comorbidities, treatments received prior to chemotherapy, type of chemotherapy received; haemoglobin, platelet and white blood cell counts at each cycle; indications for blood transfusions, total number of units received by patients, resultant effects on chemotherapy schedule amongst others.
Anaemia was defined as Hb ≤ 10g/dl.[12]

Ethical Considerations
Approval was gotten from the Health and Research Ethics Committee (HREC) of Ahmadu Bello University Teaching Hospital (ABUTH) Zaria.

Data Management

Data was stored in anonymized formats in an alpha-numeric computer with password and up-to-date commercial antivirus. All entries were backed up in secure external hard drives. Hard copies were kept in a separate, secure office with locks on at least two-levels. Only the Principal Investigator, or an authorized co-researcher had access to the data.

Data Analysis

Data recorded was analysed using Statistical Package for Social Sciences (SPSS) version 22 by International Business Machines Corporation (IBM). Test for normal distribution of variables was assessed using Shapiro-Wilk tests. Categorical variables were summarized using percentages, tables and charts while mean ± standard deviation (SD) was used to summarize numeric variables

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                    ┌─────────────────────────┐
                    │ Total number of patients│
                    │ who received chemotherapy│
                    │ within the study period │
                    │         = 527           │
                    └─────────────────────────┘
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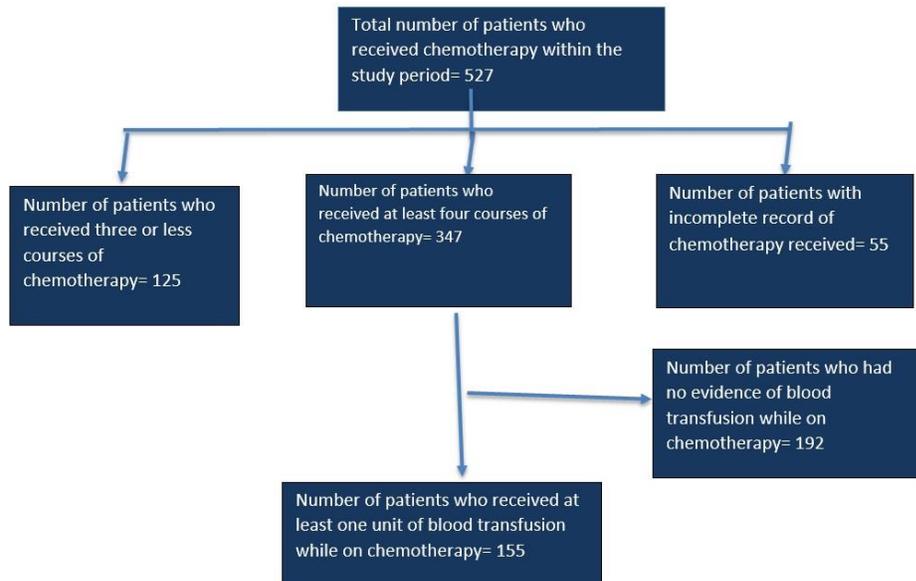
Total number of patients who received chemotherapy within the study period= 527

Number of patients who received three or less courses of chemotherapy= 125

Number of patients who received at least four courses of chemotherapy= 347

Number of patients with incomplete record of chemotherapy received= 55

Number of patients who had no evidence of blood transfusion while on chemotherapy= 192

Number of patients who received at least one unit of blood transfusion while on chemotherapy= 155

Plate 1. Flow chart showing how eligible participants were recruited for the study

RESULTS

A total of 155 patients were recruited in the study. The mean age of patients was 46.1 ± 14.8 years with half 78 (50.3%) of the participants within the 41-60 years age group (Figure 1) and majority 116 (74.5%) were females (Table 1). Cervical cancer was the commonest malignancy accounting for 69 (44.5%) of the patients (Figure 2). Most of the patients 122 (78.7%) presented with locally advanced disease, and 26 (16.7%) had metastatic disease. Most of the chemotherapy administered 111 (71.6%) were in the neoadjuvant setting and 125 (80.6%) of the chemotherapy received were platinum-based (Table 1).

Table 1. Socio-demographic and Clinical Characteristics of Patients (n= 155)

| Variable	Frequency (%)
Gender	
Male	39 (25.2)
Female	116 (74.8)
Stage of cancer	
Early	7 (4.5)
Locally Advanced	122 (78.7)
Advanced/Metastatic	26 (16.7)
Total Courses of Chemotherapy received	
4	30 (19.4)
5	26 (16.7)
6	91 (58.7)
7 & above	8 (5.2)
Type of Chemotherapy	
Neoadjuvant	111 (71.6)
Concurrent	2 (1.3)
Adjuvant	40 (25.8)
Others	2 (1.3)
Chemotherapy agent	
Platinum based	125 (80.6)
Non-Platinum based	30 (19.6)
Indication for Blood Transfusion	
Anaemia with bleeding	39 (25.2)
Anaemia without bleeding	115 (74.2)
Thrombocytopenia	1 (0.6)
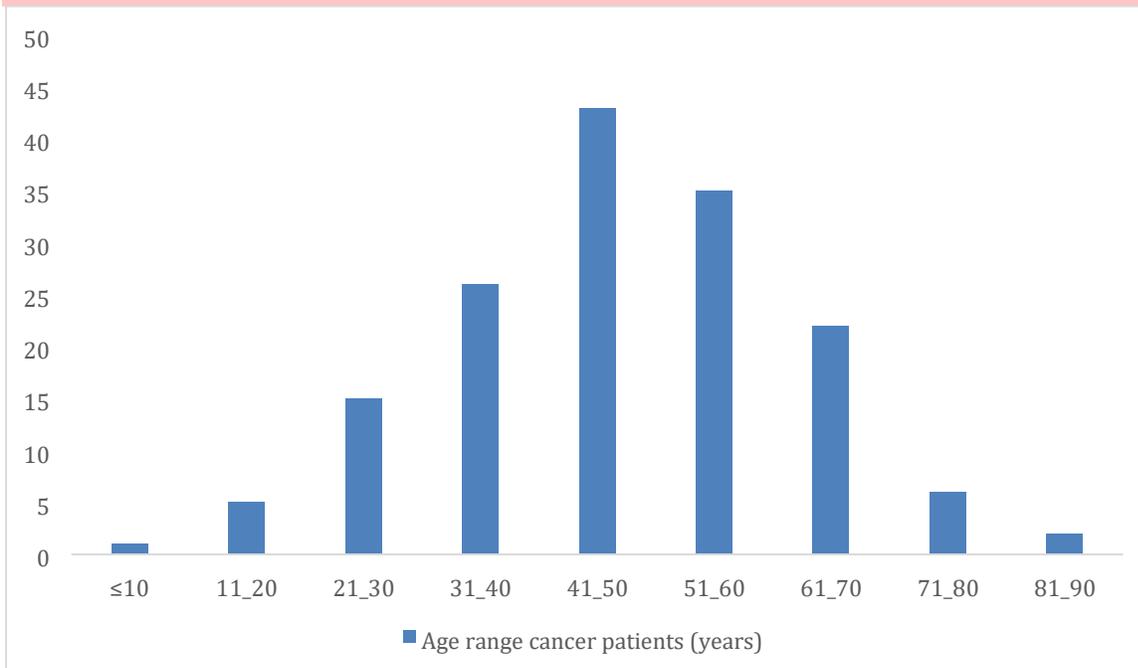
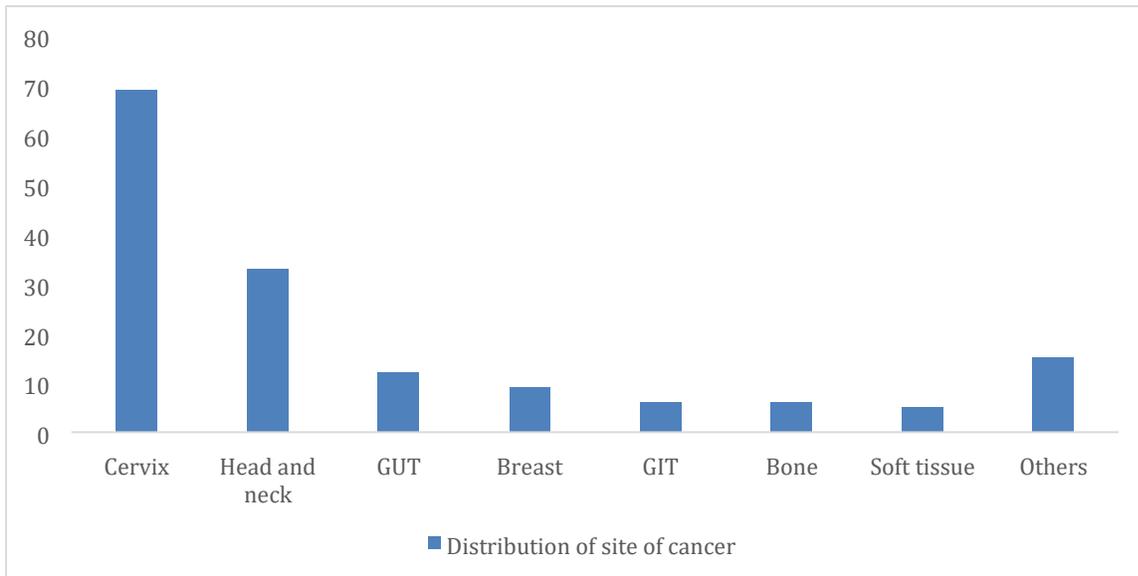**Figure 1. Age distribution of cancer patients in the study**

Figure 2. Distribution of tumour sites for patients in the study

The average baseline haemoglobin level of the patients was 9.88 ±2.15 g/dl and the average drop in haemoglobin from baseline to first transfusion was 1.25g/dl (Table 2). When data was disaggregated to tumour types, patients with cervical cancer had the lowest baseline haemoglobin

level (9.64 ±2.02 g/dl) (Table 2). There was an average of 3.92 units of blood transfused, with an average of 2.13 transfusion events (Table 2). The average units of blood transfused per transfusion event was 1.84 while the Transfusion Severity Index (TSI) was 4.88.

Table 2. Blood transfusion characteristics by specific tumor sites

Variable	Cancer site					
	Cervix (n=69)	Head & Neck (n= 33)	GUT (n=12)	Breast (n=9)	Others (n=32)	Total (N=155)
Average baseline Haemoglobin (g/dl)	9.64 ± 2.02	10.05 ± 2.11	10.81 ± 1.70	9.94 ± 1.12	10.17 ± 1.18	9.88 ± 2.15
Average drop in haemoglobin levels from baseline to first transfusion (g/dl)	1.11	1.12	2.01	1.46	1.34	1.25
Total units of blood transfused	278	130	56	37	103	604
Average units of blood transfused	4.03	4.06	4.58	4.11	3.32	3.92
Average transfusion events	2.10	2.28	2.58	2.22	1.84	2.13
Average number of bloods transfused per transfusion event	1.97	1.78	1.81	1.85	1.80	1.84
Transfusion Severity Index (TSI)	4.47	4.55	9.21	6.00	4.45	4.88

Transfusion Severity Index (TSI) = Average drop in haemoglobin levels from baseline to first transfusion (g/dl) X Average units of blood transfused; GUT: Genito- Urinary Tract

DISCUSSION

The mean age of cancer patients in this study was 46.1 ± 14.8 years with half of the patients between 41- 60 years. This finding was very similar to another study on cancer patients receiving chemotherapy where the mean age of patients was 48.5 ± 15.8 years with 47.9% of them within 40- 59 years age group.[21] This was also consistent with another study done in a cancer centre in Lagos where the mean age of cancer patients was 52 years with 45% of them between 41- 60 years age group.[22] The findings buttress the fact that cancer patients in our

settings present at a younger age compared to those from developed countries.[23-26]

Females were the majority of the cancer patients in this study accounting for about three-quarter of the total patients. This finding is consistent with other studies within similar settings where females form the majority of cancer patients.[22,26] The main explanation for the higher burden of cancer in females is because, breast and cervical cancers which are among the commonest malignancies in most low-and-middle income countries predominantly affect women.[25] Furthermore, most patients in this study presented with locally advanced or metastatic disease which is also the reality in low-resource settings where patients present late to the hospital with advanced disease.[25]

The mean baseline haemoglobin level of cancer patients was 9.88 ± 2.15 g/dl which was an indication of baseline anaemia at the time of diagnosis and before the commencement of chemotherapy. There was an average drop of 1.25g/dl in the level of haemoglobin from baseline assessment to first transfusion. This finding was supported by a study in Ethiopia which found 97 (23%) of cancer patients to be anaemic at diagnosis with a mean haemoglobin level of 9.4 ± 1.6 g/dl.[27] Furthermore, another retrospective study conducted on 95 cancer patients found the incidence of anaemia to be 50.5% with the mean haemoglobin level at diagnosis as 9.1 ± 2.1 g /dl.[28] These findings emphasize the fact that anaemia has high prevalence in cancer patients at diagnosis and worsens with commencement of treatment.

In this study an average of 3.92 units of blood was transfused per cancer patient, with an average of 2.13 transfusion events per cancer patient during the course of their treatment.

There was an average of 1.84 units of blood transfused per transfusion event, indicating that a substantive number of patients require multiple transfusions to correct their incident anaemia. This is buttressed by other studies where 75% of patients require blood transfusion with 40% of these patients requiring 7 or more units of blood during the course of chemotherapy administration.[28] Another retrospective study on 402 cancer patients in Northwest Ethiopia found that 75.4% developed chemotherapy induced anaemia which was managed using combined modalities consisting of ferrous sulphate, ferrous gluconate, ferrous fumarate and blood transfusion.[29] Furthermore, a study on cancer patients receiving chemotherapy in Zaria; Nigeria showed that 57.9% of the 140 patients involved in the study required blood transfusion to correct anaemia during the course of chemotherapy.[21]

These studies from low-resource settings have shown the prevalence of anaemia in cancer patients receiving treatment and the high demand and utilization of blood transfusion in correcting the anemia. These findings are quite contrary to what is obtainable in high resource settings. For instance, a systemic review on the management of anaemia in cancer patients in developed countries found that though anaemia is prevalent in over 60% of the patients, only 15% received blood transfusion using haemoglobin level of less than 9g/dl as the criteria for transfusion.[30] In another large European cancer anaemia survey, involving 15,367 cancer patients on chemotherapy, only 39% of these patients were found to have anaemia with haemoglobin less than 10g/dl, and only 39% of these patients received treatment for anaemia using erythropoietin stimulating agents and blood transfusion.[31]

Though blood transfusion has tremendous benefits, it is not without adverse effects.[31,32] Conversely, the safety of blood transfusion has improved over the years, repeated transfusion over a period is associated with increased risk of venous and arterial thromboembolism, immune modulation resulting in cancer recurrence; and the risk of pathogen transmission, ultimately cumulating into decreased overall survival.[31,32,33] Therefore, experts currently advocate that the cause of anaemia be assessed before deciding on the appropriate correction measures to rationalize the use of blood transfusion in the correction of anaemia in cancer patients.[33,34]

Advancement in medicine has led to the introduction of other alternatives to blood transfusion in the management of cancer patients.[35,36] These include administration of intravenous iron, and erythropoiesis-stimulating agents. These agents have some effects that address the disadvantages of blood transfusion.[35,36] These include achieving stable haemoglobin levels, outpatient administration, positive effect on patients' immune system and overall improvement in quality of life. [35,36] These advancements led to more precision in not only the diagnosis of anemia in cancer patients, but identifying the type of anemia and underlying risk factors. [35,36] The diagnostic tests should include complete blood count; reticulocyte count; iron, transferrin, folic acid and Vitamin B12 concentrations.[35,36]

These advancements have been followed closely by developing guidelines on the management of anaemia in cancer patients.[37,38,39] Generally, these guidelines have emphasized on thorough investigations to characterize anemia and its specific cause in patients. This has restricted the use of blood transfusion in favour of newer alternatives, with differing suggestions on cut off values of haemoglobin before blood transfusion is given to anaemic cancer patients.[31,32,37,39]

CONCLUSION

The study found high incidence of baseline and chemotherapy induced anaemia in cancer patients. The patients received frequent blood transfusion due to anaemia as indicated by a high transfusion severity index of 4.88. There is need for use of guidelines to streamline transfusion needs and increase the use of alternatives to blood transfusion so as to reduce the demand on blood transfusion and the accompanying adverse effects in cancer patients receiving chemotherapy.

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