

Transfusion Requirement in Anemia observed in Patients with Carcinoma Breast undergoing Chemotherapy

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ABSTRACT

Introduction: Carcinoma Breast is the second most common malignancy affecting women. Adjuvant chemotherapy is the mainstay treatment modality along with surgery. Anemia and thrombocytopenia are the hematological complications in patients with breast cancer who undergo chemotherapy. This study was carried out with an objective to identify the proportion of anemia and the requirement of Packed Red Cells transfusions in these patients.

Material and methods: This is a hospital based prospective study, done for a period of one and a half years from January 2016 to June 2017. As per the inclusion criteria 125 consecutive cases who underwent chemotherapy for Carcinoma Breast at Department of Radiotherapy, Govt. Medical College, Thiruvananthapuram were included for the study. The requirement of Packed Red Cell (PRC) was assessed in these patients. Data was analysed with SPSS software (version 21).

Results: Among the 125 patients, 60% of patients were anemic in prechemotherapy phase with a preponderance of mild anemia, haemoglobin (Hb) 11-11.9 gm/dl (as per the WHO classification of anemia in non pregnant females). In post chemotherapy phase the prevalence of anemia was 94.4% with increasing severity; majority (56%) of patients had moderate anemia (Hb 8-10.9 gm/dl). During chemotherapy, 22.4% of the study population required PRC transfusion.

Conclusion: Due to the high prevalence of chemotherapy-induced anemia and its effects on quality of life (QOL), even mild degrees of anemia should be detected and evaluated before commencing chemotherapy. PRC transfusion should be reserved for patients with severe anemia.

Key words: Anemia, Carcinoma Breast, Chemotherapy, PRC transfusion

INTRODUCTION

Carcinoma Breast is the most frequently diagnosed cancer and the leading cause of cancer death among females worldwide.¹ In India cases with age standardized incidence rate is 25.8 per 100,000 women. In Kerala, Breast cancer has an annual incidence of 14.9/100,000 population. In Thiruvananthapuram District, Carcinoma of Breast is the leading site among females and accounts for 28.5% of all cancers in women.² Presently, the percentage of women suffering from breast cancer, below fifty years of age is 47.7%.³ Main risk factors for breast cancer in Indian women are early age at menarche, late menopause, higher age at marriage, late age at first child birth, lower mean duration of breast feeding and a lower parity.⁴

Chemotherapy is one of the mainstay modalities of treatment for Carcinoma Breast apart from surgical therapy. Cytotoxic

chemotherapeutic drugs may have many hematological adverse effects. Anemia is a prevalent complication in these patients. The severity of anemia and fatigue depends on, disease type, patient's age, and other risk factors.⁵ Anemia has association with prognostic value in several types of cancer including breast cancer.⁶

Anemia may develop either by impaired function in red blood cell (RBC) production or because of renal tubular damage following treatment with cytotoxic drugs as a consequence of chemotherapy.⁷ Multiple mechanisms can impair the normal production of erythrocyte in cancer patients, including cytokines and interleukins (IL).⁷ In addition to neoplastic natural history and treatment processes, anemia can be caused by other co morbidities like infections, gastrointestinal blood loss, nutritional deficiencies, renal impairment, disorders of haematopoiesis, microangiopathy, autoimmune haemolysis, bone marrow fibrosis and displacement, or default in iron stock use.⁸ Moreover, reduced levels of erythropoietin negatively affects RBC production in bone marrow, inducing anemia.⁹

The traditional method of increasing haemoglobin (Hb) levels in patients with severe cancer associated anemia has been allogeneic blood transfusion, despite the inconvenience, cost and potential risk associated with this practice.¹⁰ Studies have shown that the administration of Erythropoiesis stimulating agents not only increases Hb levels, but also reduces transfusion requirements.¹¹ But a meta-analysis reported an increased rate of tumour progression and/or death in patients treated with these agents.¹²

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Very few studies are available from India on the proportion of anemia in patients undergoing chemotherapy for Carcinoma Breast. The current study is performed with the futuristic aim to formulate the screening of patients with anemia in the early stage of chemotherapy to prevent the consequences of it on the daily activity. It also helps to estimate the requirement of packed red cell transfusions in these patients.

MATERIAL AND METHODS

This was a Hospital based Prospective study done in the Department of Transfusion Medicine, Government Medical college, Thiruvananthapuram on female patients with Carcinoma Breast undergoing chemotherapy at the Department of Radiotherapy. The study was done for a period of one and half years from January 2016 to June 2017 after approval from the Institutional Research Committee and Institutional Human Ethics Committee. The study population comprised of 125 female patients with Carcinoma Breast, of age above 18 years on chemotherapy who were on regular follow up.

Data Collection Technique

The relevant clinical details were collected according to a structured proforma after obtaining written informed consent from patients who were enrolled as study subjects. All the patients were subjected to prechemo and post chemo hematological investigations, followed by chemotherapy regimen –AC x 4 weeks, (Doxorubicin 60mg/m² + Cyclophosphamide 600mg/m²) followed by Docetaxel

(100mg/m²) x 4 weeks. After each chemotherapy cycle, hemoglobin values assessed. Transfusion of Packed Red Cell (PRC) was done in severe anemia. Anemia classified as per WHO classification.

WHO Classification of Anemia in non pregnant females

Mild	11-11.9g/dl
Moderate	8-10.9g/dl
Severe	<8 gm/dl

Transfusion trigger was altered depending on the patient's individual requirement. Patients were followed till the end of chemotherapy sessions. The transfusion events were documented. Complications due to anemia like fatigue, Congestive cardiac failure (CCF), palpitation, wound infection, delayed healing, chest infection were noted.

STATISTICAL ANALYSIS

Data was entered in Excel sheet. Analysis was done using SPSS software version 21.

RESULTS

Out of 125 Carcinoma Breast patients undergoing Chemotherapy 75(60%) had anemia in the Pre chemotherapy phase. In Post chemotherapy phase the number of anemic patients increased to 118 (94.4%) (Table-1).

Prior to Chemotherapy majority of the patients 52 (41.6%) were with mild anemia and 23 (18.4%) showed moderate anemia (Table-2).

After administration of Chemotherapy majority of the

Anemia before Chemotherapy	Number of patients (n)	Percentage (%)	Anemia after Chemotherapy	Number of patients (n)	Percentage (%)
Present	75	60%	Present	118	94.4%
Absent	50	40%	Absent	7	5.6%
Total	125	100%	Total	125	100%

Table-1: Percentage distribution of patients with Carcinoma Breast who had anemia before chemotherapy and after chemotherapy

Anemia prior to administration of chemotherapy	Number of patients (n)	Percentage (%)
No Anemia Hb > 12	50	40%
Mild Anemia (Hb 11-11.9)	52	41.6%
Moderate Anemia (Hb 8-10.9)	23	18.4%
Severe Anemia (Hb <8)	0	0%
Total	125	100%

Table-2: Percentage distribution of patients showing severity of anemia prior to administration of chemotherapy

Anemia after administration of chemotherapy	Number of patients (n)	Percentage (%)
No Anemia (Hb > 12)	7	5.6%
Mild Anemia (Hb 11-11.9)	44	35.2%
Moderate Anemia (Hb 8-10.9)	70	56.0%
Severe Anemia (Hb <8)	4	3.2%
Total	125	100%

Table-3: Percentage distribution of patients showing severity of anemia after administration of chemotherapy

PRC	Number of patients (n)	Percentage (%)
Transfused	28	22.4%
Not transfused	97	77.6%
Total	125	100%

Table-4: Percentage Distribution of patients with Carcinoma Breast undergoing chemotherapy who received PRC Transfusion

Pre chemotherapy Anemia	PRC transfused	PRC not transfused
Present	23	37
Absent	5	60
p value = 0.000 OR =7.45(CI =2.60-21.32)		

Table-5: Comparison of Prechemotherapy Anemia and Requirement of PRC Transfusion

	Prechemotherapy anemia		Post chemotherapy anemia	
	Frequency	Percentage%	Frequency	Percentage%
Stage 2	5	8.33%	11	11.34%
Stage 3	32	53.33%	52	53.61%
Stage 4	23	38.33%	34	35.05%

Table-6: Comparison of Prechemotherapy and Post chemotherapy anemia in different stages of tumor

patients 70 (56%) developed moderate anemia, 4 patients (3.2%) with severe anemia and 44(35.2%) showed moderate anemia (Table-3).

Among 125 study subjects 28 patients required Packed Red Cell transfusion (Table-4).

Among the 28 patients who received PRC transfusion 23(82.14%) had prechemotherapy anemia compared to 5 (17.86%) of the patients who did not have prechemotherapy anemia. This difference was statistically significant with P value of 0.000 (Table-5).

So this observation points that prechemotherapy anemia had 7 times the chance of requiring PRC transfusion than those who did not have prechemotherapy anemia.

Considering the relation of tumour stages and anemia in Prechemo and Post chemo phases, higher frequency of anemia was observed among Carcinoma Breast Stage 3 patients (Table-6).

DISCUSSION

Adjuvant Chemotherapy is the mainstay treatment for Carcinoma Breast patients. Anemia is a frequent complication detected in patients with cancer.¹³ Neglecting the chemotherapy-induced anemia might be a pitfall for the physicians by making the patient unresponsive to the treatments.¹⁴

The present study gives an insight into the proportion of Anemia in female patients undergoing chemotherapy for Carcinoma Breast at Department of Radiotherapy, Govt. Medical College, Thiruvananthapuram. Patients who underwent chemotherapy from January 2016 to June 2017 were included in the study. The transfusion requirements of the patients were assessed. In addition to haemoglobin value, the influence of other variables like age, body mass index (BMI), were analysed.

In this study a total of 125 patients were included. The age of the patients ranged from 25 to 80 years. Majority of the patients were in the age group of 41-50 years (n=42, 33.6%). 71 women were postmenopausal (n= 71, 56.8%) and majority were in the overweight category (n=55, 44%, BMI=25-30) while 24.8% patients were in obese category (BMI>30), which is considered as a risk factor for carcinoma breast. Tumour sized > 5 cm (T3) had the most prevalence among (n=74, 59.8%) patients.

ABO grouping and Rh typing of the study population reflects

the incidence of general population with majority having O group (n= 51,41.8%) while Rh(D) was positive in 90.4%.

Present study population comprised of patients predominantly in the Tumor stage 3 (59.2%) followed by 32% in stage 4 while none was in the stage 1. This may be due to the fact that most of the patients were diagnosed at higher stages, because of late presentation of patients, inadequate screening programs etc.

In the present study, the Haemoglobin level of the patients indicated that 60% of patient population was anemic in the prechemotherapy phase itself. 69.33% had Mild anemia (11-11.9gm/dl) while 30.66% had Moderate anemia (8-10.9 gm/dl). It was observed that majority of the patients (n= 102, 81.2%) were having hemoglobin of more than 11gm/dl. The reason for the large number of patients in anemic population may be also due to considering the WHO scale for anemia in non-pregnant females.

The highest rate of anemia in post chemotherapy patients was observed in stage 3 with 59.32% followed by stage 4 in 31.36%. This finding was consistent with the results of Pourali et al.¹⁵ who also had the highest rate of anemia in patients with stage 3 tumour (56.9%). This might be due to the fact that most of our patients were diagnosed at higher stages (59.2% in stage 3 and 32% in stage 4), which affects the sampling in such a way that none of the patient was with low-stage breast tumour in the study.

The result of present study showed that severity of anemia increased after chemotherapy. This is in consistency with the results of the study done by Tanima et al.¹⁶

Severe anemia (Hb <8 gm/dl), which was not seen in prechemotherapy phase, was noticed in 3.2% of patients in the post chemotherapy period. This shows that the severity has increased after the administration of chemotherapy even though many other underlying disorders that can also affect the haemoglobin concentration and subsequently lead to anemia especially in Indian population (eg: malnutrition, chronic disease). This is evident from an Indian study done by Tanima et al.¹⁶ which showed Prechemotherapy anemia to be 78% while incidence of anemia to be 97% in post chemotherapy phase.

Packed red cell (PRC) transfusion is the mainstay treatment modality for severe anemia (Hb<8 gm/dl). In the present study, 28 patients (22.4%) required PRC transfusion during the chemotherapy phase due to severe anemia. This finding is

consistent with the Large-scale UK audit of blood transfusion requirements and anaemia in patients receiving cytotoxic chemotherapy by Barrett Lee et al¹⁷ who found that 19% of patients with breast cancer required blood transfusion.

Many clinical trials (23,66,89) have reported the efficacy of Recombinant Erythropoietin (EPO) in improving the haemoglobin levels in early stages as well as in advanced carcinoma breast. But Leyland-Jones et al¹⁸ had concluded that RBC transfusion should be the preferred approach for the management of anemia in this population. Apart from this, Early screening and monitoring for iron storage and rational prescription of iron supplements is also important if needed.

There has been increasing evidence that anemia leads to impaired tumour oxygenation with subsequent chemo resistance. Treatment resistance in anemic patients can be, at least partially, prevented or overcome by anemia correction, resulting in better locoregional tumor control and overall survival of patients.¹⁹

Complications related to anemia reflected in this study were Fatigue (76.8%) followed by respiratory distress (12.8%) and cardiac failure (9.6%). Respiratory distress and cardiac failures were symptomatically treated not requiring any active intervention. A study by Stasi et al.²⁰ found the incidence of fatigue to be 80% in their patients who were treated with chemotherapy.

CONCLUSION

This was a Hospital based prospective study done on 125 female patients with Carcinoma Breast, treated with standard regimen of chemotherapy in the Department of Radiotherapy, Government Medical College, Thiruvananthapuram. The study was done to analyse the proportion of female patients who had anemia and requirement of PRC transfusions during chemotherapy for carcinoma breast.

The data suggested the importance of monitoring and managing hemoglobin levels of patients at increased risk for developing chemotherapy-induced anemia. Women who begin chemotherapy with anemia experience moderate to severe anemia during chemotherapy suggesting that anemia may have been treated aggressively in this group.

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