

# Transfusion Requirement in Thrombocytopenia Observed in Patients with Carcinoma Breast Undergoing Chemotherapy

Manish Nair<sup>1</sup>, Sasikala N<sup>2</sup>, Meena D<sup>3</sup>, Mini Chellamma Viswanathan<sup>4</sup>, Soonam John<sup>5</sup>

## ABSTRACT

**Introduction:** Breast cancer is the commonest cancer in urban Indian females, and the second commonest in the rural Indian women. The estimated number of breast cancer cases in India during 2012 was 145,000 cases with an incidence rate of 25.8 per 100,000 women. In Kerala, Breast cancer has an annual incidence of 14.9/100,000 population. This study was carried out with an objective to identify the proportion of thrombocytopenia and the requirement of platelet transfusions in these patients.

**Material and methods:** This was a hospital based prospective study, done in the Department of Transfusion medicine 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 platelet transfusions were assessed in these patients. Data was analysed with SPSS software (version 21).

**Results:** Among the 125 patients, thrombocytopenia was noticed in 5.4% study population in prechemotherapy phase, majority having only grade I thrombocytopenia. In Post chemo phase thrombocytopenia was observed in 11.2% of the study group, grade I thrombocytopenia in 8.8% and grade II thrombocytopenia 2.4% of patients. Platelet transfusion was required in 5.4% of the patients during chemotherapy.

**Conclusion:** Due to the high prevalence of chemotherapy-induced hematological complications, even mild degrees of thrombocytopenia should be detected and evaluated before commencing chemotherapy. Platelet transfusion should be reserved for patients who were really required. This study gives an insight regarding the proportion of thrombocytopenia in patients with carcinoma breast undergoing chemotherapy and their platelet transfusion requirements, which will help in taking care of these patients and inventory management of the blood banks.

**Keywords:** Thrombocytopenia, Carcinoma Breast, Chemotherapy, Platelet transfusion.

## INTRODUCTION

Carcinoma breast is the most common invasive carcinoma among females and it affects 12% of the females worldwide.<sup>1</sup> The estimated number of breast cancer cases in India during 2012 was 145,000 with an incidence rate of 25.8 per 100,000 women. The estimated number of deaths in India in the year 2012 was 70,000.<sup>2</sup> In Kerala, Breast cancer has an annual incidence of 14.9/100000 population.<sup>3</sup> A few decades back, the percentage of women suffering from breast cancer, below fifty years of age were only 30 to 35%. However, presently, it is 47.7% of all women suffering from breast cancer in

Thiruvananthapuram. In these, a significant number of patients are below 30 years.<sup>4</sup> International variation in breast cancer incidence rates reflects differences in the availability of early detection as well as risk factors.

Risk factors for breast cancer include reproductive and hormonal factors such as a long menstrual history, recent use of oral contraceptives, and nulliparity. Childbirth and breastfeeding decreases the risk of breast cancer.<sup>5</sup> Potentially modifiable risk factors include weight gain after age 18 years, obesity, use of menopausal hormone therapy, physical inactivity, and alcohol consumption.<sup>6</sup> Main risk factors for breast cancer in Indian women include 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.<sup>7</sup>

Chemotherapy is one of the adjuvant modalities of treatment for Carcinoma Breast apart from surgical therapy. Cytotoxic chemotherapeutic drugs may have many haematological adverse effects. Anemia and thrombocytopenia are prevalent haematological complications in patients with breast cancer, who undergo chemotherapy. While women with breast cancer on chemotherapy are 14.6 times more likely to develop neutropenia and thrombocytopenia, and 3 times more likely to develop anemia than those not receiving chemotherapy.<sup>8</sup> Thrombocytopenia is an expected hematologic complication of patients undergoing myelosuppressive chemotherapy. Mechanism of thrombocytopenia is multifactorial. Decreased platelet production secondary to chemotherapy and/ or radiation induced myelotoxicity are already well-

<sup>1</sup>Junior Resident, Department of Transfusion Medicine, Government Medical College, Thiruvananthapuram, Kerala, <sup>2</sup>Additional Professor, Department of Transfusion Medicine, Government Medical College, Thiruvananthapuram, Kerala, <sup>3</sup>Professor and HOD, Department of Transfusion Medicine, Government Medical College, Thiruvananthapuram, Kerala, <sup>4</sup>Associate Professor, Department of Transfusion Medicine, Government Medical College, Thiruvananthapuram, Kerala, <sup>5</sup>Associate Professor, Department of Transfusion Medicine, Government Medical College, Thiruvananthapuram, Kerala, India

**Corresponding author:** Dr. Sasikala N, Additional Professor, Department of Transfusion Medicine, Government Medical College, Thiruvananthapuram, Kerala, Pin 695011, India

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established causes. Chemotherapy induced hypersplenism and hepatic damage are contributors of chemo induced thrombocytopenia.<sup>9</sup> In evaluating thrombocytopenic cancer patients, it is important to assess for other causes of thrombocytopenia, including immune thrombocytopenia, coagulopathy, infection, drug reaction, post-transfusion purpura, and thrombotic microangiopathy. The incidence of chemotherapy-induced thrombocytopenia varies greatly depending on the treatment used; the highest rates of this condition are associated with Gemcitabine- and platinum-based regimens. Each chemotherapy agent differs in how it causes thrombocytopenia: Alkylating agents affect stem cells, Cyclophosphamide affects later megakaryocytic progenitors, Bortezomib prevents platelet release from megakaryocytes, and some promote platelet apoptosis.<sup>10</sup> Thrombocytopenia in carcinoma patients can determine or preclude the administration of chemo, limit frequency and intensity of chemotherapy. If not addressed could lead to serious complications such as bleeding or in worst case, intracranial haemorrhage which can be life threatening. Platelet counts < 10,000/micro litre spontaneous bleeding can occur, <50,000/micro litre complicates the surgical procedures and platelet count <100,000, chemotherapy administration can worsen thrombocytopenia and increase the risk of bleeding. There are limited studies<sup>11,12</sup> showing the real incidence of thrombocytopenia during chemotherapy or risk factors to its development.

The traditional method of increasing platelet count in patients with cancer associated thrombocytopenia has been allogeneic blood transfusion, despite the inconvenience, cost and potential risk associated with this practice.<sup>13</sup> Risks of allogenic platelet transfusions ranges from mild allergic reactions to life threatening anaphylaxis, febrile reactions, immunomodulation, TAGVHD, TTIs and septicaemia. Recombinant thrombopoietins reduced chemotherapy – related thrombocytopenia in early trials, but antibody formation against endogenous thrombopoietin halted this trial.<sup>14</sup> Thrombopoietic growth factors are also in trial.

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

## MATERIAL AND METHODS

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

these patients ranged from 25 to 80 years.

Written informed consents were obtained from patients who were enrolled as study subjects. Patient's demographic and clinical details such as clinical history and treatment history were collected using a structured proforma. All the patients were subjected to pre chemo haematological investigations, (Blood group and Rh type, Haemoglobin, Total count, Differential count, Erythrocyte sedimentation rate, Platelet count, Liver function tests, and Renal function tests) followed by chemotherapy regimen –AC x 4 weeks, (Doxorubicin 60mg/m<sup>2</sup> + Cyclophosphamide 600mg/m<sup>2</sup>) followed by Docetaxel (100mg/m<sup>2</sup> x 4 weeks). After each chemotherapy cycle haematological investigations repeated, and platelet count assessed. Transfusion of platelet concentrate done for patients with thrombocytopenia.

Severity of thrombocytopenia in patients undergoing chemotherapy was assessed as per NCI criteria.

Grade I	75,000 to 1.5 Lakhs/ $\mu$ L
Grade II	50,000 to 75,000 / $\mu$ L
Grade III	25,000 to 50,000 / $\mu$ L
Grade IV	<25,000 / $\mu$ L

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 thrombocytopenia like bleeding were noted.

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

## RESULTS

This is a hospital based Prospective study conducted in the Department of Transfusion Medicine on 125 female patients with carcinoma breast undergoing chemotherapy at Department of Radiotherapy, Government Medical College, Thiruvananthapuram, Kerala, which is a tertiary care centre. Study period was one and a half years (from January 2016 to June 2017). In prechemotherapy phase 7 patients (5.4%) had grade 1 thrombocytopenia (table-1,2). Three of these patients got platelet concentrate transfusions

Thrombocytopenia	Number of patients (n)	Percentage (%)
before Chemotherapy		
Present	7	5.4%
Absent	118	94.6%
Total	125	100%

**Table-1:** Percentage Distribution of patients with Carcinoma Breast undergoing Chemotherapy who had prechemotherapy thrombocytopenia

Severity of prechemotherapy thrombocytopenia	Number of patients (n)	Percentage (%)
Grade 1	7	5.4%
No thrombocytopenia	118	94.6%
Total	125	100%

**Table-2:** Percentage distribution of patients showing severity of Prechemotherapy thrombocytopenia

Pre chemotherapy Thrombocytopenia	Platelet Transfused	Platlet not Transfused
Present	3	4
Absent	4	114
p value = 0.000, OR =21.37 (CI =3.53- 129.13)		

**Table-3:** Comparison of Pre chemotherapy Thrombocytopenia and Platelet Requirement

Thrombocytopenia after Chemotherapy	Number of patients (n)	Percentage (%)
Present	14	11.2%
Absent	111	88.8%
Total	125	100%

**Table-4:** Percentage Distribution of patients with Carcinoma Breast undergoing Chemotherapy who had post chemotherapy thrombocytopenia

Severity of	Number of patients (n)	Percentage (%)
postchemotherapy thrombocytopenia		
Grade 2	3	2.4%
Grade 1	11	8.8%
No thrombocytopenia	111	88.8%
Total	125	100%

**Table-5:** Percentage distribution of patients showing severity of post chemotherapy thrombocytopenia

during chemotherapy (table-3). Fourteen patients (11.2%) developed thrombocytopenia in the post chemotherapy phase (table-4). As per the NCI criteria 11 patients (8.8%) had grade I thrombocytopenia and 3 patients (2.4%) had grade II thrombocytopenia (table-5). Bleeding in the form of mucosal bleeding were noted in 3 cases (2.4%) with thrombocytopenia. The requirement of platelet products in the study population was 5.4% (n=7).

## DISCUSSION

Chemotherapy is one of the adjuvant modalities of treatment for Carcinoma Breast apart from surgery. Anemia and thrombocytopenia are prevalent haematological complications in patients with breast cancer, who undergo chemotherapy. Thrombocytopenia in carcinoma patients can determine or preclude the administration of chemo, limit frequency and intensity of chemotherapy. The incidence of chemotherapy-induced thrombocytopenia varies greatly depending on the treatment used.

The present study gives an insight into the proportion of Thrombocytopenia in patients undergoing chemotherapy for Carcinoma Breast at Department of Radiotherapy, Govt. Medical College, Thiruvananthapuram, which is a tertiary care centre. Female Patients diagnosed with Carcinoma Breast who underwent chemotherapy from January 2016 to June 2017 were included in the study. The transfusion requirements of the patients were assessed for formulating the needs in these patients.

In this study a total of 125 patients were included. Majority

of the patients were in the age group of 41-50 years (n=42, 33.6%). Mean age of study population was 53.56 years. The age ranged from 25 to 80 years with the median of 52 years. The age of study population is in concordance with the study done by Pourali et al.<sup>15</sup>

Majority of women were postmenopausal (n= 71, 56.8%) and majority were in the overweight category (n=55, 44%) while 24.8% patients were in obese category, 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%. This signifies that sampling was adequate in terms of ABO grouping and Rh typing of the study population.

Prechemotherapy thrombocytopenia was noted in 5.4% patients; all were having grade I thrombocytopenia (75,000- 1.5Lakhs/ $\mu$ l). The platelet transfusion was recommended for those, who had thrombocytopenia or bleeding manifestations irrespective of platelet count. In post chemotherapy phase 11.2% (n=14) had thrombocytopenia. 2.4% (n=3) had gradeII (50,000 to 75,000/ $\mu$ l) thrombocytopenia and 8.8%(n=11) with grade I thrombocytopenia. The requirement of platelet products in the study population was 5.4% (n=7). This is comparable to studies by Wu et al.<sup>16</sup> which showed prevalence of platelet transfusion to be 2.5% in all cancer patients treated with any type of chemotherapy.

The presence of prechemotherapy thrombocytopenia has less significance in the requirement of platelet transfusion as evidenced by the fact that only 3 patients who had prechemotherapy thrombocytopenia required platelet transfusion during chemotherapy. While 4 patients who received platelet transfusion during chemotherapy were having normal platelet counts in prechemotherapy period.

## CONCLUSION

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

Among 125 patients included in the study, 33.6% were in the age group of 41-50 years. According to BMI, 44% of patients were Overweight (BMI=25-30) while only 24.8% were in Obese category (BMI >30). ABO grouping showed 'O' as the predominant blood group (40.8%) while AB was the least (8%). Rh (D) positive were 90.4% while Rh (D) negative were 9.6%. Majority were having Stage 3 tumor (59.2%). Prechemotherapy thrombocytopenia was present in 5.4% of patient population, with grade I thrombocytopenia (75,000- 1.5Lakhs/ $\mu$ l). The incidence of thrombocytopenia showed a minimal increase in post chemotherapy phase also increasing the severity. 11.2% of study population showed

thrombocytopenia in post chemotherapy phase. 2.4% had grade II (50,000 to 75,000/ $\mu$ l) thrombocytopenia and 8.8% with grade I thrombocytopenia.

The proportion of patients with thrombocytopenia during chemotherapy is less in carcinoma breast patients and can be treated appropriately with platelet transfusions in many cases. As evidenced in the present study on carcinoma breast patients prechemotherapy thrombocytopenia has less significance in the requirement of platelet transfusion during chemotherapy. But thrombocytopenia and platelet transfusion in patients undergoing dose intensive chemotherapy may permit chemotherapy to be administered in planned and intended doses and thereby maximise a successful outcome.

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