BACTERIOLOGICAL PROFILE AND ANTIMICROBIAL SUSCEPTIBILITY OF BLOOD CULTURE ISOLATES FROM CHEMOTHERAPY- INDUCED NEUTROPENIC CANCER PATIENTS

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ABSTRACT.

The current study's findings indicate that Gram-negative bacilli were more prevalent than Grampositive cocci in the blood cultures of cancer patients. However, there is an emerging trend of Grampositive cocci. The high prevalence of multidrug-resistant Gram-negative bacilli and Methicillin Resistant Staphylococcus aureus (MRSA) is a matter of concern. These results emphasize the importance of implementing antibiotic stewardship across clinical settings. It is crucial to restrict the use of antibiotics and instead opt for narrow-spectrum antibiotics based on culture reports whenever feasible.

INTRODUCTION.

In cancer patients, particularly those with underlying haematological malignancies, infectious complications are a significant cause of illness and death. Autopsy studies have shown that approximately 60% of deaths in these patients are related to infections (1-7). Various risk factors contribute to the development of diseases, including underlying immune deficiencies, comorbidities, and treatment-related adverse effects. It is essential to recognize that multiple predisposing factors may exist in a single patient, and their cumulative burden better reflects the risk of infection. Understanding each risk factor can guide diagnosis and treatment strategies. Cancer patients with compromised immune systems are susceptible to various infectious diseases. Bacterial infections are the most common, followed by fungal infections. Viral infections also occur frequently, often due to the reactivation of latent conditions, particularly in patients with hematological malignancies. Although less common, parasitic and other unusual infections should be considered in patients with relevant exposure history (8-12).

Chemotherapy increases the risk of infections in cancer patients by suppressing the production of neutrophils and damaging the cells lining the digestive tract. Neutrophils play a crucial role in the body's against infections, being the first line of defense and a key component of innate immunity. Neutropenia, a low neutrophil count, weakens the inflammatory response to new conditions, allowing bacteria to multiply and invade the body. Neutropenic patients often present with fever as the only sign of infection, as neutropenia masks other signs and symptoms. The disease remains a frequent and severe problem in

cancer patients undergoing chemotherapy who become neutropenic. Despite advancements in the treatment of febrile neutropenia, including the use of more effective and less toxic broad-spectrum antibiotics for outpatient therapy in low-risk patients, improved empirical antifungal regimens for non-responsive cases, and increased use of granulocyte colony stimulating factors, febrile neutropenia remains a challenging issue with a significant mortality rate. These patients' most severe bacterial infections are bloodstream infections (bacteraemia), with or without a primary infection site (13). Bacteraemia during febrile neutropenia has been extensively studied in patients with haematological malignancies, especially those undergoing hematopoietic stem cell transplants (14,15). There is limited data for solid tumours, but neutropenia remains a crucial predisposing factor (16).Bacterial bloodstream infections (BSIs) are the most common infectious complications during neutropenia, and the inadequate inflammatory response often leads to sepsis, a significant cause of death in this context.

(17). The mortality rate for BSIs in cancer patients ranges from 18% to 42% (1821). Therefore, febrile neutropenia is considered a medical emergency, and prompt administration of empirical antibiotic therapy is crucial, as it has been associated with lower morbidity and mortality rates (22-24). Treatment of these infections typically relies on empirical therapy based on established guidelines, considering local microbiology and antibiotic sensitivity patterns. In recent years, there has been

notable shift in the spectrum of pathogens isolated from blood cultures of febrile neutropenic cancer patients in the United States. Gram-positive cocci have increased from 62% to 76% of isolates, while Gram-negative bacilli and fungi have decreased from 21.5% to 14% and 15% to 8%, respectively (25). A similar shift towards Gram-positive bacteria predominance has been reported in consecutive clinical trials conducted by the European Organization on the Research and Treatment of Cancer (EORTC) between 1973 and 2000, although Gram-positive and Gram-negative isolates were approximately equal in the most recent period of 1998-2000 (26).

Bloodstream infection (BSI) remains a significant problem for cancer patients, causing delays in chemotherapy, reducing effective dosage, and prolonging hospital stays. BSI can lead to inadequate treatment and higher mortality rates. While most available data on BSI in neutropenic cancer patients come from studies involving those with haematological malignancies and stem cell transplants, myelosuppressive chemotherapy and certain malignancies themselves contribute to immunosuppression and an increased infection risk. The prompt initiation of empirical antibiotic therapy for febrile neutropenia has been widely acknowledged to reduce mortality. Appropriate empirical antibiotic treatment significantly improves survival rates following BSI, particularly in neutropenic patients.Recent studies have observed a shift in the cause of BSI among febrile neutropenic patients with haematological malignancies, with Gram-negative organisms becoming more prevalent compared to Gram-positive ones. This change is likely due to improved management practices, such as enhanced catheter care and the

implementation of maximal barrier measures during catheter insertion. Additionally, a decrease in severe mucositis and the discontinuation of quinolone prophylaxis in some institutions have resulted in a decrease in viridians group streptococci but an increase in Gramnegative bacilli (GNB). Notably, the rising incidence of multidrug resistance among GNB poses a significant global therapeutic challenge.

BSI in neutropenic patients with solid tumours appears to be an underreported complication. These patients are typically treated empirically using the same antibiotic regimen as those with haematological malignancies. However, limited information is available regarding the causes of BSI in patients with solid tumours, and there are no comparative studies investigating BSI in these two distinct patient populations.

The objective of this prospective study was to identify differences in the characteristics, causes, antibiotic resistance patterns, and outcomes of BSI between neutropenic patients with haematological malignancies and those with solid tumours. We also aimed to evaluate the potential impact of these factors on empirical antibiotic therapy and clinical outcomes.

MATERIAL AND METHODS.

• Study Area:- The study was conducted in the Department of Microbiology of Modern hospital raj bagh, Srinagar.

• Study Period:- 6 months of study.

• Study Design:- Hospital-Based Descriptive Study.

• Study Population:- Patients with the clinical suspension of bloodstream infections presenting to the Radiotherapy Department of modern hospital Srinagar.

1. Inclusion Criteria:-

a. Patients presenting to the radiotherapy department with chemotherapy-induced neutropenia and suspected of having

b. bloodstream infections.

2. Exclusion Criteria:-

a. Patients on antibiotic treatment.

b. Blood cultures are received from patients presenting to departments other than the radiotherapy department.

• Sample Size:- On average, 8-9 Blood samples /month for culture & sensitivity from chemotherapy-induced neutropenic cancer patients are received in the Department of Microbiology. As the study period is six months, a total of (not least) 50 Samples will be evaluated.

• Sampling Technique:- Non-probability consecutive sampling technique will be used. Detail history was taken as per the proforma attached. The study was undertaken after the approval of the Ethical Committee.

SAMPLE COLLECTION

A region approximately 5 cm in diameter above the venepuncture site was sterilized using 70% alcohol. Then, povidone-iodine was applied in concentric circles over the place and allowed to dry for at least 1 minute. The place was then aseptically inoculated into blood culture bottles, and the exposed cap septum was disinfected with 70% isopropyl alcohol. Under sterile conditions, 5 to 10 ml of blood was collected and transferred to 50 ml bottles containing Brain Heart Infusion (BHI) broth. The bottles were gently shaken and incubated at 37ºC for 18-24 hours.

OBSERVATIONS AND RESULTS

The following observations were made in the present study:-

TABLE-1 AGE DISTRIBUTION OF STUDY POPULATION (N=50)

S. No.	Age group (years)	No. of Patients	Percentage (%)
1.	1-20	1	2
2.	21-40	10	20
3.	41-60	25	50
4.	61-80	14	28

Table 1 and Figure 1 shows that the most common age group belongs to 41-60 years (50%), followed by 61-80 years (28%). The mean age was 58

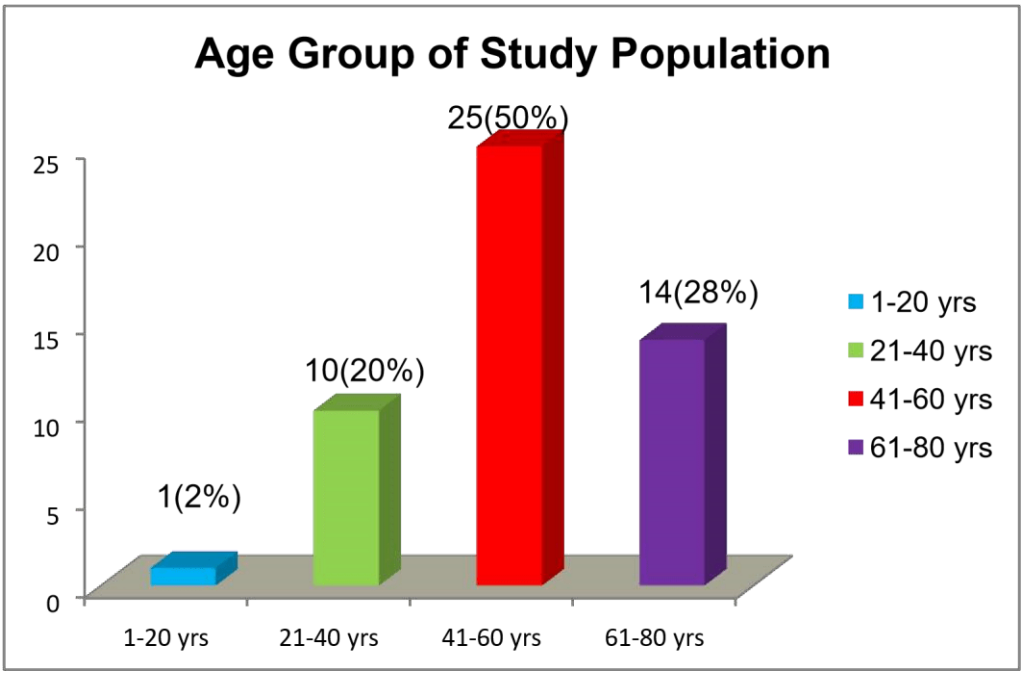

FIGURE 1:- AGE DISTRIBUTION OF STUDY POPULATION (N=50) TABLE-2 GENDER DISTRIBUTION OF STUDY POPULATION (N=50)

S. No.	Gender	No. of Patients	Percentage (%)
1.	Male	20	40
2.	Female	30	60
3.	Total	50	100

The above table shows that out of 50 patients, there was a predominance females (60%) over males (40%). Male to Female ratio was 0.67:1.

DISCUSSION

Infection remains a frequent and severe problem in cancer patients undergoing chemotherapy-induced neutropenia. Despite significant advancements in treating febrile neutropenia (FN), including more effective and less toxic broadspectrum antibiotics, FN presents a challenging therapeutic issue with a special mortality rate. One of the most severe types of bacterial infections in these patients is bloodstream infections (bacteremia), which may occur with or without a primary site of infection. Hence, this study aimed to isolate various bacteria from blood cultures in chemotherapy-induced neutropenic cancer patients and assess their antimicrobial susceptibility.

The study revealed that the most common age group among the patients was
4160 years (50%), followed by 61-80 years (28%). The mean age was 51.8 years (Table 1). Similar findings were reported by Bhat et al., where the highest number of cases of solid organ tumors was observed in the age group of 50-55 years.

Out of the 50 patients, there was a predominance of females (60%) over males (40%), with a maletofemale ratio of 0.67:1 (Table 2). Arega et al. also reported a similar female predominance with a maleto-female balance of 0.9:1. At the same time, Gaytán-Martínez et al. found a higher male predominance with a ratio of 1.6:1. In contrast, Fayyaz et al. reported a majority of male patients (70.7%).

Regarding the distribution of cancer types, the majority of patients had Chronic Myeloid Leukaemia (26%), followed by Cervical Cancer (14%), Breast Cancer, and Ovarian Cancer (10% each) (Table 3). Arega et al. also reported a predominance of leukemia cases, particularly Acute Lymphocytic
Leukaemia (ALL) is the most common hematological malignancy, and Adenocarcinoma is the most common solid organ tumor.

Bloodstream infections (BSIs) were identified as a significant cause of morbidity and mortality in the study, with a prevalence rate of 40% (Table 4). Similar results were reported by Al-Mulla et al. and Gaytan-Martínez et al., with prevalence rates of 38% and 35%, respectively. However, Prabhas et al. reported a slightly higher prevalence of 48% in cancer patients, while Babu et al. reported a lower prevalence of 15%.

The age group that exhibited the highest positive culture results was 41 to 60, followed by the 61 to 80 age group. However, the disparity in culture positivity between these age groups did not reach

statistical significance (p=0.074), according to Table 5. This finding is consistent with a study by AlMulla NA et al., which also found no significant association between age and bacteremia episodes

Regarding gender distribution, in our study, more positive bacterial cultures were obtained from females compared to males, with a male-tofemale ratio of 0.81:1.

Nevertheless, this difference was not statistically significant (p=0.768), according to Table 6. Similarly, Al-Mulla NA et al. observed no significant association between gender and bacteremia episodes (57).

In terms of the types of cancer, both hematological malignancies and solid organ tumors had an equal positivity rate of 40% each, as indicated in Table 7. This finding aligns with a study by Velasco E et al., which also reported no difference in the proportions of aerobic Gram-negative bacilli between patients with hematological malignancies and those with solid tumors (56% vs. 56.4%, respectively) (71).

In our study, Gram-negative bacilli accounted for 55% of the total bacterial isolates, while Grampositive cocci constituted only 45% (Table 8). This finding is consistent with a study conducted by Babu KG et al., where 57.8% of the isolates were Gram-negative bacilli and 39.84% were Grampositive cocci (58). The predominance of Gram-negative bacilli in febrile neutropenia has also been well-established by several other studies (47, 49, 72-74). However, Arenga B et al. reported a higher number of Gram-positive cocci (60.5%) compared to Gramnegative bacilli (39.5%) (60).

REFERENCES

1. Chang HY, Rodriguez V, Narboni GI, Bodey GP, Luna MA, Freireich EJ. Causes of death in adults with acute leukemia.

Med. 1976;55(3):259-68.

2. Hersh EM, Bodey GP, Nies BA, Freireich EJ. Causes of death in acute leukemia: A ten-year study of 414 patients from 19541963. Jama. 1965;193(2):105-9.

3. Homsi J, Walsh D, Panta R, Lagman R, Nelson KA, Longworth DL. Infectious complications of advanced cancer. Support Care Cancer. 2000;8(6):487-92.

4. Hughes WT. Fatal infections in childhood leukemia. Am J Dis Child. 1971;122(4):283-7.

5. Inagaki J, Rodriguez V, Bodey GP. Causes of death in cancer patients. Cancer. 1974;33(2):568-73.

6. Mayo JW, Wenzel RP. Rates of hospital -acquired bloodstream infections in patients with specific malignancy. Cancer. 1982;50(1):187-90.

7. Nosari A, Barberis M, Landonio G, Magnani P, Majno M, Oreste P, et al. Infections in haematologic neoplasms: autopsy findings. Hematological. 1991;76(2):135-40.

8. Freifeld AG, Kaul DR. Infection in the patient with cancer. In Abeloff's Clin Oncol. 2020:544-64.

9. Viscoli C, Castagnola E. Prophylaxis and empirical infection therapy in cancer patients. Principles and Practice of Infectious Diseases. Philadelphia, Churchill Livingstone Elsevier. 2010:3793-807.

10. Donnelly JP. Infections in the immunocompromised hosts: General principles. Principles and practice Infect Dis. 2005:3781-792.

11. Vusirikala M. Supportive care in hematologic malignancies. Wintrobe" s C Hemato ogy Phi ade: Lippincott Williams & Wilkins. 2009:1747-90.

12. Maschmeyer G, Haas A. The epidemiology and treatment of infections in cancer patients. International J Antimicrob Agents. 2008;31(3):193-7.

13. Viscoli C, Bruzzi P, Castagnola E, Boni L, Calandra T, Gaya H, et . European J Cancer. 1994;30(4):430-7.

14. Frère P, Baron F, Bonnet C, Hafraoui K, Pereira M, Willems E, et al. Infections after allogeneic hematopoietic stem cell transplantation with a nonmyeloablative conditioning regimen. Bone Marrow Transplant. 2006;37(4):411-8.

15. Nørgaard M, Larsson H, Pedersen G, Schønheyder HC, Sørensen HT. Risk of bacteremia and mortality in patients with hematological malignancies. Clin Microbiol Infect. 2006;12(3):217-23.

16. Toussaint E, Bahel-Ball E, Vekemans M, Georgala A, Al-Hakak L,
Paesmans M, et al. Causes of fever in cancer patients (prospective study over 477 episodes). Supportive Care in Cancer. 2006;14(7):763-9.

17. Bos MM, Smeets LS, Dumay I, De Jonge E. Bloodstream infections in patients with or without cancer in a large community hospital. Infect.
2013;41(5):949-58.

18. Collin BA, Leather HL, Wingard JR, Ramphal R. Evolution, incidence, and susceptibility of bacterial bloodstream isolates from 519 bone marrow transplant patients. Clin Infect Dis. 2001;33(7):947-53.

19. Krupova I, Kaiserova E, Foltinova A, Kovacicova G, Kiskova M, Krchnakova A, et al. Bacteremia and fungemia in pediatric versus adult cancer patients after chemotherapy: comparison of etiology, risk factors, and outcome. J Chemother. 1998;10(3):236-42.