International Journal of Health Sciences and Research
Vol.12; Issue: 7; July 2022
Website: www.ijhsr.org
Original Research Article *ISSN: 2249-9571*

Evaluation of the Clinical Profile and Application of MASCC Scoring in the Severity Grading of Febrile Neutropenic Patients

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DOI: https://doi.org/10.52403/ijhsr.20220742

ABSTRACT

Background: Febrile neutropenia is a major cause of mortality and morbidity in patients on chemotherapy for malignancy. [1][2] It is an oncologic emergency which requires prompt recognition, diagnosis and treatment. It is defined as the single body temperature (oral temperature) of > 38° C (101°F) or an oral temperature of ≥ 38.3◦C persisting for more than 1 hours with an absolute neutrophil count (ANC) of < 1500 cells/mm³. The Multinational Association for Supportive Care Cancer Risk Index is an internationally validated scoring system, published in the year 2000, identifies the low-risk patients to develop serious complications, who can potentially be treated as out patients with oral antibiotics. [3] [5] [6] The score quantifies the risk of FN-related complications by incorporating the patient and cancer characteristics, giving a maximum score of 26. Score more than 20 points is considered as low risk compared to those with less than or equal to 20 points with high risk for serious FN-related complications.

Methods: This is a prospective observational study conducted on 100 patients presenting to Amrita Institute of Medical Sciences (AIMS), Kochi, with Febrile Neutropenia. MASCC Risk Index Score was used to stratify patients into low-risk and high-risk groups. Blood culture and sensitivity were done for all patients apart from all relevant specific investigations.

Results: Out of 100 patients included in the study, 51 were males. FN incidence was more in the age group between 46 and 60. MASCC Risk Index Scoring was used to calculate the level of risk. 60 patients were belonging to low-risk category. Incidence of FN was more in Haematological malignancies, especially in Acute Myeloid Leukaemia. Only 32 patients were found to be having positive blood culture – most of them being found to have Gram-negative bacteria. Appropriate IV antibiotics were used for the initial treatment of the culture positive patients apart from other supportive measures. [8] Regarding patient disposal, 34 patients needed ICU care and 55 were treated in the ward. 11 patients expired - the mortality being more in culture positive patients with one or more associated co morbidities.

Conclusions: We analysed that episodes of FN were common in the middle-aged population. The MASCC score identified patients with febrile neutropenic episodes as elevated risk and low risk. [4] [7] Gram-negative bacteraemia is the predominant cause of febrile neutropenia in our setup.

Keywords: [MASCC, Febrile Neutropenia, Malignancy, Chemotherapy, Emergency]

INTRODUCTION

Febrile neutropenia (FN) is a life-threatening complication in cancer patients undergoing chemotherapy with higher mortality rate. [12] It is an onco-medical emergency which needs prompt recognition, early diagnosis, and immediate management. Febrile neutropenia is defined as the single body temperature (oral temperature) of > 38° C (101°F) or an oral temperature of ≥ 38.3◦C persisting for more than 1 hours with an absolute neutrophil

count (ANC) of < 1500 cells/mm³. These immune-compromised febrile neutropenic patients are at higher risk of infection even from the commensal organisms present in their own body – in the oral cavity, gut, skin etc. The severity of infection is also high causing mortality in many of these patients.

The Multinational Association for Supportive Care Cancer Risk Index is an internationally validated scoring system, published in the year 2000, identifies the low-risk patients to develop serious complications, who can potentially be treated as out patients with early antibiotics. The score quantifies the risk of FN-related complications by incorporating the patient and his or her cancer characteristics. The maximum score is 26. Score of more than 20 is considered as low risk and the score of 20 or less as high risk to develop FN related serious complications.

AIM

Evaluation of the clinical profile and application of MASCC scoring in the severity grading of Febrile Neutropenic Patients

OBJECTIVES

1. To evaluate the clinical profile and outcome of Febrile Neutropenia patients.
2. To evaluate validity of the MASCC Risk Index Score in the severity assessment of Febrile Neutropenia patients.

MATERIALS & METHODS

The study was conducted on 100 successive febrile neutropenic patients fitting in the inclusion criteria (vide infra) presenting to the Emergency Department and Oncology Out Patient Department of Amrita Institute of Medical Sciences, a quaternary Medical Centre in Kochi, Kerala, India' The study period was between November 2020 and March 2021.

Inclusion Criteria:

1. Febrile Neutropenic patients on chemotherapy.
2. Histological diagnosis of malignancy.
3. Age group - from 1 to 90 years
4. Oral Temperature greater than 101˚F
5. ANC < 1500 cells/mm3

Exclusion Criteria:

1. Pregnancy
2. HIV Patients with cancer
3. HCV patients
4. ANC > 150

The data collected for the study included:

1. Sociodemographic data: Sex, Age
2. Clinical data: Presenting complaints, type of cancer, treatment details, co morbidities
3. Vitals: Temperature, heart rate, respiratory rate, oxygen saturation and blood pressure.
4. Laboratory investigations: Complete Blood Count including WBC count – Total count and differential count, absolute neutrophil counts, C-reactive protein, blood culture and sensitivity.
5. MASCC Risk Index Scoring: Max score 26: Low risk > 21; High risk ≤ 21

- Burden of Illness (Symptom severity) None or mild +5: Moderate +3: Severe 0
- No hypotension – 5 points
- No chronic obstructive pulmonary disease – 5 points
- Solid tumour or no previous fungal infection – 4 points
- No dehydration requiring parenteral fluids – 3 points
- Outpatient status – 3 points
- Age <60 years – 2 points

Statistical Analysis

This is a prospective observational study on subjects fitted to the inclusion and exclusion criteria.

RESULT

Of the 100 Febrile Neutropenic patients studied 51 were males, the incidence being more in the age group between 46 and 60 years (25 patients). The incidence was more common in haematological malignancies, especially in Acute Myeloid Leukaemia (32 patients) and B-Acute Lymphoid Leukaemia (25 patients). Blood culture was sterile in 66 patients; in most of the patients gram negative bacterial predominance was there

(22 patients). According to MASCC Risk Index Scoring 60 patients belonged to low-risk group. 34 patients needed ICU care while 55 patients were treated in the ward. The rest 11 patients died, who were found to have positive blood culture, belonging to high risk group with multiple comorbidities. While 17 patients did not have any comorbidity, 60 patients had 2 and rest had more than 2 comorbidities. In this study severe neutropenia (ANC <500) was found in 72 patients; in 16 patients ANC was more than 1000 while in the rest it was between 500 and 1000. Most of these patients were on 3+7 regimen chemotherapy (30 patients), being followed next by BFM 95 protocol (16 patients).

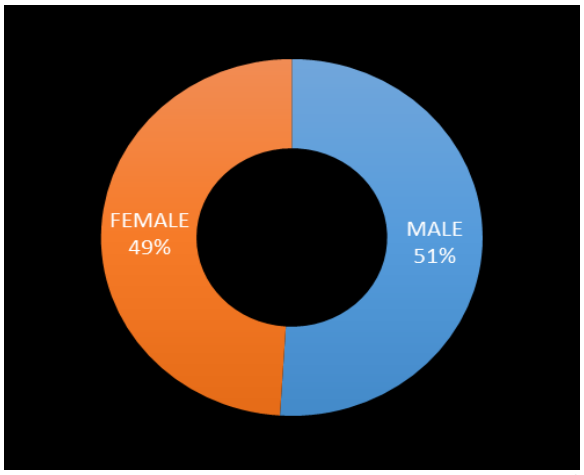

Figure 1: Doughnut diagram showing the distribution of gender.

A total of 100 patients were included in the study satisfying the inclusion criteria, 51% are male and 49% are female.

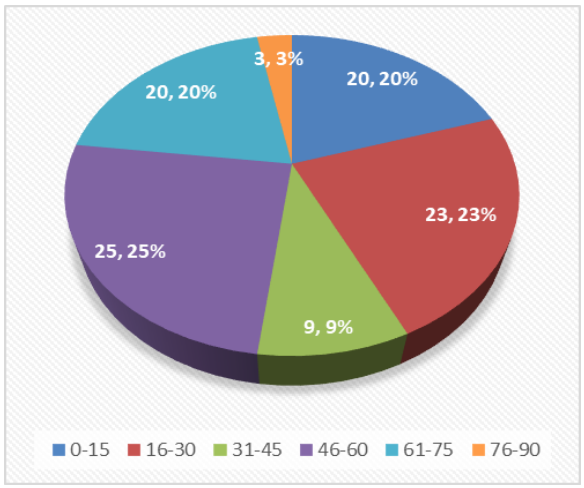

Figure 2: Pie in the 3-D graph showing the distribution of age

A total of 100 patients included in the study satisfying inclusion criteria, age distribution group between 0-15 has 20%, 16-30 has 23%,31-45 has 9%, 46-60 has 25%,61-75 has 20% and 76-90 has 3%.

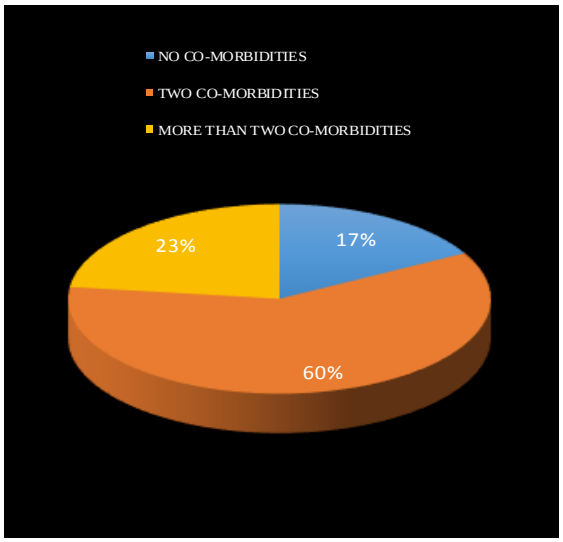

Figure 3: pie in 3-d showing distribution of comorbidities.

A total of 100 patients included in the study, 60% have two co-morbidities,23% have more than two co-morbidities and 17% have no co-morbidities. (co-morbidities includes diabetes mellitus, hypertension, coronary artery disease, chronic kidney disease, chronic liver disease, chronic obstructive pulmonary disease etc)

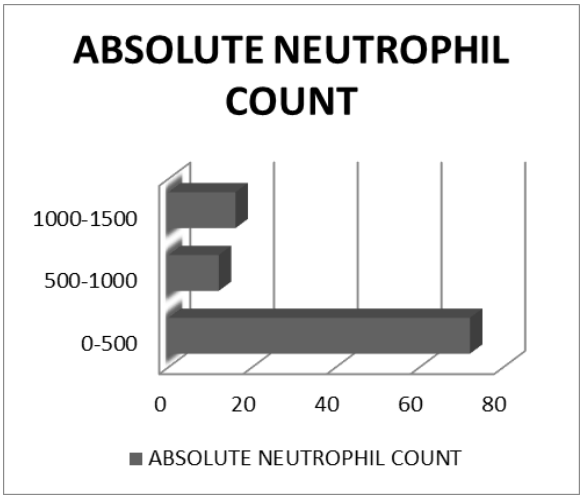

Figure 4: Clustered graph showing the distribution of ANC

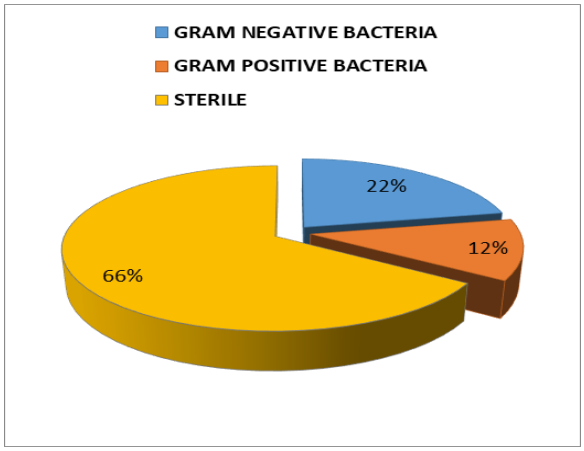

Figure 5: Pie in the 3-D graph showing the distribution of gram staining.

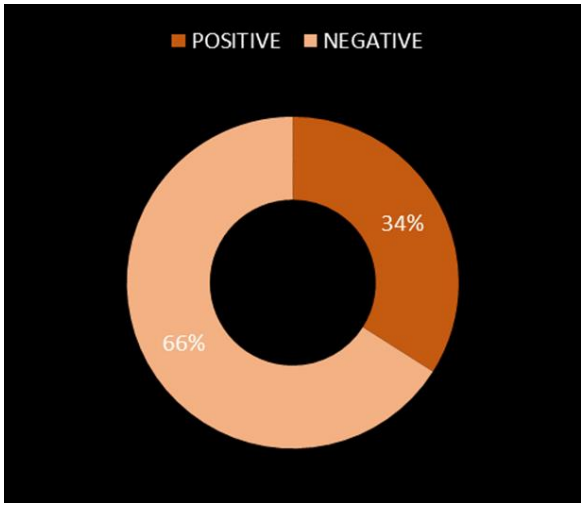

Figure 6: doughnut diagram showing blood culture report

Among 100 patients included in the study,72% of patients having their ANC lies between 0-500, 12% lies between 500-1000, and 16% lies between 1000-1500.

A total of 100 patients were included in the study, 66% are sterile, 22% are gram-negative staining and 12% are gram-positive staining. [9]

A total of 100 patients included in the study, 66% patients are having negative blood culture and 34% of patients are having positive blood culture

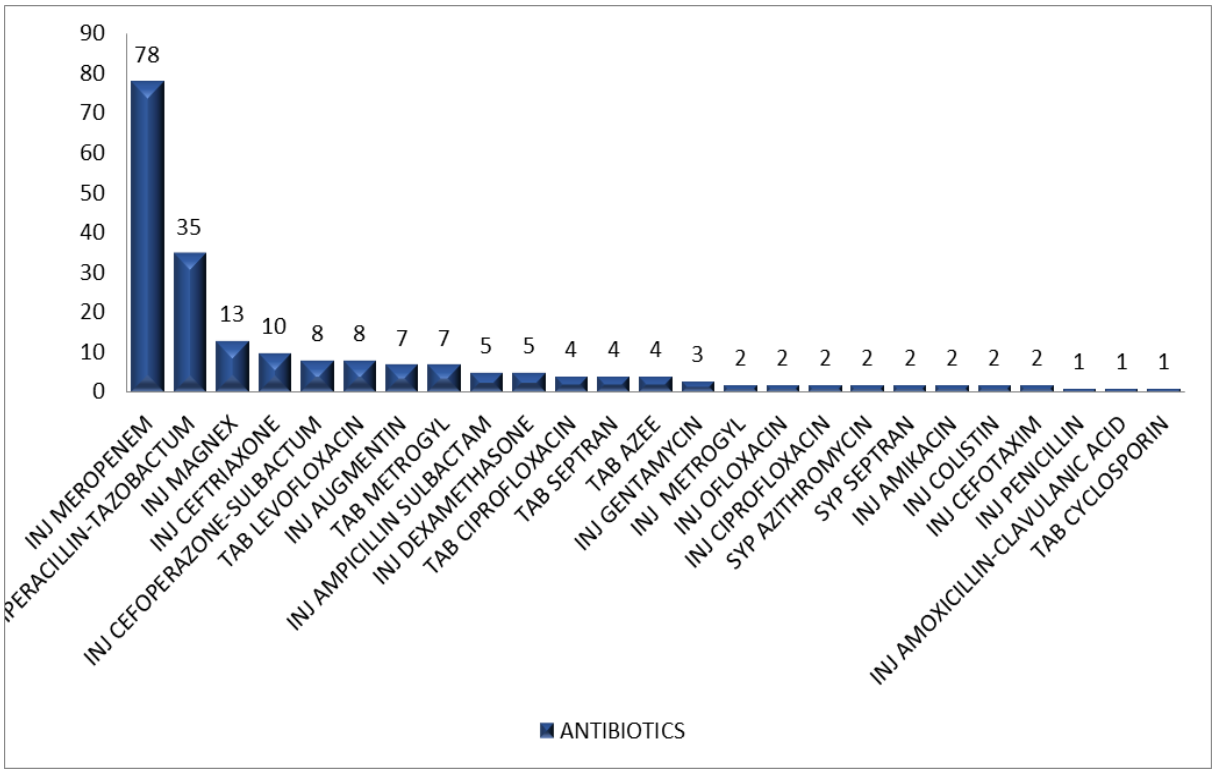

Figure 7: clustered column showing the distribution of antibiotic

Among the 100 patients included in the study, 78% of patients were treated with Inj meropenem, 35% with Inj piperacillin and tazobactam, 13% with Inj magnex, 10% with Inj ceftriaxone, 8% with Inj cefoperazone-sulbactam and Tab levofloxacin,7% with Inj augmentin and tab metrogyl, 5% with Inj ampicillin-sulbactam

and Inj dexamethasone, 4% with Tab ciprofloxacin, tab septran and tab azithromycin, 3% with Inj gentamycin and 2% with Inj Ciprofloxacin, Syrup Azithromycin, syrup septran, Inj amikacin, Inj colistin, and Inj cefotaxime and 1% with Inj penicillin, Inj amoxicillin-clavulanic acid, and Tab cyclosporine. [10] [11]

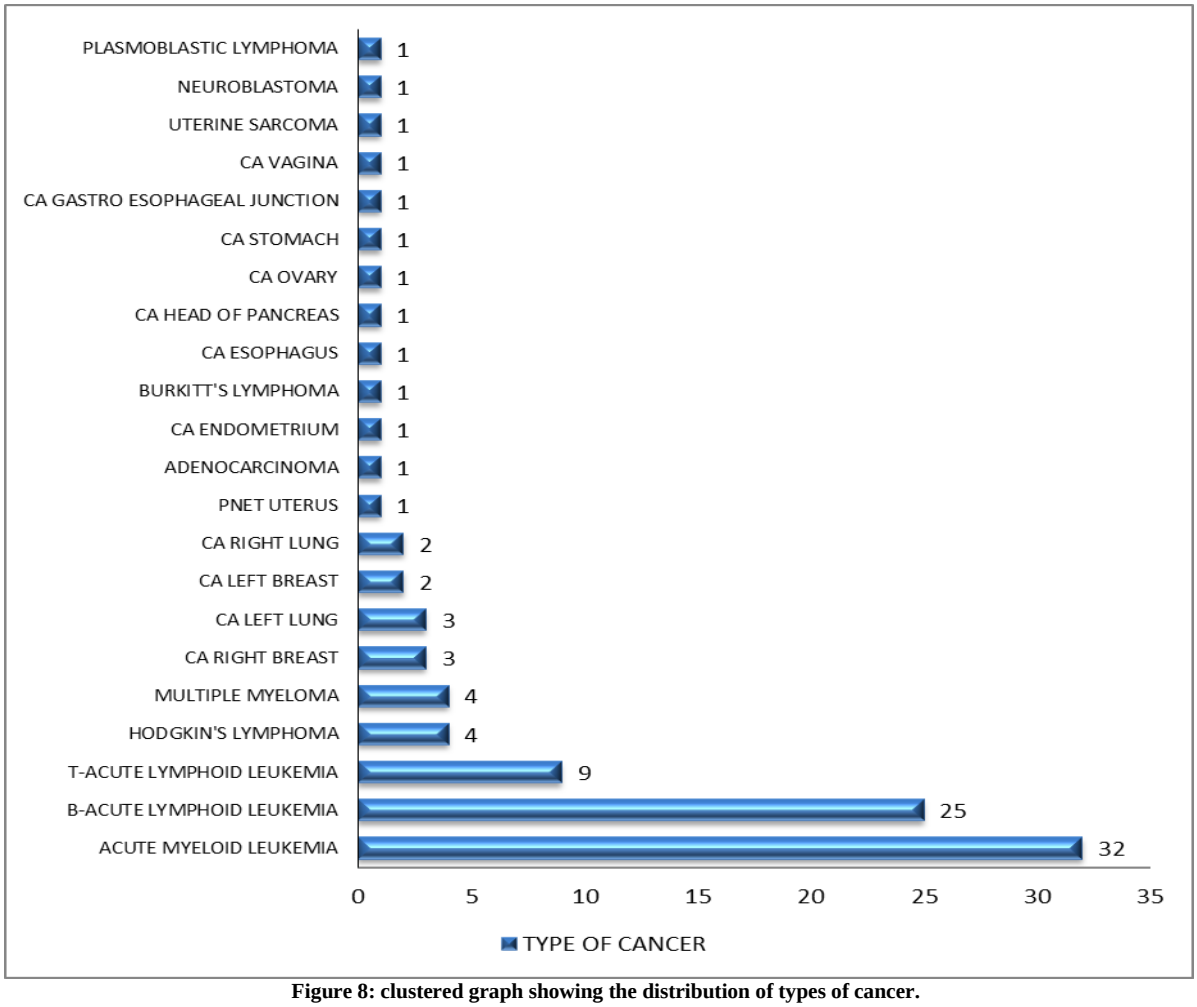

Figure 8: clustered graph showing the distribution of types of cancer.

A total of 100 patients were included in the study. 32% have acute myeloid leukemia, 25% have B-acute lymphoid leukemia, 9% have T-acute lymphoid leukemia, 4% have Hodgkin's lymphoma and multiple myeloma, 3% have CA left lung and right breast, 2 % have CA left breast and right lung, 1% had PNET uterus, adenocarcinoma, CA endometrium, Burkitt's lymphoma, CA gastroesophageal junction, CA esophagus, CA head of the pancreas, CA ovary, CA stomach, CA vagina, uterine sarcoma, neuroblastoma, plasmoblastic lymphoma. [116]

Among the 100 patients included in the study, 30% under the chemotherapy using 3+7 regimen, 16% with BFM 95 protocol,11% with BFM 2009 protocol, 6% with docetaxel, 5% with carboplatin, 4% with taxol and ABVD regimen, 3% with CVAD and CYBORD, 2% with PACLITAXEL and 6 FEC and 1% with R IVAC protocol, MP regimen, GEM CAP, EPOCH, CLADARABINE, CCG, BEP regimen, AZACYTIDINE, and BFM 2002 protocol. (17)

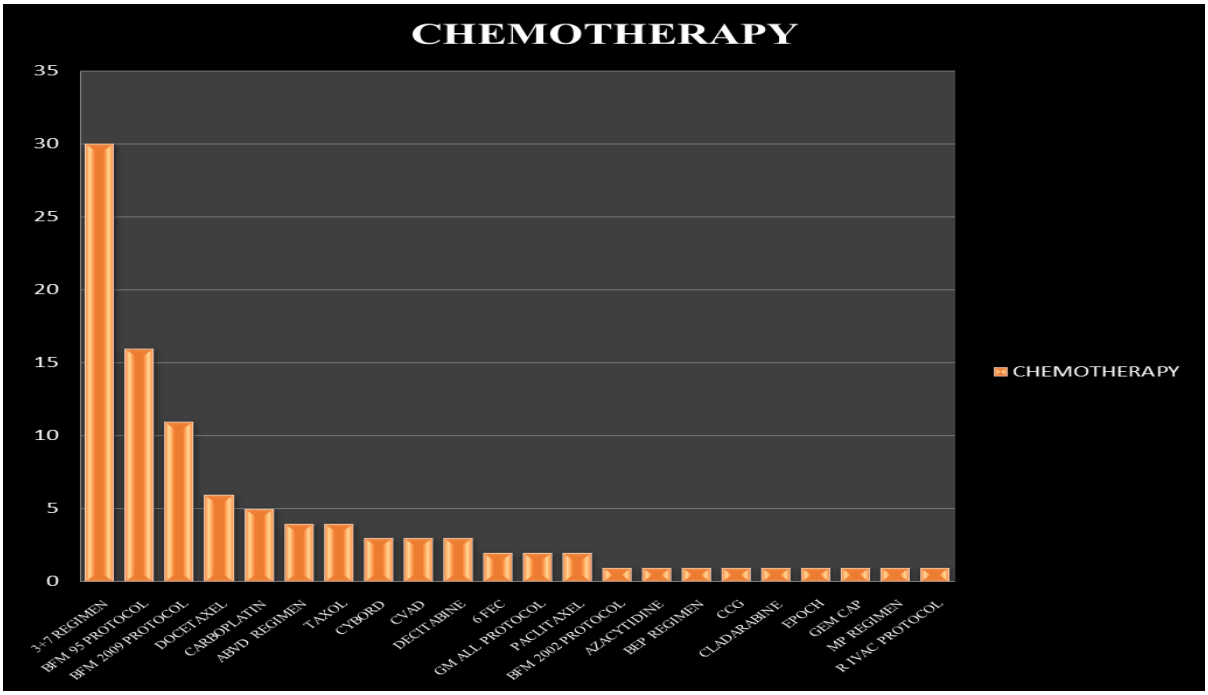

Figure 9: clustered graph showing the distribution of types of chemotherapy.

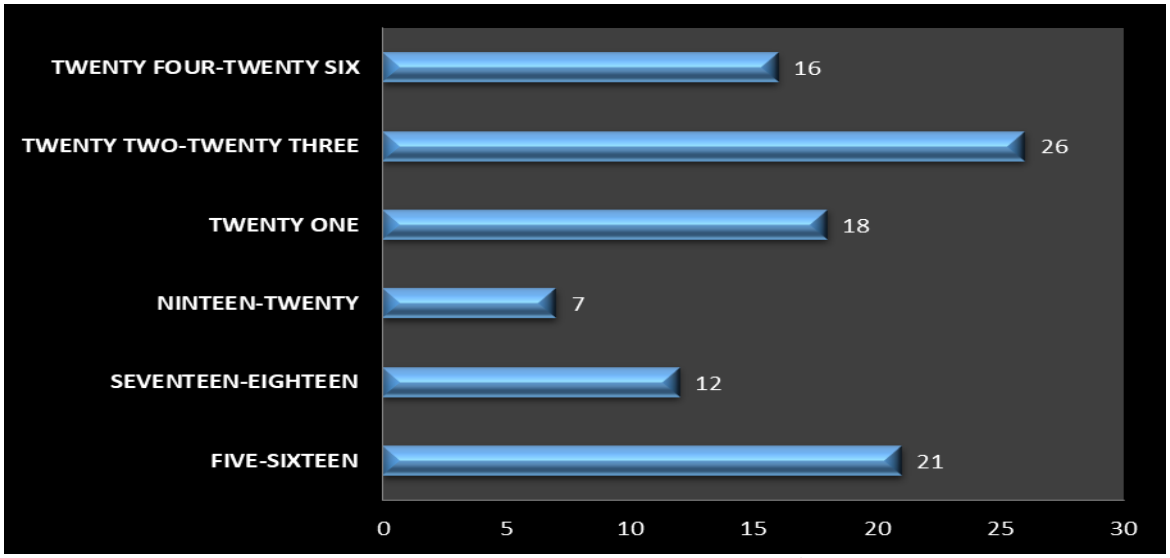

Figure 10: clustered bar graph showing the distribution of MASCC score

Among 100 patients included in the study, 16% of patients are having MASCC scoring of 24-26. 26% of patients are having MASCC scoring of 22-23. 18% of patients are having a MASCC scoring of 21. 7% of patients are having MASCC scoring of 19-20. 12% of patients are having MASCC scoring of 17-18. 21% of patients are having MASCC scoring of 5-16. [15] [16] [17]

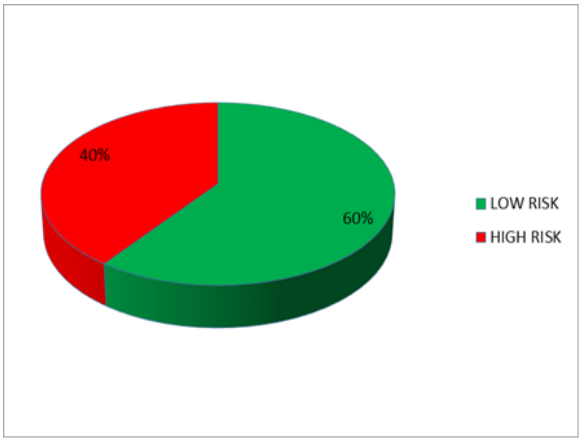

Figure 11: pie in a 3-D chart showing the distribution of level of risk

Among 100 patients included in the study, 60% patients are at low risk and 40% patients are at high risk.

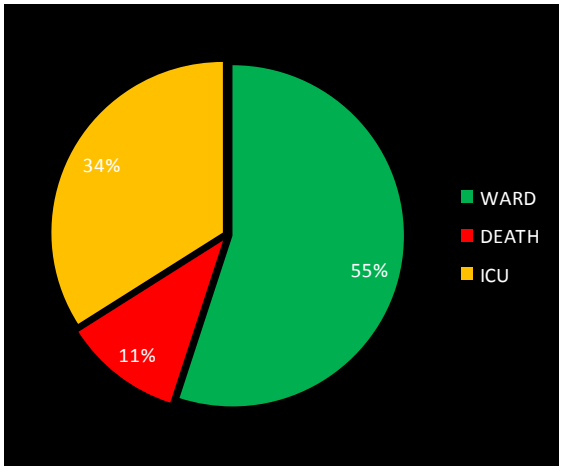

Figure 12: exploded pie chart showing the distribution of outcome

A total of 100 patients were included in the study satisfying the inclusion criteria, 55% of patients shifted to the ward, 34% patients shifted to ICU and 11% patients expired.

DISCUSSION

Febrile Neutropenic episodes commonly occur following chemotherapy. Incidences are noted more in haematological malignancies than solid tumours. The association of febrile neutropenia with acute leukaemia was first demonstrated by Bodey. In our study, out of 100 cases of FN, there were 51 males and 49 females with FN episodes. Out of this, 66 were haematological malignancies and 34 were solid tumours. [18] Acute myeloid leukaemia was the commonest underlying haematological malignancies. The presence of medical comorbidities also predicted poor outcomes. 3+7 regimen was commonly used chemotherapy (30%). Absolute neutrophil count (ANC) is less than 500 cells/mm3 for 72% of patients. Blood culture showed positive in 34 cases, among which 22 were gram-negative and 12 gram-positive species. This study helped us find that the MASCC risk-index score is a useful tool to identify patients at low risk of complications. Using the MASCC score, the level of risk was calculated. 60% low risk and 40 % elevated risk were documented. In patients with a MASCC score of >21 better response to treatment was observed in the study which showed very high statistical significance. Elevation of C-reactive protein (a sign of serious infection) was noticed in FN patients in this study also. 78% of patients were treated with beta-lactam antibiotics. IV meropenem was the first-line drug. The oral treatment was given with ciprofloxacin. In our study, in-patient status at the onset of fever, presence of medical co-morbidities, ANC <50 cells/mm3, demonstrable bacteraemia had a poor outcome.1[3] [14][15]1

Recent studies report a wide range of mortality rates (7– 33%) in FN patients. The mortality in our study was 11% which is comparable to other studies.

CONCLUSION

Febrile Neutropenia episodes with tachypnoea, hypotension, temperature >103°F, inpatient status at the onset of fever, ANC <100 cells/mm3, elevated CRP, and demonstrable bacteraemia had a poor outcome in terms of mortality and length of hospital stay. The initial step should be risk stratification of patients using a validated risk assessment tool like the MASCC Risk Index Score. High risk and low risk of complication are identified using this scoring system and treated with IV and oral antibiotics respectively. [19] [20] Gram-negative bacteraemia is the predominant cause of febrile neutropenia in our setup. Significant higher mortality was observed in those episodes with positive cultures and elevated risk.

We conclude that the MASCC risk index score is a tool that helps identify FN patients at low risk of complications. In the future, applying this score would help in treating high-risk patients aggressively from the start and at the same time identifying low-risk patients who may be treated less aggressively with a potential early discharge and a marked reduction in hospital cost.

Acknowledgement: None
Conflict of Interest: None

Source of Funding: None

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How to cite this article: Binu Bright, Aiswarya Ravi, Dhanasekaran B. S et.al. Evaluation of the clinical profile and application of MASCC scoring in the severity grading of febrile neutropenic patients. *Int J Health Sci Res.* 2022; 12(7):298-306.
DOI: *https://doi.org/10.52403/ijhsr.20220742*

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