

Early Outcome of Hospitalized Febrile Neutropenic Patients in Medicine Department of Dhaka Medical College Hospital (DMCH)

Dr. Md. Riad Hossain

Registrar

Department of Medicine

DMCH

Background

Neutropenic fever is defined as a single oral temperature greater than or equal to 101⁰ F (38.3⁰ C) or a temperature greater than or equal to 100.4⁰ F (38⁰ C) for at least an hour, with an ANC of less than 1500/mcL in blood. A neutropenic patient may show few signs of infection because they lack the white blood cells needed to initiate an inflammatory response .

An infection in neutropenic patient can quickly progress to sepsis which can be fatal.

Rationale of the study

- As febrile neutropenia is a medical emergency with high morbidity & mortality and its complications are preventable with early administration of judicious use of antibiotics .
- The study is done to evaluate early outcome of febrile neutropenia to develop empirical antibiotic guidelines for the initial management of febrile neutropenia.

Materials and Methods:

- **Study Design:** Prospective observational study.
- **Place of Study:** Department of Medicine, Dhaka Medical College Hospital.
- **Study Period:**12 months.
- **Study population:** Total 100 febrile neutropenic patients admitted to the medicine ward of DMCH.
- **Sampling Method:** Purposive sampling

Objective

- **General :**
- To determine the early outcome of hospitalized febrile neutropenic patients

Objective

- **Specific :**

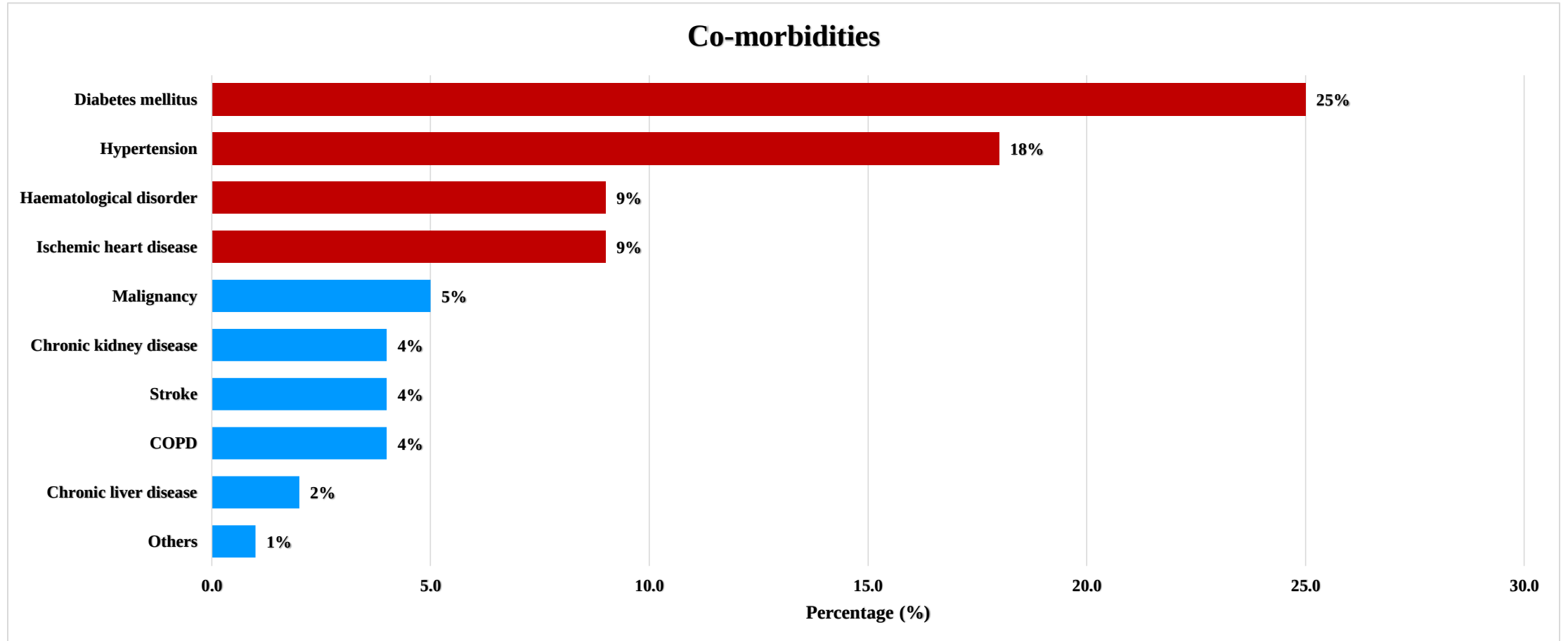
- To observe the progression of febrile neutropenic patients in 7 days.
- To evaluate the cause of febrile neutropenia.
- To evaluate the complications of febrile neutropenia.

Results

Presenting complaints of the febrile patients in the study (n=100).

Sign symptoms	Frequency (n)	Percentage (%)
Fever	100	100
Vomiting	39	39
Headache	25	25
Confusion	24	24
Abdominal pain	20	20
Breathlessness	17	17
Rash	13	13
Cough	13	13
Dysuria	13	13
Gum bleeding	13	13
Drowsiness	12	12
Joint pain	7	7
Chest pain	5	5
Convulsion	5	5
Diarrhoea	3	3

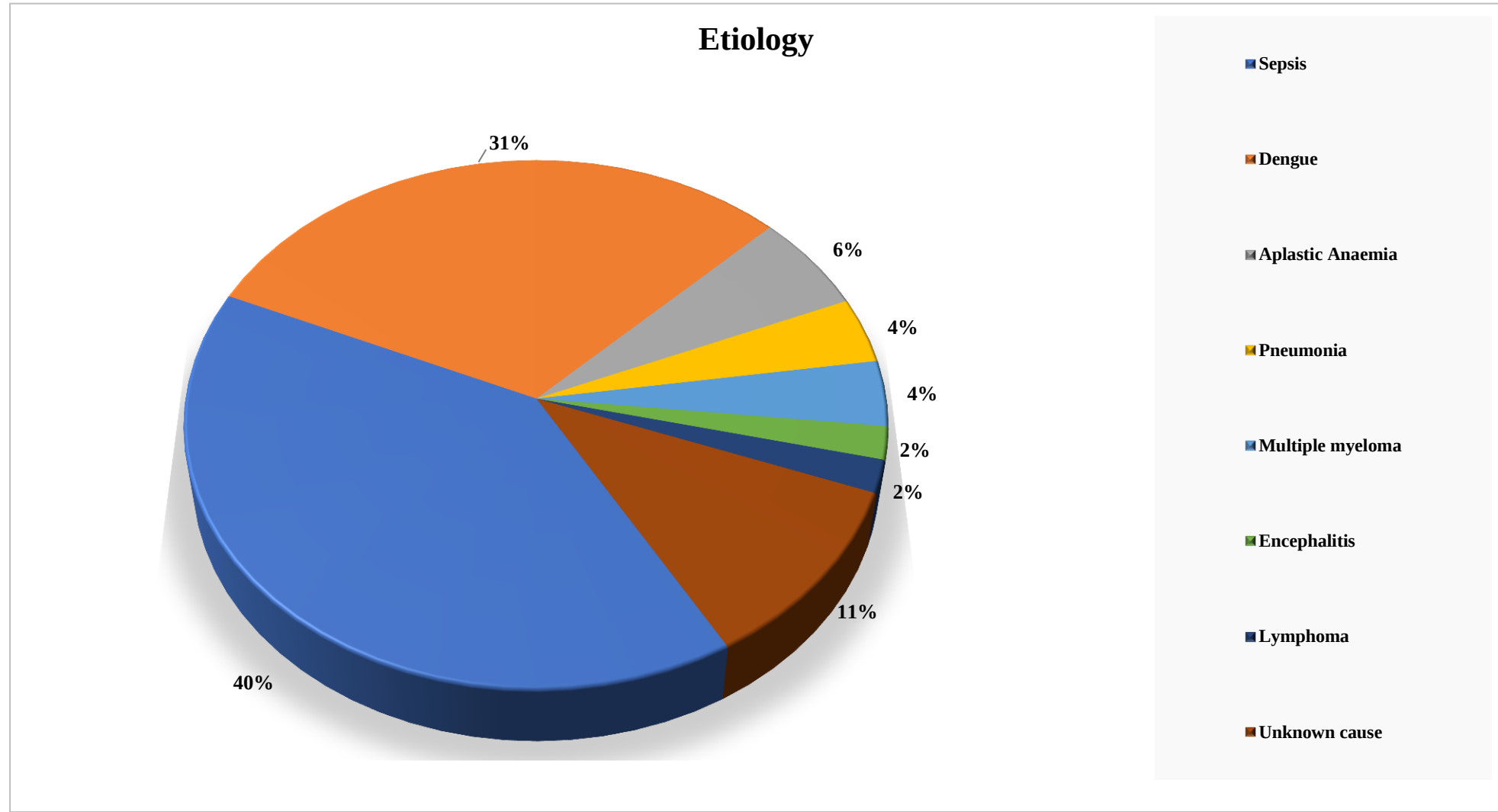
Co-morbidities among study participants (n=100).



Descriptive statistics for biophysical parameters and vital signs of study participants (n=100).

Variables	Mean±SD	Min-Max
Height, m	1.53±0.05	1.45-1.67
Weight, Kg	50.40±6.94	37.0-78.0
BMI, Kgm ⁻²	21.54±2.78	16.40-31.57
Temperature, °F	102.36±0.69	101.0-105.0
Heart rate, beats/min	101.84±13.88	80-140
SBP, mmHg	89.10±11.20	70-120
DBP, mmHg	58.50±9.14	40-80
Respiratory rate, breaths/min	21.48±3.20	16-28

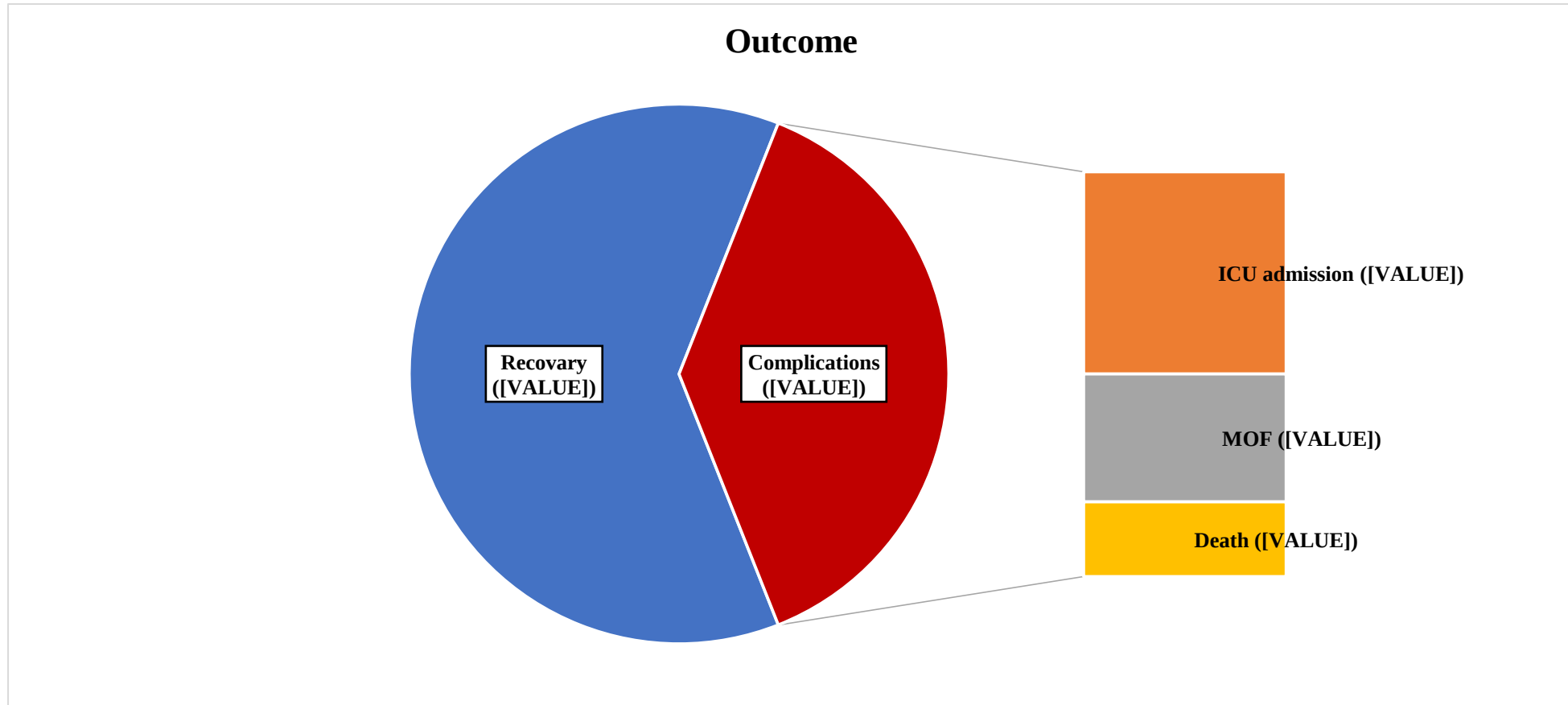
Etiological diagnosis of febrile neutropenia patients in the study (n=100).



Neutrophil count of the study population (n=100).

Neutrophil count	Descriptive statistics
Mean±SD Neutrophil count, /mCL	1056.83±404.61
Min-Max	130/mCL – 2435/mCL
Neutropenia category	
Mild (1000 to 1500 /mCL)	55 (55.0%)
Moderate (500 to 1000 /mCL)	34 (34.0%)
Severe (<500 /mCL)	11 (11.0%)

Clinical outcome of the study population (n=100).



Spectrum of bacterial isolates in the study (n=100).

Isolated microorganisms	Frequency	Percentage
Blood Culture		
Positive	7	7.0
E. coli	5	5.0
Staphylococcus spp.	2	2.0
Negative	93	93.0
Urine Culture		
Positive	13	13.0
E. coli	8	8.0
Staphylococcus spp	1	1.0
Acinetobacter spp.	1	1.0
Enterococcus spp.	1	1.0
Klebsiella spp.	2	2.0
Negative	87	87.0

Outcome of the patients in relation to etiology of febrile neutropenia in the study (n=100).

Etiology	Outcome				P value*
	Recovery (n=62)	ICU admission (n=19)	Multi organ failure (n=12)	Death (n=7)	
Sepsis	13 (32.5%)	13 (32.5%)	10 (25.0%)	4 (10.0%)	
Pneumonia	1 (25.0%)	2 (50.0%)	0	1 (25.0%)	
Dengue	29 (93.5%)	0	0	2 (6.5%)	
Multiple myeloma	3 (75.0%)	1 (25.0%)	0	0	0.002
Encephalitis	1 (50.0%)	0	1 (50.0%)	0	
Aplastic Anaemia	5 (83.3%)	1 (16.7%)	0	0	
Lymphoma	1 (50.0%)	1 (50.0%)	0	0	
Unknown cause	9 (81.8%)	1 (9.1%)	1 (9.1%)	0	

Outcome of the patients in relation to neutropenia severity (n=100).

Neutrophil count	Outcome				P value
	Recovery (n=62)	ICU admission (n=19)	Multi organ failure (n=12)	Death (n=7)	
Mean ($\pm$ SD) neutrophil count /mCL	1077.46 $\pm$ 439.24	909.47 $\pm$ 337.30	1072.5 $\pm$ 354.94	1247.14 $\pm$ 227.06	0.237†
Neutropenia severity					
Mild	34 (61.8%)	8 (14.5%)	7 (12.7%)	6 (10.9%)	0.647*
Moderate	21 (61.8%)	8 (23.5%)	4 (11.8%)	1 (2.9%)	
Severe	7 (63.6%)	3 (27.3%)	1 (9.1%)	0	

Discussion

- Among the 100 patients, the highest frequency was observed in the 18-30 years age group, constituting 38% of the total cohort.
- A previous study in Bangladesh reported a higher incidence of febrile neutropenia among younger individuals.

Ref. : Bahar T, Rahman S, Chowdhury ZZ, Kabir T, Akther F, Haque S, et al. Clinical Consequences and Economic Burden Associated with Febrile Neutropenia in Hospitalized Cancer Patients: A Prospective Study. J Med. 2022;23(1):48–53.

Discussion contd.

Other studies in different parts of the world have different findings regarding this.

1. Wang XJ, Wong M, Hsu LY, Chan A. Costs associated with febrile neutropenia in solid tumor and lymphoma patients - An observational study in Singapore. BMC Health Serv Res. 2014;14(1):1–9.
2. Lugtenburg P, Silvestre AS, Rossi FG, Noens L, Krall W, Bendall K, et al. Impact of age group on febrile neutropenia risk assessment and management in patients with diffuse large B-cell lymphoma treated with R-CHOP regimens. Clin Lymphoma, Myeloma Leuk. 2012;12(5):297–305

Discussion contd.

- **In terms of socioeconomic status, the majority fell within the lower middle-class category (60%),** a finding consistent with studies reporting a higher representation of individuals with modest income levels in febrile neutropenic populations. Economic factors play a crucial role in healthcare-seeking behavior, access to medical facilities, and compliance with recommended preventive measures.

Discussion contd.

- **Fever was universal, occurring in all cases followed by vomiting , headache (25%) and confusion (24%) indicated potential underlying infections.** Abdominal pain (20%) and breathlessness (17%) ,skin-related symptoms, including rash (13%) and gum bleeding (13%), were also observed.
- The diverse range of symptoms underscores the importance of comprehensive clinical assessments in febrile cases, enabling timely interventions for optimized patient outcomes.

Discussion contd.

- **Diabetes mellitus emerges as the most prevalent co-morbidity, afflicting a quarter of the patients (25.0%).** This high incidence aligns with previous studies, emphasizing the association between diabetes and susceptibility to infections, particularly in neutropenic individuals.^{1,2}
Hypertension (18.0%) and ischemic heart disease (9.0%) constitute significant cardiovascular co-morbidities, reflecting the intricate interplay between cardiovascular health and febrile neutropenia.³

Ref. 1. Abu-Ashour W, Twells L, Valcour J, Randell A, Donnan J, Howse P, et al. The association between diabetes mellitus and incident infections: A systematic review and meta-analysis of observational studies. *BMJ Open Diabetes Res Care*. 2017;5(1):1–10. 2. Chávez-Reyes J, Escárcega-González CE, Chavira-Suárez E, León-Buitimea A, Vázquez-León P, Morones-Ramírez JR, et al. Susceptibility for Some Infectious Diseases in Patients With Diabetes: The Key Role of Glycemia. *Front Public Heal*. 2021;9(2):1–18. 3. Hosiriluck N, Klomjit S, Rassameehiran S. Prognostic factors for mortality with febrile neutropenia in hospitalized patients. *Southwest Respir Crit Care Chronicles*. 2015;3(9):3–13.

Discussion contd.

- **Haematological disorders (9.0%) and malignancies (5.0%) represent pertinent underlying conditions,** emphasizing the vulnerability of individuals with pre-existing hematologic conditions to febrile neutropenia.

Ref. Lakshmaiah K, Malabagi A, Shetty R, Sinha M, Jayashree R, Govindbabu. Febrile neutropenia in hematological malignancies: Clinical and microbiological profile and outcome in high risk patients. J Lab Physicians. 2015;7(2):116–20.

Discussion contd.

- Sepsis (40.0%) emerges as the predominant cause, which aligns with previous studies emphasizing sepsis as a major contributor to febrile neutropenic episodes, underscoring the critical need for vigilant infection control measures.^{1,2} **Dengue fever (40.0%) is the second most prevalent etiology,. The presence of dengue fever as a significant cause of febrile neutropenia in my study is a noteworthy observation, especially in the context of the ongoing outbreak in Bangladesh.**³

Ref. 1.Penack O, Becker C, Buchheidt D, Christopeit M, Kiehl M, Von Lilienfeld-Toal M, et al. Management of sepsis in neutropenic patients: 2014 Updated guidelines from the Infectious Diseases Working Party of the German Society of Hematology and Medical Oncology (AGIHO). Ann Hematol. 2014;93(7):1083–95. 2.Thompson W, Stephen R, Wilson MK. Neutropenic Sepsis. In: Textbook of Palliative Care. Cham: Springer International Publishing; 2019. 1383–98. 3. 3.Dengue - Bangladesh. World Health Organization. 2023. Available at:<https://short-link.me/uuZy/>(Last accessed 07, April 2023);1-2

Discussion contd.

- Among all patients, blood culture was positive in 7 (7.0%) and urine culture was positive in cases 13.0. Bloodstream infection rates were reported to be between 11-38% in other studies.^{1,2}

Ref. 1. Penack O, Becker C, Buchheidt D, Christopeit M, Kiehl M, Von Lilienfeld-Toal M, et al. Management of sepsis in neutropenic patients: 2014 Updated guidelines from the Infectious Diseases Working Party of the German Society of Hematology and Medical Oncology (AGIHO). *Ann Hematol.* 2014;93(7):1083–95.

2. Thompson W, Stephen R, Wilson MK. Neutropenic Sepsis. In: *Textbook of Palliative Care*. Cham: Springer International Publishing; 2019. 1383–98.

Discussion contd.

- In this study, ICU admission was needed in 13 (32.5%) sepsis, 2 (50%) pneumonia, 1 (25%) multiple myeloma), 1 (16.7%) aplastic anaemia, 1 (50%) lymphoma patients.
- Death was observed in 4 (10%) sepsis patients, 1 (25%) pneumonia), and 2 (6.5%) dengue patients.

Ref. Asif Husain Osmani,Adnan Abdul Jabbar,Manesh Kumar Gangwani,and Bilal Hassan . Outcomes of High Risk Patients with Febrile Neutropenia at a Tertiary Care Center . Asian Pac J cancer Prev._2017; 18(10): 2741–2746.

Conclusion

- Study results found that almost one-third of the febrile neutropenic patients had early adverse outcome.
- Diabetes mellitus and hypertension were the most frequent co-morbidities .
- Sepsis and dengue were the most common etiologies of febrile neutropenia.
- However, further multicenter study with longer follow up is needed to corroborate my research findings in our country perspective.

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Thank You!