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## ORIGINAL RESEARCH

# Assessment of clinical and microbiological profile of pathogens in febrile neutropenia in haematological malignancies

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***ABSTRACT***

***Background: Febrile neutropenia is a medical emergency. The present study was conducted to assess clinical and microbiological profile of pathogens in febrile neutropenia in haematological malignancies.***

***Materials & Methods: 70 patients of haematological malignancies who developed neutropenia (<500/mm3) and fever ≥ $100^0$ F were selected. Microbiological culture of urine and blood was carried out. Clinical profile and sensitivity pattern of isolated microorganisms was recorded.***

***Results: Out of 70 patients, males were 40 and females were 30. Clinical features were fever in 56, GI symptoms in 34, bleeding in 15, vertigo in 2, infection in 7, splenomegaly in 5 and hepatomegaly in 17. The difference was significant (P< 0.05). Haematological disorders found to be ALL in 20, AML in 15, aplastic anemia in 10, lymphoma in 6, CML in 4, APML in 3 and other in 2 patients. Gram positive organism found were MRSA in 2, MSSA in 3, Strep. spp. In 4, and enterococcus spp.in 3 cases. Gram negative organism found were E. coli in 24, K. pneumoniae in 16, Klebsiella spp.in 8, pseudomonas spp.in 6 and P. aeruginosa in 2 cases. In maximum cases antibiotic sensitivity was found against PIP/TAZO, CEFO/SAL and CEFTAZI.***

***Conclusion: Gram negative bacteria found to be the causative agent in maximum cases. In maximum cases antibiotic sensitivity was found against PIP/TAZO, CEFO/SAL and CEFTAZI.***

***Key words: Febrile neutropenia, Haematological disorders, Culture***

## INTRODUCTION

Febrile neutropenia (FN) or neutropenic fever is defined as asingle oral temperature of ≥38.3°C (101°F) sustained over a 1-hour period along withan absolute neutrophil count (ANC) of <500 cells/mm3, or anANC that is expected to decrease to <500 cells/mm3during thenext 48 hours.It is seen among 80% and 10 to 50% of those with haematological andsolid malignancies respectively. It is known as a serious complication of chemotherapy.[1]

Febrile neutropenia is an emergency in medical science. Fever in neutropenia is influenced by prolonged duration and severity of neutropenia.[2]It is the cause of prolonged hospital stay, increasecost of treatment, morbidity and mortality, affecting gastrointestinal tract (GIT), where chemotherapy induced mucosal damage causes blood stream invasion by gut flora.

Invasive devices like central venous catheter (CVC) also become a source for blood stream infections.[3]

The risk of blood stream infections (BSIs) is a major cause of concern in these patients. BSIs are responsible for 10 to 25% of all febrile episodes in neutropenic patients, with an incidence as high as 13 to 60% in hematopoietic stem cell transplantation recipients.[4] Severe sepsis and septic shock have been, respectively estimated to occur in 20 to 30% and 5 to 10% of FN patients.[5] Crude mortality rates reaching 40% have been reported in FN patients with underlying haematological malignancies.[6]The present study was conducted to assess clinical and microbiological profile of pathogens in febrile neutropenia in haematological malignancies.

## MATERIALS & METHODS

The present study comprised of 70 patients of haematological malignancies of both genders. Patients who developed neutropenia (<500/mm3) and fever ≥ $100^0$ F were selected. All gave their written consent for the participation in the study.

Data such as name, age, gender etc. was recorded. A thorough clinical examination was carried out. A case history performa was created and parameters such as LFT, RFT, CBC etc. was done. Microbiological culture of urine and blood was carried out. Clinical profile and sensitivity pattern of isolated microorganisms was recorded. Data thus obtained were subjected to statistical analysis. P value < 0.05 was considered significant.

## RESULTS

**Table I Distribution of patients**

| Total- 70 | | |
|---|---|---|
| **Gender** | **Males** | **Females** |
| Number | 40 | 30 |

Table I shows that out of 70 patients, males were 40 and females were 30.

**Table II Assessment of clinical features**

| Clinical features | Number | P value |
|---|---|---|
| Fever | 56 | 0.01 |
| GI symptoms | 34 | |
| Bleeding | 15 | |
| Vertigo | 2 | |
| Infection | 7 | |
| Splenomegaly | 5 | |
| Hepatomegaly | 17 | |

Table II, graph I shows that clinical features were fever in 56, GI symptoms in 34, bleeding in 15, vertigo in 2, infection in 7, splenomegaly in 5 and hepatomegaly in 17. The difference was significant (P< 0.05).

**Graph I: Assessment of clinical features**

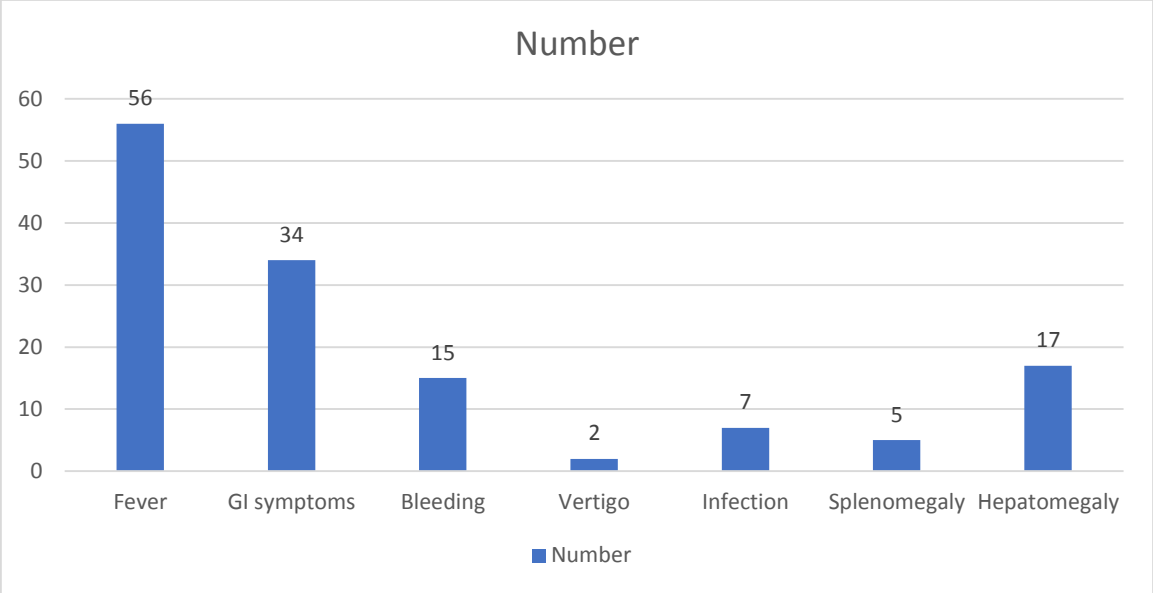


**Table III: Hematological disorders**

| Hematological disorders | Number | P value |
|---|---|---|
| ALL | 20 | 0.03 |
| AML | 15 | |
| Aplastic anemia | 10 | |
| Lymphoma | 6 | |
| CML | 4 | |
| APML | 3 | |
| Other | 2 | |

Table III shows that haematological disorders found to be ALL in 20, AML in 15, aplastic anemia in 10, lymphoma in 6, CML in 4, APML in 3 and other in 2 patients.

**Table IV Culture and sensitivity pattern of isolated microorganisms**

| | | PIP/TAZO | CEFO/SAL | CEFTAZI | CEFTRI | CARBEP |
|---|---|---|---|---|---|---|
| Gram positive organism | MRSA (2) | 2 | 2 | | | |
| | MSSA (3) | 3 | 3 | 2 | | |
| | Strep. spp. (4) | 2 | 4 | 3 | | |
| | Enterococcus spp (3) | 2 | 1 | 1 | | |
| Gram negative organism | E. coli (24) | 14 | 13 | 10 | 8 | 6 |
| | K. pneumoniae (16) | 12 | 11 | 10 | 7 | 4 |
| | Klebsiella spp (8) | 5 | 2 | 4 | 2 | 1 |
| | Pseudomonas spp (6) | 4 | 3 | 5 | 2 | 3 |
| | P. aeruginosa (2) | 2 | 2 | 1 | 1 | 1 |

Table IV shows that gram positive organism found were MRSA in 2, MSSA in 3, Strep. spp. In 4, and enterococcus spp in 3 cases. Gram negative organism found were E. coli in 24, K. pneumoniae in 16, Klebsiella spp in 8, pseudomonas spp in 6 and P. aeruginosa in 2 cases. IN maximum cases antibiotic sensitivity was found against PIP/TAZO, CEFO/SAL and CEFTAZI.

## DISCUSSION

Studies have shown shift in the spectrum of microorganisms isolated from FN patients in last couple of years. Escherichia coli, Klebsiella spp., and Pseudomonas aeruginosa among gram-negative bacilli and Staphylococcus aureus among gram-positive cocciwere the most frequently isolated organisms from these patients.[7,8]With time these have been replaced by coagulase-negative staphylococci (CoNS) and viridans group of streptococci. Later on gram-negative bacilli were the predominant cause of BSIs in neutropenic patients which were gradually replaced by gram-positive cocci in the 1990s.[9]Researches have reported a shift in prevalence from gram-positive to gram-negative bacteremia with rise and successful dissemination of MDR gram-negative bacterial infections.[10,11]The present study was conducted to assess clinical and microbiological profile of pathogens in febrile neutropenia in haematological malignancies.

We found that out of 70 patients, males were 40 and females were 30. Lakshmaiah KCet al[12]determined clinical profile, microbiological profile, antibiotic sensitivity pattern, and outcome in 72 patients with hematologic malignancies with febrile neutropenia. Results showed that most of the patients had acute myeloid leukemia. Overall culture positivity was 29.62%. Gram-negative bacilli was present in 63.64% and Escherichia coli was the most frequent pathogen. Sensitivity pattern for pipercillin-tazoactum, meropenem, cefoperazone-sulbactum, amikacin, ceftazidime, ciprofloxacin found to be 85.71%, 78.26%, 69.52%, 63.64%, 41.66% and 47.05% respectively. Overall mortality was 13.5%. Most of the patients responded to empiric antibiotic cefoperazone-sulbactum.

We found that clinical features were fever in 56, GI symptoms in 34, bleeding in 15, vertigo in 2, infection in 7, splenomegaly in 5 and hepatomegaly in 17. Paul et al[13]microbiological profile and antibiotic resistance pattern of blood stream infections in 306 consecutive febrile neutropenic cancer patients. 74.18% patients were suffering from hematological malignancies. Percentage resistance values of gram-negative bacilli to aminoglycosides, β-lactam/β-lactamase inhibitor combinations, fluoroquinolones, cephalosporins, carbapenems, chloramphenicol, ampicillin, co-trimoxazole, and doxycycline were 26.6 to 91.7%, 8.3 to 86.6%, 10 to 66.7%, 13.3 to 73.3%, 8.3 to 73.3%, 80 to 93.3%, 13.3 to 20%, 16.7 to 66.6%, and 13.3 to 16.7%, respectively.

We found that haematological disorders found to be ALL in 20, AML in 15, aplastic anemia in 10, lymphoma in 6, CML in 4, APML in 3 and other in 2 patients. We found that gram positive organism found were MRSA in 2, MSSA in 3, Strep. spp. In 4, and enterococcus spp in 3 cases. Gram negative organism found were E. coli in 24, K. pneumoniae in 16, Klebsiella spp in 8, pseudomonas spp in 6 and P. aeruginosa in 2 cases. IN maximum cases antibiotic sensitivity was found against PIP/TAZO, CEFO/SAL and CEFTAZI. Taj et al[14] conducted a study on 226 cases in which 173 were males and 53 were females. Clinically documented infections were 104 (46.01%) and microbiologically documented infections were 80 (35.39%), while 42 (18.58%) had pyrexia of undetermined origin. Gram negative infections accounted for 68 (85%) and Escherichia coli was the commonest isolate. Gram positive microorganisms were isolated in 12 (15%) cases and most common was Staphylococcus aureus. First-line empirical treatment with piperacillin/tazobactam and amikacin showed response in 184 patients (85.9%) till 72 hours.

The limitation the study is small sample size.

## CONCLUSION

Authors found that gram negative bacteria found to be the causative agent in maximum cases. In maximum cases antibiotic sensitivity was found against PIP/TAZO, CEFO/SAL and CEFTAZI.

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