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RESEARCH ARTICLE

Clinical and Microbiological Profile of Pathogens in Febrile Neutropenia in Haematology Malignancies: A Single Center cross-sectional type of observational study

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ABSTRACT

Background

Neutropenia is a clinical condition in a body occurs when a low number of neutrophils in the blood. Febrile neutropenia is a clinical condition in which development of a high fever with signs of infection in the body. It is a most common postoperative complication of anticancer treatment. The aim of the study was to evaluate the current practices used in the institution and for culture sensitivity in isolated microorganisms.

Material and methods: 50 hospitalized patients are selected for the study. All the patients are provided informed consent before starting of the study.

Results: 50 patients selected from the study 36 were males and 14 were females. 42 Patients were found the gram negative infections. The most common bacteria found in the culture media was Escherichia coli. 8 (15%) Patients were found the gram positive microorganisms stain and most common bacteria found in the culture media was Staphylococcus aureus.

Conclusion: In our study we concluded that there decrease in the level of infection in the body due to gram positive microorganisms. For doctor the main concern was the gram negative microorganisms and further surveillance needed. In our study the results shows that the sensitivity for antibiotic therapy in antibiogram.

KEYWORDS

cost, hospitalization, heart failure, Madagascar.

History

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INTRODUCTION

One of most common hematological emergency occur in medical practices was febrile neutropenia which occur due to treatment of hematological malignancies. In literature review, many studies shows that it is life threatening infection occur in the body and can seen in 60-65% case of febrile neutropenia.[1]

Gastrointestinal tract (GIT) affects more commonly in patients of FN, due to chemotherapy the damage of upper lining of the epithelium of gastrointestinal tract and decrease the gut flora. One of the important sources of infection is invasive devices used in the FN patients like central venous catheter (CVC) in blood stream infection. Other than GIT the most common affected area are respiratory system and skin infections.

Due to antibiotic therapy the rate of mortality is decrease in patients of FN reduced in Cancer patients up to 60 % cases. In patients of FN broad spectrum of antibiotics are recommended with high regimens of chemotherapeutic drugs. There are less studies reported the cases of FN in India, so current study conducted in patients FN in hematology malignancies.

MATERIALS & METHODS

Study setting: The study was performed in the Department of Medicine, Haematology and Microbiology VMMC and Safdarjung Hospital, New Delhi.

Study design: A single centre cross-sectional type of observational study

Study subjects:
50 consecutive patients of febrile neutropenia undergoing indoor treatment in the Department of Haematology are selected for the study after taking the signed informed consent.

INCLUSION CRITERIA:

- Aged >18 years patients were selected for the study.

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- Patients of febrile neutropenia with hematological malignancies.

EXCLUSION CRITERIA:

- Patient with cause of fever other then febrile neutropenia.
- Patients on antibiotics.
- Patient with documented HIV
- Patients with non hematological malignancies.

INVESTIGATIONS

The subjects underwent following investigations to reach a definitive diagnosis:

Routine Investigations:

a) Complete blood count& ESR
b) Urine for routine and microscopic examination
c) Chest X-ray
d) Kidney Function Tests
e) Liver Function Tests
f) Serum Electrolytes
g) Random Blood Sugar

Microbiological Investigations:

a) Blood for bacterial culture and sensitivity
b) Urine for bacterial culture and sensitivity
c) Sputum for bacterial culture and sensitivity
d) Nasal & tracheal aspirate for bacterial culture and sensitivity

Special Investigations (wherever clinically indicated):

a) Broncho-alveolar lavage (BAL) for bacterial culture and sensitivity.

METHODOLOGY

I. All the patients are given written informed consent signed with guardian and prior starting the study the approval was taken by the institutional ethical committee. Patients were evaluated by detailed history and clinical examination, upon the development of fever of any duration. Once the diagnosis of Febrile Neutropenia was confirmed the patients underwent routine and microbiological investigations.
ii. The pathogens isolated from these specimens were tested to determine their sensitivity patterns to antibiotics,
iii. All the samples collected as per standard procedure and processed immediately in the department of microbiology by routine bacteriological procedures.

OBSERVATIONS AND RESULTS

This study was a cross-sectional type of observational study aimed to find bacterial spectrum and their sensitivity pattern. The study population consisted of febrile neutropenic patients with hematological malignancy and it was carried out in departments of Haematology, Medicine and Microbiology at Vardhman Mahavir Medical College & Safdarjung Hospital, New Delhi. Data collected & analysed by using WHONET 5.4 SOFTWARE. The results and observations of study have been compiled after applying various statistical tools, wherever applicable, and are as follows:
50 patients with FN and hematological malignancies were enrolled and profiled as a part of study. After taking written informed consent from the patients a detail history was taken and clinical examination was done. Blood sample was taken and sent for culture and sensitivity in department of microbiology

Distribution of patients as per MASCC criteria for risk assessment (**Figure:1**)

• Group A :Patients at high risk (score< 21)	10
• Group B :Patients at low risk (score > 21)	40

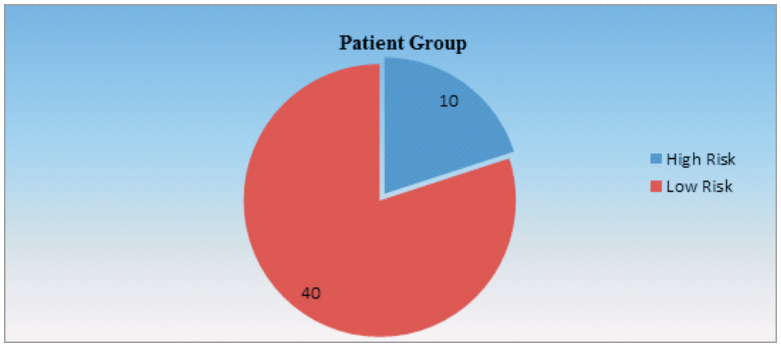


Table 1: Underlying hematological malignancy documented (%).

Acute myeloblastic leukemia(AML)	18(36%)
Acute lymphoblastic leukemia(ALL)	14(28%)
Myelodysplastic syndrome(MDS)	15(30%)
Lymphoma(LL)	3(6%)

- 36% of patients registered were diagnosed to have acute myeloid leukemia and 28% had acute lymphoblastic leukemia.
- 30% of the patients had myelodysplastic syndrome and 6% patients had lymphomas(fig 5).
- More no. of male patients in each group of malignancies as compared to females(fig 6).
- Most of the patients of AML i.e.66% were on induction phase and 33% were in consolidation phase of chemotherapy.
- Patients of ALL on chemotherapy were on BMF 85 protocol.
- All patients of lymphoma were on CHOP (Cyclophosphamide, Doxorubicin, Vincristine and Prednisolone. therapy.

Figure 2 : Distribution of pathogens amongst hematological malignancies.

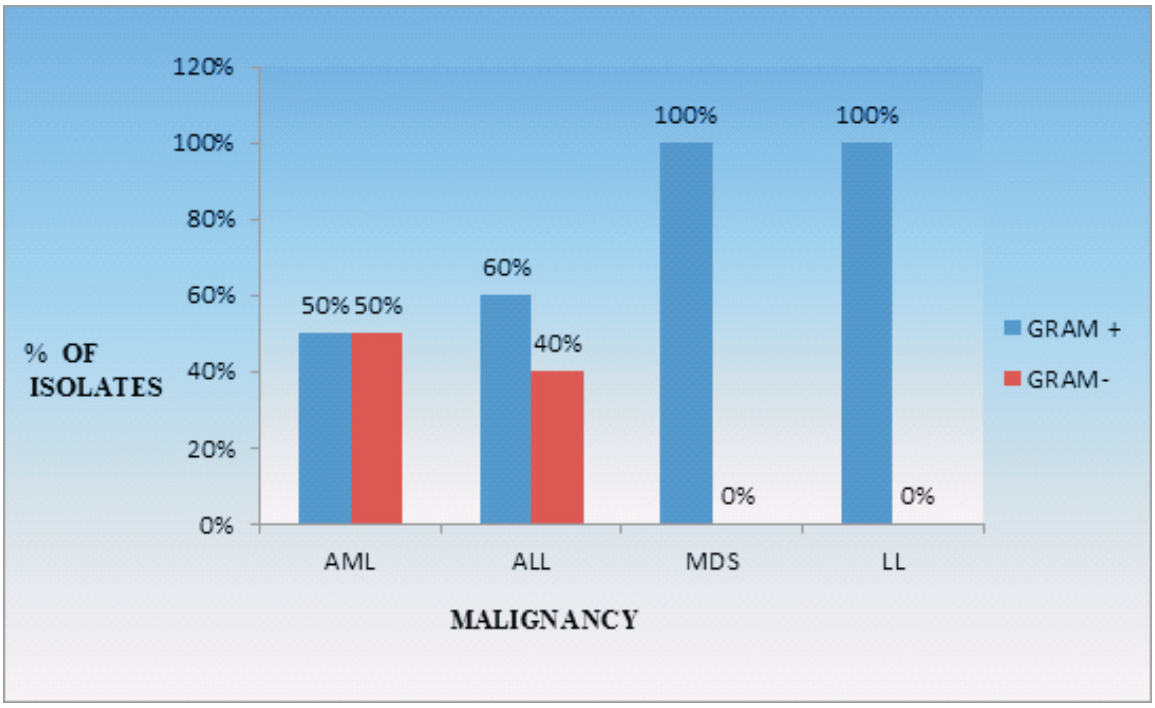
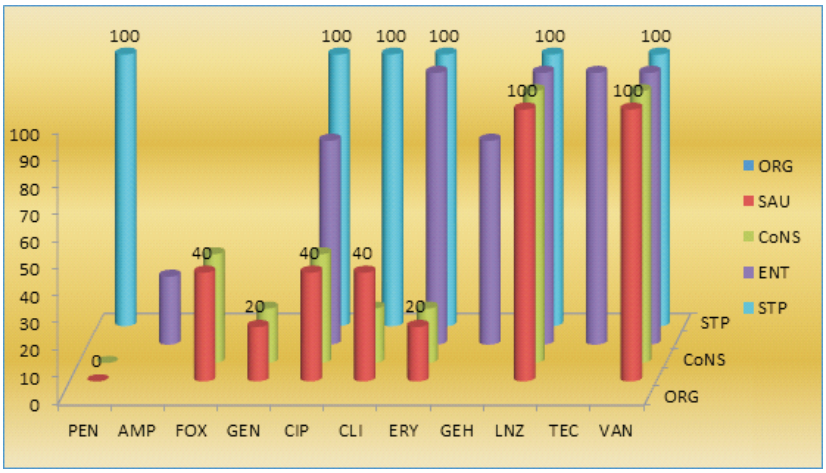


Figure 3 : Gram-negative.

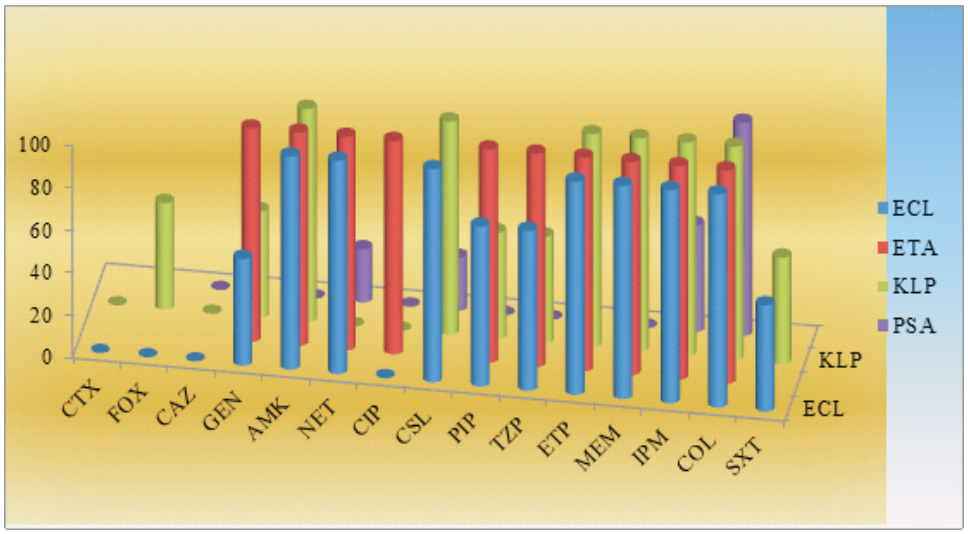


- E.coli were 100% ESBL susceptibile to amikacin, netilmicin, cefoperazon-salbactum, ertapenem, meropenem, imipenem and colistin. 75% susceptibility to pipracillin and tazobactum. 50% susceptibility towards gentamicin and cotrimoxazol.
- E.coli were resistant to cefotaxim,cefoxitin, ceftazidime and ciprofloxacin.
- Enterobacter was found only in one blood culture which was 100% susceptible to gentamycin, amikacin, netilmicin, ciprofloxacin, pipracillin, tazobactum, ertapenem, meropenem, imipenem and colistin.
- Klebsiella were 100% susceptible to , amikacin,cefoperazon-salbactum, ertapenem, meropenem, imipenem and colistin. 50% susceptible tocefoxitin,gentamycinpipracillin, tazobactumand cotrimoxazol. 50% were found to be ESBL.
- Klebsiella were resistant to cefotaxim, ceftazidime, netilmicin and ciprofloxacin.
- All Pseudomonas were susceptible to colositin , 50% were susceptible to imipenem. Susceptibility to netilmicin and cefoperazon-salbactum was 25%. Resistant to ceftazidime, amikacin , pipracillin, tazobactum and meropenem(fig 15).

Table 2 % Susceptibility

ORG	CTX	FOX	CAZ	GEN	AMK	NET	CIP	CSL	PIP	TZP	ETP	MEM	IPM	COL	SXT
ECL	0	0	0	50	100	100	0	100	75	75	100	100	100	100	50
ETA				100	100	100	100		100	100	100	100	100	100	
KLP	0	50	0	50	100	0	0	100	50	50	100	100	100	100	50
PSA			0		0	25	0	25	0	0		0	50	100	

Figure 4 : Empirical Antibiotic therapy.



In this institution following antibiotic regimen is used for patients of chemotherapy induced febrile neutropenia till cultures are awaited.

- cefoperazon-salbactum, Amikacin, ciprofloxacin pipracillin-tazobactum, ceftriaxon, meropenem, gentamicin, clindamycin.
- Antibiotic therapy was revised as per the patients clinical response and pathogen isolated. Carbepenem and vancomycin was added to therapy of patients not responding to initial regimen. As it was not a prospective study follow up of antibiotictherapy was not possible.

DISCUSSION

This study was done in 50 FN patients with high risk of Hematological Malignancies. The above study elevation of clinical profile, effect of antibiotic, effect on severity of infection. The result of the study found that FN many found in acute myeloid patients on chemotherapy. Lyman GH et al in 2014[3] was seen the similar results as compared to our study. We see the higher incidences of FN in acute myeloid leukemia patients because in the treatment of these patients intensive chemotherapy are performed which leads to profound neutropenia and increase the risk factor of severe infection in the body. One of the Kuderer et al[5] Febrile neutropenia commonly seen in during the course of treatment induction chemotherapy than in maintenance chemotherapy.

Bacterial culture yielded pathogens in 29.62% of the FN episodes. Freifeld et al[6] study results shows that positive culture have been identified in 15–38% patients. Fluoroquinolone are the drug of choice to decease the bacterial count of gram negative bacteria.

In contrast to the Western studies, studies from India including the present one still find GNB as the predominant infection in HM.[7] Overall E. coli was found to be the most common isolate including all cultures and S. aureus was the most common isolate from blood. Similar results were also reported from other studies.[8]

In our study low count of bacteria S. aureus infection in our study is due to infrequent use of CVCs. Increased incidence of S. aureus isolates from the blood in our study was due to use of CVCs in all acute leukemia patients.[9] Also Gram-negative isolates from only two cases produced extended spectrum beta lactamases. We found that GNB were highly sensitive to imipenem, piperacillin/tazobactum and meropenem.[10]

They were also moderately sensitive to amikacin and cefoperazone/sulbactum. Most of the GNB showed high resistance to third generation cephalosporins.[11] Similar antibiotic sensitivity pattern of high sensitivity of GNB to carbapenems, piperacillin/tazobactum, cefoperazone/sulbactum and resistance to third generation cephalosporins has been reported in studies.[12]

Even though, in vitro sensitivity to cefoperazone/sulbactum was low, most patients responded to it clinically, when administered empirically. Sensitivity to fluoroquinolones is low among GNB with higher resistance seen in E. coli. All S.aureus including MRSA were highly sensitive to amikacin, linezolid, vancomycin, teicoplanin, and levofloxacin.[13] Overall mortality in this study was 13.50%. All the deaths were attributed to infections. Similar results have been found in other studies both from India and abroad.[14]

The most reason of occurrence of FN in cancer patient are immune deficiency with underling systemic disease which causes breach in the mucosal layer of GIT due to chemotherapy and 80 % infection due to endogenous flora. Furthermore, the importance of clinical judgment and not chasing laboratory reports is well emphasized through this study.[15] For instance though cefoperazone-sulbactum was only 70% sensitive according to the culture sensitivity, 70% of episodes did respond to the first line antibiotic suggesting an in vivo and in vitro discordance, which has been proven before. This study help in oncologists in treatment FN in India.The weakness of this study is that it is a nonrandomsied observational study.[16]

CONCLUSION

Hematological malignancies are the major contributing factor in morbidity and mortality in post chemotherapy period. Escherichia coli with gram negative infection most commonly find infection in body. GNM infection most commonly seen infection in body but showing considerable sensitivity to first line antibiotic cover. Further studies needed to be done with large sample size to see the relation between hematological malignancies with febrile neutropenia.

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