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## Microbiological Profile of Neutropenic Patients with Fever: A Case Series Study.

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### Case Report

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#### ABSTRACT

A systematic study of the etiological profile of these fevers would help to formulate a suitable antibiotic policy as well as effective infection control measures. The study material was collected from the hospitals of M. S. Ramaiah Medical College, Bangalore. A detailed history was taken and physical examination was done in all patients. They were subjected to appropriate investigations to find out the cause of fever. In this study, 74 patients with febrile neutropenia were the study subjects and among them 65% were males and 35% were females. Majority were in the age group of 39 – 58 years (51.4%). Pathogens isolated in 15(20.27%) of 74 febrile neutropenic cases. An understanding of the epidemiology of febrile neutropenic episodes is crucial for the implementation of strategies that may contribute to preventing and controlling these infections.

#### INTRODUCTION

Fever among neutropenic patients may be infectious and non infectious. Different organisms isolated in these patients include gram positive organisms, gram negative organisms, invasive mycoses, mycobacteriae and viruses. Gram positive bacteriae like *Staphylococcus aureus*, Coagulase-negative *Staphylococci* and *Streptococcal* species e.g. alpha-hemolytic *Streptococci* were isolated in these patients. Gram negative aerobic bacteria like *Escherichia coli*, *Klebsiella pneumoniae* and *Pseudomonas aeruginosa* have been isolated in these patients. Gram negative anaerobic organisms such as *Leptotrichia buccalis*, *Clostridium septicum*, *C.tertium* and *C.difficile* have been identified in neutropenic patients. Invasive mycoses like species of *Candida* and *Aspergillus* are isolated in these patients. Mycobacteriae such as *Mycobacterium chelonae* and *M.fortuitum*, herpes viruses especially *Herpes simplex virus*, *Varicella zoster virus* and *Cytomegalovirus* have also been identified in these patients [1]. Infections are a major cause of morbidity and mortality in cancer patients. The risk of infections is principally related to the intensity and duration of the immune suppressive chemotherapy. In the 1980's there was a shift in the relative prevalence of specific pathogens afflicting patients with cancer. Whereas in the 1960's and 1970's Gram negative bacterial pathogens [*Enterobacteriaceae* and *pseudomonas aeruginosa*] were the principal cause of bacteremia, in 1980's and 1990's Gram positive bacterial pathogens became predominant [2]. The spectrum of invasive fungal infections has dramatically increased in patients with prolonged neutropenia. Examples of such emerging pathogens include *Fusarium*, *Acremonium* & *Scedosporium*. Most infections occur about 12-14 days after the 1<sup>st</sup> day of chemotherapy [3]. Although the precise reasons for the changing patterns of bacterial pathogens are unknown, the use of intensive chemotherapeutic regimens ( with associated immune suppression and mucositis) [4], antibacterial prophylaxis targeted against gram negative bacilli, selective gut decontamination, invasive procedures/catheters have all been cited as possible contributing factors. Antibiotic resistant bacteria

tend to be more prevalent in neutropenic patients because they are exposed to prolonged courses of broad spectrum antimicrobials e.g. Entero bacteriaceae expressing extended spectrum  $\beta$  lactamases (ESBL); fluoroquinolone resistant E coli, methicillin resistant staphylococci & vancomycin resistant enterococci. . An early increase in infections attributable to viridians streptococci is also a common; these infections can result in severe complications [ARDS, Shock] in neutropenic patients [5]. There are many studies regarding empirical use of broad spectrum antibiotics in this group of patients. Systematic study of the etiological profile of these fevers would help to formulate antibiotic policy as well as effective infection control measures. There are only a few Indian studies in the literature addressing similar issues. Our study will attempt to investigate the microbiological profile of these infections.

## METHODOLOGY

A case series study was conducted at M. S. Ramaiah Medical College, Bangalore in the Department of General Medicine. Totally 74 patients, who had episodes of fever and neutropenia on admission or anytime during hospital stay, were studied during a period of two years. A semi structured questionnaire was used as study tool. After taking written informed consent from patient, A detailed history was taken and physical examination was done in all patients. They were subjected to appropriate investigations to find out the cause of fever. These included complete blood counts, urine microscopy, chest x-ray & blood smear for malarial parasites. Blood - sputum - stool - urine and access device cultures done if clinically indicated. Cultures from any other suspicious/focal lesions were taken. CT scan of the chest, abdomen & pelvis were done if clinically indicated. Elisa for HIV was done if considered relevant.

## RESULTS

In this study, 74 patients with febrile neutropenia were the study subjects and among them 65% were males and 35% were females.

Table 1: Age wise distribution of study subjects

Age group	Frequency	Percentage
18-38 years	10	13.5
39-58 years	38	51.4
59-78 years	24	32.4
79-98 years	02	02.7
Total	74	100

Among total study subjects, majority were in the age group of 39 – 58 years (51.4%) followed by 59 – 78 years (32.4%), 18 – 38 years (13.5%) and only 2.7% in the age group of 79 – 98 years

Table 2: Distribution based on source of infection

Source of infection	Frequency	Percentage
Found	42	56.7
Not found	32	43.3
Total	74	100

Source of infection was observed in only 56.7% of study subjects

Table 3: Distribution based on source of infection (Observed)

Source of infection found	Frequency	Percentage
Respiratory	18	42.8
Abdominal	10	23.8
Urinary	04	09.5
Oral mucositis	04	09.5
CVC related	03	07.1
Infected hemorrhagic bullae	02	04.8
Perianal abscess	01	02.4
Total	42	100

Among 74 cases, source of infection was observed among 42 patients. Among 42 patients, source of infection was respiratory (42.8%), abdominal (23.8%), Urinary (9.5%) and others

## Pathogens isolated in 15(20.27%) of 74 febrile neutropenic cases

Unimicrobial: 13  
Polymicrobial: 02

### Pathogens are as follows:

E Coli (ESBL): 04  
Coagulase negative staphylococci: 03  
Staphylococcus aureus: 02  
Klebsiella spp: 02  
Candida species: 02  
Streptococcus pneumoniae: 01  
Enterococcus faecalis: 01  
Citrobacter Freundii: 01  
Acinetobacter species: 01

## DISCUSSION

In a study done by I. Hann, C. Viscoli et al<sup>[6]</sup> there was no significant difference in overall rates of bacteria in children less than 18 years and adults. The present study shows largest numbers of infections were seen middle and elderly age groups. Children under 18 years developed more streptococcal infections where as adults developed more staphylococcal infections, in a study done by I. Hann, C.Viscoli et al. In this study, in all cases of gram positive bacteremia, staphylococcus was the predominant organism isolated. An Indian study by RR Dutta et al in New Delhi showed the common foci of infections to be pneumonia, perianal abscess, thrombophlebitis, furuncle and oral mucositis. The organisms isolated were Coagulase negative Staphylococcus aureus, Streptococcus pyogenes, E-coli, Pseudomonas aeruginosa, Proteus vulgaris and Klebsiella pneumoniae. They concluded that gram-positive infections especially staphylococcal infections were common<sup>[7]</sup>.

A shift in the bacteriological spectrum was shown in a study by Stephen H. Zinner, in this showed that there has been a clear shift in infecting organisms, such that 60 -70% of bacteremias with single organisms are due to gram positive organisms compared to the spectrum two decades earlier. In this study gram negative organisms were still the most common infectious organisms making 52.94% of total cases where causative organism was isolated. In a study by Stephen H.Zinner<sup>2</sup> some of the causes of shift towards gram positive infections include oral mucositis as a result of increase in use of potent chemotherapeutic regimens, profound and prolonged neutropenia, increasing use of long dwelling intravascular catheters, use of antacids and H2 blockers. In this study the use of chemotherapeutic agents and profound neutropenia were shown to be associated with increased frequency of infections. Long dwelling intravascular and urinary catheters were found to be associated with gram negative infections.

In the study by Vicki A. Morrison<sup>[8]</sup> both gram positive and gram negative organisms were isolated from respiratory tract in which staphylococcus aureus and pseudomonas were predominant. In this study gram positive organism streptococcus pneumonia and acinetobacter species organisms isolated from respiratory tract.

A study by Eduardo Velasco et al<sup>[9]</sup> showed a predominance of primary infections with a high frequency of episodes of unknown origin. This significant finding can be attributed to the prompt institution of broad-spectrum antibiotics for febrile cancer patients. In our study also episodes of unknown origin were common. In a study Philip A.Pizzo<sup>[10]</sup>, monotherapy with some 3<sup>rd</sup> generation cephalosporins which have bacterial activity against enterobacteriaceae, P.Aeuruginosa and many gram positive organisms can be a safe and cost effective alternative to combination regimens containing an aminoglycoside. In this study large numbers of patients having neutropenia were treated with monotherapy involving ceftazidime and cefoperazone and patients whose ANC was expected to fall in next few days (i.e. less than 500 / cubic mm) responded satisfactorily to combination of 3<sup>rd</sup> generation cephalosporins and amino glycosides.

## CONCLUSION

In this study majority of the patients were middle aged and elderly group and a large number of

patients presented with clinical signs and symptoms suggestive of respiratory system involvement. Gram positive infections especially Staphylococci species were a common cause of febrile neutropenia.

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