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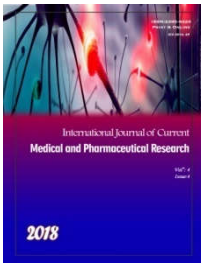

ETIOLOGICAL PROFILE OF FEBRILE NEUTROPENIA IN CHILDHOOD MALIGNANCY

***Dr. Raja Periyasamy and Dr. Kannan Ramamoorthy**

Department of Paediatrics, Government Tiruvarur Medical College, Tiruvarur

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ABSTRACT

Objective: To study the etiological profile of febrile neutropenia in childhood malignancy.
Methods: Children of either sex under 12 years who with haematological malignancy developed fever were subjected to absolute neutrophil count. Children with ANC less than 1500 are included, they are worked up in detail including complete history, physical examination, haematological profile, radiological investigation as required. Concern to the study was obtained. Investigations like blood culture, urine culture, throat swab, ear swab, CSF study was collected and microorganism isolated was presented as proportions.
Results: 75 children were worked up. Acute lymphoblastic leukemia was the commonest haematological malignancy accounting for 83 % (62 /75) of children recruited followed by Acute Myelogenous Leukemia (13%) and Non Hodgkins lymphoma (4%). Among the 75 cases culture was positive in 45 % (34/75). Fungal growth was positive in 12 % of isolates. Among the organism isolated 82 % (28/34) was from children with Acute lymphoblastic leukemia. 12 % (4/34) from children with Acute Myelogenous Leukemia and 6% (2/34) from children with Non Hodgkins Lymphoma.
Conclusion: Culture positivity is more if the ANC is less than 500. Gram negative organism particularly *E.coli* was most commonly isolated in malignant children with febrile neutropenia. Amikacin in combination with other drugs would be the first drug choice in the management of suspected febrile neutropenia.

INTRODUCTION

Despite a considerable reduction over the past decades in infection-related mortality in patients with cancers who present with fever and neutropenia (FN), infections remain a major cause of morbidity and mortality in this susceptible population[1]. The strategy of using empiric antibiotics has greatly influenced the outcome of fever in a neutropenic host [2]. Critical to this strategy is its ongoing update based on the spectrum and resistance patterns of pathogens isolated from patients and known etiologies as determined by the diagnostic modalities currently available to clinicians. The major causes of febrile neutropenia in childhood malignancy are chemotherapy, systemic infections, immunosuppression and immunodeficiency associated with cancer[3]. A systemic review of literature showed that age, nutritional status, chemotherapy dose and intensity, low base line blood counts are all risk factors for greater mortality and morbidity[4,5]. Fever is defined as a single oral measurement of 38.3°C or 2 measurements of 38°C separated by atleast one hour[6]. Mild neutropenia is defined as absolute neutrophilic count (% PMN neutrophils + % band forms) <1500, moderate neutropenia ANC 500-1000, severe neutropenia <500[7]. Traditionally children with malignant disease who present with fever and neutropenia are hospitalised for parenteral antibiotics. The foundation for such a practice is based on the study by Bodey in 1966 indicating that an ANC < 500 cells/mm^3 conferred a high risk of bacteremia[8]. We planned our study to determine the spectrum and antimicrobial susceptibility pattern of bacteria causing blood stream infections in febrile neutropenic patients with malignancies.

MATERIALS AND METHODS

All the children under 12 years with malignancy attending haematology department between Feb. 2017 and Jan. 2018 were enrolled. Those with ANC<1500 were included. Predesigned, structured questionnaire was filled up. These children were worked up in detail including complete history, physical examination, haematological profile and radiological investigations as required. Blood specimens for culture and antimicrobial susceptibility testing were obtained from peripheral vein. Urine samples are collected by obtaining the mid stream flow by the clean catch technique. In suspected cases throat swab or Ear swab were taken in a sterile swab. In children with CNS symptoms CSF should be sent for cell count, biochemistry, culture and sensitivity. Blood agar and Chocolate agar was used for CSF culture. Statistical analysis of data using SPSS software 16.

Corresponding author:* **Dr. Raja Periyasamy
Department of Paediatrics, Government Tiruvarur Medical College, Tiruvarur.

RESULTS

A total of 127 children were recruited in the study period.Out of these, 75 children were included as per the inclusion criteria. Among them Acute lymphoblastic leukemia was the commonest haematological malignancy accounting for 83% (62/75), followed by acute myelogenous leukemia (13%) and Non-Hodgkin lymphoma (4%). There was male preponderance, with male Constituting 54% against 46% of female children. (M:F Ratio 1.17:1). The total count in 56% children were between 3000-4000. There were 33% of children with total count between 2000-3000 and only 10.67% of children with total count <2000. Majority (86.67%) of the children had severe degree of neutropenia and 10.67% had moderate neutropenia. Only 2.67% had mild degree of neutropenia. Majority (82%) of the febrile neutropenic episodes had occurred in Acute lymphoblastic leukemia which is statistically significant (p<0.05).

Table 1 Type of Malignancy and Degree of Neutropenia

ANC	MALIGNANCY			TOTAL	
	ALL	AML	NHL	NUMBERS	%
<500	54	10	1	65	86.67
500-1000	6	-	2	8	10.67
1000-1500	2	-	-	2	2.67

P= <0.05

Table 2 Type of Malignancy and Organisms

Isolates	Type of Malignancy			Total	
	ALL	AML	NHL	Numbers	%
E.Coli	11	-	1	12	36
Pseudomonas	9	2	-	11	32
Klebsiella	4	1	-	5	14
Proteus	1	-	-	1	3
Staph.aureus	-	1	-	1	3
Candida	3	-	-	3	9
Aspergillus flavus	-	-	1	1	3

P= <0.05

Of the 75 cases studied, culture was positive in 45% (34/75) out of which, 85% of the isolates were gram negative and 3% was gram positive. Fungal growth was seen in 12% of the isolates, out of these candida was seen in 3 cases and *Aspergillus flavus* was present in one case. Among the organisms isolated 82% (28/34) were from children with ALL followed by AML (12%) and NHL (6%). Among the children with ALL, *E.coli* was the commonest organism (39%) isolated followed by *pseudomonas* 32%. In children with AML, *Pseudomonas* was the commonest organism (50%) isolated. Out of the 3 children with NHL, one child found to have *E.Coli* and the other child had *Aspergillus flavus.* All the candida isolated were in children with ALL. Amikacin was 100% sensitive to all the isolated gram positive and gram negative organisms.

All the candida were 100% sensitive to *Fluconzole*, *Ketoconazole* and *Amphotericin* B. *Aspergillus flavus* was 100% sensitive to Amphotericin B. During the study, 3 children died. All of them had severe neutropenia and pseudomonas was grown in their blood. Out of the 3 children, 2 had ALL and 1 child had AML.

CONCLUSION

From this study we analyzed the various parameters associated with febrile neutropenia in children.

- No clinical signs or localising signs need to be present to suspect septicaemia in febrile neutropenia.
- Culture positivity is more if ANC<500.
- Gram negative organisms particularly *E.Coli* was most commonly isolated in malignant children with febrile neutropenia.
- Amikacin in combination with other drugs would be the drug of first choice in the management of suspected febrile neutropenia.
- Mortality can be lessened with appropriate antibiotics and adequate supportive therapy.

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