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Original Research Article

Title: To determine the spectrum of infection with Acute Leukemic in adults.

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Abstract

Background & Methods: The aim of the study is to determine the spectrum of infection with Acute Leukemic in adults. Aspiration of septic nodules will be done and sent for Gram's stain & culture & sensitivity if present. CSF analysis if needed. CT Chest will be taken in suspected fungal pneumonia.

Results: The most common and important sites of infection in patients with acute leukemia. Overall, the respiratory tract is the most common site of infection. Approximately 33 % of patients with acute leukemia will develop a pulmonary infiltrate during an episode of neutropenia lasting 10 days or longer. Other parts of the respiratory tract including the oropharynx, upper airways, and the paranasal sinuses are also frequent sites of infection.

Conclusion: Infections cause a substantial amount of morbidity and mortality in patients with acute leukemia and other hematologic malignancies. Neutropenia is the predominant predisposing factor, although other factors also contribute to the development of infection. Bacterial infections predominate during the initial phases of severe neutropenia. Invasive fungal infections develop in patients with persistent and profound neutropenia. Viral infections appear to be increasing in frequency and severity. Early diagnosis and the administration of pre-emptive therapy, especially when dealing with invasive fungal infections, are important as infection prevention.

Keywords: spectrum, infection, acute, leukemic & adults.

Study Design: Observational Study

Introduction

Acute leukemias are hematological neoplasms featured by altered proliferation and/or differentiation of hematopoietic progenitors, leading to accumulation of immature cells in the bone marrow and peripheral blood[1]. The clinical consequences are due to bone marrow failure and infiltration of extra hematological sites by leukemic cells causing organ function impairment.

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Leukemia is classified as lymphoid and myeloid depending on the lineage of progenitor cells involved. Leukemia is again classified depending on natural history as acute leukemia and chronic leukemia. Acute leukemia is classified as Acute lymphoblastic leukemia(ALL) and Acute myeloid leukemia(AML) [2].

ALL is characterized by clonal expansion of lymphoid blasts in peripheral blood and bone marrow. AML is characterized by clonal expansion of myeloid blasts. The main key for cure in leukemia is early diagnosis and early treatment. The curative rate is around 40% in adults[3]. In adults leukemia have a devastating course. In India the cure rate is low compared to western countries. The reasons for this is multiple which includes high number of high risk population, limited data on cytogenetics ,febrile neutropenia, infections, relapse, drug toxicity and mainly delay in diagnosis of disease.

Despite significant advances in supportive care, infections continue to be a significant cause of morbidity and mortality in leukemic patients. The implementation of empirical antibiotic therapy in febrile neutropenia led to dramatic reduction in mortality.[4] Nonetheless , the development of more effective and dose intensive salvage chemotherapy regime, incorporation of monoclonal antibodies, use of consolidation and maintenance strategies and increased use of indwelling catheters have increased the susceptibility to infections and changed the spectrum of infections.[5]There is emergence of multidrug resistant organism and organisms which were previously considered innocuous[6-7].

Material and Methods

Present study was conducted at MGM Medical College, Indore for 01 Year. Detailed history (fever, cough, breathlessness, skin abscess, purulent discharge, dysuria, altered level of consciousness, seizure, diarrhoea, dysentry) will be elicited. Thorough head to foot clinical examination with emphasis on oral cavity, perianal region, skin for any lesion, venipuncture, and bone marrow & LP site for infection. For all patients CBC, CRP, BACTEC, Urine routine, Urine culture, USG will be done. X Ray will be taken if there is cough or clinical signs of pneumonia. All patients will be screened for HIV and HAV, HBV, HCV at the time of induction and at the time of jaundice. Any ear discharge or pus from abscess will be sent for Gram's stain & culture & sensitivity.

INCLUSION CRITERIA:

All Patients diagnosed with acute leukemia (ALL and AML) with infection as evidenced by at least one of the following criteria:

Febrile: Single temperature higher than 38.3°C or a sustained temperature >38°c for more than 1 hr.

Afebrile: clinical focus of infection like cellulitis, abscess, oral thrush, herpetic lesions, chicken pox, mumps, measles, diarrhea, dysentery, pneumonia or clinical evidence of systemic infections.

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EXCLUSION CRITERIA:

1. Patient whose parents do not give consent for the study.
2. Patient with primary immunodeficiency.
3. Patient with relapse.

Result

Table No. 1: Demographic Profile

S. No.	Parameter	No.	Percentage	P Value
1	Male	61	61	0.659912
2	Female	39	39	
	Diagnosis	No.	Percentage	
1	ALL	94	94	0.031258
2	AML	06	06	
	Duration of Fever	No.	Percentage	0.049657
1	<7 Days	68	68	
2	1-2 Weeks	17	17	
3	>2 Weeks	15	15	

Table No. 2: Infections in Patients with Acute Leukemia

S. No.	Parameter	No.	Percentage	P Value
1	Unexplained fever	42	42	.022965
2	Clinically documented infections	28	28	
3	Microbiologically documented infections	25	25	
4	Non-infectious cause	05	05	

Clinically documented infections account for 28 % of febrile episodes in neutropenic patients. They are defined by the presence of a site suggestive of an infection such as cellulitis, pneumonia, esophagitis, or enterocolitis, without microbiological documentation of the causative pathogen for the infection. Microbiologically documented infections also account for 25% of febrile episodes in neutropenic patients. The majority of these are monomicrobial (i.e., caused by a single pathogen), but polymicrobial infections are being documented with increasing frequency. Recent data show that ~15–25 % of bacteremias in neutropenic patients, including catheter-related infections, are polymicrobial. The chi-square statistic is 5.1711. The p-value is .022965. The result is significant at $p < .05$.

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Table No. 3: Common sites of infection in patients with acute leukemia

S. No.	Site of infection	No.	Percentage	P Value
1	Respiratory tract	33	33	.024624
2	Bloodstream	21	21	
3	Urinary tract	14	14	
4	Skin and skin structure	10	10	
5	Intestinal tract	09	09	
6	Other sites	13	13	

The most common and important sites of infection in patients with acute leukemia. Overall, the respiratory tract is the most common site of infection. Approximately 33 % of patients with acute leukemia will develop a pulmonary infiltrate during an episode of neutropenia lasting 10 days or longer. Other parts of the respiratory tract including the oropharynx, upper airways, and the paranasal sinuses are also frequent sites of infection. The chi-square statistic is 2.6589. The *p*-value is .024624. The result is significant at $p < .05$.

Table No. 4: Analysis of Complaints

S. No.	Complaints	No.	Percentage	P Value
1	Fever	93	93	.004348
2	Rash	03	03	
3	Abscess/Cellulitis	03	03	
4	Ear discharge	02	02	
5	Loose Stool	09	09	
6	Blood in stool	00	00	
7	Oral Ulcer	01	01	
8	Breathlessness	09	09	
9	Cough	31	31	
10	Dysuria	05	05	
11	ALOC	00	00	
12	Seizure	00	00	

The chi-square statistic is 13.1378. The *p*-value is .004348. The result is significant at $p < .05$.

Discussion

Recent epidemiologic data document a predominance of gram-positive pathogens from microbiologically documented infections [8]. Unfortunately, these data focus on monomicrobial bacteremic infections, and do not provide details from most other sites of infection, or from polymicrobial infections. This gives an incomplete and skewed view about the microbiology of these infections since bacteremias are caused most often by gram-positive organisms that colonize the skin, whereas infections at most other sites (lung, intestinal tract, urinary tract) have a predominance of gram-negative pathogens [9]. Additionally ~80 % of polymicrobial infections have a gram-negative component, and ~33 % are caused by multiple gram-negative species. When all sites of infection and polymicrobial

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infections are taken into consideration, a substantially different picture emerges, with gramnegative pathogens being almost as frequent as gram-positive pathogens [10].

Indeed, some institutions are now reporting a predominance of gram-negative pathogens. Knowledge of local epidemiologic patterns is critical as empiric regimens need to be designed with this information in mind. The gastrointestinal tract serves as an important source of infection in neutropenic patients, with the predominant pathogens being enteric gram-negative bacilli. The use of antibacterial prophylaxis in high-risk patients including those with acute leukemia has led to a reduction in the frequency of documented gram-negative infections, although some centers are reporting a reversal of this trend [11]. Nevertheless, gram-negative infections, when they do occur, are generally associated with greater morbidity and mortality than infections caused by their grampositive counterparts. Multiple surveillance studies have shown that E. coli, Klebsiella spp., and P. aeruginosa remain the three most commonly isolated gramnegative organisms from neutropenic patients and collectively cause 65–75 % of microbiologically documented gram-negative infections [12]. Other Enterobacteriaceae such as Enterobacter spp., Citrobacter spp., Serratia spp., and Proteus spp. are less common, although institutional differences do exist. Despite the overall decline in the frequency of gram-negative infections in neutropenic patients, there has been an increase in the proportion of such infections caused by non-fermentative gram-negative bacilli (NFGNB) such as Acinetobacter spp., nonaeruginosa Pseudomonas spp., and Stenotrophomonas maltophilia. Collectively, NFGNB now cause ~38 % of documented gram-negative infections, a proportion that has gradually increased over the years.

Conclusion

As patients with leukemia are subjected to ever increasingly intense chemotherapeutic regimens, it is imperative to maximize the efforts in preventing the infections. Strict attention to infection control measures like cooked food diets, strict asepsis during any invasive procedure, strict hygienic measures, and prompt institution of empirical broad spectrum antibiotic, in the management of patients with neutropenia who are at risk of infection. This study shows that septicaemia was the most common infection in adult with leukemia, MRSA being the most frequently isolated organism followed by gram negative pathogens like E. coli and Klebsiella.

Infections cause a substantial amount of morbidity and mortality in patients with acute leukemia and other hematologic malignancies. Neutropenia is the predominant predisposing factor, although other factors also contribute to the development of infection. Bacterial infections predominate during the initial phases of severe neutropenia. Invasive fungal infections develop in patients with persistent and profound neutropenia. Viral infections appear to be increasing in frequency and severity. Early diagnosis and the administration of pre-emptive therapy, especially when dealing with invasive fungal infections, are important as infection prevention.

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