RESEARCH ARTICLE

A Pattern of Bacterial Infections in Acute Leukemia Patients with Neutropenic Fever in Middle Euphrates Region of Iraq

Ahmed Mjali[1]*, Bushra N. H. Al Baroodi[2], Anmar Alharganee[3]

[1,2]*Department of Hematology and Oncology, Al- Hussein Medical City, Karbala, Iraq*
[3]*Department of Oncology, Nottingham University Hospital (NHS UK), Baghdad, Oncology Teaching Hospital, Baghdad, Iraq*

Received: 18th March, 2021; Revised: 09th April, 2021; Accepted: 20th May, 2021; Available Online: 25th June, 2021

ABSTRACT

Our research aims to evaluate causative bacterial microorganisms in acute leukemia patients with neutropenic fever in the Al-Hussein cancer center at Karbala province of Iraq.

Patients and methods: Data was collected prospectively from 59 patients with acute leukemia, hospitalized for neutropenic fever from December 2016 till February 2020.

Results: Out of fifty-nine patients with acute leukemia, 36 patients (61.02%) were female, and 23 patients (38.98%) were male. Twenty-two patients (37.29%) were ALL type, and 37 patients (62.71%) were AML type. Blood was the common site of infection at 27 patients (45.76%), followed by sputum at 12 patients (20.34%), skin infection with 11 patients (18.64%), urine infection with 5 patients (8.48%), and stool infection 4 patients (6.78%). The most common types of bacteria were gram-negative that infected 59.32% of total patients (E. coli was the most common type). Whereas gram-positive bacteria-infected was 40.68% of the total patients (streptococcus pneumonia was the most common type).

Conclusion: Gram-negative microorganisms are the most common bacterial microorganism in our center. Thus, gram-positive infections remain a matter of serious concern.

Keywords: Acute leukemia, Iraq, Neutropenic fever.

International Journal of Drug Delivery Technology (2021); DOI: 10.25258/ijddt.11.2.1

How to cite this article: Mjali A, Al Baroodi BNH, Alharganee A. A Pattern of Bacterial Infections in Acute Leukemia Patients with Neutropenic Fever in Middle Euphrates Region of Iraq. International Journal of Drug Delivery Technology. 2021;11(2):248-251.

Source of support: Nil.

Conflict of interest: None

INTRODUCTION

There are two major types of Acute leukemia: acute lymphoblastic leukemia (ALL) and acute myeloid leukemia (AML).[1] In Iraq, leukemia account >6% of cancer patients, and acute leukemia represents more than 60% of leukemia patients.[2,3]

Aggressive therapeutic options for these patients, such as chemotherapy and stem-cell transplantation, induce neutropenia and increase the risk of infection.[4,5] Despite advances in the development of antibiotics, neutropenic fever was life-threatening condition & considered one of the severe complications during therapy.[6] Through the early phases of a neutropenia episode, bacterial infections are predominant, while invasive fungal infections happen later. Antimicrobial treatment needs to be based upon clinical, radiographic, and microbiological cultures.[7,8] In this study, we tried to find out the common microorganism that affects leukemic patients with febrile neutropenia at Karbala province and develop future leukemia treatment strategies and local guidelines in our country.

PATIENTS AND METHODS

All cases of acute leukemia with neutropenic fever admitted at Al-Hussein cancer center were collected prospectively from December 2016 till February 2020. This center was established in November 2011 with oncology & hematology wards. It covers the Karbala population and other patients from the Middle Euphrates region in Iraq who were referred to this center for solid & hematological malignancy treatment.[9] Neutropenic fever is an acute complication in immune-compromised patients, it is described as a single oral temperature of >38.3°C (101°F) or > 38°C (100°F) for more than one hour in a patient with an absolute neutrophil count (ANC) of < 500/cumm or < 1000/cumm, with an expected fast decrease.[10]

Primary diagnosis with acute leukemia (Acute Myeloid Leukaemia AML or ALL) was made on clinical examination, peripheral smear examinations, bone marrow aspiration, and immunophenotyping if available. Patients with neutropenic fever sets of cultures were taken: blood samples, central venous line, urine, sputum, skin lesions or any suspected site for identifying the organisms. All specimens went through

**Author for Correspondence: ahmedmajly@yahoo.com*

culture and sensitivity tests in the laboratory by culturing organisms on appropriate media growth (e.g., blood, chocolate, and McConky agar). Final diagnosis and sensitivity results were discovered by Vitek 2 systems used to confirm the biochemical test. The assay has been carried out according to the instructions of the manufacturer (Biomerieux-France); in short, after dilution in 0.45% saline, the cell density of the remaining bacterial suspension was changed to a density of 0.5 McFarland; 145 µL of the bacterial suspension was dipped into 3 mL of 0.45 percent of saline solution to additional bacterial cell density change. Vitek cards were inoculated with the suspension vials and loaded into the Vitek 2 automated reader-incubator.[11]

RESULTS

Fifty-nine acute leukemia patients with neutropenic fever were enrolled in our study, mean age was 34.3 ± 14.17, while the median was 30 years. The number of female patients was 36 (61.02%), male patients were 23 (38.98%). Thirty-seven patients (62.71%) were AML, and 22 patients (37.29%) were ALL (Table 1).

The site of infection was distributed to different sites of the body where specimens were taken. Blood was the most common site with 27 specimens (45.76%), followed by sputum 12 specimens (20.34%), skin swabs 11 specimens (18.64%), urine 5 specimens (8.48%) and stool 4 specimens (6.77%). Gram negative bacteria were most common in 35 patients (59.32%), while gram-positive were 24 patients (40.68%) as shown in Table 1.

The most frequent gram-negative type is *E. coli* with 23 patients (65.71%) followed by *Klebsiella pneumonia* with 5 patients (14.29%), *Enterobacter aerogenes* with two patients (5.71%), *Pseudomonas aeruginosa* with two patients (5.71%), Aeromonas hydrophila/caviae with one patient (2.86%), Proteus mirabilis with 1 patient (2.86%), and *Enterobacter cloacae* with one patient (2.86%) as shown in Table 2.

On the other hand, *Streptococcus pneumonia* was the most common isolated gram-positive bacteria presenting about one-quarter of cases as 6 patients (25%), followed by *Staphylococcus hominis* with 4 patients (16.66%), Staphylococcus saprophyticus with 2 patients (8.33%), *Enterococcus faecalis* with 2 patients (8.33%), *Streptococcus oralis* with 2 patients (8.33%), Streptococcus pyogenes with 2 patients (8.33%), *Staphylococcus epidermis* with 1 patient (4.17%), *Streptococcus agalactiae* with 1 patient (4.17%), *Staphylococcus warneri* with 1 patient (4.17%), *Staphylococcus pseudintermedius* with 1 patient (4.17%), *Staphylococcus aureus* with 1 patient (4.17%), and *kocuria varians* with 1 patient (4.17%).

Table 1: Characteristics of the baseline (n=59).

Characteristics of patients	
Age (years)	
Mean	34.3 ± 14.17
Median	30
Gender	
Male	23 (38.98%)
Female	36 (61.02%)
Types of acute leukemia	
ALL	22 (37.29%)
AML	37 (62.71%)
Specimen collection	
Blood	27 (45.76%)
Sputum	12 (20.34%)
Skin swab	11 (18.64%)
Urine	5 (8.48%)
Stool	4 (6.78%)
Type of Bacteria	
Gram positive	24 (40.68%)
Gram negative	35 (59.32%)

DISCUSSION

Since patients with acute leukemia require urgent care with effective chemotherapy regimens, most of them appear to be neutropenic after diagnosis, making them at risk with high mortality rates.[6] Old-time, in the evolution of chemotherapy, gram-negative microorganisms were the most frequent in the 1960s and 1970s. Later, gram-positive species becoming more widespread during the 1980s and 1990s. This shifting

Table 2: Types of isolated bacteria.

Isolated microorganism	*Numbers*
Gram-negative	
E. coli	23 (65.71%)
Klebsiella pneumonia	5 (14.29%)
Enterobacter aerogenes	2 (5.71%)
Psedomonas aeruginosa	2 (5.71%)
Aeromonas hydrophila/caviae	1 (2.86%)
Proteus mirabilis	1 (2.86%)
Enterobacter cloacae	1 (2.86%)
Total	35 (100%)
Gram-positive	
Streptoccoccus pneumonia	6 (25%)
Staphylococcus hominis	4 (16.66%)
Staphylococcus saprophyticus	2 (8.33%)
Enterococcus faecalis	2 (8.33%)
Streptococcus oralis	2 (8.33%)
Streptococcus pyogenes	2 (8.33%)
Staphylococcus epidermis	1 (4.17%)
Streptococcus agalactiae	1 (4.17%)
Staphylococcus warneri	1 (4.17%)
Staphylococcus pseudintermedius	1 (4.17%)
Staphylococcus aureus	1 (4.17%)
Kocuria varians	1 (4.17%)
Total	24 (100%)

may result from using fluoroquinolone as prophylaxis and increased usage of plastic venous catheters.[7,12-14] In our study, gram-negative microorganisms still the predominant type in acute leukemia patients with neutropenic fever. Which consistent with other studies done in Italy, Iran, Thailand, India, and Taiwan, where gram-negative bacteria still the predominant type.[6,14-19]

Since *E. Coli* can colonize the gastrointestinal tract of humans, it is one of the most common bacterial microorganisms in human fecal flora.[14] Therefore, it presents a common cause of Gram-negative microorganisms in neutropenic patients in our study. Which also was the most common isolated gram-negative bacteria in previous studies in Iran, Thailand, Taiwan, and India.[6,15,17,18] In most centers, coagulase-negative staphylococci were the most frequent gram-positive bacteria, but Streptococcus pneumonia was the most frequent gram-positive bacteria presenting about one-quarter of cases.[6,8, 14,15,17,20]

In our study, bloodstream infection is the most common infection site, followed by respiratory tract infection, same results in a study done by Karanwal *et al*., where blood and sputum were the common sites.[18] While studies from Iran and Thailand, blood and urine were the most common sites.[6,15] On the other hand, Menzo *et al*., showed that respiratory tract infections were the frequent site then bloodstream infections.[14]

CONCLUSION

Gram-negative bacteria were the most frequent in our center. E. Coli is the most common isolated gram-negative bacteria. On the other hand, gram-positive was still of great concern, and Streptococcus pneumonia is the predominant gram-positive organism. Bloodstream infection was the most frequent site, followed by a chest infection. Further studies in other parts of Iraq are needed to cover the paucity of data regarding the incidence of bacterial infection in Iraqi patients with acute leukemia. It is empirical to apply strict infection control guidelines and be followed by healthcare personnel to undermine the severity and frequency of febrile neutropenia figures at hematological centers where rates seem to surge.

DECLARATION

Acknowledgments

We would like to thank Mr. Hekmat Hamada Baqir from Karbala Cancer Registry Center; without his help, this study couldn't see the light of day.

Authors' Contribution

All authors listed have made a substantial, direct, and intellectual contribution to the work and approved it for publication.

Funding

None.

Data Availability

All datasets analyzed in the study are included in the manuscript and presented as tables.

Ethics Statement

The selected topic was accepted by the scientific committee; official acceptance was taken from health authorities to conduct this study. Collected information was kept confidential.

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