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Current spectrum of bacterial infections in patients with nosocomial fever and neutropenia

Abstract

Background: Neutropenic patients are vulnerable to a wide spectrum of infectious agents. The aim of this study was to determine the current frequency of bacterial infections in patients with nosocomial fever and neutropenia.

Methods: In a retrospective study, the neutropenic patients' specimens with nosocomial fever were cultured on blood and MacConkey agar plates and evaluated at microbiology laboratory. Ninety-five significant isolates as species level were recognized by bacteriological techniques.

Results: The most observed microorganism was *Escherichia coli*, followed by *Pseudomonas aeruginosa*, *Acinetobacter baumannii*, *Klebsiella pneumoniae*, Coagulase positive staphylococci and Coagulase negative staphylococci. One fungal infection was also observed. Overall, 67% of the organisms were gram negative, 29.8% gram positive, and 3.2% polymicrobial.

Conclusion: The changing pattern of infectious agents in neutropenic patients overtime postulates the necessity of other studies to give the most up-to-date insight of the organisms to physicians.

Keywords: Bacterial Infections, Spectrum, Nosocomial, Fever, Neutropenia

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Neutropenic patients are vulnerable to a wide spectrum of infectious agents which cause substantial mortality and morbidity among them (1-6). Neutropenia is defined as a neutrophil count of <500 cells/mm³, or a count of <1000 cells/mm³ with a predicted decrease to <500 cells/mm³ (4). The increasing use of cytotoxic chemotherapy in patients with hematologic malignancies and solid tumors has increased the number of patients who have neutropenia (6). Chemotherapy disrupts skin and mucosal barriers, too. Furthermore, exposures to pathogens have been increased because of the frequent insertion of Foley and venous catheters in patients with cancers. (7). Thus, these patients are prone to infections. Both gram-negative and gram-positive bacteria are responsible for infection in neutropenic patients but there has been a shift in etiology from gram-negative rods to gram-positive cocci during the previous years (3, 4, 8, 9).

Although the many different mechanisms cause fever in immunocompromised patients, specific clinical and immunologic evidences can help clinicians to distinguish between the causes and the duration of immune deficit can strongly predict the possible infecting organisms (4). Many studies have investigated the causes of infection and fever in neutropenic patients (10-16), but the changing face of the responsible bacterial spectrum necessitates further ongoing studies in this field, and succinct local data are lacking. Thus, we aimed to investigate the current spectrum of bacterial infections in nosocomial febrile neutropenic patients in one of the hospitals in Tehran, Iran in order to help verify the choices of antibiotic therapy in this setting.

Methods

From September 2007 to September 2009, the specimens from all the neutropenic patients with nosocomial fever were sent to the laboratory in a hospital in Tehran, Iran. Fever was considered as a single oral temperature of $\geq 38.3^{\circ}\text{C}$ or a temperature of $\geq 38^{\circ}\text{C}$ for ≥ 1 hour and absolute neutrophil count of $<500/\text{mm}^3$. Nosocomial infection was considered when a patient was diagnosed with an infection 48–72 hours after admission, or at most one week after discharge from the hospital (4).

The patients who were already on antimicrobial therapy or had fever due to a non-infectious cause, such as drug infusion, blood transfusion, and others were excluded from the study. The following data were recorded from the patients; age, gender, admitted ward, final diagnosis, source of culture, and the isolates.

The specimens were inoculated on blood and MacConkey agar plates at microbiology laboratory. The plates had been incubated at 37°C for 24 hours and 95 significant isolates as species level were recognized by bacteriological techniques. We used control organisms *Escherichia coli* ATCC 35218, *Klebsiella pneumoniae* ATCC 700603, *Pseudomonas aeruginosa* ATCC 27853, *Acinetobacter baumannii* ATCC BAA-747, *Staphylococcus epidermidis* ATCC 12228, *Staphylococcus aureus* ATCC 29213, *Staphylococcus saprophyticus* BAA-750, *Enterococcus faecalis* ATCC 29212, *Enterobacter aerogenes* ATCC 13048, *Streptococcus pneumoniae* ATCC 49619, and *Salmonella typhimurium* ATCC 14028 to check the quality of media and evaluate color stability.

We used three control American type culture collection (ATCC) organisms for each test, and each test was tested for each new varied group. The data were collected and analyzed.

Results

Ninety-five subjects (63 males, 32 females) with the mean age of 43.87 ± 17.2 years (ranged 13–88 years) were evaluated. Among the 95 patients, 44 were admitted in hematology ward, 26 in bone marrow transplantation ward, 14 in oncology ward, 5 in nephrology ward, 4 in intensive care unit, and 2 in gastroenterology ward.

Twenty-four (25.3%) of patients were admitted for bone marrow transplantation, 15 (15.8%) of them were diagnosed with acute lymphocytic leukemia, 14 (14.7%) and 18

(18.9%) of patients had acute myeloid leukemia and other malignancies, mostly hematologic, respectively. The final diagnosis for 6 (6.3%) of patients was an infection. Sixty-three (66.3%) of patients had positive blood cultures and 17 (17.9%) positive urine cultures. Positive sputum and wound cultures were seen in 13 (13.7%) and 2 (2.1%) patients, respectively. The most observed microorganism was *Escherichia coli* (27.7%), followed by *Pseudomonas aeruginosa* (16%), *Acinetobacter baumannii* (10.5%), *Klebsiella pneumoniae* (8%), Coagulase positive staphylococci (8%) and Coagulase negative staphylococci (8%). One fungal infection was also observed (table 1). Overall, 67% of the organisms were gram-negative, 29.8% gram-positive, and 3.2% polymicrobial. This percentage in contrast to the source of culture is shown in table 2.

Table 1. The Frequency (Percentage) of Pathogens in Nosocomial Fever and Neutropenia

| | N | Percentage |
|----------------------------------|------------|--------------|
| <i>Escherichia coli</i> | 27 | 27.6 % |
| <i>Pseudomonas aeruginosa</i> | 16 | 16.3 % |
| <i>Acinetobacter baumannii</i> | 12 | 12.2 % |
| <i>Klebsiella pneumoniae</i> | 8 | 8.2 % |
| Coagulase positive staphylococci | 8 | 8.2 % |
| Coagulase negative staphylococci | 8 | 8.2 % |
| <i>Enterococcus faecalis</i> | 6 | 6.1 % |
| <i>Staphylococcus aureus</i> | 5 | 5.1 % |
| <i>Enterobacter aerogenes</i> | 4 | 4.1 % |
| <i>Streptococcus pneumoniae</i> | 2 | 2 % |
| <i>Salmonella typhimurium</i> | 1 | 1 % |
| Yeast | 1 | 1 % |
| Total | 98* | 100 % |

* Total number of organisms is assumed after considering polymicrobial infections

Table 2. The Frequency (Percentage) of Pathogens in Contrast to the Source of Culture

| Organism | Source of culture | | | |
|---------------|-------------------|-----------|-----------|----------|
| | Blood | Urine | Sputum | Wound |
| Gram Negative | 43 | 12 | 7 | 1 |
| Gram Positive | 19 | 5 | 4 | 0 |
| Polymicrobial | 1 | 0 | 1 | 1 |
| All | 63 | 17 | 12 | 2 |

* One patient was infected with fungus.

Discussion

Febrile neutropenia is of specific concern in immunocompromised patients as this state makes them prone to bacterial infections (1-3, 6, 17, 18). The pattern of bacterial infections in these patients has changed overtime. There has been a shift in etiology from gram-negative rods to gram-positive cocci during the previous years (3, 8, 9). Furthermore, because of higher morbidity and mortality of infection in these patients, antibiotic therapy should be started as soon as possible. Thus, the local data of common pathogens is important to initiate the appropriate empirical antibiotic therapy (19). Our study demonstrated 67% gram-negative, 29.8% gram-positive, and 3.2% polymicrobial infections in the patients. The most observed microorganism was *Escherichia coli* in the gram-negative group and coagulase negative staphylococci in gram-positive group. Although fungal infections are not common in neutropenic patients, there are studies assessing fungal infections in these patients (20). We found one fungal infection in our patients. Butt et al. conducted a study on bacterial spectrum and antimicrobial susceptibility pattern of organisms causing bloodstream infections in febrile neutropenic patients over a period of nine months. They observed gram-negative rods in many cultures, in which *Escherichia coli* was mostly seen among them, and gram-positive cocci in the rest of cultures among which coagulase negative staphylococci were the most common (11).

Saeidpour et al. performed a non-randomized study on hospitalized children of the emergency and pediatric hematology and oncology units in Iran. They found that the most common pathogen was gram-negative bacteria, and *Pseudomonas aeruginosa* and *Staphylococcus aureus* were the most frequent gram-negative and gram-positive isolates, respectively. *Candida spp.* was the only isolated fungus (12). These two studies are compatible with our results.

Syrjälä et al. reported the frequency of blood stream infections during neutropenia in different cycles of intensive chemotherapy treatment in patients with acute myeloid leukemia (AML). Gram-positive organisms were seen in 71.7% of cultures, which coagulase negative staphylococci being the most prominent (13). Chong et al. showed the similar rate in gram positive and negative, in febrile neutropenic patients (14). Meidani et al. reported 56.4% gram-positive bacteria, 17.4% gram-negative bacillus, 3% anaerobic bacilli, 4.3% atypical bacteria, and 17.4% fungi in their patients (15). In a study performed in Japan, Kanamaru

and Tatsumi compared infecting pathogens among febrile neutropenic patients and the general patient population. They found that 57% of the isolated organisms were gram-positive among general patients but this proportion was 37% in febrile neutropenic patients. Although coagulase negative staphylococci were the most common in general population, streptococci were the most observed in patients with febrile neutropenia. Gram-negative bacteria were seen in neutropenic patients more than the others. Among this group of organisms, enterobacteriaceae were the most common in general patients and *Pseudomonas aeruginosa* was the most seen in febrile neutropenic patients. None of fungi and anaerobes was seen in neutropenic patients (9).

Meidani et al. in Iran performed their study on neutropenic patients with fever. They found 68.4% of medical documents with no result for culture of any body fluid. Only 2.6% of patients had positive blood culture (16).

These reports are not consistent with our results and show that the spectrum of pathogens in neutropenic patients is not the same in different countries. The higher rates of gram-positive pathogens in some studies may be explained by some factors; For example, the use of prophylactic antibiotics such as fluoroquinolones, the frequent use of central venous catheters, and oral and intestinal mucosal damaging as a result of chemotherapy (7). Because of obtaining samples from patients with nosocomial fever and neutropenia in our study, the higher rates of gram-negative pathogens may be reasonable. There are different findings in other studies in Iran (12, 15). Based on the above findings, we cannot demonstrate the definite change in the spectrum of bacterial infection in Iran. To sum up, previous studies have found several organisms (both gram negative and gram positive) as common infecting organisms among neutropenic patients and the pattern of organisms is different in these patients compared to the general population.

In our study, gram-negative bacteria were seen more than other organisms in febrile neutropenic patients, and *Escherichia coli* was the most common pathogen. The changing pattern of infectious agents in neutropenic patients overtime postulates the necessity of other studies to give the most up-to-date insight of the organisms to physicians.

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