Summary

Infectious complications during neutropenia account for about 70% of fatal complications in patients with acute leukemia **(Buchheidt et al., 2003)**.Bacteremia and fungemia are the most commonly documented infections in hematological patients undergoing chemotherapy; they thus have great clinical and prognostic significance **(Fatkenheuer et al., 2003)**.Because of the high frequency of bacteremia and fungemia, most neutropenic patients with fever were admitted to the hospital and treated with broad-spectrum parenteral antibiotics.

The aim of our study was to detect clinical, radiological and laboratory parameters that were associated with low risk of bacteremia and fungemia in children with acute lymphoblastic leukemia who were presented with FN so that they may be potential candidates for outpatient management. In our study, we also identified the type of bacterial and fungal isolates in these children.

This study comprised 30 patients admitted to the Hematology and Oncology Unit, Benha Specialized Children's Hospital, diagnosed as acute lymphoblastic leukemia and have been treated with chemotherapy [Children's Cancer Group(CCG) protocol]. 98 attacks of FN were recorded in these patients during the period between August 2007 and April 2010.

These patients were 18 males and 12 females with a mean age of 5.2 years ranging from 1.5-12 (SD 2.7). In each attack of FN, complete history taking and careful physical examination were done with particular attention to areas that may hide a site of infection unless closely examined particularly the oral cavity and the perianal area.

The following laboratory parameters were done in each attack of FN:

a) Complete blood picture with differential count

b) C-reactive protein

c) Blood culture for both bacteria and fungi

d) Surveillance cultures based on clinical findings

e) Chest x-ray

In our study the prevalence of infection was 53.1% (n=52 out of 98 attacks of FN). Bacterial infection only was 30.6% (n=30), fungal infection only was 16.3% (n=16) and combined bacterial and fungal infections were 6.1% (n=6).

The results of bacterial blood culture showed that 36.7% (n=36) of febrile neutropenic attacks had documented bacterial infection (true bacteremia) in the form of positive bacterial blood culture. Gram-positive organisms constituted 63.9% (n=23) while Gram-negative organisms constituted 36.1% (n=13) of febrile neutropenic attacks that had documented bacterial infection (n=36). Staph aureus constituted 91.3% (n=21) and beta-hemolytic streptococci constituted 8.7% (n=2) of Gram-positive organisms (n=23). E.coli constituted 46.1% (n=6), klebsiella 30.8% (n=4), pseudomonas 15.4% (n=2) and acinetobacter constituted 7.7% (n=1) of Gram-negative organisms (n=13).

In our study, positive fungal blood culture was found in 22 out of 98 attacks of FN (22.4%).

Aspergillus fumigatus spp. Constituted 45.5% (n=10), aspergillus niger spp. 22.7% (n=5), candida albicans 27.3% (n=6) and candida tropicalis constituted 4.5% (n=1) of febrile neutropenic attacks that had documented fungal culture.

Based on the data obtained, as regards clinical and radiological parameters, we found that higher degrees of temperature, longer duration of neutropenia, presence of hypotension, chest manifestations and chest x-ray abnormalities were highly significant ($p<0.001$) in attacks of FN with infection (either bacterial,fungal or both) versus attacks without infection.

As regards laboratory parameters, there were highly significant ($p<0.001$) lower values of ANC, AMC, APC and platelets in attacks of FN with infection (either bacterial,fungal or both) versus attacks without infection. Also there were highly significant ($p<0.001$) higher values of CRP in attacks of FN with infection versus attacks without infection.

On the other hand, TLC showed non significant differences ($p>0.05$) between both groups.

There were non significant differences ($p>0.05$) between attacks of FN with Gram-positive versus attacks with Gram-negative organisms as regards clinical, radiological and laboratory parameters except for CRP which showed significantly ($p<0.05$) higher values in attacks of FN with Gram-positive organisms.

There were significantly ($p<0.05$) higher degrees of temperature in attacks of FN with only bacterial infection versus attacks with only fungal infection. Also, presence of chest manifestations and chest x-ray abnormalities was highly significant ($p<0.001$) in attacks of FN with only fungal infection versus attacks with only bacterial infection. On the other hand, duration of neutropenia and hypotension showed non significant ($p>0.05$) differences between both groups.

There were significantly ($p<0.05$) lower values of TLC and platelets in attacks of FN with only bacterial infection versus attacks with only fungal infection. On the other hand, other laboratory parameters showed non significant differences ($p>0.05$) between both groups.

Conclusion

- Not all acute lymphoblastic leukemic patients who develop FN have the same risk for bacteremia and fungemia.
- Higher degrees of temperature, longer duration of neutropenia, presence of hypotension, chest manifestations and chest x-ray abnormalities were considered high risk factors for infection in acute lymphoblastic leukemic patients with FN.
- Acute lymphoblastic leukemic patients with FN with higher values of CRP and lower values of ANC, AMC, APC and platelets at time of presentation had a high-risk for infection.
- Patients at high-risk for infection must be hospitalized and treated with empirical broad-spectrum intravenous antibiotics to decrease the incidence of infection-related morbidity and mortality while patients at low-risk for infection could be safely treated in outpatient setting with minimal antibiotic treatment.
- Acute lymphoblastic leukemic patients with FN and presented with chest manifestations and chest x-ray abnormalities were considered at high-risk for fungal infection so antifungal therapy must be recommended.