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# Cause-Specific Mortality in Childhood Acute Lymphoblastic Leukemia at a Single Center in Iran

**Khadijeh Arjmandi Rafsanjani, Azadeh Kiumarsi* and Leila Hashami**

*Pediatric hematology oncology department, St Aliasghar Hospital, Tehran, Iran

## Abstract

**Background:** We studided the etiologies of mortality in childhood Acute Lymphoblastic Leukaemia (ALL) patients at Paediatric Oncology Department of St Aliasghar Hospital.

**Methods:** In our hospital, between years of 2005 to 2012, we had 442 registered cases of ALL whose data was collected and analyzed regarding to different factors including their age, sex, WBC count, immune phenotype, treatment response and timing of death and the etiologies of their mortality.

**Results:** Among the new registered cases of ALL in the study period, 80 (18%) died. Infection was accountable for deaths in 58 (72.5%) cases. Septicemia, pulmonary infections were documented in 41 (51.25%), and 12 (15%) cases respectively. Eleven (13.8%) died due to haemorrhage.

**Conclusion:** Infection was the chief etiology of mortality in our ALL patients. For improving survival it is very important to advance our supportive care particularly prevention and treatment of infection. By studying mortality causes in clinical and demographic subgroups, one gains insights into development of strategies and interventions to modify treatment to decrease mortality.

**Keywords:** Acute Lymphoblastic Leukaemi; Mortality; Infection

***Corresponding Author:** Azadeh Kiumarsi, MD, Pediatric hematology oncology department, St Aliasghar Hospital, Tehran, Iran; Tel: 00982123046411; E-mail: raha1221@yahoo.com

## Introduction

For children younger than 15 years of age, cancer is one of the most important contributors to loss of life. While the available mortality data are adequate for assessing the importance of childhood cancer relative to other diseases, they cannot provide the necessary detail for determining the cause of death in specific pediatric cancers. The major causes of treatment related mortality in acute leukemia in developing countries are infections, haemorrhage, and chemotherapy induced toxicity [1, 2].

We conducted this study due to the small number of studies about the mortality etiologies in childhood leukemia from developing countries. The statistics reported by studies from developed countries could not precisely our population. For that reason, we conducted a retrospective study at the Paediatric Oncology department of St Ali asghar Hospital, Tehran, Iran.

## Patients and Methods

We reviewed the medical records of all paediatric patients treated for ALL between the ages of 1 and 18 years, registered at our hospital between 2005 to 2012 and in the next step, the records of the patients who died during this period were further analyzed.

The diagnosis of ALL at presentation was made according to bone marrow morphology and immunophenotyping. Children were treated in accordance with the BFM 2002 protocol.

We documented the patients' age, sex, initial White Blood Cell (WBC) count, immunophenotype, timing of death with respect to disease status and the cause of death.

The mortality etiologies were divided into three major categories: (i) Infections; (ii) Haemorrhagic complications; (iii) Other causes.

The study was approved by the hospital ethics committee.

Data were analyzed using (SPSS) version 16.

## Results

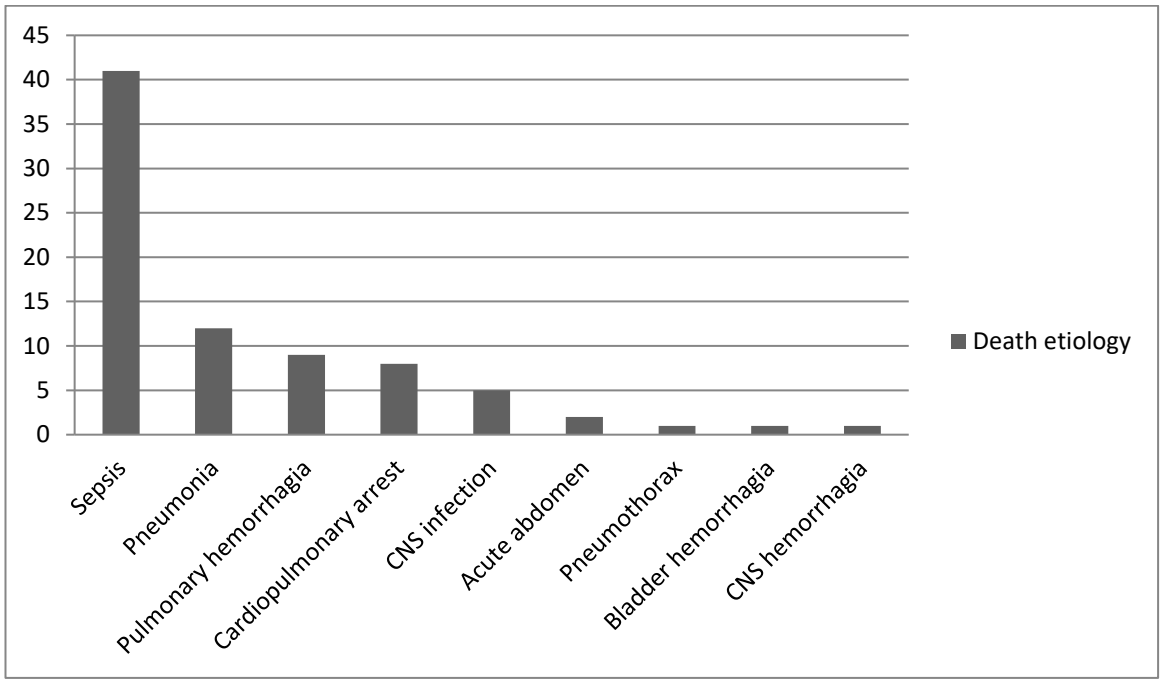
A total of 442 new cases of ALL were registered during the study period. Among them, 80 (18.1%) cases died. The mean age of mortality was 8.6 years (range 2-18 years). Fifty one (63.8%) cases were males. The initial WBC count at presentation was less than 10 x $10^3$/L in 37 (46.3%) and more than 50 x $10^3$/L in 19 (23.8%). Immunophenotyping performed by flow cytometry established that 60 (75%) had precursor B and 20 (25%) had precursor-T ALL. In light microscopic evaluation 55 (69%) cases had L1 morphology, 18 (23%) L2 morphology and 7 (8%) cases had L3 morphology.

Fourty nine (61.25%) of cases had relapse while they were under treatment and 28 (35%) had relapse after the treatment cessation.

Of 80 deaths, 58 (72.5%) patients died of infection, 11 (13.8%) of haemorrhage and 11 (13.8%) died of other causes. Fourty one (51.2%) infective deaths were due to sepsis and 12 (15%) had pneumonia. Five (6.3%) had central nervous system infections.

Haemorrhage resulted in 11 (13.8%) deaths. Major sites of haemmorrhage were pulmonary in 9 (11.3%), intracranial and genitourinary in 3.1 (3.9%) cases each. Of the 11 (13.8%) cases with other causes of mortality, 8 (10%) were due to cardiopulmonary compromise, 2 (2.5%) due to acute abdomen and 3.1 (3.9%) due to pneumothorax (Figure 1).

**Figure 1:** Distribution of death etiology among patients




## Discussion

The most common childhood malignancy is leukemia which accounts for 30% of all cancers diagnosed in children less than 15 years of age [3]. The employment of multi-modal therapies over the past years has increased survival noticeably in most types of pediatric cancers [4]. Advances in antimicrobial therapy, supportive care and improvement in intensive care have enhanced the patients' overall survival.

A sex-specific difference in frequency of deaths has been reported in different studies. In our study, 63.8% of deaths were seen in male patients. Mertens et al., also reported a higher rate of death in male patients and they indicated that treatment had not achieved a cure within the first 5 years for some males. In their study, females demonstrated consistently higher mortality due to non – recurrence mortality than males [5, 6].

Infection remains a major reason for therapy associated morbidity and mortality [7]. Patients with leukemia who are under chemotherapy regimens experience severe and potentially lethal infections due to epithelial barriers' breakage, immune dysfunction, malnutrition and invasive therapeutic interventions. The haematopoietic and lymphoid system are also affected by the malignant process which itself aggravates the immunocompromised state. Neutrophils are the key component of cellular defense against most bacteria and chemotherapy induced neutropenia is associated with life-threatening infections, particularly adding together with delayed treatment [8]. Asim et al., in Pakistan reported that in their study, mortality was mostly due to infective and haemorrhagic complications of therapy rather than treatment failure or relapse [9].

In the present study, 72.5% of patients died due to infection. Choudhry et al., [10] from India and Gao et al., [11] from China also reported that infections were accountable for mortality in the majority of their ALL cases.

The leading non-infective cause of mortality in leukaemic patients is haemmorrhage. In our study, haemorrhage resulted in 13.8% of deaths and pulmonary hemorrhagia was the most common site. Choudhry et al., [10] and Asim et al., [9] also reported haemorrhage as the second major cause of mortality.

By studying mortality rates within specific therapeutic modalities as well as in clinical and demographic subgroups, one gains insights into the therapeutic modalities that are associated with greatest mortality, identification of patients who require closer follow up, and development of strategies and interventions to modify treatment to decrease mortality without sacrificing survival. In conclusion, although complete elimination of deaths due to infection may be impossible, early and intensive treatment of patients may lessen mortality.

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