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# Cytogenetic Profile of Childhood Acute Lymphoblastic Leukemia in Oman

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*Background.* Chromosomal abnormalities have important diagnostic and prognostic significance in acute lymphoblastic leukemia (ALL). The purpose of this study was to define and classify the frequency and type of chromosomal abnormalities among newly diagnosed children with ALL and compare the results with those reported from other geographical regions of the world.

*Methods.* Bone marrow chromosomal studies with GTG banding were performed in untreated ALL pediatric patients aged from 7 days to 14 years.

*Results.* Among Omani children examined with ALL, 47 (81%) patients yielded results, with 26 (55.3%) showing an abnormal karyotype [10 (21.3%) pseudodiploid, 2 (4.3%) hypodiploid and 14 (29.7%) hyperdiploidy] and 21 (44.6%) had normal diploidy. Structural abnormalities were observed in 16 (34%), of which 11 (23.4%) cases were translocations, the most frequent being t(9;22) observed in three (6.4%) of our patients. Uncommon translocations such as t(9;15)(p11;q10), t(3;6)(p12;q11), t(1;6)(?31;?q23), t(1;19)(q12;q12), der(18)t(12;18)(q11;p11), and other structural aberrations add(2)(q22), add(6)(q16), add(18)(q22), add(14)(q32) along with deletions del(10)(q22), del(12)(p11), del(12)(p12), del(18)(q11) were also observed.

*Conclusions.* The study showed a good correlation and concordance between the ploidy distribution by cytogenetics and flow cytometry. The patterns of chromosomal anomalies in our patients showed some variations in the frequency of aberrations reported. It is therefore necessary that newer techniques like fluorescence in situ hybridization (FISH) along with reverse transcriptase polymerase chain reaction (RT-PCR) and spectral karyotyping will help us identify chromosomal aberrations not detected by conventional cytogenetic methods in the near future. To our knowledge, this is the first report from the Middle East of a cytogenetic study on childhood ALL. © 2007 IMSS. Published by Elsevier Inc.

*Key Words:* Cytogenetic analysis, Acute lymphoblastic leukemia, Chromosomal abnormalities.

## Introduction

Acute lymphoblastic leukemia (ALL) is a disease characterized by the abnormal proliferation of immature lymphoid cells (1). In this disease, non-random chromosomal abnormalities have important biological, diagnostic, and prognostic significance (2). Karyotyping is a valuable diagnostic tool with many specific chromosomal rearrangements being identified, and in ALL it is of increasing importance owing

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to its role in the subclassification and prediction of outcome. Currently, the results of cytogenetic analyses have independent prognostic significance (3).

The majority of ALL patients have acquired chromosomal abnormalities in leukemic cells. Cytogenetic changes also indicate the genes involved in the leukemic process and provide a starting point for unraveling the complex genetic mechanisms involved in leukemogenesis. Further advances continue to be made, with the discovery of new, recurring chromosomal abnormalities in childhood ALL (4).

Here we describe the clinical, immunophenotypical, morphological, and cytogenetic pattern in Omani children with ALL. Our aim was to define and classify the frequency and type of chromosomal abnormalities among newly diagnosed Omani children with ALL, for comparison with those reported in the literature from populations in other geographical regions of the world. This is the first report of cytogenetic analysis on childhood ALL from Omani children.

## Materials and Methods

### *Patients*

A total of 58 children were studied (35 male and 23 female). Successful results from 47 children (30 boys, 17 girls; age range: 7 days–14 years) presenting at the Paediatric Haematology Department, Sultan Qaboos University Hospital from February 2002 to June 2005 were analyzed. The diagnosis of ALL was based on French-American-British (FAB) cytomorphology criteria and the immunophenotyping of bone marrow. We divide ALL into B- and T-lineages with B-lineage further subdivided into B-cell, pre-B-cell, and early B-precursor types [CD10 + ve or neg] (5).

### *Immunofluorescence Analysis*

Immunophenotyping was performed using an acute leukemia panel of monoclonal antibodies consisting of CD2, CD3, CD4, CD5, CD7 (T-cell lineage), CD10 (CALLA), CD19, CD20, CD22 (B-cell lineage), cytoplasmic IgM heavy chain μ (Pre-B ALL), CD 11, CD14, CD15, CD33, CD34 (myeloid markers), CD117(c-kit), and TdT. DNA indexing was done using flow cytometry.

### *Chromosomal Analysis*

Chromosomal analysis was performed using heparinized bone marrow aspirates at the time of diagnosis, just before treatment. Chromosome preparation was done by standard short-term culture (24 and 48 h) techniques using RPMI-1640 marrow max medium (GIBCO cat. # 12260–022) incubated at 37°C. Karyomax–Colcemid solution (final concentration 0.05 μg/mL) was added for the final 30 min of culture. Cells were subjected to hypotonic treatment (KCl 0.075 M) for 30 min at 37°C and fixed in methanol:acetic acid (3:1). Chromosome analysis was performed on GTG-banded preparations using the Applied Imaging Cytovision Automated Karyotyping System. International System for Human Cytogenetic Nomenclature (ISCN) criteria (2005) was used for assessing the presence of clones with numerical and structural abnormalities (6). Structural abnormalities were classified as primary non-random abnormalities when they were recurrent and had known significance with respect to the prognosis or as secondary non-random abnormalities when less specific and found with the primary abnormality. Clonal abnormality was established only when two or more cells had the same extra chromosome or structural abnormality and there were three or more cells with the same missing chromosome. Fluorescence in situ hybridization (FISH) could not be performed due to current lack of facility.

## Results

The clinical, morphological, immunophenotypical and cytogenetic findings are summarized in Table 1. Forty-seven yielded successful cytogenetics results. The disease was more frequent in males (30) than females (17). Ages ranged between 7 days and 14 years. Six patients were $<1$ year of age, 36 were between the ages of 1 and 10, and five were $>10$ years old. Thirty-one patients were in the prognostically better age range of 2–8 years.

Morphologically, 24 children were classified as FAB L1, and 22 were FAB L2, with data on one case unavailable. There were no patients with FAB L3 morphology (Figure 1). Immunophenotypically, 19 children were classified as pre-B ALL, 20 were precursor B-cell ALL, seven were T-cell, and data on one case was not available (Table 2; Figure 1). Patients were followed in the hematology clinics from initial diagnosis and received the standard Pediatric Oncology Group (POG) treatment protocol according to the type of the ALL and risk stratification (mean follow-up of 3.5 years; range 0.5–5 years). Overall, 33 patients are alive and in remission, two had relapsed but were alive, six had relapsed and died, and two died without a relapse. Four patients were lost to follow-up.

Among the patients analyzed, 26 showed an abnormal karyotype. A normal diploid count was observed in 21 children, pseudodiploidy in 10, hypodiploid with $<46$ chromosomes in 2, low hyperdiploidy with 47–50 chromosomes in 5, and high hyperdiploidy (or low hypotriploid) with 51–65 chromosomes in 9 patients, respectively (Table 2). This study showed a good correlation and concordance between the ploidy and distribution by cytogenetics and flow cytometry.

In our patients, frequent chromosome gain occurred most frequently in chromosome 21, followed in decreasing order by 6 (as observed in other populations), equal gains of