INTRODUCTION

Neoplastic proliferation with differentiation of lymphoid progenitors seen on bone marrow characterizes acute lymphoblastic leukemia (ALL). Various classifications of ALL have been documented based on prognostic significance and their biological behavior. Immature lymphoid cell lines at different stages of maturation may show cell cycle arrest resulting in the malignant transformation.¹

In Pakistan insufficient data is available regarding the incidence and chromosomal abnormalities of ALL.² The most common age involvement of ALL is below the age of fifteen years. In a retrospective study in Karachi conducted by Yasmeen et al revealed 32% frequency regarding the cases of childhood ALL.²

Various abnormalities involving the chromosomal deletions and translocations have been reported in the literature. Many of these often show dysregulation of the gene expression. The karyotypic changes in children with ALL have been documented to affect 80% children ³ whereas in adults it is reported around 79% cases with ALL.¹,⁴

The normal diploid 2n number of chromosomes may show either decrease or increase in patients with ALL showing aneuploidy. A significant variation in the childhood ALL and adults show hyperploidy with more than 2n chromosomes.

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ABSTRACT... Objectives: The aim of the present study is to evaluate the frequency of chromosomal abnormalities in childhood acute lymphoblastic leukemia at a tertiary care hospital of Sindh. Study design: Observation study. Place of study: Isra University Hospital, Hyderabad and Oncology Unit Liaquat University of Medical and Health Sciences, Jamshoro. Duration of study: From January 2014 to March 2015. Materials and Methods: Cytogenetic analysis was conducted on peripheral blood and bone marrow samples of 100 diagnosed cases of acute lymphoblastic leukemia (ALL). Peripheral blood and bone marrow samples were collected and putted into sodium heparinized bottles. Cytogenetic analysis was performed by karyotyping according to the ISCN guidelines for human cytogenetic nomenclature using cytovision+ system for image analysis. Data was analyzed on statistic 8.1 USA and expressed as means, percentage and chi-square with P-value of ≤ 0.05 being defined significant. Results: Chromosomal abnormalities were found in 53% of the ALL cases. Numerical abnormalities were found in 71% whereas 35% cases showed structural abnormalities. 29% cases of ALL showed diploidy and aneuploidy was found in 69% of cases and 2% cases were unknown. Highest number of patients 51% showed hyperploidy followed by 12% cases of hypoploidy and 6% showed pseudoploidy. Chromosomal translocations t(9; 22) (q34; q11) and t(8; 22) (q24; q11) were noted in 6% each and t(8; 14) (q22; q32) were seen in 5% of the cases of childhood ALL. Conclusion: The present study reports chromosomal abnormalities in 53% of cases. Numerical abnormalities were found in 71% whereas 35% cases showed structural abnormalities.

Key words: Childhood Acute lymphoblastic leukemia, Chromosomal, Numerical and structural abnormalities

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in about 30% and 5% cases respectively.\textsuperscript{5,6} Trisomies may involve the specific chromosomal involvement.\textsuperscript{7}

In addition decreased chromosomal number less than diploid 2n may be the second common ALL related abnormality in childhood. However the incidence is somewhat lower affecting about 6% cases of ALL.\textsuperscript{8} The most common chromosomal defect is hypoploidy with 45 chromosomes.\textsuperscript{8,9} Comparatively it has poor prognosis when compared with hyperploidy.\textsuperscript{8-10} The gold standard method of choice for the diagnosis of cytogenetic abnormalities is with conventional chromosomal analysis in patients with suspected leukemia.\textsuperscript{1,10}

A search of literature shows a few reported studies from Pakistan in general and Sindh in particular, hence more studies are needed to explore chromosomal abnormalities in acute lymphoblastic leukemia in our population.

**MATERIAL AND METHODS**

A Cross sectional study was conducted at Isra University Hospital, Hyderabad and Liaquat University of Medical and Health Sciences, Jamshoro from January 2014 to March 2015. One hundred diagnosed cases of ALL were selected according to inclusion and exclusion criteria through non-probability purposive sampling. Diagnosed cases of ALL were included, while patients of other types of acute leukemia, lymphoma, and multiple myeloma were excluded from study.

Informed written consent was taken from parents/guardians. The study was approved by ethics committee of institute. Peripheral blood and bone marrow samples were drawn from the diagnosed cases of acute lymphoblastic leukemia and putted into sodium heparinized bottle for cytogenetic analysis. CBC was performed on haematology analyzer sysmex 1000i. Cytogenetic analyses were performed from samples heparinized tube and cultured (RPMI medium) and stimulated with mitogen phytohaemeagglutinin (PHA) & incubated at 37 degree centigrade. Incubate in 0.075 M KCl (Hypotonic solution in water bath).

Fixed examined on slide. Karyotype analysis were performed and classified according to the International System for Human Cytogenetic Nomenclature (ISCN) using cytovision system for image analysis.

The statistical analysis of data was done through SPSS version 21.0 and graphical representation with Microsoft excel. The student’s t test was applied for the continuous variables whereas $\chi^2$ test for the categorical variables. The p-value of $\leq 0.05$ is defined as significant.

**RESULTS**

Mean age of the subjects was $7.5 \pm 3.2$ years. The most frequent age groups were 5-10 years and $<5$ years noted in 59(59%) and 35(35%) respectively. The gender wise distribution of the ALL cases showed 57% and 43% cases of males and females respectively with p-value = 0.09. The ratio of male to female ratio was found to be 1.32:1. Hemoglobin concentration of $< 08g/\text{dl}$ in 9% and 8-10g/dl in 49% more than 10g/\text{dl} in 42% of the cases. In approximately 33% of the ALL patients showed more than 5million/\mu L count of red blood cells whereas maximum number 61% patients with ALL showed red blood cell counts of 2-5million/\mu L followed by 6% cases showing less than 2million/\mu L RBC count with p-value=0.001. The maximum number 59% patients of ALL showed more than 100,000/\mu L white blood cell count followed by 17% and 15% ALL cases showing 10,000-50,000 and 50,000-100,000 white blood cell count. Only 9% of ALL cases showed less than 10,000 white blood cell with p-value=0.0001.

Chromosomal abnormalities were noted in 53% patients while numerical and structural abnormalities were found in 71% and 35% cases respectively. Diploidy and aneuploidy were noted in 29% and 69% of cases while 2% showed unknown. 51 cases of hyperploidy, 6% were found to have hypoploidy 12% had pseudoploidy (Table-I & Figure-I).
Chromosomal translocations found in the present study are summarized in Table-I. Chromosomal translocations t(9; 22) (q343; q11) and t(8; 22) (q24; q11) were noted 6% in each. The second common Chromosomal translocation were t(8;14) (q24;q32) in 5% cases. However unknown translocations were seen in 13% of the cases (Table-II & Fig-2).

**Table-I. Chromosomal Numerical abnormalities**

<table>
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<tr>
<th>Chromosomal abnormality</th>
<th>No. of Pt</th>
<th>%</th>
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<tr>
<td>Hyperploidy</td>
<td>51</td>
<td>51</td>
</tr>
<tr>
<td>Hypoploidy</td>
<td>6</td>
<td>6</td>
</tr>
<tr>
<td>Pseudoploidy</td>
<td>12</td>
<td>12</td>
</tr>
<tr>
<td>Unknown</td>
<td>2</td>
<td>2</td>
</tr>
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</table>

In the present study the gender wise distribution of the ALL cases showed 57% and 43% cases of males and females respectively with p-value = 0.09. The ratio of male to female ratio was found to be 1.32:1. The finding in accordance with previous studies which reported a male to female ratio of 1.8:1 and 1.7:1 in Pakistani children respectively. The findings suggest a male predominance in childhood ALL.

Chromosomal abnormalities were noted in 53%, numerical and structural abnormalities were found in 71% and 35% respectively. Diploidy, aneuploidy and unknown were noted in 29%, 69% and 2% of cases respectively. Numerical abnormalities were found, hyperploidy in 51% cases, hypoploidy in 6% of cases, pseudoploidy in 12% of cases. Frequency of chromosomal abnormalities of present is consistent with previous study which had reported a frequency of 48.8% which is in accordance with the findings of the present study.

Another previous study showed chromosomal abnormalities in 64% of cases. The numerical abnormalities involved 53% of the cases followed by 26% cases revealing structural abnormalities. Moreover both the structural as well as numerical abnormalities were found in about 21% cases. The findings are consistent with present study.

The finding of hyperploidy is consistent with a previous study, but Shaikh et al reported lower frequency of hyperploidy which is not in agreement with present study. One reason of low frequency in Shaikh et al was the obsolete...
technique they used, while present study used more sophisticated conventional Keryotyping. The differences might had occurred because of this reason. Nonetheless the sample size of present is larger as compared to previous study from Karachi.

Another previous study reported cytogenetic abnormalities being present in of the patients with only patients showing normal diploid 2n karyotype. In another study by revealed structural abnormalities in approximately 62% of the cases with 26% cases showing hyperdiploidy. The findings of present study are parallel to above and other previous studies.

In the present study Philadelphia t(9; 22) (q34; q11.2) was noted in 6% of ALL cases which is comparable to 3-5% of pediatric ALL reported previously. However, a previous study has reported Philadelphia chromosome in 7.08% of cases.

The lymphoid B or T cell immunophenotype results are not presented in the current study however, the prognostic importance of ALL with cytogenetic abnormalities can be of valuable importance shown in the present study.

It is thus concluded that hyperploidy with greater than normal diploid 2n chromosomal number having good prognosis is an important finding. Frequency of chromosomal aberrations like Philadelphia chromosome having poor prognosis and hypoploidy are consistent with findings of world literature.

The inclusion and exclusion criteria with prospective design of the present study have strengthened the objective goals. However the sample size in the present study blocks the findings of the present study to be generalized for the whole population.

CONCLUSION
Chromosomal abnormalities were found in 53% of the ALL cases. Numerical abnormalities were found in 71% whereas 35% cases showed structural abnormalities. 29% cases of ALL showed diploidy and aneuploidy was found in 69% of cases and 2% cases were unknown. Highest number of patients 51% showed hyperploidy followed by 12% cases of hypoploidy and 6% showed pseudoploidy. Chromosomal translocations t (9; 22) (q34; q11) and t(8; 22) (q24; q11) were noted 6% in each whereas (8; 14) (q22; q32) in 5% of the cases of childhood ALL. Overall, this study provides further understanding of cytogenetic and molecular abnormalities in ALL cases.

REFERENCES
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**AUTHORSHIP AND CONTRIBUTION DECLARATION**

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