Osman Demirhana*, Nilgün Tanrıverdia and Dilara Süleymanovaa

Department of Medical Biology and Genetics, Faculty of Medicine, Çukurova University, Balcali-Adana/Turkey

Received: 08 August, 2019
Accepted: 13 August, 2019
Published: 14 August, 2019

*Corresponding author: Dr. Osman Demirhan, Professor, Department of Medical Biology and Genetics, Faculty of Medicine, Çukurova University, 01330 Balcali-Adana, Turkey, Tel: 05060229765; E-mail: osdemir@cu.edu.tr, edemirhan42@gmail.com

Keywords: Acute lymphoblastic leukemia; Chromosomal aberrations

Research Article

Frequency and types of chromosomal abnormalities in acute lymphoblastic leukemia patients in Turkey

Abstract

Objectives: Acute lymphoblastic leukemia (ALL) is the most common malignancy in children and is usually associated with numerical and structural chromosomal changes. The correlations of specific cytogenetic findings with presenting clinical features indicate the prognostic significance of chromosomal abnormalities (CAs) in patients with ALL.

Design and methods: The aim of this study was to describe the types and frequencies of CAs in the childhood and adult ALL patients. To date, this was the largest study to date in children with ALL in Turkey, and presented the general cytogenetic characteristics of 260 patients diagnosed as having ALL in a 17-year period. The cytogenetic analyses were performed in the diagnosis of ALL patients.

Results: The karyotype results were normal in 76.9% of 260 patients. However, CAs were detected in 23.1% of all patients. The male-female ratio was 1.5 and median age at diagnosis was 8.58 years in children. The incidence of abnormal karyotype was higher in males than that of females (the male-female ratio=2.62). The 18.1% of these CAs was structural aberrations, and numerical aberrations were 5.0%. The Ph chromosome t(9;22) translocation was present in 0.8% of children. CAs in addition to Ph+ was observed in one case. Specifically, deletions are the most common karyotype (5.8%) among the patients, duplications was present in 6 (2.3%) patients. Inversions were detected in two patients (0.8%). The ratio of fragilities and other CAs was 1.9% and 2.3% of all patients, respectively. Among numerical chromosome abnormalities, 7 patients (2.7%) had aneuploidies and poliploidies. One patient also had microchimeric cells.

Conclusion: This study showed that anomalies detected in ALL patients have shown correlations between specific abnormalities and clinical characteristics of the patients. This information could contribute to an understanding of the role of chromosomal changes in ALL malignancy, and confirms the previously reported association between level of CAs and cancer risk.

Introduction

ALL is a malignant disorder of the bone marrow in which a lymphoid progenitor cell becomes genetically altered. It is the most common malignancy of childhood with an annual incidence rate of 3–4 cases per 100,000 children. The disease is most common in children but can occur at any age. Although, there are few identified factors associated with an increased risk of developing ALL such as genetic, parental and environmental factors, the etiology of the disease remains largely unknown [1,2]. Prognostic impact of CAs in ALL patients is complex. The disease has a bimodal distribution: a sharp peak in incidence among children aged 2–5 years [3]. ALL results from somatic mutation in a single lymphoid progenitor cell at one of several discrete stages of development.

The lymphoblasts have acquired genetic changes included both the number and structure of chromosomes. The translocations, inversions, deletions and duplications affect gene expression in ways that subvert normal programs of cell differentiation, proliferation, and survival, and these factors likely act in concert with each other in multistep pathways leading to leukemic transformation. Specific genetic abnormalities have been useful in diagnosis and defining prognostically important patient subgroups [4]. Several numerical and structural CAs are associated with childhood leukemia. The clonal origin of ALL has been established by cytogenetic analysis. Numerous genetic alterations have been and continue to be discovered in ALL, and it has been repeatedly shown that specific genetic abnormalities are present in the majority of successfully karyotyped patients with ALL [5–7]. Aneuploidy is seen in 30–40% of all cases of
childhood ALL. Numeric chromosomal changes are usually encountered in chromosomes 4, 6, 8, 10, 14, 17, 18, 20 and 21 [8-11]. Recurrent chromosome translocations play a critical role in the pathogenesis of ALL, and many translocations have important prognostic significance. Moreover, the molecular characterization of breakpoints from such rearrangements has led to the identification of oncogenes and to the design of novel therapeutic approaches. The most common structural change is the t(12;21) translocation, which accounts for 25% of cases of ALL [12].

This study was presented the cytogenetic characteristics of pediatric patients diagnosed as having ALL within a 17-year period.

Materials and Methods

The childhood and adult ALL patients referred to our genetics laboratory from 1 May 1992 to 28 April 2009 were recruited. The diagnosis of ALL was made on the basis of a chromosomal analysis. In this study, karyotypes of patients referred with AAL were retrospectively analysed. ALL was initially, diagnosed by the referring clinical hematologist, based on the available clinical details. The cytogenetic analyses were performed in the Cytogenetics Laboratory, at the Department of Medical Biology and Genetics, Faculty of Medicine, Çukurova University. Metaphase chromosome preparations from peripheral blood were made according to the standard cytogenetic protocols. Fifty metaphases were analyzed in all the patients, but in cases of abnormalities and mosaicism the study was extended up to 100 metaphases. All CAs were reported according to the current international standard nomenclature (ISCN, 2009).

Results

Cytogenetics was performed in 260 patients diagnosed with ALL. The male–female ratio was 1.5 and median age at diagnosis was 8.58 years. The incidence of abnormal karyotype was higher in males (n=43, 72,4%) than that of females (n=17, 27,6%). The male–female ratio with abnormal karyotype was 2.62. Out of 260 patients, 60 (23,1%) were found to have abnormal karyotype and rest of 200 (76,9%) were normal. The results of abnormal karyotype were divided into three categories: Philadelphia chromosome–positive (Ph+), CAs in addition to Ph+ and the others CAs were shown in Table 1.

The structural aberrations (translocations, deletions, inversions, duplications and fragilities) and numerical aberrations were 18,1% and 5,0%, respectively. The Ph chromosome t(9;22) translocation was present in approximately 1,2% of children. CAs in addition to Ph+ was observed in one case [46,XY,Ph+(90%),dup(1)(q12;q23)]. Specifically, deletions are the most common karyotype (5,8% and 15 cases) among the patients, followed by 46,XY,del(1p22); 46,XY,del(4p13); 46,XX,del(6q16); 46,XY,del(6q-); 46,XY,del(7q32); 46,XY,del(8q24); 46,XY,del(11q11); 46,XY,del(11q); 46,XY,del(12p13); 46,XX,del(12p13); 46,XY,del(14q22) and 46,XY,del(17p11). The ratio of translocations in all CAs was 3,9% (10 cases),

| Sex/Age | Karyotypes | No. of cases | Frequency in all cases (%) |
|---------|------------|--------------|---------------------------|
| Normal  | 200        | 76.9         |
| Abnormal| 60         | 23.1         |
| General Total | 260       |              |
| Abnormalities |          |              |
| F/54 M/29 Philadelphia chromosome positive (Ph+) | 1       | 1            |
| Chromosomal aberrations in addition to Ph+ |  |              |
| M/2 46,XY, Ph+(90%), dup(1)(q12;q23) | 1       |              |
| Total 3 1.2 |
| Ph-, the others chromosomal aberrations |  |              |
| Structural chromosome abnormalities |  |              |
| Deletions |  |              |
| M/2 46,XY,del(1p22) |  |              |
| M/2 46,XY,del(4p13)x2 |  |              |
| M/7 46,XX,del(6q16) |  |              |
| M/6 46,XY,del(6q-) |  |              |
| M/3 46,XY,del(7q32) |  |              |
| M/5 46,XY,del(7q11)(50%) |  |              |
| M/6 46,XY,del(8q24) |  |              |
| M/2 46,XY,del(11q11)(50%) |  |              |
| M/1 46,XY,del(11q) |  |              |
| M/3 46,XY,del(12p13) |  |              |
| F/13 46,XX,del(1q21) |  |              |
| M/3 46,XY,del(12p13)x1 |  |              |
| M/5 46,XY,del(14q22)x1 |  |              |
| M/6 46,XY,del(17p11), fra(8%) |  |              |
| Total 15 5.8 |
| Translocations |  |              |
| F/8 46,XX,t(1;2)(q12;q37) |  |              |
| M/2 46,XY,t(1;11)(q21;q23) |  |              |
| M/4 46,XY,t(2;6)(q25;p21.3) |  |              |
| M/5 46,XY,t(4;11)(q25;p5) |  |              |
| F/11 46,XX,t(4;11) |  |              |
| M/5 46,XY,t(4;11) |  |              |
| M/4 46,XY,t(4;9),del(11q) |  |              |
| F/7 46,XY,t(8q7) |  |              |
| F/6 46,XX,t(11;14) |  |              |
| F/3 46,XX,t(15;17) |  |              |
| Total 10 3.8 |
| Duplications |  |              |
| M/2 46,XY,dup(1)(q12;q23) |  |              |
| M/4 46,XY,1q+ |  |              |
| M/6 46,XY,1qh+ |  |              |
| M/10 46,XX,14q+ |  |              |
| M/7 46,XY,Aq+CA (16%) |  |              |
| F/2 46,XY,Yqh+ |  |              |
| Total 6 2.3 |
| Inversions |  |              |
| M/1 46,XY,inv(2)(q1) CA (10%) |  |              |
| F/4 46,XX,inv(9)(p11;q12) |  |              |
| Total 10 3.8 |
| Fragilities |  |              |
| M/1 46,XY,inv(2)(q1) CA (10%) |  |              |
| F/4 46,XX,inv(9)(p11;q12) |  |              |
The frequency of genetic abnormalities observed in our study and previous reports was lower than that of previous reports [14-18]. The difference between the findings of our study and previous reports was our some patients show different clinical presentations which, sometimetime, are mixing with clinical features of CML, AML and ALL.

In our study, deletions were found to be the most frequent structural abnormalities (5.8%), and 15 chromosomal deletions. Losses of these regions were identified at 1p22, 4p13, 6q16, 4q-, 7q32, 7q11, 8q24, 11q11, 11q-, 12p13, 12q11, 1q22, 17p11, suggesting the presence of multiple tumor suppressor genes (Table 1). We detected one del(1p22), two t(1;2)(q12;q37), t(1;11)(q21;q23), one dup(1)(q12; q23) and 1q+ in 5 patients. The numerical and structural aberrations of chromosome 1 have been observed in chronic and acute leukemias and solid tumors as well. Previous reports on a CML–BC patient found the involvement of the long arm of chromosome 1 [19]. It was marked that consistent breaks and deletions involving specific ongenes/tumor suppressor genes were present in 1p36 and other regions of chromosome 1, such as 1p22–q21 [20,21]. It is remarkable to have found the ABL2 gene in 1q25, which is a proto-oncogene whose protein is a non–receptor tyrosine kinase, and the TPR gene in the same region; its extreme 5’-end fuses with several different kinase genes in some neoplasias and could be involved in leukemogenesis mechanisms [22]. Gene deletions and translocations are responsible for initiating of cancer progression. The loss or inactivation of one or more tumor suppressor genes are associated with many types of cancer, as chromosomal regions associated with tumor suppressors are commonly deleted or mutated.

Aberrations involving chromosome 6q are common in childhood ALL occurring in 7–18% of patients [23,24]. Frequently, the breakpoints are 6q15, 6q21–23 regions and interstitial deletion are also common in both B lineage and T lineage. Overall the breakpoints occur predominantly in 6q21 [25]. The deleted region is mostly large, involving a number of genes and genes affected by the deletion are presumably essential for normal cellular homeostasis. FOXO3A, a transcription factor involved in the control of proliferation and apoptosis, is one of the candidate genes located in the deleted 6q21 region. In the present study, 3 patients also had del(6q) and t(2;6)(p25;p21.3), and this break point was in the region of 6p21.3. Sinclair et al. [26] also suggested that the incidence of balanced rearrangements involving 6q in ALL may be much higher than previously thought. These findings show that the (6q) abnormality is a good prognostic indicator. In present study, we also found del(7q) in two patients, and there was a correlation between an isolated deletions of the long arm of chromosome 7 (q31, q32 and q-) and patients with ALL. The partial deletions of 7q might represent a secondary event in the context of preexisting genomic instability. Complete loss of chromosome 7 or partial deletion involving its long arm are highly recurrent CAs in myeloid disorders [27,28]. Also, we found deletion at bands 8q24 in a patient. These results were consistent with the hypothesis that the 8q24 region affected tumorigenicity [29,30]. About 50% of hematopoietic neoplasms...

| Chromosome Abnormalities | Total | M/3 | F/15 | F/6 | M/6 | M/1 |
|--------------------------|-------|-----|------|-----|-----|-----|
| 45,XY, fra(32%), CA (22%) | 5     | 1.9 |
| 46,XX, fra(25%)          |       |     |
| 46,XX, fra(20%)          |       |     |
| 46,XY, del(17p11-ter), fra(8%) |       |     |
| 46,XY, fra(3p21)         |       |     |
| Total                    | 6     | 2.3 |
| General total            | 47    | 18.1|

Numerical chromosome abnormalities

| Chromosome Abnormalities | Total | M/3 | F/15 | F/6 | M/6 | M/1 |
|--------------------------|-------|-----|------|-----|-----|-----|
| 47,XX, +21               | 7     | 2.7 |
| 47,XY, +21               |       |     |
| 47,XX, +21               |       |     |
| 47,XX, +21, (15;17)(p12;q23) |       |     |
| 47,XYX                   |       |     |
| 46,XY, 45, X (23%)       |       |     |
| Total                    | 6     | 2.3 |
| General total            | 13    | 5.0 |

Aneuploidies and poliploidies

| Chromosome Abnormalities | Total | M/3 | F/15 | F/6 | M/6 | M/1 |
|--------------------------|-------|-----|------|-----|-----|-----|
| 46,XX, aneaploidy        | 7     | 2.7 |
| 46,XX, poliploidy        |       |     |
| 46,XX, aneaploidy        |       |     |
| 46,XX, aneaploidy        |       |     |
| 46,XX, aneaploidy        |       |     |
| 46,XX, aneaploidy        |       |     |
| Total                    | 7     | 2.7 |
| General total            | 13    | 5.0 |
somatically acquire translocations, which activate proto-oncogenes in most cases. The major translocations in ALL affect proteins that have critical functions in cell proliferation, differentiation, or survival [31]. The translocations in all metaphases were found in 10 patients with ALL (3.8%). These translocations were found in specific regions of chromosomes 1q12, 1q21, 2q37, 2p25, 4q25, t(4;11)x[2], t(4;9), 6p21.3, t(8q;?), 11p13, 11q23, 11q, t(11;14) and t(15;17) (Table 1). First, rearrangements affecting the same chromosomal region may involve different genes and represent clinically and biologically diverse entities. For example, the t(11q23) translocation is a poor prognostic factor, accounting for 2-4% of childhood ALL, and it is expressed in 80% of all infants with ALL [32]. In the present study, chromosomes 11 translocation was found to be most frequently involved in structural abnormalities (in six cases). In particular, translocations between 11 and 4 chromosomes in three patients are noteworthy. Similarly, in other Turkish study, the t(11q23) translocation was found in one patient of thirty four patients with childhood ALL [14]. The chromosomal translocation t(4;11)(q21;q23) is associated with high-risk ALL of infants. These findings show that 11 chromosomes are very important in the prognosis of ALL. Because, chromosomal translocations that activate specific genes are a defining characteristic of human leukemias and of acute lymphoblastic leukemia in particular. Translocation t(4;11)(q21;q23)/KMT2A-AFF1 was the most frequent rearrangement found. In a recent study, five most common fusion genes i.e. BCR-ABL (t 9;22), TCF3-PBX1 (t 1;19), ET6V-RUNX1 (t 12;21), MLL-AF4 (t 4;11) and SIL-TAL1 (del 1p32) were found in 79% of the patients, and MLL-AF4 (t 4;11) positivity characterized a subset of adult ALL patients with aggressive clinical behaviour and a poor outcome [33]. This study also supports our findings. 12p13 and 12q11 deletions were detected in two patients. The prognostic importance of simultaneously occurring 12p13 deletions is currently unknown. Thus, we suggested that more information should be obtained from patients with different variants of deletions. The role of the 12p–q deletions in prognosis, incidence of relapse and follow-up should also be evaluated. In addition, we observed rare structural chromosomal rearrangements on 17 chromosome (del(17p11), (15;17)). The p53 mutation occurs rarely in ALL. Kim et al., [34], have also shown a case with acute promyelocytic leukemia of t(15;17)(q22;q21) rearrangement asociated with other abnormalities. Our results, in addition to other previously reported findings, suggested that losses and structural rearrangements of chromosome 17 could play a role in the pathogenesis of ALL. These deletions might have an overall unfavorable prognosis in our patients.

In the present study, the Ph chromosome t(9;22) translocation was present in approximately 1,2% of children. CAs in addition to Ph+ was observed in one case [Ph+(90%), dup(1)(q12;q32)]. Ph chromosome was the most frequent recurrent abnormality (29%). Its incidence increased with age, as already reported [35], but peaked in the 40- to 50-year-old age range. Thus, two of our three Ph-positive patients were older (29 and 54 years). Gene duplications and increases in gene copy numbers can also contribute to cancer. We describe six patients (2,3%) of a rare type of duplications, such as dup(1)(q21;q23), 1q+, 1qh+, 14q+, 4q+ and Yqh+ (Table 1).

These chromosomal gains may be relevant to the pathogenesis of ALL transformation in some cases. Balanced rearrangements are infrequent and can occur as a single additional abnormality or as a part of complex cytogenetic changes. In our study, The inversions were evaluated in 2 patients (0,8%) such as inv(9) (p11;q12) and inv(2) (Table 1). Some genes on chromosomes 2 that are known to play a role for tumor development. Therefore, 2p-q could play a role in the pathogenesis of ALL. However, there have been very few reports on the inv(9) variation as an acquired CAs in hematologic malignancies [36]. It has reported pericentric inversion in chromosome 9 at a frequency of 0.8–2% in normal population and at a similar frequency in ALL patients. This inversion is usually considered as a polymorphism, and its clinical consequences remain unclear [37].

Autosomal recessive genetic diseases associated with increased chromosomal fragilitie (FSs) and a predisposition to ALL include ataxia–telangiectasia, Nijmegen breakage syndrome, and Bloom syndrome [38]. FSs are known to be associated with genes that relate to tumorigenesis. They have been found the FSs in 8–32% of our patients–cells (1,9%) (Table 1), and ALL children have the others CAs in 10–20% of cells (2,3%). These CAs may affect the susceptibility to tumors. These aberrations are also the most common ones in ALL cases with variant translocations and additional abnormalities. The most interesting finding in this study was the involvement of microchimeric cells [46,XY/46,XX(20%)] was seen in one patient (Table 1). Microchimerism is the existence of small amounts of DNA in the body coming from a genetically different person. It recently found male microchimerism presence to be associated with a 70% reduced odds of developing breast cancer, and a 4-fold increased odds of developing colon cancer [39]. In one other study, FMc were identified in 50% of papillary thyroid tumors [40]. Unfortunately, we were not able to determine the nature of these cells. This suggests to us that the can microchimerism take place in the etiology of cancer?

Numerous genetic alterations have been and continue to be discovered in ALL, and it has been repeatedly shown that specific genetic abnormalities are present in the majority of successfully karyotyped patients with ALL [3,41]. In the present study, 5% of the patients revealed numerical CAs (Table 1). The rate of chromosomal gains and losses can lead to aneuploidy was termed chromosomal instability. Aneuploidy is also features of cancers that are usually associated with poor prognosis. Aneuploidy is a remarkably common feature of human cancer, present in ~90% of solid human tumours and >50% of haematopoietic cancers [42]. The common aneuploidy observed in our patients (2,3%), occurring in 10–15% of metaphases (Table 1). Several studies have shown that aneusomies of different chromosomes were associated with aggressive tumor behavior [11,12]. For example, gain of chromosome 8 is found in ~10–20% of cases of acute myeloid leukemia [43,44]. Autosomal monosomies are observed to be the most frequent in our patients, and the most frequently observed numerical changes involve the chromosomes -8, -7, -17, -21, +21, -22 and -Y. Trisomy of chromosome 8 is frequently reported in myeloid lineage disorders and also detected in lymphoid neoplasms as well as solid tumors. 

Citation: Demirhana O, Tannverdia N, Süleymanova D (2019) Frequency and types of chromosomal abnormalities in acute lymphoblastic leukemia patients in Turkey. Arch Community Med Public Health 5(2): 055-061. DOI: http://dx.doi.org/10.17352/2455-5479.000055
suggesting its role in neoplastic progression in general. These chromosomal aneuploidies may affect the susceptibility to tumors.

One of the main results in our patients, the 1.7% of them revealed the trisomy 21 chromosome (Down syndrome=DS), and one patient has one translocation of 15p12 and 17q23 in addition to the presence of trisomy 21 chromosome. Just as, children with DS have a 10– to 30-fold increased risk of leukemia. DS cases are more likely to have B-cell precursor ALL, and their leukemic cells lack adverse genetic abnormalities [45]. Leukemia cells with either i(21q10) or trisomy 21 have the potential for basophil formation [46]. It has reported a transient leukemic condition in a phenotypically normal newborn bearing i(21q10) clones, suggesting that the q arm of chromosome 21 contains sufficient genetic information for the development of transient leukemia [47]. Consistent with the literature, in our study hyperdiploidy was detected in 26% of ALL patients, with the most common copy gains seen in chromosomes 4, 6, 10, 21 and X. Previous studies have suggested that gaining a copy of chromosomes 4, 10 or 17 is associated with favorable prognosis; however, trisomy of chromosome 5 confers poorer outcome among hyperdiploid patients [48,49]. In the present study, we observed the complete or partial loss of chromosome 7 in several metaphases (Table 1). Monosomy 7 was also observed in several clones analyzed. An association between the complete or partial loss of chromosome 7 and ALL has been recognized from the early days of tumor cytogenetic analysis. Detection of such abnormalities usually heralds a poor prognosis [50]. Amare [51], reported monosomy of chromosomes 7 and 17 as secondary CAs that occur when disease progresses from CML to a more aggressive blastic phase or transforms into lymphoid leukemia like acute myeloid, lymphoid leukemia, or lymphoid blast crisis of CML. Sabine [52], have shown that monosomy 7/del(7q) causes loss an important tumor suppressor, and upregulation of oncogene in AML.

We detected two patients with 47,XXX (Klinefelter’s syndrome) and 46,XY/45,X−Y (23%) (Table 1). Sex chromosome aneuploidies may be affect susceptibility to the tumors. The 47,XXX karyotype in hematological disorders has not been clearly established yet. Gain of an X chromosome is relatively common in leukemias, lymphomas and prostate cancer, and generally occurs in association with other karyotypic changes [53,54]. Risk of acquiring breast carcinoma in 47,XXX is relatively increased, with relative risk exceeding 200 times. It is generally not known whether this gain involves the active or the inactive X chromosome. Although, there are numerous X-linked genes that may be involved in neoplasia, including the MAGE tumor-specific antigen loci [55], the pseudautosomal GM–CSFR gene that likely escapes X chromosome inactivation [56], and the ARAF1 [57], ELK1 [58], and MCF2 [59], oncogenes. With regard to Y chromosome, deletions have been shown to be involved in prostate cancer [60,61], male breast carcinomas [62,63], and pancreatic adenocarcinomas [64]. Loss of Y chromosomes is a common secondary change in cancer cells and in a few leukemias [65]. Possible significance of loss of Y chromosome in neoplasia have been postulated as; Y chromosome harbors a tumor suppressor gene, which when lost or modified, gene(s) presumably located on the X chromosome may be affected leading to abnormal proliferation. Polyploidy and endoreduplication of chromosomes occur more often in patients with disseminated cancer and vary with the extent of disease.

Conclusion

The patients showed a high frequency of loss and gains of chromosome increased incidence of deletions, translocations, duplications, inversions, chromatin breaks and aneuploidies, along with other chromosomal alterations, could contribute to the progression of the disease. This study could detect a wide variety of common, rare and novel chromosomal abnormalities in patients with hematological disorders, providing valuable diagnostic and prognostic information. In addition, aneuploidies of X can play a role in the pathogenesis of ALL. Further understanding of the CAs may help in anticipating its implications in hematological cancers.

Ethics

Ethics Committee Approval: The study was a retrospective, the results analyzed in our laboratory were used.

Authorship Contributions

Concept: Osman Demirhana, Nilgün Tanrverdica, Dilara Süleymanovaa; cytogenetic analysis. Osman Demirhana; date collection and writing of the article.

References

1. Pui CH, Relling MV, Downing JR (2004) Acute lymphoblastic leukemia. N Engl J Med 350: 1535-1548. Link: http://bit.ly/33w4hbK
2. Carroll WL, Bhoyjani D, Min DJ, Raetz E, Relling M, et al. (2003) Pediatric acute lymphoblastic leukemia. Hematology Am Soc Hematol Educ Program 1: 102-131. Link: http://bit.ly/31vjk2K
3. Erik F, Kjeld S (2006) The incidence peaks of the childhood acute leukemias reflect specific cytogenetic aberrations. J Pediatr Hematol Oncol 28: 486-495. Link: http://bit.ly/2N6QPv
4. Chai YH, Lü H, Li JQ, Lu J, Xiao PF, et al. (2007) Classical and molecular cytogenetic abnormalities in 124 pediatric patients with acute lymphoblastic leukemia. Zhonghua Er Ke Za Zhi 9: 684-686. Link: http://bit.ly/2YyAhE
5. Matasar MJ, Ritchie EK, Consedine N, Magai C, Neugut AI (2006) Consedine N. Incidence rates of the major leukemia subtypes among US Hispanics, Blacks, and non-Hispanic Whites. Leuk Lymphoma 47: 2365-2370. Link: http://bit.ly/2MgLczH
6. Michel G, von der Weid NX, Zawahen M, Redmond S, et al. (2008) Swiss Paediatric Oncology Group (SPOG). Incidence of childhood cancer in Switzerland: the Swiss childhood cancer registry. Pediatr Blood Cancer 50: 46-51. Link: http://bit.ly/2XvXGz
7. Bhatia S, Sather HN, Heerema NA, Trigg ME, Gaynon PS, et al. (2002) Racial and ethnic differences in survival of children with acute lymphoblastic leukemia. Blood 100: 1957-1964. Link: http://bit.ly/2H5AaF
8. Raimondi SC (1993) Current status of cytogenetic research in childhood acute lymphoblastic leukemia. Blood 81: 2237-2251. Link: http://bit.ly/2HJuVib
9. Moorman AV, Clark R, Farrell M, Hawkins JM, Martinneau M, et al. (1996) Probes for hidden hyperdiploidy in acute lymphoblastic leukemia. Genes Chromosomes Cancer 16: 40-45. Link: http://bit.ly/2yYDS16
10. Pui C-H, Crist WM, Look AT (1990) Biology and clinical significance of cytogenetic abnormalities in childhood acute lymphoblastic leukemia. Blood 76: 1449-1463. Link: http://bit.ly/2TwEPqX

11. Mertens F, Johansson B, Mitelman F (1996) Dichotomy of hyperdiploid acute lymphoblastic leukemia on the basis of the distribution of gained chromosomes. Cancer Genet Cytogenet 92: 8-10. Link: http://bit.ly/2N2YYDf

12. Harrison CJ (2001) The detection and significance of chromosomal abnormalities in childhood acute lymphoblastic leukaemia. Blood Rev 15: 49-59. Link: http://bit.ly/2Z1gYED

13. Harrison CJ (2000) The genetics of childhood acute lymphoblastic leukaemia. Baillieres Best Pract Res Clin Haematol 13: 427-439. Link: http://bit.ly/31EoInC

14. Karkucak M, Gorukmez O, Yakut T, Baytan B, Gorukmez Ö, et al. (2012) Molecular cytogenetic findings in cases with childhood acute lymphoblastic leukemia. International Journal of Hematology and Oncology 2: 67-72. Link: http://bit.ly/31Bmpo3

15. Andreasson P, Hoplund M, Bekassy AN, Garwicz S, Heldrup J, et al. (2000) Cytogenetic and FISH studies of a single center consecutive series of 152 childhood acute lymphoblastic leukemias. Haematologica 85: 15-21. Link: http://bit.ly/2H4XlLHJ

16. Silverman LB, Gelber RD, Dalton VK, Asselin BL, Barr RD, et al. (2001) Improved outcome for children with acute lymphoblastic leukemia: results of Dana-Farber Consortium Protocol 91-01. Blood 97: 1211-1218. Link: http://bit.ly/31B9eab

17. Moghrabi A, Levy DE, Asselin B, Barr R, Clavell L, et al. (2007) Results of the Dana-Farber Cancer Institute ALL Consortium Protocol 95-01 for children with acute lymphoblastic leukemia. Blood 109: 896-904. Link: http://bit.ly/2Zbo313

18. Schneider NR, Carroll AJ, Shuster JJ, Pullen DJ, Link MP, et al. (2000) New recurring cytogenetic abnormalities and association of blast cell karyotypes with prognosis in childhood T-cell acute lymphoblastic leukemia: a Pediatric Oncology Group report of 343 cases. Blood 96: 2543-2549. Link: http://bit.ly/2Z78yb7

19. Heim S, Mitelman F (1995) Cancer cytogenetics: Chromosomal and Molecular Aberrations of Tumor Cells, 2nd Ed. S Heim, F Mitelman, eds. Wiley-Liss, New York 33-68. Link: http://bit.ly/2KvoUpj

20. Smedley D, Sidhar S, Birdsal S, Bennett D, Herlyn M, et al. (2000) Molecular pathology of melanoma. Cancer Genet Cytogenet 116: 34-40. Link: http://bit.ly/2YNbpuu

21. Hibi K, Takahashi T, Yamakawa K, Ueda R, Sekido Y, et al. (1992) Three distinct regions involved in 3p deletion in human lung cancer. Oncogene 7: 445-449. Link: http://bit.ly/2MdJxsB

22. Huret JL, Ahmad M, Arasaban M, Bernheim A, Cigna J, et al. (2013) Atlas of genetics and cytogenetics in oncology and haematology in 2013. Nucleic Acids Res 41: D920-D924. Link: http://bit.ly/2N2qeIN

23. Tszuki S, Karnan S, Horibe K, Matsumoto K, Kato K, et al. (2007) Genetic abnormalities in (12;21) TEL-AML1 acute lymphoblastic leukemia: analysis by means of array-based comparative genomic hybridization. Cancer Sci 98: 698-706. Link: http://bit.ly/220LLPT

24. Hayashi Y, Raimondi SC, Look AT, Behm FG, Kitchingman GR, et al. (1990) Abnormalities of the long arm of chromosome 5 in childhood acute lymphoblastic leukemia. Blood 76: 1626-1630. Link: http://bit.ly/2KsWVp0

25. Borowitz MJ, Chan JKC (2008) WHO classification of tumors of Haematopoietic and Lymphoid Tissues. Int Agency Res Cancer 9: 173-174.

26. Sinclair PB, Harrison CJ, JL Forni, Jarosová M (2005) Analysis of balanced rearrangements of chromosome 6 in acute leukemia: clustered breakpoints in q22-q23 and possible involvement of c-MYB in a new recurrent translocation, t(6;7)(q23;q22). Blood 106: 602-611. Link: http://bit.ly/2Mhltbgm

27. Slovak ML, Kopecky KJ, Cassileth PA, Harrington DH, Theil KS, et al. (2000) Karyotypic analysis predicts outcome of preremission and postremission therapy in adult acute myeloid leukemia: a Southwest Oncology Group/ Eastern Cooperative Oncology Group Study. Blood 96: 4075-4083. Link: http://bit.ly/31Dh6je

28. Jerez A, Sugimoto Y, Makishima H, Verma A, Jankowska AM, et al. (2012) Loss of heterozygosity in 7q myeloid disorders: clinical associations and genomic pathogenesis. Blood 119: 6109-6117. Link: http://bit.ly/2KJlgJc

29. Aplin PD (2006) Causes of oncogenic chromosomal translocation. Trends Genet 22: 46-55. Link: http://bit.ly/33xBRiy

30. Mitelman F, Johansson B, Mertens F (2007) The impact of translocations and gene fusions on cancer causation. Nat Rev Cancer 7: 233-245. Link: http://bit.ly/2KXXcic

31. Look AT (1997) Oncogenic transcription factors in the human acute leukemias. Science 278: 1059-1064. Link: http://bit.ly/2YVABMr

32. Silverman LB (2007) Acute lymphoblastic leukemia in infancy. Pediatr Blood Cancer 49: 1070-1073. Link: http://bit.ly/2MfKvQn

33. Sabir N, Iqbal Z, Awan A, Taeem T, Naeem T, et al. (2012) Prognostically Significant Fusion Oncogenes in Pakistani Patients with Adult Acute Lymphoblastic Leukemia and their Association with Disease Biology and Outcome. Asian Pacif J Cancer Prev 13: 3349-3355. Link: http://bit.ly/2N5sXe3

34. Kim M, Lee SA, Park HI, Oh EJ, Park CW, et al. (2010) Two distinct clonal populations in acute promyelocytic leukemia, one involving chromosome 17 and the other involving an isochromosome 17. Cancer Genet Cytogenet 197: 185-188. Link: http://bit.ly/2YRu88g

35. Secker-Walker LM, Craig JM, Hawkins JM, Hoffbrand AV (1991) Philadelphia positive acute lymphoblastic leukemia in adults: Age distribution, BCR breakpoint and prognostic significance. Leukemia 5: 196-199. Link: http://bit.ly/2T1W3Ex

36. Han TS, Ma SK, Chan LC (2000) Acquired pericentric inversion of chromosome 9 in essential thrombocythemia. Hum Genet 106: 669-670. Link: http://bit.ly/2N296Df

37. Keung YK, Knovich MA, Powell BL, Buss DH, Pettenucci M (2003) Constitutional pericentric inversion of chromosome 9 and acute leukemia. Cancer Genet Cytogenet 145: 82-85. Link: http://bit.ly/2YNbpuu

38. Vanasse GJ, Concannon P, Willerford DM (1999) Regulated genomic instability and neoplasia in the lymphoid lineage. Blood 94: 3997-4010. Link: http://bit.ly/2KzZxm

39. Kamper-Jørgensen M, Biggar RJ, Tjønneland A, Hjalgrim H, Kroman N, et al. (2012) Opposite effects of microchimerism on breast and colon cancer. Eur J Cancer 48: 2227-2235. Link: http://bit.ly/2OSxWUJ

40. Srivatsa B, Srivatsa S, Johnson KL, Bianchi DW (2003) Maternal cell microchimerism in newborn tissues. J Pediatr 142: 31-35. Link: http://bit.ly/2YBmxXt

41. Michel G, von der Weid NX, Zwahlen M, Redmond S, Strippoli MP, et al. (2008) Swiss Paediatric Oncology Group (SPOG): Incidence of childhood cancer in Switzerland: the Swiss childhood cancer registry. Pediatr Blood Cancer 50: 46-51. Link: http://bit.ly/2KxWwMQ

42. Secker-Walker LM, Prentice HG, Durrant J, Richards S, Hall E, et al. (1997) Cytogenetics adds independent prognostic information in adults with acute lymphoblastic leukaemia on MRC trial UKALL XA. MRC Adult Leukaemia Working Party. Br J Haematol 96: 601-610. Link: http://bit.ly/2KJRKPd

43. Mitelman F, Johansson B, Mertens F (2012) Mitelman Database of Chromosome Aberrations and Gene Fusions in Cancer.
58. Heerema NA, Sather HN, Sensel MG, et al. (2000) Prognostic impact of trisomies of chromosomes 10, 17, and 5 and among children with acute lymphoblastic leukemia and Highhyperdiploidy (>50 chromosomes). J Clin Oncol 18: 1876-1887. Link: http://bit.ly/2YNvURE

59. Johnson E, Cotter FE (1997) Monosomy 7 and 7q- associated with myeloid malignancy. Blood Rev 11: 46-55. Link: http://bit.ly/2MY12QN

60. Jordan JJ, Hanlon AL, Al-SaleemTI, Greenberg RE, Tricoli JV (2001) Loss of the short arm of the Y chromosome in human prostate carcinoma. Cancer Genet Cytoget 124: 122-126. Link: http://bit.ly/2ZKk3tT

61. Vijayakumar S, Garcia D, Hensel CH, Banerjee M, Bracht T, et al. (2005) The human Y chromosome suppresses the tumorigenicity of PC-3, a human prostate cancer cell line, in a thymic nude mice. Genes Chromosomes Cancer 44: 365-372. Link: http://bit.ly/33wugsz

62. Teixeira MR, P andis N, Dietrich CU, Reed W, Andersen J, et al. (1998) Chromosome banding analysis of gynecomas and breast carcinomas in men. Genes Chromosomes Cancer 23: 16-20. Link: http://bit.ly/2yZniVZs

63. Rudas M, Schmidinger M, Wenzel C, Okamoto I, Budinsky A, et al. (2000) Karyotypic findings in two cases of male breast cancer. Cancer Genet Cytoget 121:190-193. Link: http://bit.ly/2MgYyD0

64. Wallrapp C, Hahnel S, Boeck W, Soder A, Mincheva A, et al. (2001) Loss of the Y chromosome in a frequent chromosomal imbalance in pancreatic cancer and allows differentiation to chronic pancreatitis. Int J Cancer 91:340-344. Link: http://bit.ly/2yXPGtT

65. Mohanty D (2004) Sex chromosome loss and malignancy: Does a relationship established? Indian Journal of Human Genetics 10. Link: http://bit.ly/2yYODjK

Highlights

- Signatory publisher of ORCID
- Signatory Publisher of DORA (San Francisco Declaration on Research Assessment)
- Articles archived in worlds' renowned service providers such as Portico, CNKI, AGRIS, TNDnet, Base (Bielefeld University Library), CrossRef, Scilit, J-Gate etc.
- Journals indexed in ICMJE, SHERPA/ROMEO, Google Scholar etc.
- OAI-PMH (Open Archives Initiative Protocol for Metadata Harvesting)
- Dedicated Editorial Board for every journal
- Accurate and rapid peer-review process
- Increased citations of published articles through promotions
- Reduced timeline for article publication

Submit your articles and experience a new surge in publication services

Discover a bigger Impact and Visibility of your article publication with Peertechz Publications

Submit your articles and experience a new surge in publication services

Peertechz journals wishes everlasting success in your every endeavours.

Copyright: © 2019 Demirhana O, et al. This is an open-access article distributed under the terms of the Creative Commons Attribution License, which permits unrestricted use, distribution, and reproduction in any medium, provided the original author and source are credited.

Citation: Demirhana O, Tanriverdia N, Süleymanova D (2019) Frequency and types of chromosomal abnormalities in acute lymphoblastic leukemia patients in Turkey. Arch Community Med Public Health 5(2): 055-061. DOI: http://dx.doi.org/10.17352/2455-5479.000055