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Recurrent genetic abnormalities detected by FISH in adult B ALL and association with hematological parameters

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Abstract

Background: Recurrent genetic abnormalities influence prognosis in B lymphoblastic leukemia. *BCR-ABL* rearrangement is associated with higher leukocyte counts and older age at presentation. Among adults, *BCR -ABL* - is the commonest recurrent abnormality whereas, *IgH* rearrangements are rare.

Aim: Aim of this study was to identify common recurrent genetic abnormalities in adult B ALL and study their association with hematological findings.

Methods: Bone marrow and peripheral blood from patients with B acute lymphoblastic leukemia were analyzed for complete blood counts, bone marrow morphology and cytogenetic abnormalities. The study group was divided into smaller groups based on cytogenetic abnormalities. Hematological parameters and presence of recurrent genetic abnormalities was compared across age groups and gender by non parametric tests.

Results: *BCR-ABL* positive group had a higher leukocyte count than *BCR-ABL* negative group. Among groups 1 to 5, group 1 with gains of chromosomes was associated with leucopenia and higher age at presentation. *BCR-ABL* is commonest recurrent abnormality followed by *IgH* rearrangements.

Conclusion: Patients with gains of chromosomes alone have low total leukocyte counts at presentation.

KEYWORDS

B acute lymphoblastic leukemia, *BCR-ABL*, *IgH* rearrangement, *MLL*, *MYC*, *TCF3/PBX*

1 | INTRODUCTION

In adults, acute lymphoblastic leukemia (ALL) is B-cell type in 75% to 85% of patients.[1,2] Increasing age is associated with shorter duration of remissions.[3] Adults and adolescents have worse outcomes than younger children.[4] Among recurrent genetic abnormalities, Philadelphia chromosome increases from childhood to adults and its prevalence is approximately 5% to 7%.[5-8] Some authors have reported a higher prevalence of *BCR-ABL* -approximately 33% in adult ALL and 5% in paediatric ALL.[9,10] Among other recurrent genetic abnormalities, *TCF3/PBX* translocations have been reported in nearly 6% of patients with B ALL, among which 25% of patients have a pre-B immunophenotype.[9,11] *BCR-ABL* positivity is associated with older age and higher white cell counts.[12] Male preponderance in ALL as well as younger age at presentation has been reported by investigators.[13] *MLL* gene rearrangements have been reported in 20% of ALL, of which 10% are seen in older children and adults.[14] Identifying recurrent genetic abnormalities helps to classify ALL and predict prognosis.[15] Traditionally, total leukocyte

counts have been associated with prognosis in acute B ALL.[18,19] However, studies associating complete blood counts with genetic abnormalities have been limited to total leukocyte counts.

The aim of this study was to identify common recurrent genetic abnormalities in adult B ALL by fluorescence in situ hybridization (FISH) and study their association with hematological findings.

2 | MATERIALS AND METHODS

Adults diagnosed with de novo acute B ALL were included in the study. The study included all adults with B ALL whose samples were submitted between 2014 and 2019. Patients with history of relapsed acute lymphoblastic leukemia were excluded. Peripheral blood samples were processed in automated analyzer (ADVIA 2120, Siemens), and blood smears stained with Leishman stain were examined for blast count and blast morphology. Bone marrow aspirate samples were subjected to morphological examination, immunophenotyping and fluorescence in situ hybridization. A differential count of 200 leukocytes on peripheral smear and at least 500 nucleated cells on the marrow was recorded separately by two observers. Fluorescence in situ hybridization (Cytovision system capture station software 7.4v Leica fluorescent microscope): Cell pellets of bone marrow /peripheral blood were prepared by adding 5 mL of RPMI solution, centrifugation at 1000 rpm for 5 minute and resuspension in 10 mL of KCl for 10 minutes. Pellet was recentrifuged with Carnoys fixative and washed thrice in fixative. A drop of the pellet was placed on a clean slide, air dried and immersed in 1XPBS and 4% buffered formalin for five minutes each. The slides were then placed in dehydrating solutions of 70%, 85%, and 100% ethanol for two minutes each and air dried. The following probes were applied - Vysis BCR-ABL/ASS1 Tricolour DF, Vysis TCF3/PBX1 Dual colour DF, Vysis MYC Dual colour Break-apart rearrangement, Vysis MLL Dual colour Break-apart rearrangement and Vysis IGH Dual colour Break-apart rearrangement probe. Slides were placed in the hybridiser and programmed as follows—denaturation at 72 ° C for 5 minutes and hybridization at 37 ° C for 16 hours. Slides were then washed with post hybridization solution –0.4 XSSC, dried and cover slipped. Signal pattern was interpreted after observing 400 nucleii. The normal and abnormal signal patterns were interpreted as shown in Figures 5-9. Statistical:

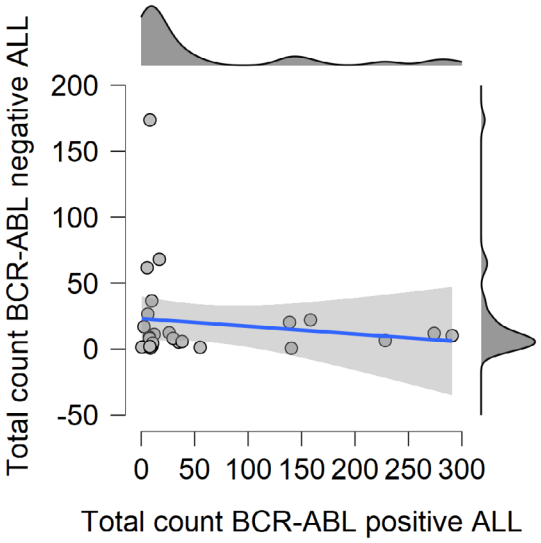

FIGURE 2 Bivariate relationship between *BCR-ABL* positive and *BCR-ABL* negative patients. Median leukocyte counts in *BCR-ABL* positive group (10.7×10^9/L) were higher than *BCR-ABL* negative group (7.8×10^9/L) (p = 0.02). Note that at lower counts there is no relationship between the two whereas, at higher counts there is a mild, negative, linear relationship

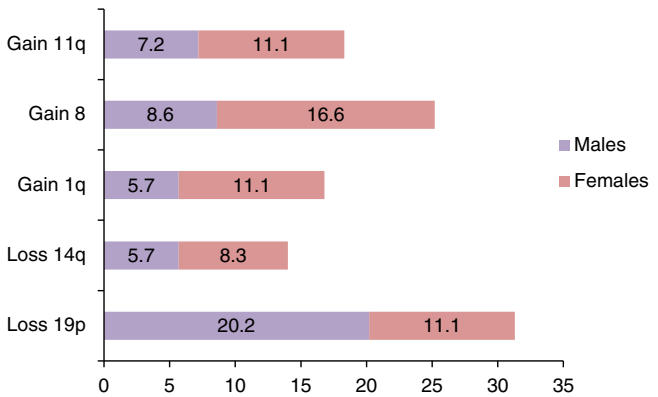

FIGURE 1 Common gains and losses of various chromosome arms in B-ALL (n=105) in males (n=69) and females (n=36). In addition, (not shown in the figure) males had loss of 11q (4.3 %), loss of 9q (2.8%), gain 14q (4.3%), gain 22q (2.8%) and gain 9q (2.8%). Females had (not shown in figure) loss of 22q (2.7%), loss of 8 (2.7%), gain 22q (2.7%) and gain 14q (11.1%). All frequencies in the figure above are in percentages

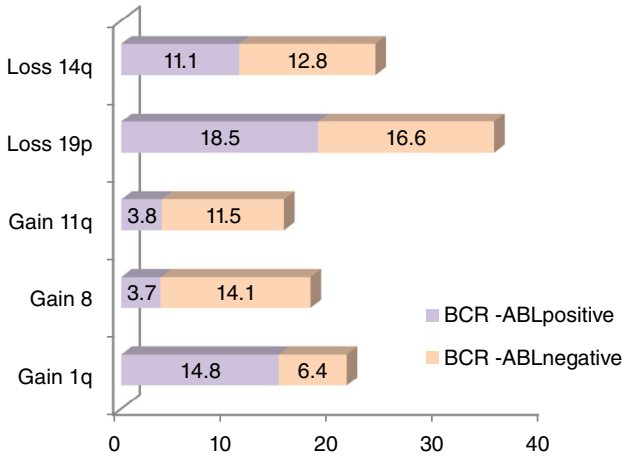

FIGURE 3 Additional cytogenetic abnormalities: Gains and losses of chromosomes in *BCR-ABL* positive and negative groups. *BCR-ABL* positive patients in addition (not shown in figure) had IgH rearrangements (11.1%), loss of chromosome 11q (3.7%) and loss of 14q (11.1%). *BCR-ABL* negative patients in addition (not shown in figure) had IgH rearrangements (8.9%), gain 14q (8.9%) and loss 11q (3./8%). X-axis shows percentage of positive patients

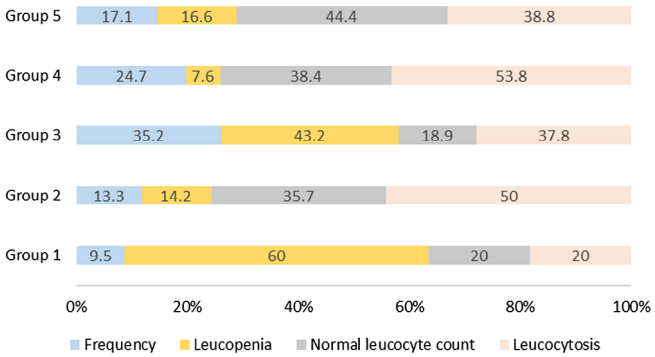

FIGURE 4 Classification of the study group based on cytogenetic abnormalities. Group 1 had gains of partial or entire chromosome arm only. Group 2 had loss of partial arm or entire chromosome arm. Group 3 had no cytogenetic abnormalities. Group 4 had recurrent genetic abnormalities and Group 5 had recurrent genetic abnormalities with gains and/or loss of chromosomes. Leukocytosis was seen in 2,7,14,14 and 7 patients in group 1,2,3,4 and 5 respectively. Leukopenia was seen in 6,2,16,2 and 3 patients in group 1,2,3,4 and 5 respectively. Normal leukocyte counts were seen in 2,5,7,10 and 8 patients in group 1,2,3,4 and 5 respectively

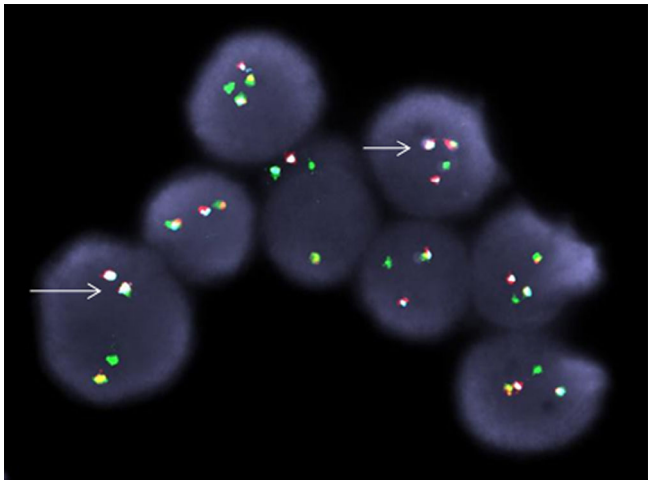

FIGURE 5 *BCR-ABL* positive ALL indicated by two fusion signals (yellow, one green (chromosome 22) and one orange signal (chromosome 9), indicated by arrows). Spectrum Green LSI (locus specific identifier) *BCR* probe consists of two probes located at chromosome 22q11.2. Spectrum Orange LSI *ABL1* probe spans the ABL1 and *ASS1* genes on chromosome 9q34. (Magnification 630 x)

Continuous variables were represented as mean and SD when normally distributed and as median and interquartile range when otherwise. Categorical variables were coded as 1 when present and 0 when absent. Categorical variables were represented as frequencies and percentages. Continuous variables and categorical variables were compared by Mann Whitney U test and Kruskal Wallis test (XLSTAT Version May 3, 2014, JASP [Version 0.12.2]). Two tailed p values less than 0.05 were considered significant. Multiple regression analysis (MS Excel 2016) was used to predict total leukocyte counts from categorical variables.1

3 | RESULTS

A total of 105 adults with B-lymphoblastic leukemia were included in this study. There were 69 (65.7%) males and 36 (34.2%) females with a median age of 38 years (Interquartile range [IQR] = 25 years). The youngest patient was 17 years and the oldest 72 years. The male female ratio was 1.9:1. Thirty-three patients (31.4%) were less than 30 years, 26 (24.7%) patients were in the 30-40-year age group, 16 (15.2%) were aged between 41 and 50 years, 19 (18.0%) were aged between 51 and 61 years and 11 (10.4%) were more than 61 years of age.

The median haemoglobin was 88 g/L (IQR = 37 g/L, range 33.0-143.0 g/L). Total leukocyte count varied from 1 $\times 10^9$/L to 359.0 $\times 10^9$/L. Median leukocyte count was 8.4 $\times 10^9$/L (IQR = 24.6 $\times 10^9$/L). Normal leukocyte count (4-11$\times 10^9$/L) was seen in 33 (31.4%), leukopenia (less than 4 $\times 10^9$/L) in 28 (26.6%) and leucocytosis (more than 11 $\times 10^9$/L) in 44 (41.9%) patients. The median platelet count was 72 $\times 10^9$/L (IQR = 104 $\times 10^9$/L) with a minimum of 5 $\times 10^9$/L and a maximum of 624 $\times 10^9$/L. Hemoglobin (U = 1264, P = .88), total leukocyte count (u = 1161.5, P = .58), and platelet counts (u = 1198, P = .86) did not differ significantly between males and females. Table 1 and figure 1 show the median distribution of haematological parameters, recurrent genetic abnormalities as well as gains and losses of partial or complete chromosomes.

BCR-ABL fusion was detected in 27 patients (25.7%), *TCF3/PBX* fusion in three patients (2.8%), *MYC* rearrangement in six (5.7%), *MLL* rearrangement in two (1.9%) and *IgH* rearrangement in 10 patients (9.5%). There was no significant difference in recurrent genetic abnormalities across gender (Table 1). Multiple linear regression analysis was conducted to predict total leukocyte count (dependent variable) with *BCR-ABL*, *TCF3/PBX*, *MLL* rearrangement, *MYC*, *IgH* rearrangements and gains/losses of chromosomes as independent variables. Regression was not found to be significant {F (15, 89) =1.11, P = .35 with R^2 of 0.158}.

3.1 | *BCR -ABL* positive group compared with *BCR-ABL* negative group

BCR-ABL fusion was absent in 78 (74.2%) patients. Leukocyte counts in *BCR-ABL* positive group were significantly higher than *BCR-ABL* negative group (U = 738.5, P = .02), whereas, median age was not significantly different (U = 967, P = .52) between the two groups (Figure 2). Median age in the *BCR-ABL* positive group was 36 years whereas; it was 39.5 years in the negative group. Median haemoglobin was 94 g/L in the *BCR-ABL* positive group whereas it was 86.5 g/L in the negative group (U = 971.5, P = .55). Total leukocyte counts above 50$\times 10^9$/l were seen in 11 patients in the *BCR-ABL* negative group whereas; it was seen in seven patients in the *BCR-ABL* positive group (P < .0001). In the *BCR-ABL* positive group, 13 patients had leukocytosis (48.2%) whereas; in the *BCR-ABL* negative group 31(39.7%) patients had leukocytosis. In the *BCR-ABL* negative group, median leukocyte count was 7.8 $\times 10^9$/L (range 0.1-359 $\times 10^9$/L). In the *BCR-ABL* positive group, median leukocyte count was 10.7 $\times 10^9$/L (range 0.6-290 $\times 10^9$/L) Additional cytogenetic abnormalities in *BCR-ABL*

Parameters	Males, n = 69 (IQR)	Females, n = 36 (IQR)	*P* value
Median age in years	35 (27)	39.5 (19.5)	.10
Median Hemoglobin g/dl	88 (37)	86.5 (34.2)	.88
Total leukocyte count × 10^9/L	8.1 (25.6)	9.9 (14.4)	.58
Platelet count × 10^9/L	72.5 (90.5)	72.6 (132.7)	.86
BCR-ABL fusion	21.7%	33.3%	.24
TCF3/PBX fusion	4.3%	0	.31
MYC rearrangement	8.6%	0	.09
MLL rearrangement	2.8%	2.7%	.73
IgH rearrangement	8.6%	11.1%	.73

TABLE 1 Distribution of haemoglobin, total leukocyte count and recurrent genetic abnormalities in males and females

Note: No significant difference was seen in the two groups ($P > .05$ by Mann Whitney *U* test/Fishers exact test).

TABLE 2 Comparison of median hematological parameters in the five groups

Parameter	Group1, n = 10	Group 2, n = 14	Group3, n = 37	Group 4, n = 26	Group 5, n = 18	*P*-value
Median age in years	59	31.5	36	38	34	0.04
Median Hb in gm/L	81.5	87.5	86	100.5	81	0.16
Median leukocyte count × 10^9/L	1.9	10.6	8.4	12.0	8.9	0.01
Median platelet count × 10^9/L	79.5	98.5	58.5	88.5	54	0.51

Note: Group 1 had significantly lower total leukocyte counts ($P = .01$)and higher age at presentation ($P = .04$) when compared to the other groups (Kruskal-Wallis test). Group 1 had gains of partial or entire chromosome arm only. Group 2 had loss of partial arm or entire chromosome arm. Group 3 had no cytogenetic abnormalities. Group 4 had recurrent genetic abnormalities and Group 5 had recurrent genetic abnormalities with gains and/or loss of chromosomes.

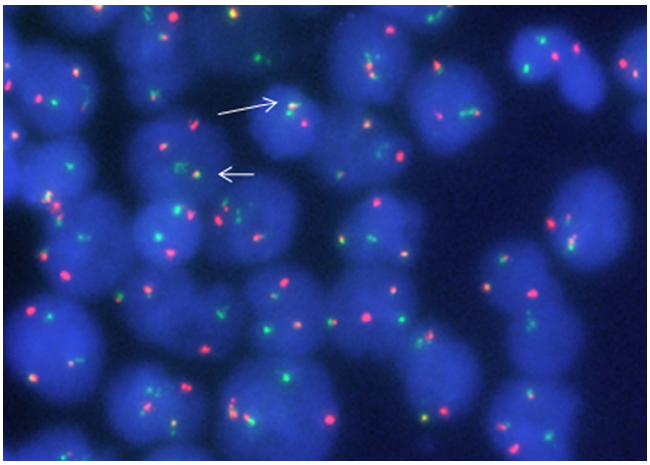

FIGURE 6 *TCF3/PBX* positive ALL with one orange, one green and one fusion signal (indicated by arrows). Spectrum green probe spans the *TCF3* region on chromosome 19p 13.3 and Spectrum orange covers the *PBX* gene on chromosome 1q23 (Magnification 630x).

positive group and negative group are summarised in figure 3 Results of Fishers exact test indicated that there was no significant difference in additional cytogenetic abnormalities between the two groups ($P = .58$ for gains and $P = .46$ for losses).

IgH rearrangements were seen in ten (9.5%) patients. In four patients, *IgH* rearrangements coexisted with *MYC* rearrangement and in three patients it coexisted with *BCR-ABL* rearrangements.

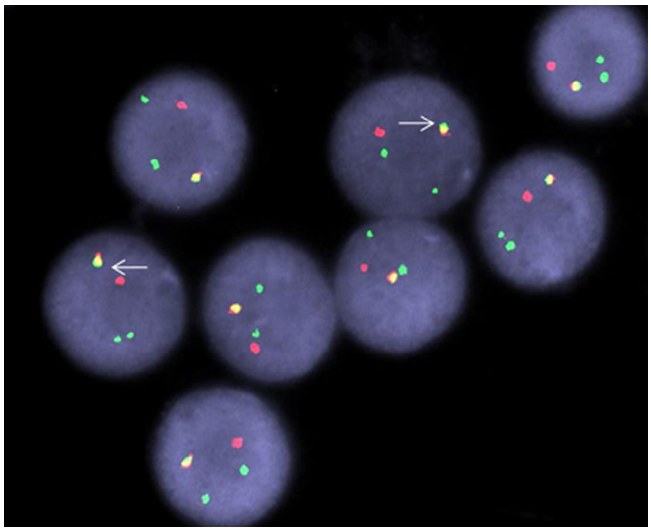

FIGURE 7 *ALL* positive for *MLL* rearrangement indicated by one orange signal, one green signal and one fusion signal (arrows). This is a break apart rearrangement probe. The 5′ (centromeric) Spectrum Green *MLL* probe begins between *MLL* exons 6 and 8 and extends toward the chromosome 11 centromere. The 3′ (telomeric) Spectrum Orange *MLL* probe starts between *MLL* exons 4 and 6 and extends toward the 11q telomere (Magnification 630x)

The study group was divided in to five groups- group 1 through to group 5, based on cytogenetic abnormalities. Group 1 had gains of chromosomes only. There were 10 (9.5%) patients in this group (seven

males and three females). Age varied from 25 to 79 years. There were 14 (13.3%) patients in group 2 (10 males and four females). Group 2 comprised of patients who had loss of partial or entire chromosomes. Their age varied from 23 to 64 years. Group 3 comprised patients with no cytogenetic abnormalities There were 37 (35.2%) patients in group 3 (24 male, 13 female). Their age varied from 17 to 76 years. Patients with one or more recurrent genetic abnormalities were grouped into group 4. In this group there were 26 (24.7%) patients of which, 15 were male and 11 were female. Their age varied from 18 to 63 years. Group 5 was a heterogeneous group with patients having recurrent genetic abnormalities and gains and/or losses of chromosomes. There were 18(17.1%) patients in this group (13 males and five females). Their age varied from 18 to 63 years. Median hematological parameters in the different groups are summarised in table 2 and figure 4. Distribution of haemoglobin and platelets were not found to be significantly different between the five groups {h = 6.46 (4, n = 105) P = .16 for haemoglobin and h = 3.2 (4, n = 105), P = .51 for platelet count, Kruskal Wallis test}. Total leukocyte count and age was found to significantly differ between the groups {h = 12.1 (4, n = 105), P = .01 for total leukocyte count and h = 9.57 (4, n = 105), P = .04 for age distribution, Kruskal Wallis test}. None of the five age groups (less than 30, 30-40, 41-50, 51-60, and 61 and above) were found to have significant differences in hematological parameters as well as cytogenetic abnormalities (Table 3).

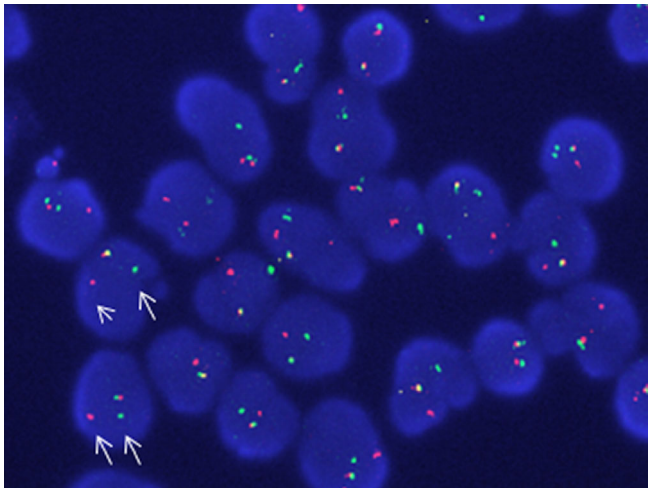

FIGURE 8 ALL with *IgH* rearrangement indicated by one orange signal, one green signal and one fusion signal (arrows) . This is a break apart rearrangement probe Spectrum Green *LSI IGHV* (IGH-variable) probe covers essentially the entire *IGH* variable region. Spectrum Orange LSI *IGH* 3′ probe lies 3′ (centromeric) to the IGH locus. (Magnification 630x).

Discussion: In this study which included 105 adults with B ALL, males outnumber females by a ratio of 1.9:1. There was no difference in cytogenetic abnormalities with respect to gender. *BCR-ABL* rearrangement was seen in 25.7%, followed by *IgH* rearrangements (9.5%), *MYC* (5.7%), *TCF3/PBX* (2.8%) and MLL rearrangements (1.9%). Loss of short arm of chromosome 19 (13%) and gain of chromosome 8(15.2%) were other common cytogenetic abnormalities. *BCR-ABL* positive group had a significantly higher leukocyte count than *BCR-ABL* negative group. However, none of the other hematological parameters, age or other cytogenetic abnormalities were significantly different in the *BCR-ABL* positive group. Leukocyte count significantly differed between groups classified on the basis of cytogenetic abnormalities. Group 1 (gains of chromosomes alone) had higher median age at presentation and lower median leukocyte counts.

TABLE 3 Hematological parameters and frequency of recurrent genetic abnormalities in the different age groups

Parameters	Age less than 30 (n = 33)	30 to 40 years (n = 26)	41 to 50 years (n = 16)	51 to 60 years (n = 19)	More than 61 years (n = 11)	*P* value and H statistic
Median age in years	23	35.5	44.5	55	64	$P < .0001$ H = 98.0
Hemoglobin gm/l	89	102	78.5	82	91	$P = .28$ H = 5
Total leukocyte count × 10^9/l	12.0	7.9	7.4	8.4	4.5	$P = .37$ H = 4.2
Median platelet count × 10^9/l	62.0	84.0	54.5	87.0	88.0	$P = .72$ H = 2
BCR-ABL positive % of patients	24.2	38.4	18.7	21	18.1	$P = .76$ H = 1.8
TCF3/PBX positive % of patients	6	3.8	0	0	0	$P = .99$ H = 0.21
MLL % of patients with rearrangement	3	7.6	0	0	0	$P = .99$ H = 0.29
MYC % of patients with rearrangement	3	3.8	6.2	10.5	9	$P = .99$ H = 0.26
IgH % of patients with rearrangement	3	19.2	6.2	10.5	9	$P = .87$ H = 1.19

Note: None of the parameters and genetic abnormalities were significantly different across various age groups ($P > .05$ by Kruskal Wallis test).

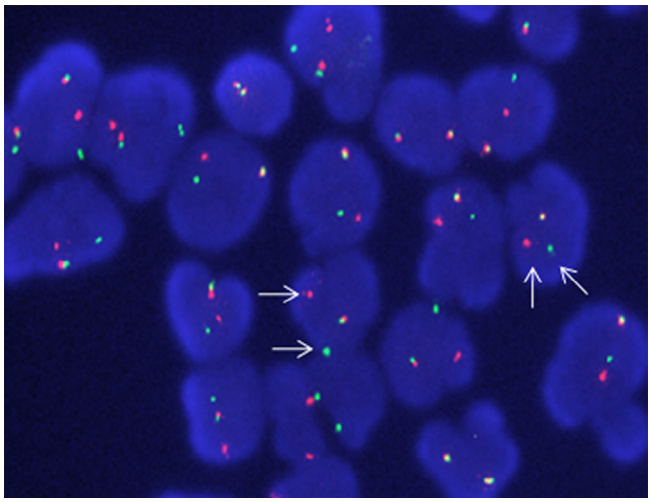

FIGURE 9 ALL positive for *MYC* rearrangement indicated by a normal fusion signal and abnormal separated green and orange signals. Spectrum Orange probe starts centromeric to *MYC* and is centromeric to the breakpoint region. Spectrum Green begins telomeric to *MYC* gene and is telomeric to the break point region (Magnification 630 x).

31.4% patients were aged between 17 and 29 years, 24.7% were aged between 30 and 40 years, 15.2% were aged between 41 and 50 years, 18% were aged between 51 and 61 years and 10.4% were more than 61 years of age. This incidence is higher than that reported by the Italian study where 74% ALL was seen in patients less than 18 years. 8.5% were between 18 and 30 years of age, 6.2% between 30 and 40 years, 5.5% between 40 and 50 years, and 5.3% between 50 and 60 years.[2] This study involved 5202 adults and children with both T and B ALL whereas; our study involved only adults with B-ALL, which could be the reason for these differences in frequency among the various age groups. In the same study, *TCF3/PBX1* was seen in nearly seven % of patients who were less than 30 years of age.[2] Similar to their study, *TCF3/PBX* was infrequent and seen in 2.8% of our patients of which, 6% of patients were less than 30 years and 3.8% of patients were between 30 and 40 years. In the present study, *BCR-ABL was* found to be nearly uniform across the age groups except for a slightly higher frequency (38.4%) in patients aged between 30 and 40 years. In contrast, in the earlier Italian study, frequency of *BCR-ABL* increased with age- 14.4% in 18-25-year age group, 26% in 25 to -30 years, 37.3% in 30 to 40 years, 42.8% at 40 to 50 years and 52.7% at 50 to 60 years. In their study, patients with total leukocyte counts of $>50 \times 10^9$/L had higher frequency of *BCR-ABL* positivity ($P < .0001$) whereas we found total leukocyte counts of $>50\times 10^9$/L was seen more frequently in the *BCR-ABL* negative group ($P < .0001$). This difference could be due to the limited number of patients in the older age groups in our study. This could also be the reason for discrepancy in *MLL* frequency. *MLL* was seen in only 2.5% of patients in our study and was limited to two age groups: one less than 30 years and other 30 to 40 years of age. However in the study by the Italian group, it was seen to progressively increase from 3.8% in the 18-25-year age group to 6.4% (25-30 years) to 7.9% (30-40 years) and to 11.7% (40-50 years). They found that *MLL* rearrangement was associated with higher leukocyte counts across all age groups. We found MLL rearrangement in only two patients in our study group. One of the patients had leukocytosis whereas, the other had leukopenia. In another study, on patients aged 60 and above, it was found that 18% of ALL occurs in elderly. *BCR-ABL* positivity was observed in 24% of these patients.[3] In our study, BCR-*ABL* positivity was seen in 18.1% of patients above 61 years. Only 10.4% of our patients were above 61 years. In another study, involving 321 adolescents and young adults aged between 16 and 20 years, *BCR-ABL* positivity was seen in 4.7% and *MLL* rearrangement in 2.7%.[4] Similarly, in our study, *MLL* gene rearrangement was seen in 3% of patients aged less than 30 years. However, in the same age group our *BCR-ABL* positivity was 24.2%. This discrepancy could be due to the limited number of patients in our study (33 patients were less than 30 years of age). In the GMALL study group, *BCR-ABL* positivity was seen in 36.2% which is slightly higher than our study (25.7%). In this study, it was also seen that *BCR-ABL* positivity increased with age from 12.7% (15-24 years), to 30.6% (25-34 years) to 43.7 (35-44 years).[8] We noticed an increase from 24.2% (less than 30 years) to 38.4% (30-40-years). However, a decline was seen in patients aged between 41 and 50 years (18.7%) which remained nearly constant across patients aged between 51 and 61-years and patients aged over 61 years. In the German multicentre trial, *BCR-ABL* positivity was prevalent in 37%, with positive patients having a higher white cell count than *BCR-ABL* negative patients (23.8×10^9/L vs 11.5×10^9/L, $P = .0001$). Patients in the *BCR-ABL* positive group had a higher median age than negative patients (45 vs 30 years) as well as a marginally higher haemoglobin (102 vs 92 g/L, $P = .004$).[12] In our study, median leukocyte counts in the *BCR-ABL* positive group was significantly higher than the *BCR-ABL* negative group ($P = .02$). However, unlike the German study, age and haemoglobin were not seen to vary significantly between the two groups. Among Chinese patients, the mean age of presentation was significantly higher in females than males (19.5 years vs 16.4 years, $P = .007$). Percentage of patients positive for Philadelphia chromosome did not differ in the two groups (17.7% in males and 17.4% in females, $P = .93$).[13] However, in our study, age at presentation though marginally higher in females, did not differ significantly among males and females (39.5 years in females and 35 in males, $P = .10$). Frequency of *BCR-ABL* positivity also did not differ significantly between males and females ($P = 0.24$).

In an UK based study, males at presentation were found to be younger than females and a slight male preponderance was observed.[15] Prevalence of *BCR-ABL* was found to be 15% and like our study, positivity increased with age from 5% (15-19 years) to 11% (20-29 years), to 15% (30-39 years) and 24% (40-49 years) after which, incidence declined and a plateau was reached.[15] In our study, a similar decline and plateau was evident after the fourth decade. The second most common abnormality was *MYC* rearrangement which was seen in 7%, followed by *TCF3/PBX1* in 3% and *MLL* rearrangement in 4%.[15] In our study too, we found *MYC* rearrangement in 5.7%, followed by *TCF3/PBX* in 2.8% and *MLL* in 1.9%. Liu et al reported MLL rearrangement in 7.6%, *TCF3/PBX* rearrangements in 9.8% and *BCR-ABL* positivity in 26.1%.[16] *IgH* rearrangements have been reported in association with hyperdiploidy, *BCR-ABL* positivity, DUX4 overexpression and *MLL* gene rearrangements.[16,17] In our patients,

IgH rearrangements were seen in 9.5%, of which 40% were associated with *MYC* rearrangement and 30% with *BCR-ABL* rearrangement.

Our study suffers from some limitations. The study group is small and flow cytometry as well as karyotyping findings have not been correlated. The findings must be correlated with prognosis and survival. In this study, we found that *BCR-ABL* is the commonest recurrent genetic abnormality in adult B ALL. Positivity for this rearrangement is related to high leukocyte counts. None of the other hematological parameters have any association with cytogenetic abnormalities. Patients with gains of chromosome only had lower leukocyte counts at presentation and were older at presentation compared to other groups. None of the cytogenetic abnormalities have any predilection for particular age or gender. We need to further investigate this in larger groups to study prognosis and therapeutic response.

ETHICAL STATEMENT

Data were collected from the hospital information system and anonymised. Samples were collected after obtaining informed consent from patients. Ethics approval for the study and publication was obtained retrospectively from the institution ethics committee (Ethics approval number-AMH-C-S-014/07-20).

CONFLICT OF INTEREST

The authors declare no potential conflict of interest.

AUTHOR CONTRIBUTIONS

Anil Tarigopula: Conceptualization; data curation; formal analysis; investigation; methodology; project administration; supervision; validation; visualization; writing-original draft; writing-review and editing. **Vani Chandrashekar:** Conceptualization; data curation; formal analysis; investigation; methodology; project administration; software; supervision; validation; visualization; writing-original draft; writing-review and editing. **Perumal Govindasami:** Conceptualization; formal analysis; investigation; methodology; software; supervision; validation; visualization; writing-original draft; writing-review and editing.

DATA AVAILABILITY STATEMENT

The data that support the findings of this study are available on request from the corresponding author. The data are not publicly available due to privacy or ethical restrictions.

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