Results

Table (15): Clinical data of the studied children with ALL at the time of diagnosis

	Group 1: (N= 23) No detectable chromosomal translocation	Group 2: (N= 17) chromosomal translocation	Controls (N) 8
Age (years)	(2-16) 6.25 ±1.36	(1-16) 4.5±0.963	(1.5- 16) 7.25±1.52
Sex (M/F)	13/10	10/7	5/3
Fever	18 (78.2%)	12 (70.5%)	--
Bone aches	5 (21.7%)	5 (29.4%)	--
Pallor	20 (86.9%)	15 (88.2%)	--
Purpura	18 (78.2%)	12 (70.5%)	--
HSM	14 (60.8%)	14 (82.3%)	--
GLA	16 (69.5%)	13 (76.4%)	--

HSM= Hepatosplenomegaly.

GL= Generalized lymphadenopathy.

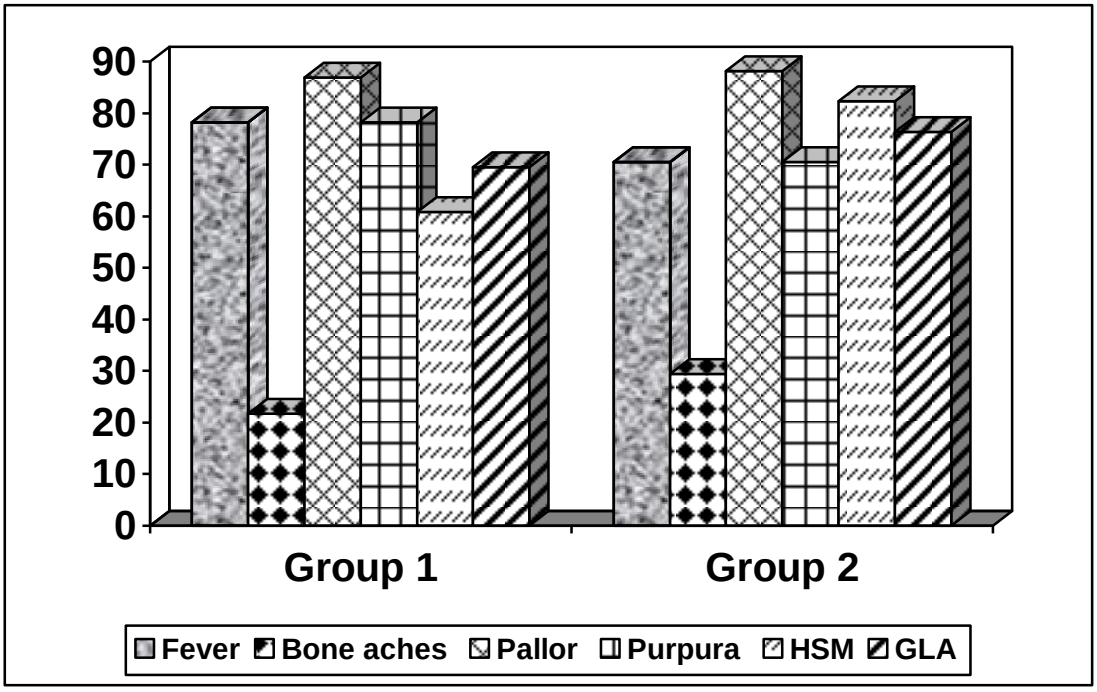


Fig. (41): Clinical data of the studied children with ALL at the time of diagnosis

Table (16): Peripheral blood picture and BM Blasts in ALL patients at diagnosis

	Group 1 (N= 23)	**Group 2 (N= 17)**	**Controls (N= 8)**
Peripheral blood:			
Haemoglobin (gm%)	(4.5-10) 6.30±1.31	(4-11.8) 6.78±2.32	(10.5- 13.8) 11.88±0.91
Platelets (10^3/c.mm.)	(70-110) 46.95±5.74	(63-120) 55.17±7.25	(200- 380) 230±44.2
WBCs (x 10^3/c.mm.)	(4.2-65.5) 31.09±13.9	(3.8- 70.2) 39.07±4.79	(2.5- 8.8) 5.02±2.01
Blasts (%)	(30-55) 35.60±12.97	(36-68) 44.17±4.52	-- --
Bone marrow:			
Blast (%)	25- 50 38.17±8.82	30-74 40.88±11.54	-- --

Group 1: ALL children without translocations.

Group 2: ALL children with translocations.

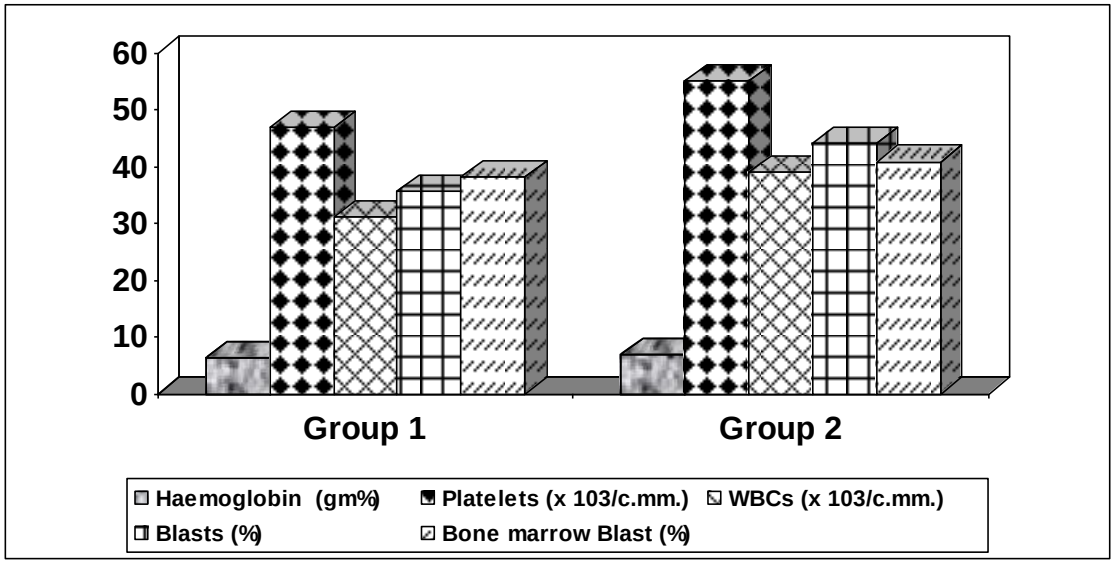


Fig. (42): Peripheral blood picture and BM Blasts in ALL patients at

diagnosis

Table (16): summarizes the hematological finding at diagnosis in group I without detectable translocation versus group II with translocation.

- As regard Hb gm/dl there was insignificant differences with mean Hb 6.3±1.31 and 6.78±2.32 respectively (P>0.05). while in control group it was 11.88±91.
- Platelet count $x10^3$/ C.mm. There was thrombocytopenia in the ALL patients with mean values of 46.95±5.74 and 55.17±7.25 $x10^3$/cm in group I and II respectively with statistical insignificant difference (P>0.05). By comparing the 2 groups with the control group (mean 230±44.2 x 10^3/cm) there was highly significant difference (P<0.1).
- The mean value of leucocytic count $x10^3$/ C.mm in group I and II was 31.09±13.9 and 39.07±4.79 with insignificant difference (P>0.05).
- By comparing with the control group (mean value 5.02±2.01), there was a highly significant increase in the ALL groups (P<0.01).
- As regard the blast % in group I and II in peripheral blood, the mean values was 35.6±12.97 and 44.17±4.52 respectively, which was insignificantly different (P>0.05)
- The BM blast % in group I and II was 38.17±8.82 and 40.88±11.54 respectively which also was statistically insignificantly different (P>0.05).

Table (17): Distribution of fusion genes in relation to Hb, TLC, platelets, Blasts % in BM and PB

Translocation N=17 (42.5%)		**Hb (gm %)**	**TLC (x 10^3/c.mm)**	**Platelets (x 10^3/c. mm)**	**PB-Blast %**	**BM-Blast %**
T(4;11) N=2 (5%)	Range	(4.0-10.2)	(50.5-65)	(20-25)	(50-58)	(48-52)
	Mean±SD	7.1 ± 1.36	52.75 ± 13.2	22.5± 9.58	54± 14.5	50± 15.3
t(12;21) N= 8 (20%)	Range	(4.5- 100)	(6.5- 32)	(30- 118)	(20-44)	(28-46)
	Mean±SD	6.275± 1.52	20.625± 3.65	77.87± 20.3	28.25± 6.9	31.5± 8.3
t(1; 19) N= 3 (7.5%)	Range	(5.2 -6.8)	(50-60.4)	(30-50)	(52-64)	(38-50)
	Mean±SD	6.17± 0.86	54.133± 10.3	40± 8.78	58.66± 15.9	42.667±8.64
t(9; 22) N= 4 (10%0	Range	(5.6- 11.8)	(42.6- 678)	(20-60)	(55-68)	(44-63)
	Mean±SD	8.1 ± 2.36	55.85± 13.6	37.5± 7.63	60.25 ± 17.6	53.75± 12.3

t(4; 11): One case out of two died after 28 days from indication chemotherapy. The other case died after 360 days

t(12; 21): One case died after 360 days and seven cases live till day 720.

t(1; 19): Once case died after 20 days form indication chemotherapy, one case died after 360 days, one live tell day 720.

t(9; 22): Two cases died after 360 days and two cases live till day 720.

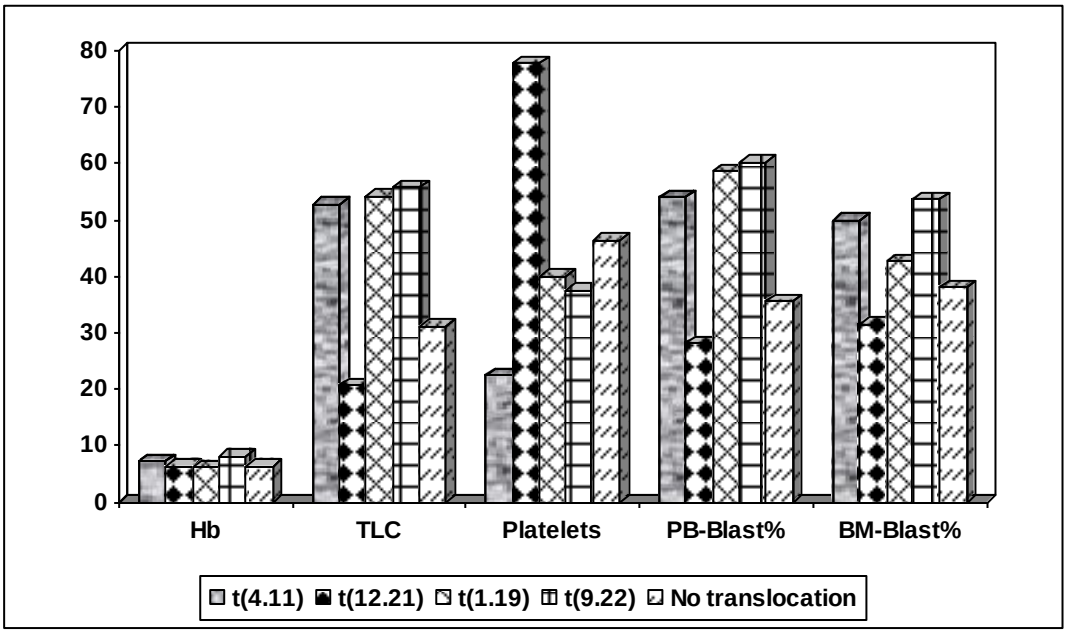


Fig. (43): Distribution of fusion genes in relation to Hb, TLC, platelets, Blasts % in BM and PB

Table (17): summarizes the distribution of fusion genes in relation to Hb gm%, TLC $x10^3$/C.mm, platelet count $x10^3$/ C.mm, peripheral blood blast cells % and BM blast cells %.

- The mean values of Hb% in the different translocations shows insignificant difference (P>0.05).
- The mean value of total leucocytic count in ALL patients with t(12; 21) was 20.625±3.65 $x10^3$/C.mm which was statistically significantly lower than the mean leucocytic count in the t(4; 11), t(1; 19) and t(9; 22) with mean values of 52.75±13.2, 54.133±10.3 and 55.85±13.6 respectively (P<0.05).
- The mean values of blast cells % in peripheral blood and BM in ALL patients with t(12; 21) was 28.25±6.9 and 31.5±8.3 respectively, which was statistically significantly lower than the mean values of other translocations (P<0.05).
- The mean value of the platelet count in ALL patients with t(12; 21) was statistically more than the mean platelet count in the t(4; 11), t(1; 19) and t(9; 22) with (P<0.05).

Table (18): Distribution of fusion genes in relation to immunophenotypes

Translocation No. 17 (42.5%)	**Early Pre-B**	**Pre-B**	**CALL**
2 (5%) t (4;11)	1	1	--
8 (20%) t(12;21)	--	3	5
3 (7.5%) t(1;19)	1	1	1
4 (10%) t (9; 22)	--	--	4
No detectable translocation No. 23 (57.5%)	7	6	10
	9 (22.5%)	11 (27.5%)	20 (50%)

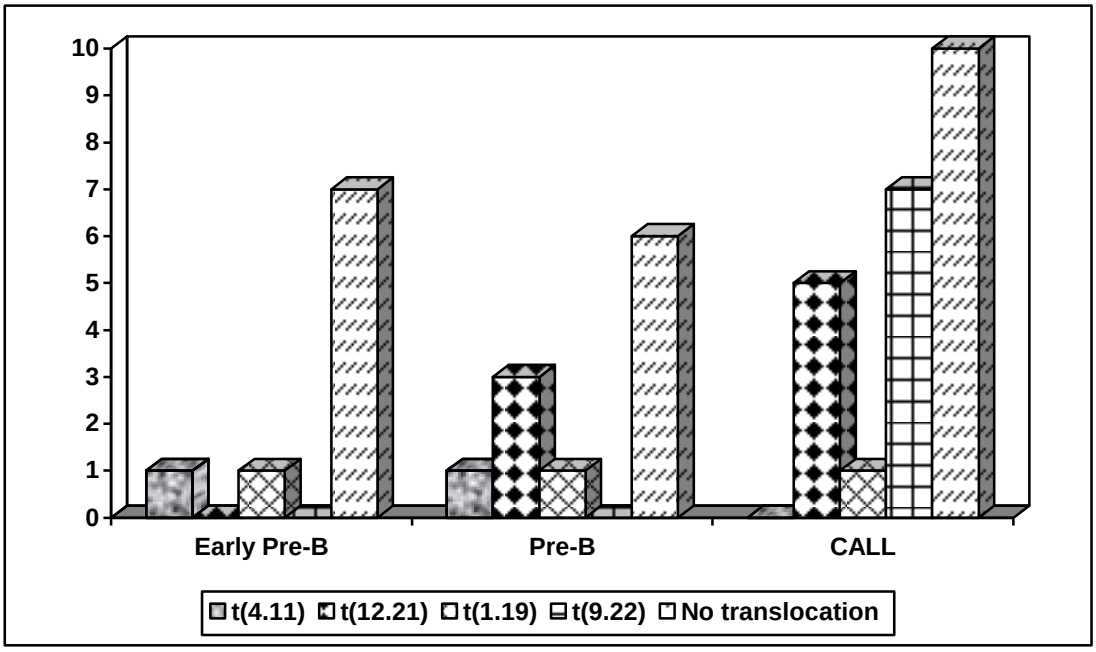


Fig. (44): Distribution of fusion genes in relation to immunophenotypes

Table (18): summarize the distribution of fusion genes in relation to immunophenotypes.

- Nine cases were early pre-B(22.5%), one case t(4; 11), one case t(1; 19) and 7 cases without detectable translocations.
- Eleven cases were pre-B(27.5%), one case t(4;11), 3 cases t(12; 21), one case t(1; 19) and six cases without detectable translocations.
- Twenty cases were CALL (50%), 5 cases t(12; 21), one case t(1; 19), 4 cases t(9; 22) and 10 cases without detectable translocations.

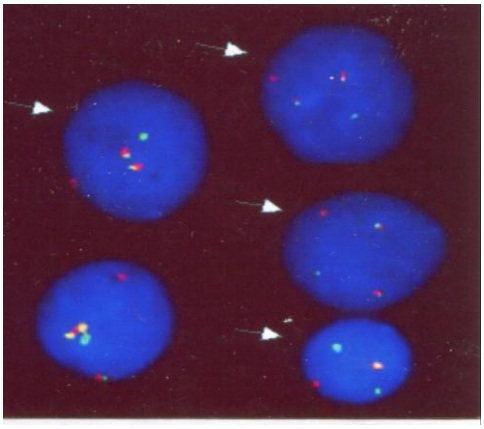


Fig. (45): t(12; 21) TEL-AML1 fusion dual colour FISH (one red, one green and two fused signals) 8 cases (20%)

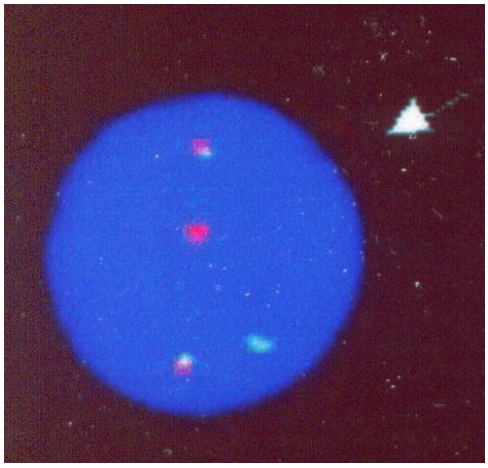


Fig. (46): t(1; 19) ETO-PBX fusion dual colour FISH (one red, one green and two fused signals) 3 cases (7.5%)

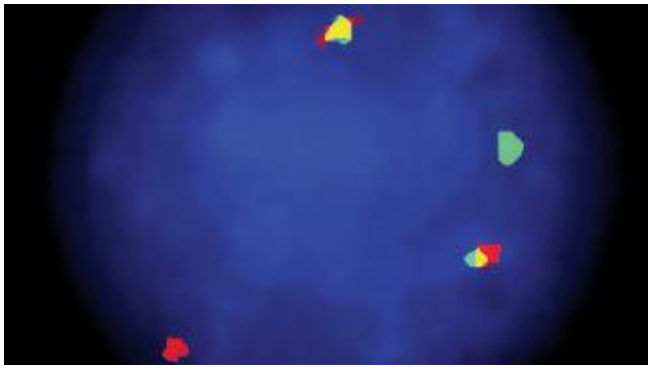
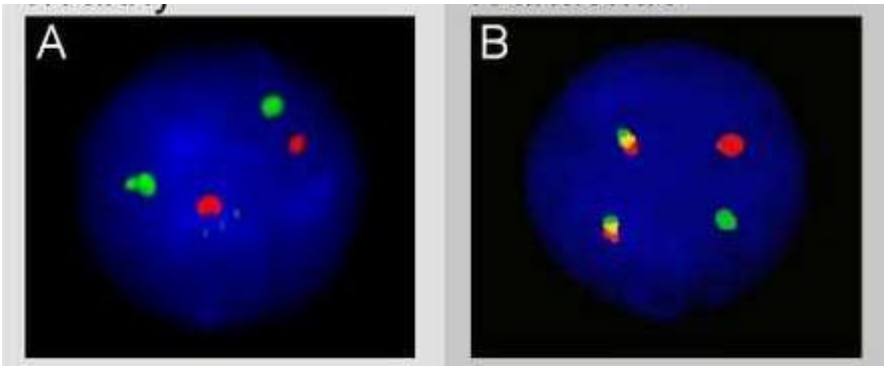


Fig. (47): t(9; 22) BCR-ABL fusion dual colour FISH (one red, one green and two fused signals) 4 cases (10%)



Normal **ALL**

Fig. (48): t(4; 11) MLL-AF4 fusion dual colour FISH (one red, one green and two fused signals) 2 cases (5%)

Patient's response after induction therapy and disease free survival (DFS):

- Two cases died one during induction chemotherapy at day 20 with t(1; 19) and the other case died at the end of induction therapy day 28 with t(4; 11).
- The disease free survival (DFS) after 360 days:
  4 cases live till 360 days; one case with t(12; 21), one with t(1; 19) and 2 cases with t(9; 22).
- The disease free survival (DFS) after 720 days:
  10 cases live till 720 days; 7 cases with t(12; 21), 1 case 2with t(1; 19) and 2 cases with t(9; 22).

- Life table estimates were calculated using Kaplan-Meier method, and the standard error of the life table estimates was calculated with Green-Wood formula. Patients without adverse events were censored on the date of the last reported contact.
- The differences between curves were tested for statistical significance using were tested for statistical significant using the log rank test.
- The overall DFS was 72% for t(12; 21)
  51% for t(4; 11)
  58% for t(1; 19)
  69% for t(9; 22)

Using Kaplan-Meier, a significant differences in DFS between group I without detectable translocations and t(4; 11), t(1; 19), and t(9; 22), while there was no significant differences in DFS between group I and t(12; 21). Also there was significant difference in DFS between t(12; 21) versus t(4; 11), t(1; 19) and t(9; 22). This means that t(12; 21) was associated with good prognosis while t(4; 11), t(1; 19) was associated with poor prognosis.

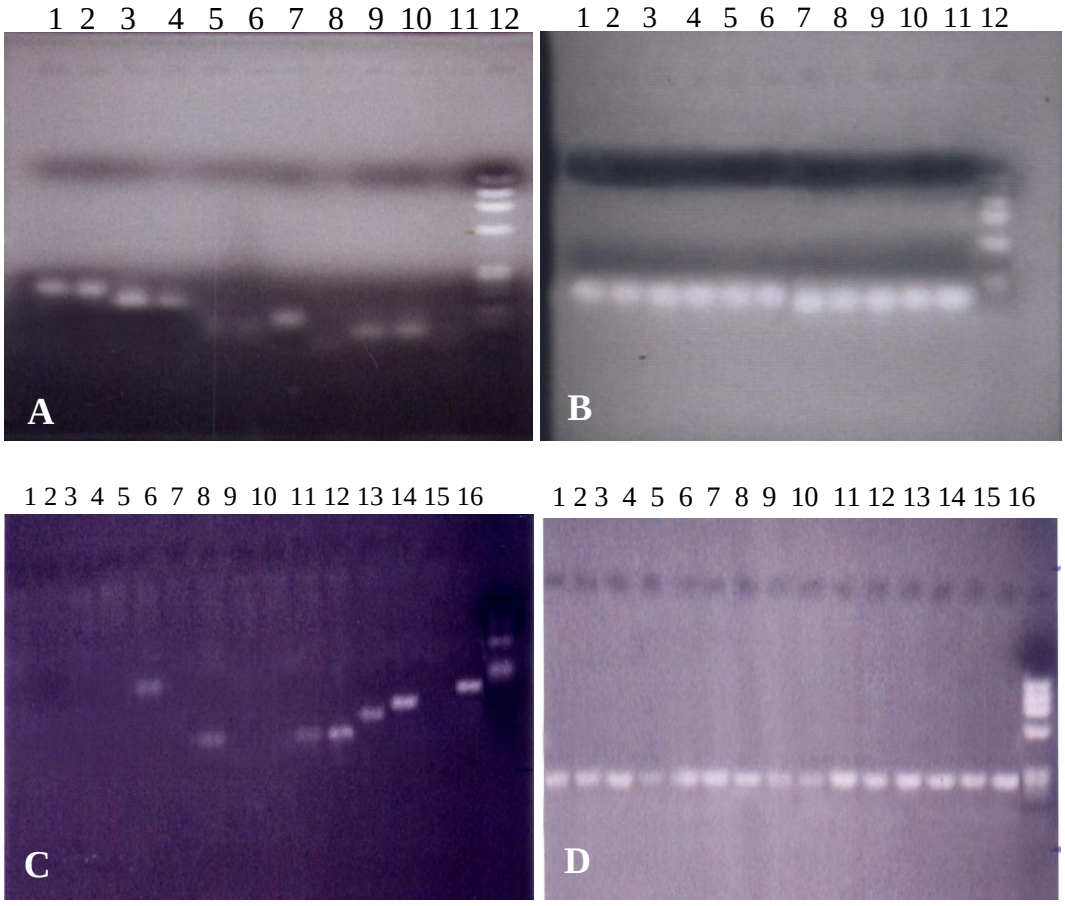


Fig. (49): PCR amplification of the four studied fusion transcripts. A) Wells 1,2 show BCR ABL fusion transcript**,** 3.4 wells are MLL-AF4, well No. 7 represent E2A PBX1 fusion gene, wells 9,10 show TE1-AML fusion gene, 5,6,8,11 wells are negative for fusion transcripts, well 12 is DNA ladder (100bp). C) 5,15 wells show BCR ABL fusion transcript, wells 7,10,11 show TE1-AML fusion gene, well 12, E2A PBX1 transcript, well 13 AML-AF4 transcript and 1,2,3,4,6,8,9,14 are negative for translocation. B&D) Represent GAPDAH internal control for normalization

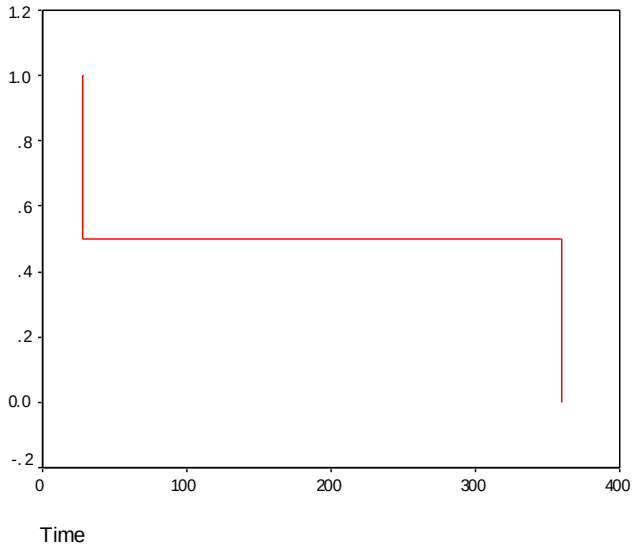


Fig. (49): Diseases free survival between group I without detectable translocations and t(4; 11), t(1; 19), and t(9; 22)

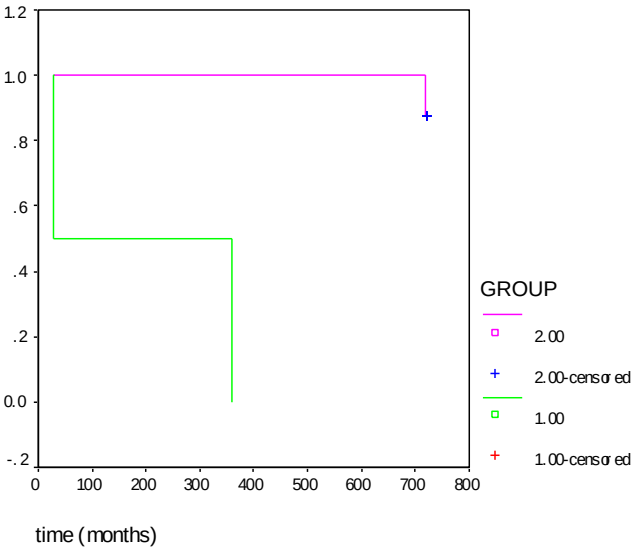


Fig. (50): Kaplan-Meier diseases free survival between t(4; 11), t(1; 19), and t(9; 22) versus t(12; 21)

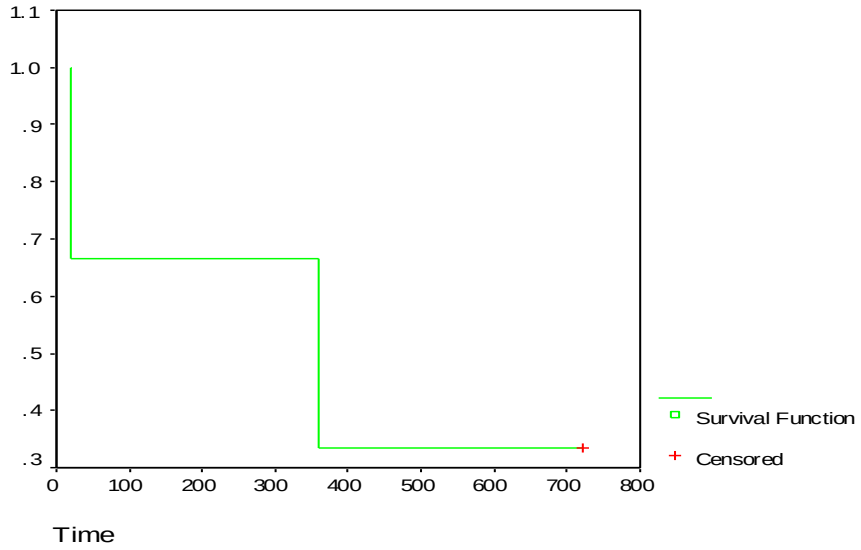


Fig. (51): Kaplan-Meier diseases free survival for all cases

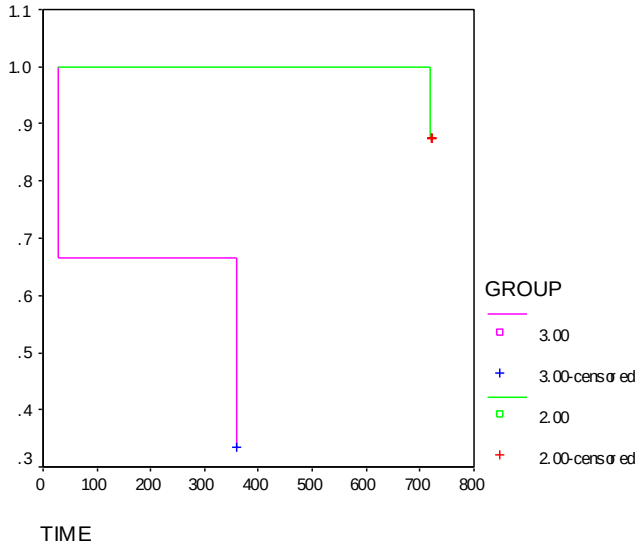


Fig. (52) Kaplan-Meier diseases free survival between t(1; 19), vs t(12; 21)

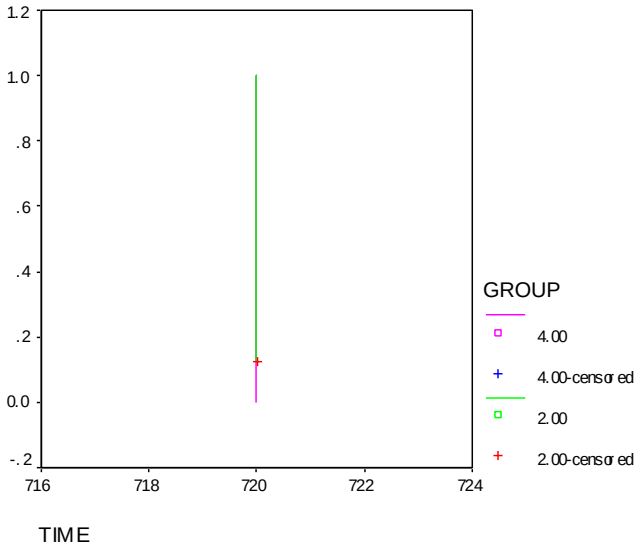


Fig. (53): Kaplan-Meier disease free survival of t(4;11), t(1;19) and t(9;22) vs group with no translocation

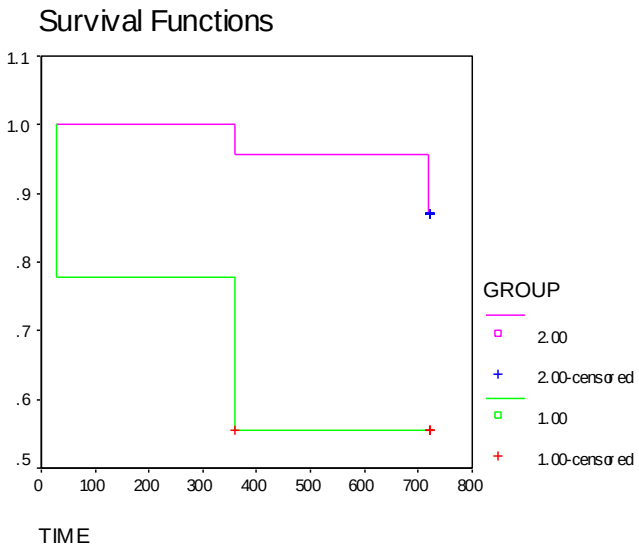


Fig. (54): Kaplan-Meier disease free survival of t(12; 21) vs group with no translocation

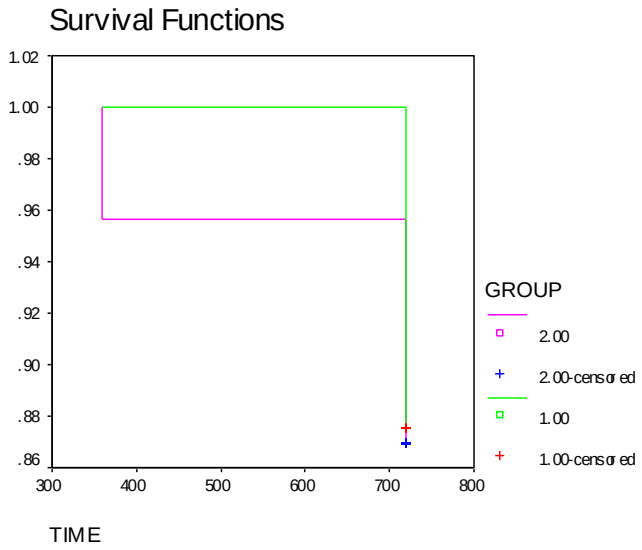


Fig. (55): Kaplan-Meier disease free survival of t(12; 21) vs group with no translocation

Table (19): ALL cases with chromosomal translocations t(12; 21), t(4; 11), (1; 19) and t(9; 22) (group I) (n=17)

Trans.	Age years	Hb Gm%	WBC $X10^3/\mu L$	Plat $X10^3/\mu L$	PB Blast %	BM Blast %
(12; 21)	2	4.5	6.5	110	20	30
(12; 21)	5	6	15.8	100	22	28
(12; 21)	8	7.2	22.5	118	25	30
(12; 21)	1	10	32	85	40	46
(12; 21)	10	4.5	16	30	22	30
(12; 21)	3	5.5	20	35	25	30
(12; 21)	7	5	20	80	28	30
(12; 21)	12	7.5	30.2	65	44	28
(1; 19)	10	6.5	60.4	50	64	40
(1; 19)	16	5.2	50	40	52	38
(1; 19)	6	6.8	52	30	60	50
(4; 11)	11	4	65	25	58	52
(4; 11)	1	10.2	50.5	20	50	48
(9; 22)	8	6	58	20	58	44
(9; 22)	4	5.6	42.6	60	68	60
(9; 22)	1	9	45.8	40	55	48
(9; 22)	14	11.8	68	30	60	63

Table (20): ALL cases without detectable chromosomal translocations under the study (group II)

Trans.	Age years	Hb Gm%	WBC $X10^3/\mu L$	Plat $X10^3/\mu L$	PB Blast %	BM Blast %
	3.25	9	44	36	20	32
	3	5.2	30	30	28	30
	2.25	6.4	26.5	34	30	35
	1	8	24	40	22	30
	2	6.5	18.6	50	20	32
	8	6	28	60	24	31
	2.5	5	10.8	44	50	60
	2.5	4.8	15.6	32	46	50
	1.5	5.6	22	30	38	40
	15	6	20	25	40	46
	11	10	30.5	40	36	30
	9	8	24	44	28	38
	3	7	28.5	50	30	32
	12	6	36	65	28	33
	1.25	5.5	50.8	20	48	40
	3	5.8	60.2	30	66	54
	6	5.2	22	120	30	32
	5	6	19.6	100	27	33
	3.75	7.4	32	90	25	30
	3	5	20	80	30	36
	3.5	4.5	60	10	52	48
	4.25	6	52	20	60	50
	4.5	8	40	30	44	36

Table (21): ITP cases as control group (group III)

Trans.	Age years	Hb Gm%	WBC X103/µL	Plat X103/µL	PB Blast %	BM Blast %
	5	10.5	6.5	90	0	0
	4	11.4	6	80	0	0
	8	11.8	8.8	60	0	0
	12	12	5	38	0	0
	10	12.5	6.2	36	0	0
	9	13	8.5	70	0	0
	5	12.8	3	60	0	0
	6	11.8	2.5	40	0	0
	4	10.5	2.8	30	0	0
	13	12	5	40	0	0
	12	12.5	6	25	0	0
	8	13	2	50	0	0
	10	13.8	2.8	44	0	0
	11	12	3	30	0	0
	13	12.2	8	30	0	0
	6	11.9	5.8	40	0	0
	8	10.8	3	30	0	0
	9	11.6	2.8	45	0	0
	10	10.5	6.8	25	0	0
	5	11	6	30	0	0