RESULTS

- Twenty six newly diagnosed patients with acute lymphoblastic leukemia were included in the present study. The individual clinical and laboratory data of all patients are shown in the appendix.
- The study included 13 male patients and 13 female patients. They were children (age ranged from 1.5 to 18 years).

♦ Presenting symptoms:

Table (13): Presenting symptoms of the studied group

Symptom	No. N=26	% (100%)
Fatigue	18	69.2
Pallor	20	76.9
Purpura	15	57.7
Abdominal swelling	18	69.2
Bone aches	12	46.2
Epistaxis	14	53.8
Neck swelling	21	80.8

The most common presenting symptom among the study group was neck swelling (80.8%) while the least common was bone aches (46.2%).

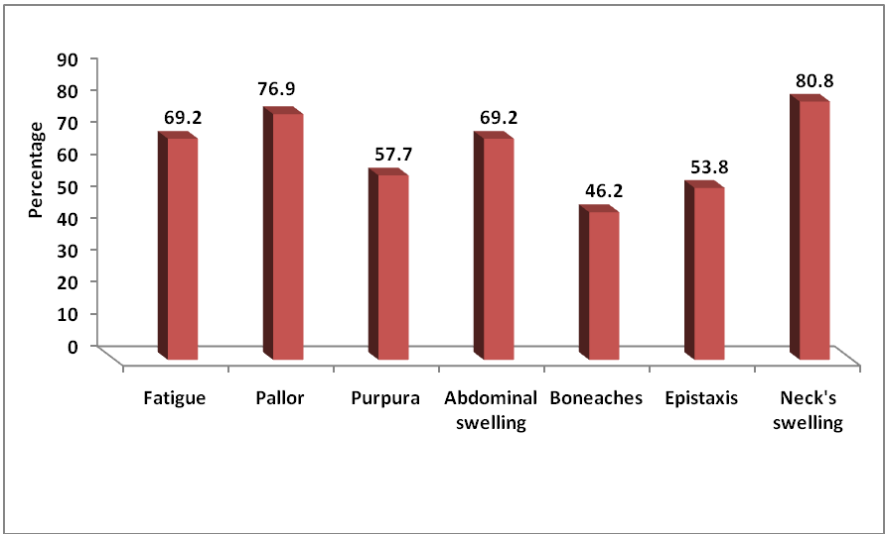


Figure (17): *Presenting symptoms of the studied group*

♦ Clinical findings:

Table (14): Clinical signs of the studied group

Sign	No. N=26	% (100%)
Fever	16	61.5
Lymphadenopathy	21	80.8
Hepatomegaly	14	53.8
Splenomegaly	21	80.8

The most common clinical signs among the studied group were lymphadenopathy (80.8%) and splenomegaly (80.8%) while the least common was hepatomegaly (53.8%).

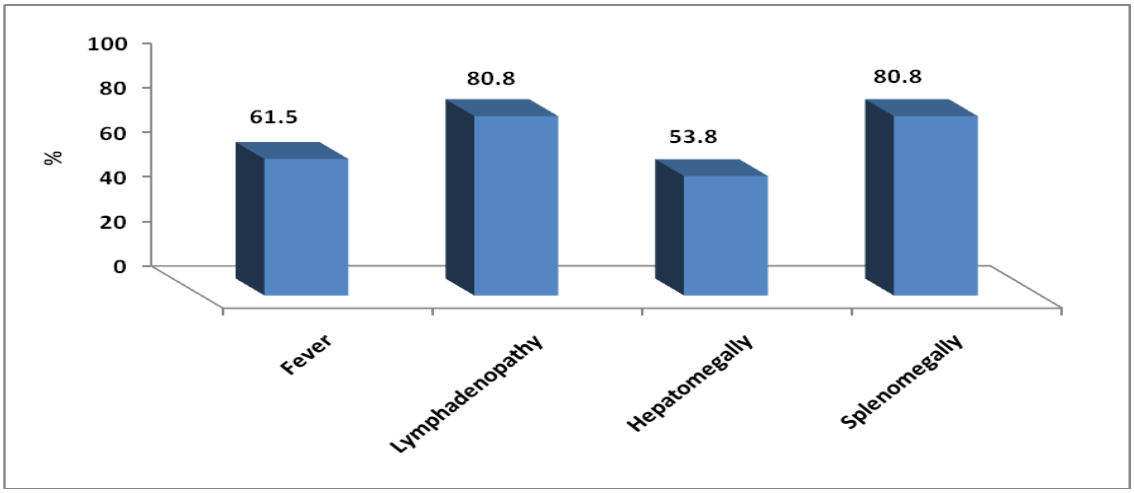


Figure (18): Clinical signs of the studied group

♦ Laboratory findings:

Table (15): Laboratory findings of the studied group at diagnosis

Item	Range	Mean±SD
Hb (g/dL)	5.8-13.7	9.09±2.23
TLC(x10^3/µL)	1.6-240	32.12±50.43
Plt (x10^3/µL)	16-650	117.4±128.56
Blasts in PB (%)	2-100	47.8±28.42
Blasts in BM (%)	20-100	64.8±26.45
LDH(U/L)	270-3250	960.1±758.4
ESR(mm)	25-150	73.5±32.96

Table (16): The hemogram abnormalities of the studied group

Item	No=26	%	Z	P
Hb:				
Below 9 g/dL	14	53.8	0.39	>0.05
Above 9 g/dL	12	46.2		
TLC:				
Below 50 x 10^3/µL	22	84.6	4.6	**<0.001***
Above 50 x 10^3/µL	4	15.4		
Plt:				
Below 50 x 10^3/µL	8	30.8	2.125	**<0.05***
From 50 - 100 x 10^3/µL	18	69.2		

Significant P<0.05 and P<0.001

There was no statistically significant difference in number of patients whose hemoglobin level was below 9 g/dl and above 9 g/dl (p>0.05).

However, there was statistically significant increase in number of patients with total leukocytic count below 50x10^3/µL rather than those with total leukocytic count above 50x10^3/µL (p<0.001), and statistically significant increase in the number of patients with platelets count from 50-100x10^3/µl more than those with platelets count less than 50x10^3/µl (p<0.05).

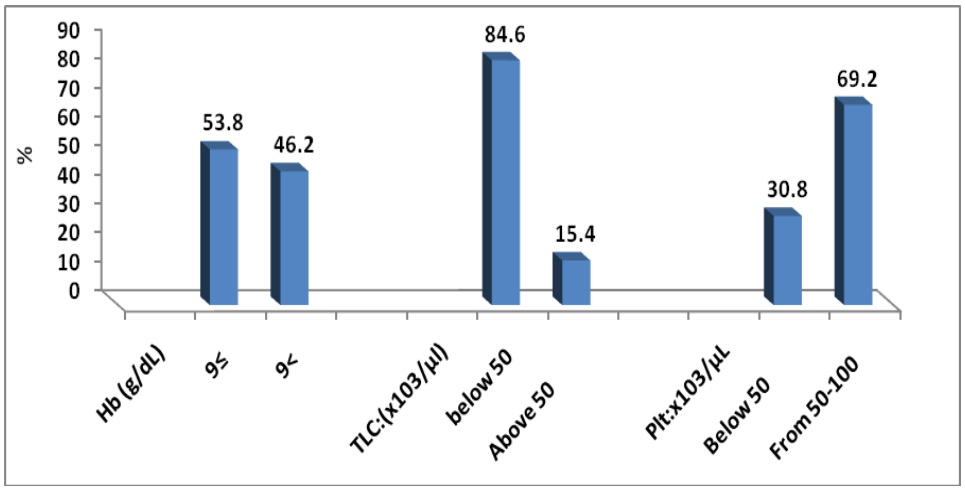


Figure (19): The hemogram abnormalities of the studied group

♦ Morphological characteristics (FAB classification):

Table (17): FAB classification of patients

FAB classification	No. of patients	%
L1	13	50
L2	11	42.3
L1/L2	2	7.7
Total	26	100

The most common FAB classification among the studied group was L1 type (50%) and the least common was L1/L2 type (7.7%).

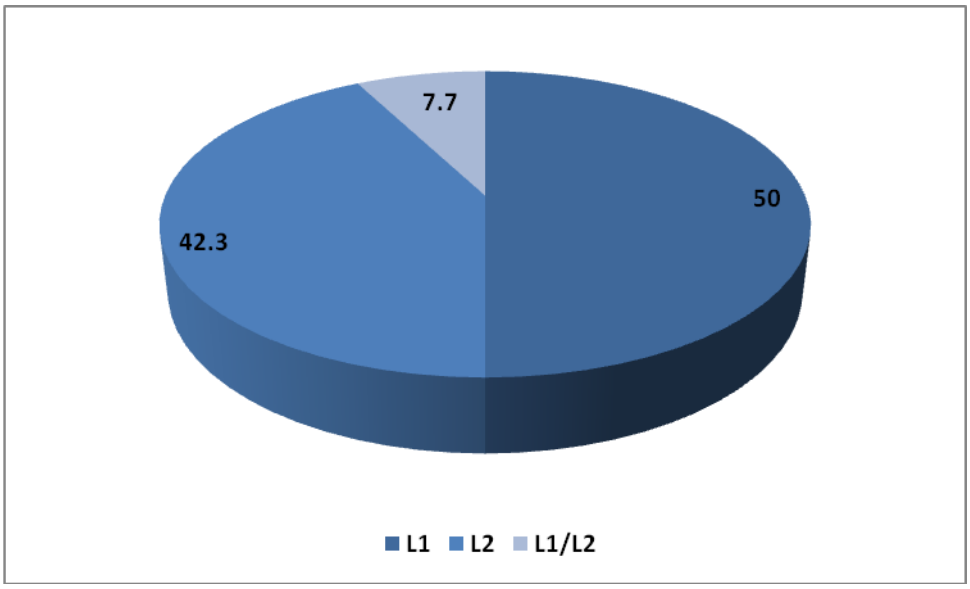


Figure (20): FAB classification of patients

Results of t(1;19):

Table (18): Incidence of t(1;19)

t(1;19)	No. of cases (26)	Frequency %	Z	P
Positive	6	23.1	3.3	**< 0.001***
Negative	20	76.9		

Significant P<0.05

FISH was performed for t(1;19) on the 26 newly diagnosed cases with ALL. Out of the analyzed samples (26), there were 6 cases positive for t(1;19) which represents 23.1% positivity that shows a high statistical significance (p<0.001).

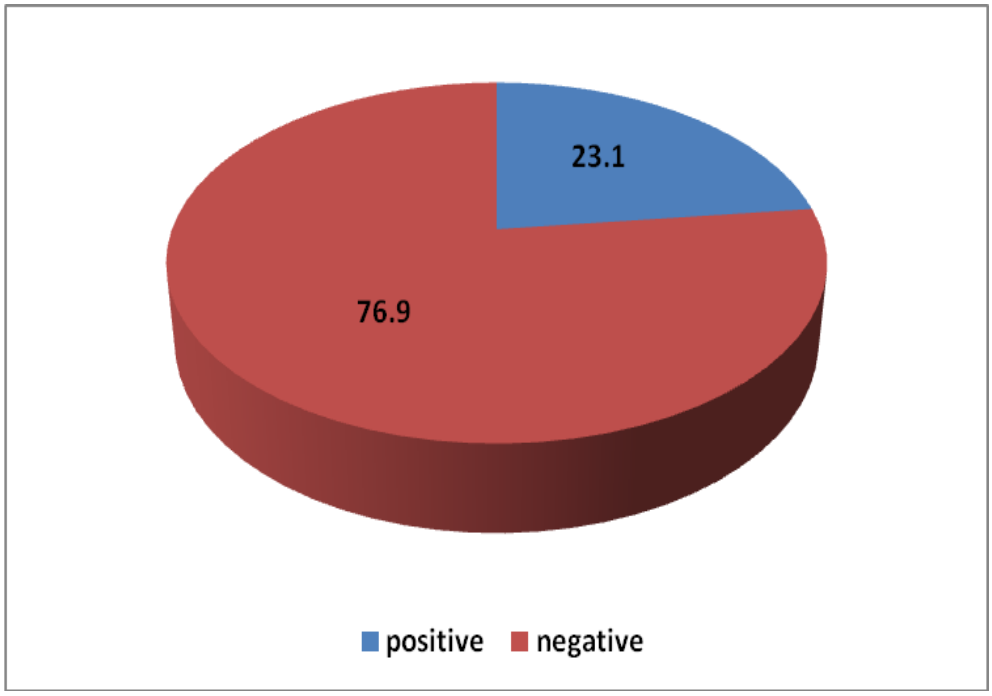


Figure (21): Incidence of t(1;19)

Table (19): **Clinical and hematological data of t(1;19) positive cases**

Patient No.	FAB Diagnosis	Age	Sex	Hb	TLC	Plt	PB BL%	BM BL%	Fate	Alive/ Dead
1	L2	10	Male	10.7	13.3	210	85	95	Relapse	Died
7	L2	8	Female	8.5	2.5	45	100	100	Remission	Alive
8	L1	2	Male	7	43.3	64	40	87	No remission	Alive
15	L2	4	Female	12.4	45	220	40	90	Relapse	Died
21	L1	18	Male	8.5	79.5	166	70	90	Relapse	Died
24	L2	4.5	Male	8.6	18.9	16	90	93	No remission	Died

Table (20): Age distribution in t(1;19) cases

t(1;19)	No.	Range	Mean age±S.D	Student "t"	P. value
Positive	6	2-18	7.8±5.8	0.38	0.707
Negative	20	1.5-16	8.7±5.1		

Significant P<0.05

There was no statistically significant difference between both negative and positive groups for t(1;19) as regard to the age of patients (p>0.05).

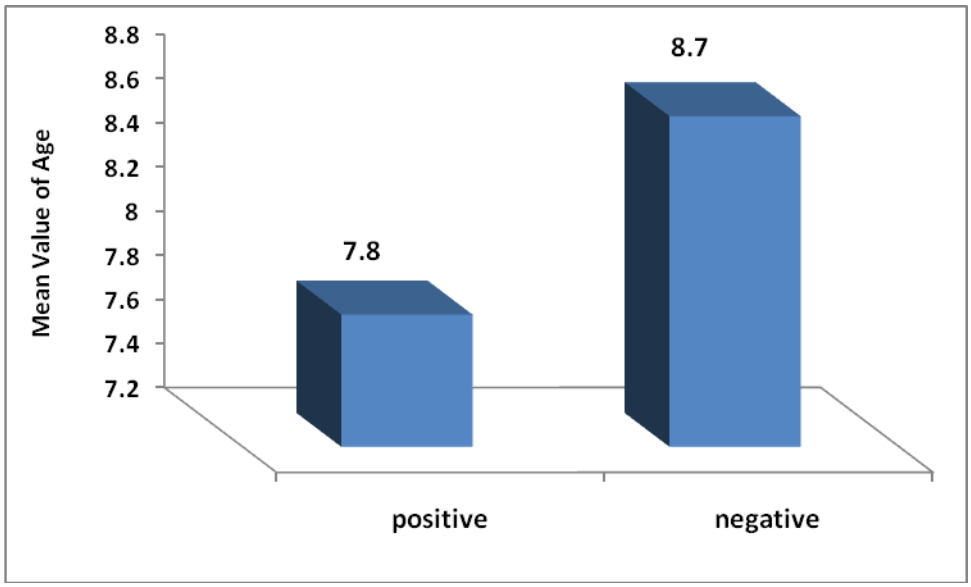


Figure (22): Age distribution in t(1;19) cases

Table (21): Sex distribution in t(1;19) cases:

Gender	Positive		Negative		Total	
	No.	%	No.	%	No.	%
Male	4	66.7	9	45	13	50
Female	2	33.3	11	55	13	50
Corrected X^2	0.217					
P	>0.05					

Significant P<0.05

There was no statistically significant difference between both negative and positive groups for t(1;19) as regard to sex of the studied group (p>0.05).

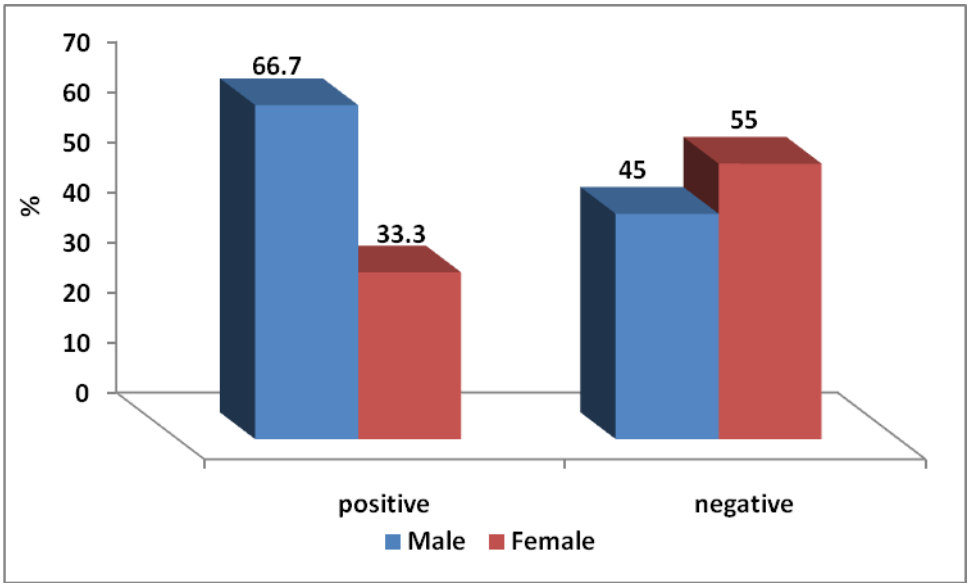


Figure (23): *Sex distribution in t(1;19)*

♦ Hematological findings:

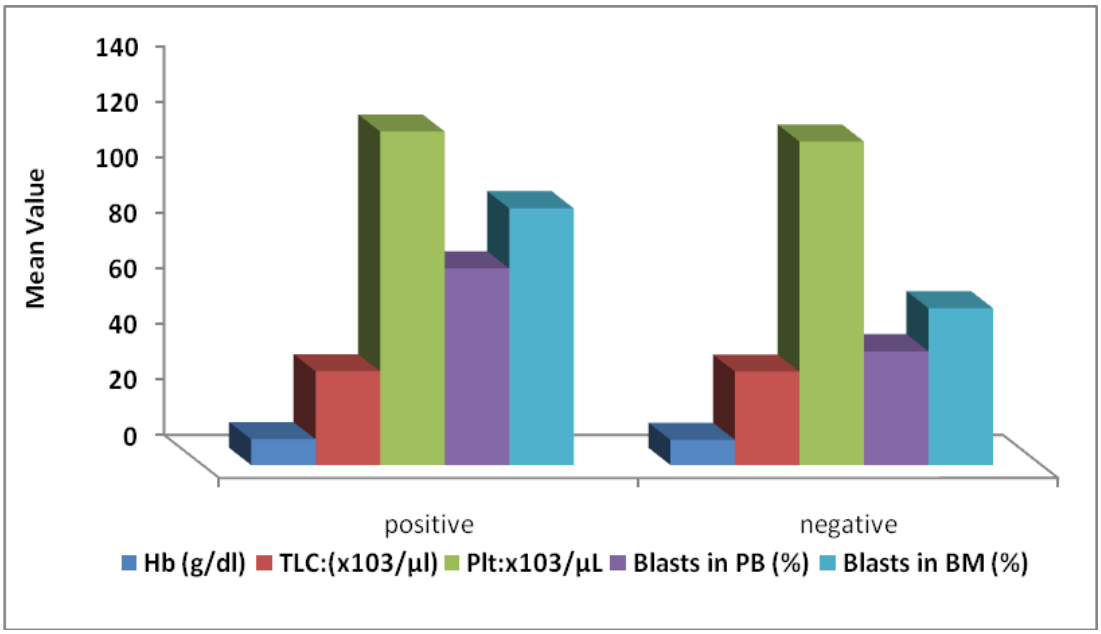
Table (22): Comparison between t(1;19) positive and negative cases regarding the hematological parameters

Parameter	Positive		Negative		T	P	Sig.
	Range	Mean±SD	Range	Mean±SD			
Hb g/dl	7-12.4	9.28±1.93	5.8-13.7	9.04±2.35	0.23	0.82	>0.05
TLC x10$^{3/}$µL	2.5-79.5	33.75±28.02	1.6-240	31.63±56.02	0.09	0.93	>0.05
Plt x10$^{3/}$µL	16-220	120.17±89.21	20-650	116.55±140.18	0.06	0.95	>0.05
PB blasts %	40-100	70.83±25.77	2-87	40.95±25.91	2.48	**0.021**	**<0.05***
BM blasts %	87-100	92.5±4.59	20-96	56.5±24.49	3.53	**0.002**	**<0.01***
LDH U/L	531-2311	1325.33±741.39	270-3250	850.55±746.59	1.37	0.18	>0.05
ESR mm	60-120	92.5±27.52	25-150	67.85±32.91	1.66	0.11	>0.05

****Significant P<0.05 and <0.01***

Statistical analysis of the hematological parameters of both positive and negative cases for t(1;19) shows significant increase in the blast cell percentage both in peripheral blood and bone marrow in positive cases ($p<0.05$ for peripheral blood blast cell% and $p<0.01$for bone marrow blast cell%).

However, there was no statistically significant difference between both negative and positive groups for t(1;19) as regard to hemoglobin level, total leukocytic count, platelet count, serum LDH level and ESR level.



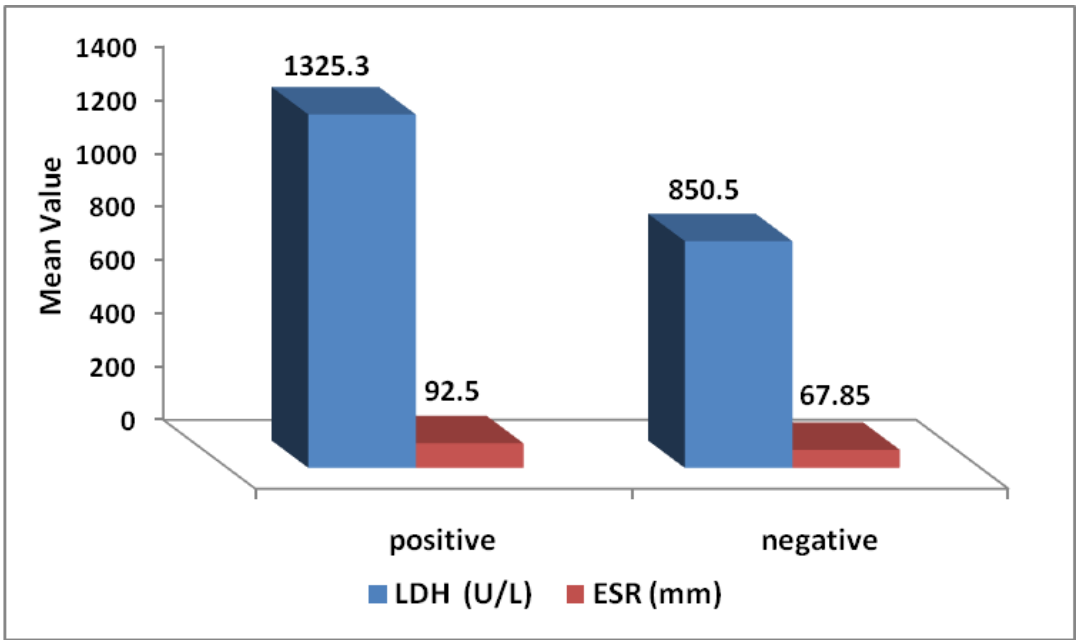


Figure (24): Comparison between t(1;19) positive and negative cases regarding the hematological parameters.

♦ FAB classification:

Table (23): FAB classification of t(1;19) groups

FAB	Positive		Negative		Total		Z	P. value
	No.	%	No.	%	No.	%		
L1	2	33.3	11	55	13	50	0.93	>0.05
L2	4	66.7	7	35	11	42.3	-1.4	>0.05
L1/L2	0	0	2	10	2	7.7	0.8	>0.05
Total	6	100	20	100	26	100		

Significant P<0.05

There was no statistically significant difference between both negative and positive groups for t(1;19) as regard the FAB subtype (p>0.05). However, L2 is more common among positive cases but, L1 is more common among negative cases.

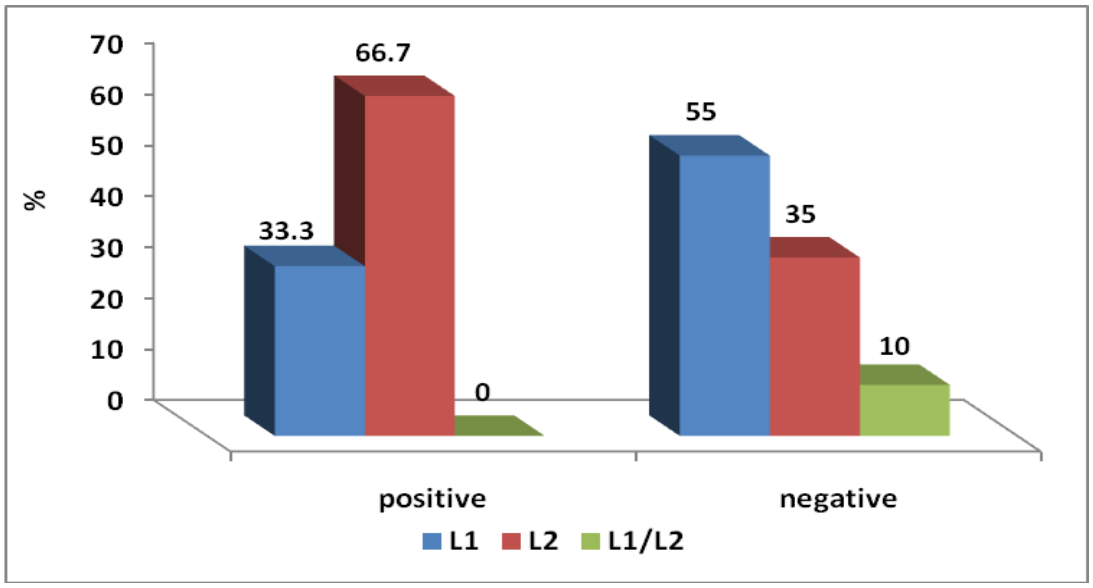


Figure (25): FAB classification of t(1;19) groups

- **Prognosis:**

Table (24): Fate of t(1; 19) positive and negative cases

Fate	Positive (6)		Negative (20)		Z	P
	No.	%	No.	%		
Remission	1	16.7	12	60	1.86	**<0.05***
Complete Rem.	0	0	3	15	1.01	>0.05
No Remission	2	33.3	1	5	1.9	**<0.05***
Relapse	3	50	4	20	1.45	>0.05

Significant P<0.05

As regard the fate of t(1;19) positive and negative cases, there was statistically significant increase in number of positive cases who resist treatment or achieved remission when compared with negative cases (p<0.05). However, there was no statistically significant difference between both positive and negative cases who achieved either complete remission or suffered from relapses (p>0.05).

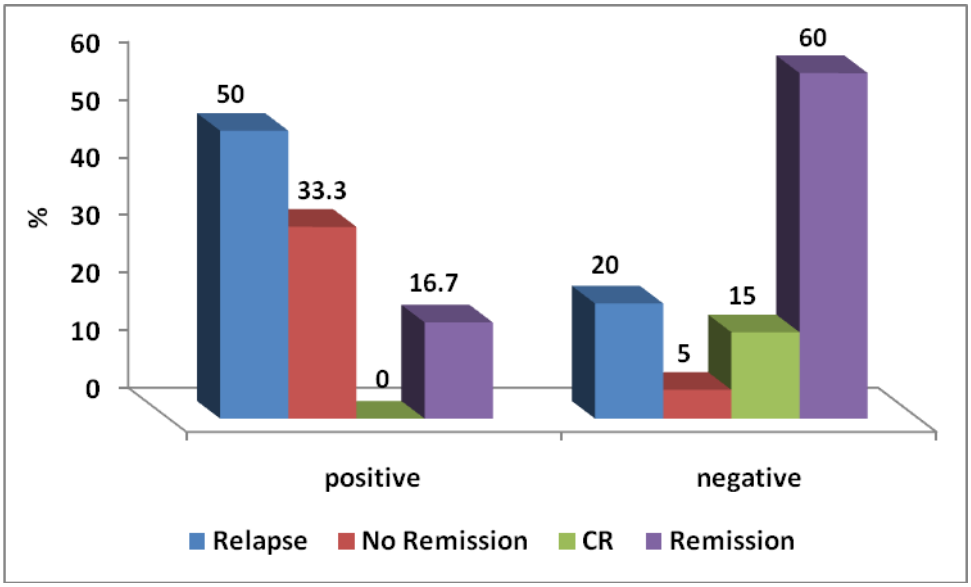


Figure (26): Fate of t(1; 19) positive and negative cases.

Table (25): Survival of t(1;19) positive and negative cases

Alive/Died	Positive (6)		Negative (20)		Total	
	No.	%	No.	%	No.	%
Alive	2	33.3	15	75	17	65.4
Died	4	66.7	5	25	9	34.6
X^2	1.94					
P	> 0.05					

Significant P<0.05

Statistical analysis reveals no significant difference between both positive and negative groups for t(1;19) regarding the survival of the patients (*p>0.05).*

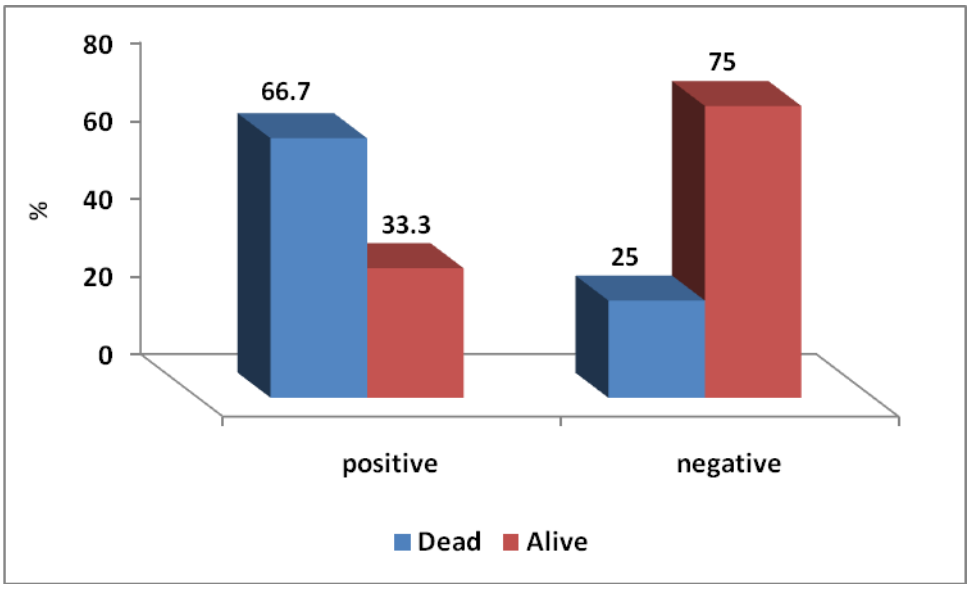


Figure (27): Survival of t(8;21) positive and negative cases

The relation between t(1;19)[PBX1/E2A] and t(9;22)[ABL/BCR]

Table (26): Relation between t(1;19) and t(9;22):

		t(1;19)		Total	Z	P
		Negative	Positive			
t(9;22)	Negative	7 (35%)	3 (50%)	10 (38.5%)	0.66	>0.05
	Positive	9 (45%)	2 (33.3%)	11 (42.3%)	0.51	>0.05
	Not Recorded	4 (20%)	1 (16.7%)	5 (19.2%)	0.18	>0.05
Total		20 (100%)	6 (100%)	26 (100%)	----	----

% of t(9;22) within t(1;19)results
Significant P<0.05

The statistical analysis of cases positive and negative for t(1;19) and/or t(9;22) reveals no significant correlation.

Table (27): Frequencies of t(1;19) and t(9;22):

	No.	%
Both Negative	7	26.9
One Positive	12	46.2
Both Positive	2	7.7
Not Recorded t(9;22) results	5	19.2
Total	26	100

By studing the frequency of both t(1;19) and t(9;22) among the studied group, only 2 cases (7.7%) are positive for both translocations, 7 cases (26.9%) are negative for both translocations and 12 cases (46.2%) are positive for only one of them.

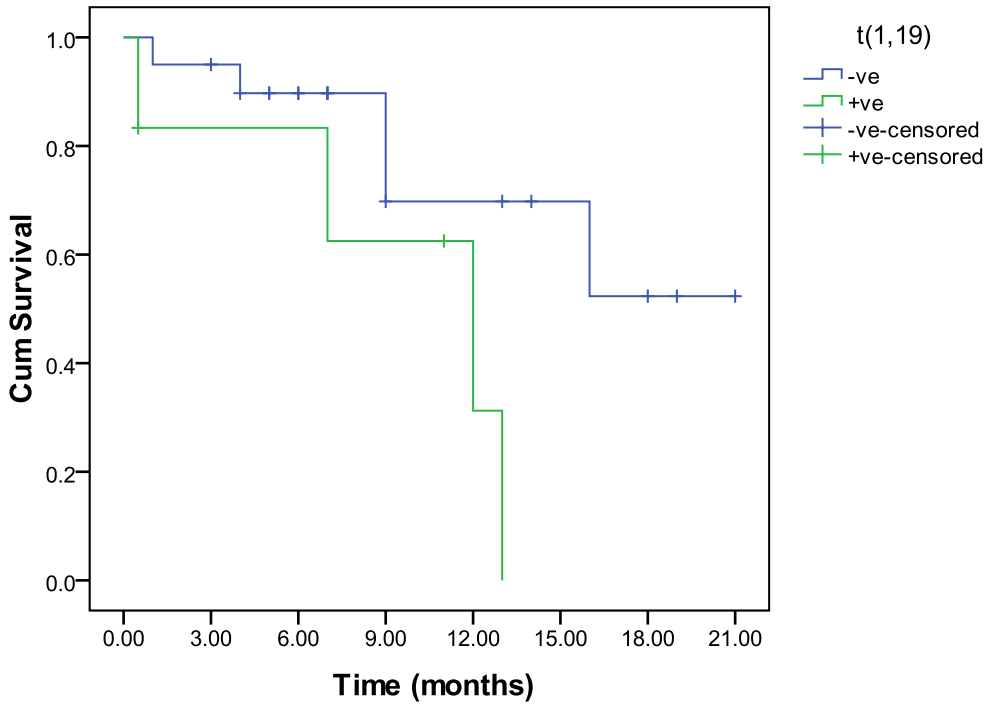
Table (28): Fate of t(1;19) and t(9;22):

		t(1;19) & t(9;22)			Total
		Both -ve	One +ve	Both +ve	
Fate	Remission	5 (71.4%)	6 (50%)	0 (0%)	5 (23.8%)
	Complete Rem.	0 (0%)	3 (25%)	0 (0%)	2 (9.5%)
	No Remission	0 (0%)	1 (8.3%)	1 (50%)	3 (14.3%)
	Relapse	2 (28.6%)	2 (16.7%)	1 (50%)	11 (52.4%)
Total		7 (100%)	12 (100%)	2 (100%)	21 (100%)
X^2		9.7			
P		>0.05			

Significant P<0.05

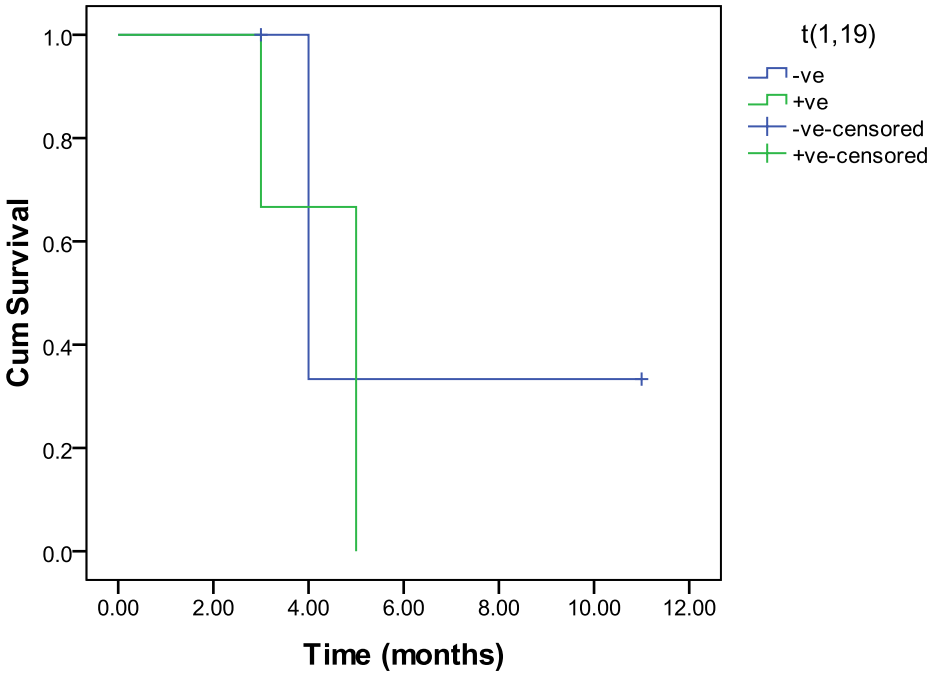
Regarding the fate of the t(1;19) and t(9;22) cases, statistical analysis reveals no significant difference between cases of both negative, both positive or one positive ($p>0.05$).

Kaplan-Meier analysis of overall survival, disease free interval and event free survival was used as prognostic test and showed a statistically significant decease in survival between patients positive and negative for FISH detected chromosomal abnormality in t(1;19). Bad prognosis observed in patients with FISH detected abnormality in t(1;19).



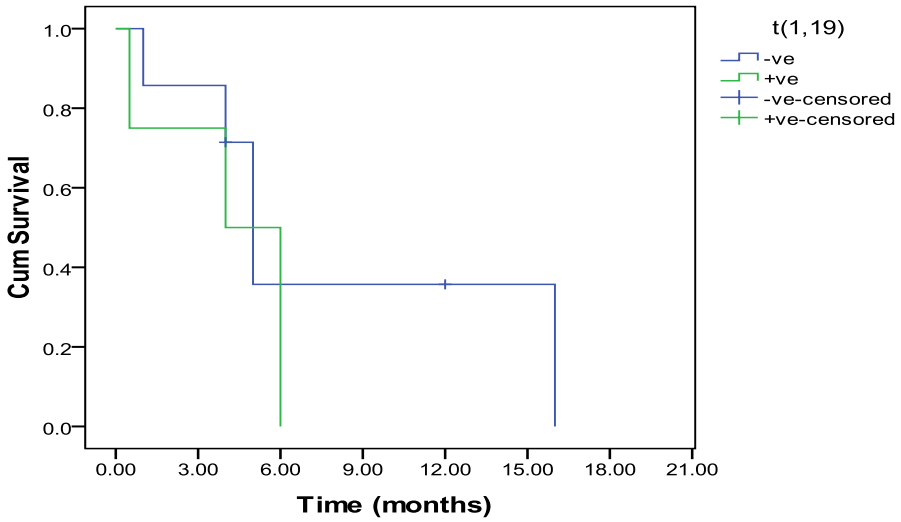
Log Rank test =3.98 P<0.05* (0.046)

Figure (28): Kaplan-Meier analysis of overall survival (OS) in cases with t(1;19) in studied group showed significant decrease in survival in these patients (P<0.05).



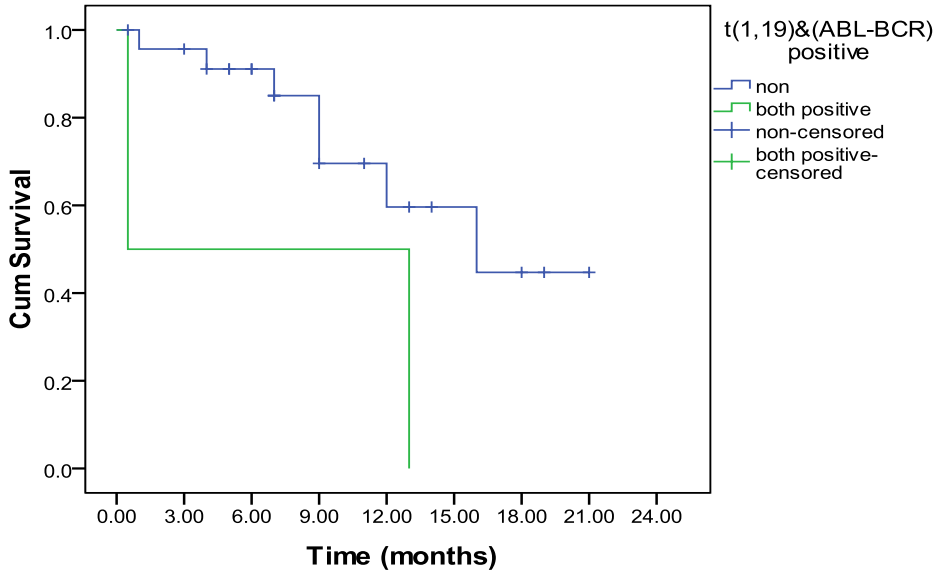
Log Rank test =0.23 P>0.05

Figure (29): Kaplan-Meier analysis of disease free interval (DFI) in cases with t(1;19) in studied group showed non significance in DFI in these patients (P>0.05)



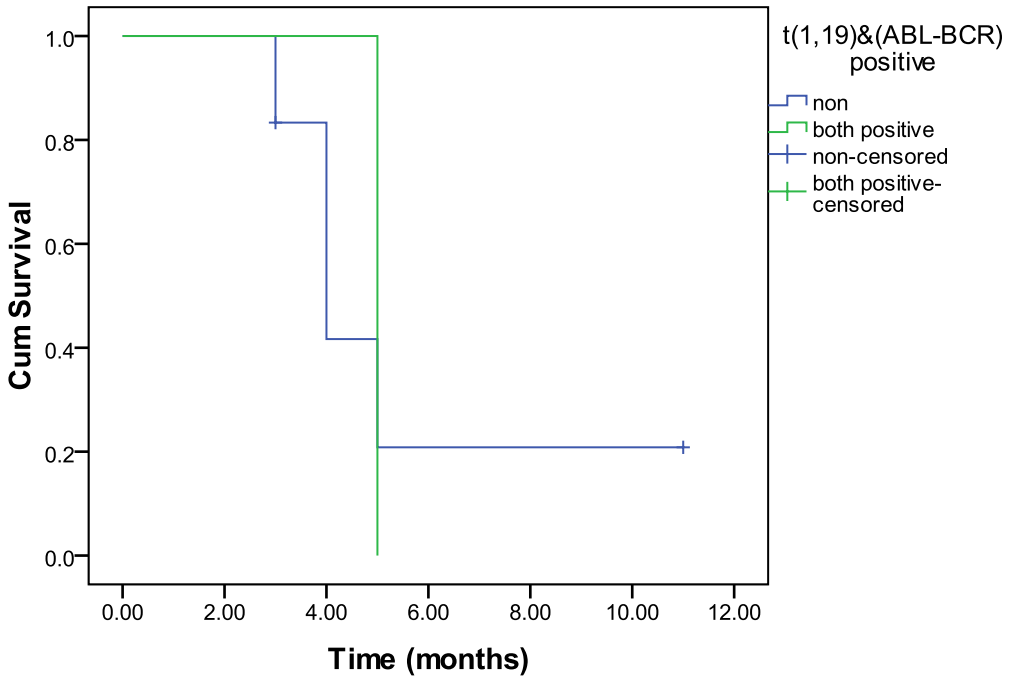
Log Rank test =0.66 P>0.05

Figure (30): Kaplan-Meier analysis of event free survival (EFS) in cases with t(1;19) in studied group showed non significance in EFS in these patients (P>0.05)



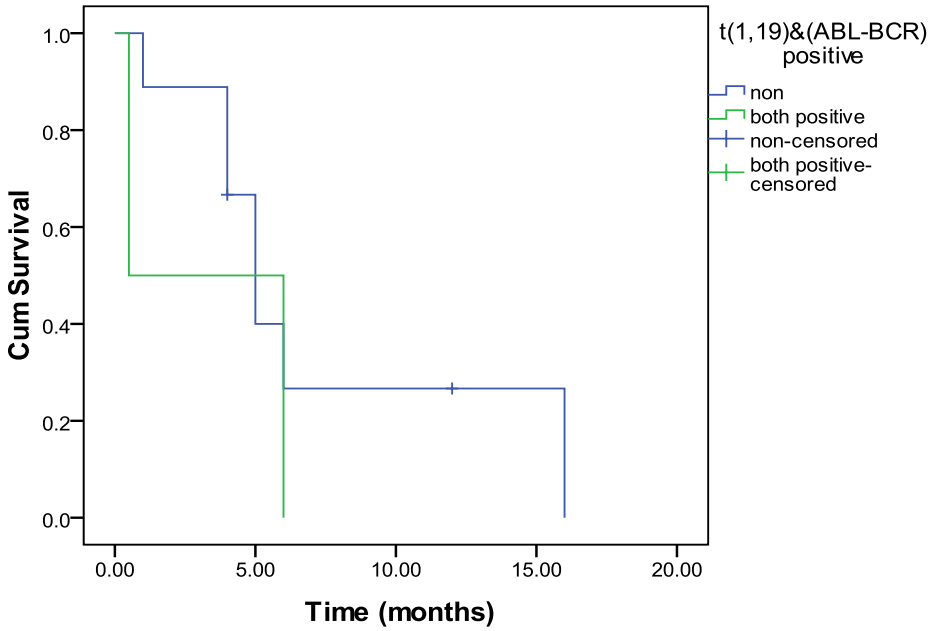
Log Rank test =3.07 P>0.05 (0.08)

Figure (31): Kaplan-Meier analysis of overall survival in cases with both t(1;19) and t(9;22)[ABL/BCR] in studied group showed non significance in survival in these patients.(P>0.05)



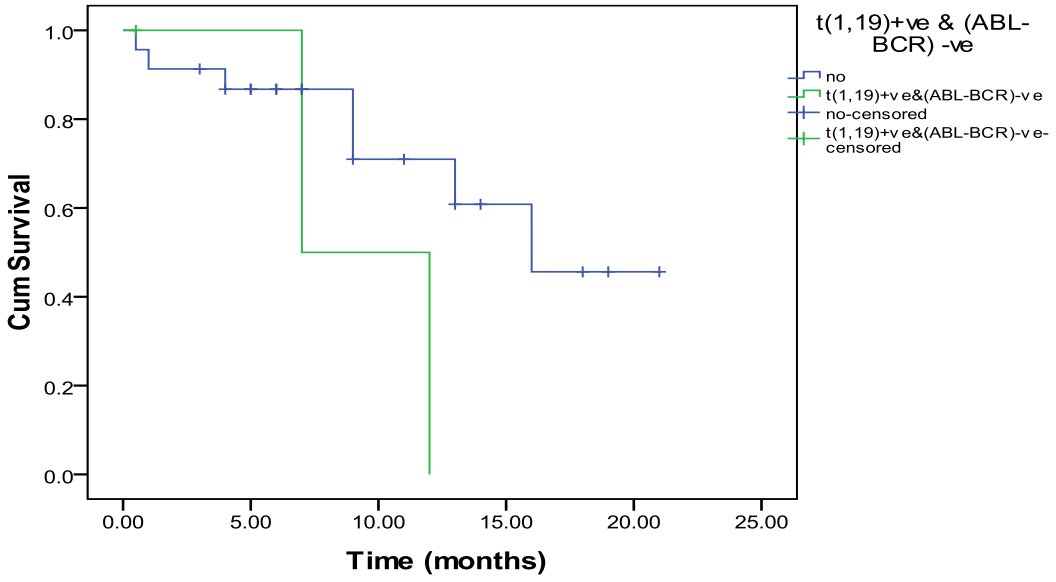
Log Rank test =0.075 P>0.05

Figure (32): Kaplan-Meier analysis of disease free interval (DFI) in cases with both t(1;19) and t(9;22) [ABL/BCR] in studied group showed non significance in DFI in these patients (P>0.05)



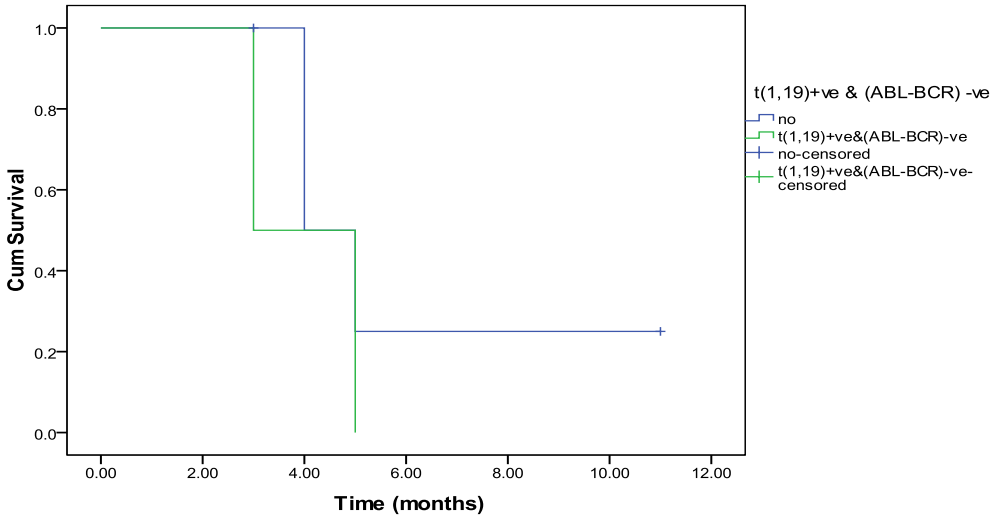
Log Rank test =0.497 P>0.05

Figure (33): Kaplan-Meier analysis of event free survival (EFS) in cases with both t(1;19) and t(9;22) [ABL/BCR] in studied group showed non significance in EFS in these patients (P>0.05)



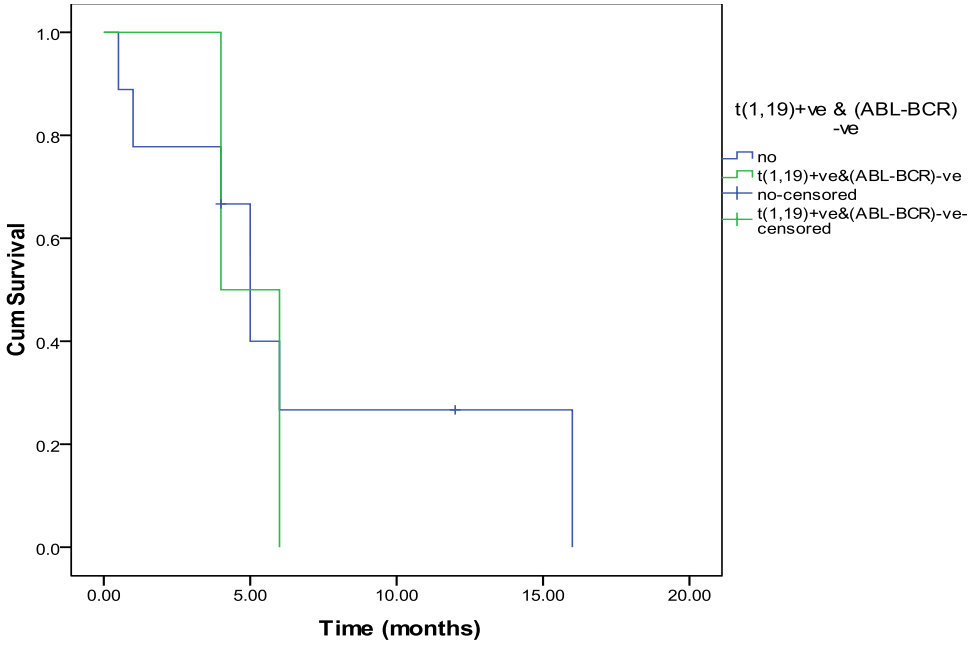
Log Rank test =2.7 P>0.05

Figure (34): Kaplan-Meier analysis of overall survival in cases with t(1;19) positive and t(9;22)[ABL/BCR] negative in studied group showed non significance in survival in these patients.(P>0.05)



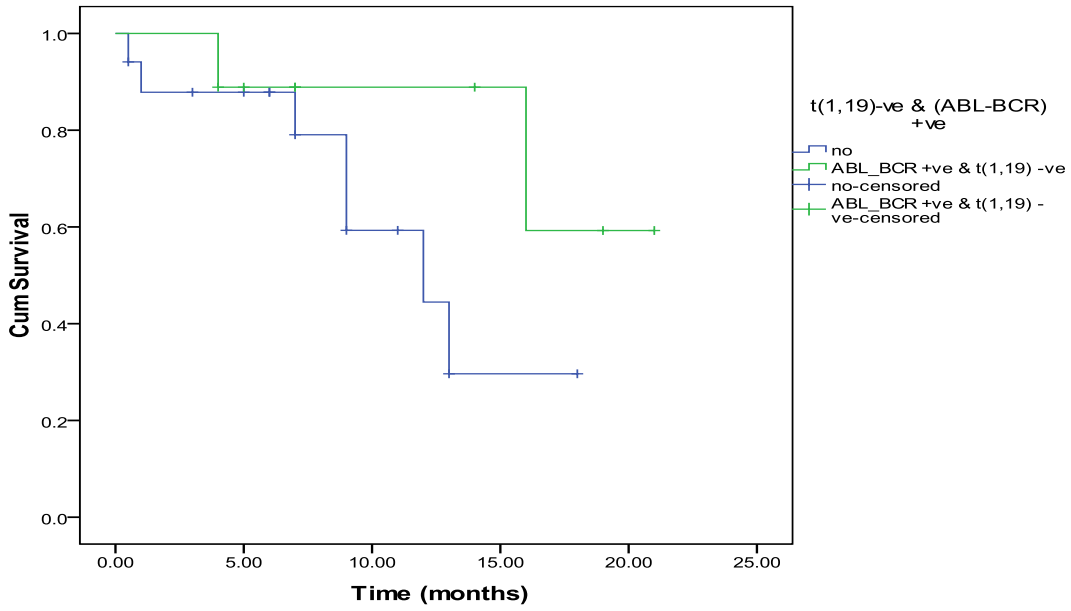
Log Rank test =0.63 P>0.05

Figure (35): Kaplan-Meier analysis of disease free interval (DFI) in cases with t(1;19) positive and t(9;22)[ABL/BCR] negative in studied group showed non significance in DFI in these patients.(P>0.05)



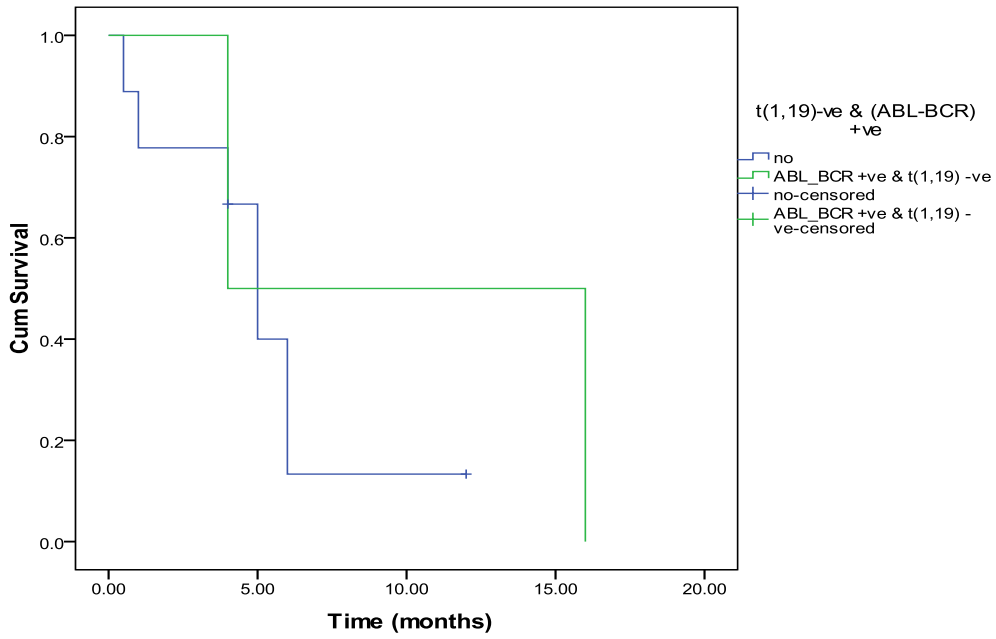
Log Rank test =0.107 P>0.05

Figure (36): Kaplan-Meier analysis of event free survival (EFS) in cases with t(1;19) positive and t(9;22)[ABL/BCR] negative in studied group showed non significance in EFS in these patients.(P>0.05)



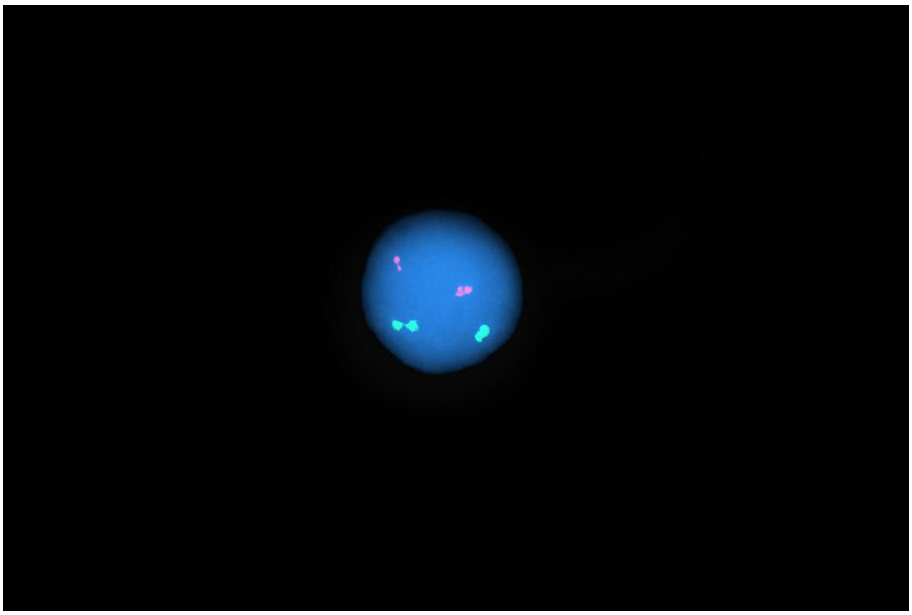
Log Rank test =1.96 P>0.05

Figure (37): Kaplan-Meier analysis of overall survival in cases with t(1;19) negative and t(9;22)[ABL/BCR] positive in studied group showed non significance in survival in these patients.(P>0.05)

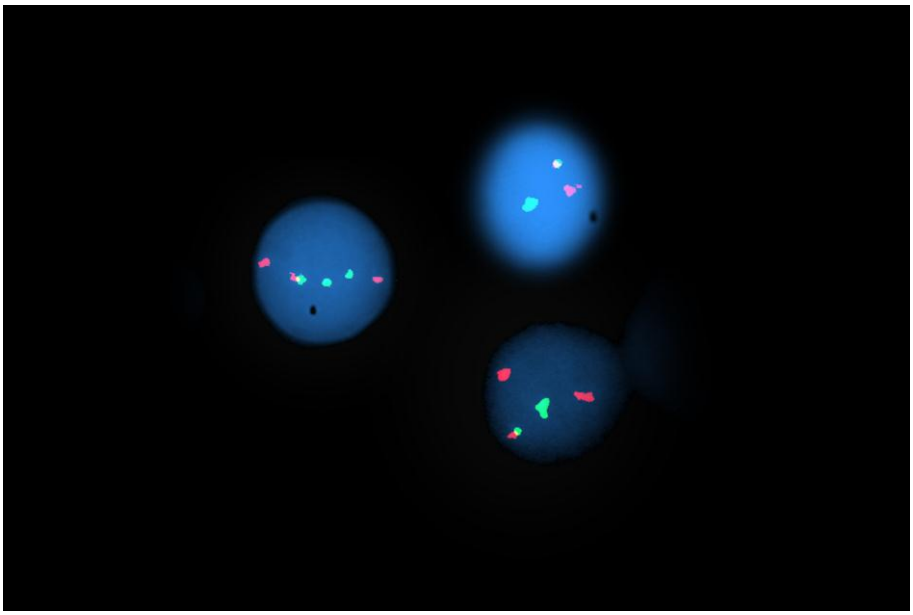


Log Rank test = 0.4 P>0.05

Figure (38): Kaplan-Meier analysis of event free survival in cases with t(1;19) negative and t(9;22)[ABL/BCR] positive in studied group showed non significance in EFS in these patients.(P>0.05)



Photograph 1: Fluorescence in situ hybridization (FISH) analysis of bone marrow cells using the Vysis LSI TCF3/PBX1 Dual Color, Dual Fusion Translocation Probe showing cell negative for t(1;19) containing the two orange signals for (PBX1) and two green signals for (TCF3).



Photograph 2: Fluorescence in situ hybridization (FISH) analysis of bone marrow cells using the Vysis LSI TCF3/PBX1 Dual Color, Dual Fusion Translocation Probe showing different cells positive for t(1;19) containing the TCF3/PBX1 fusion gene, as the orange signal for (PBX1), the green signal for (TCF3), and the orange/green (yellow) signal for the fusion gene are observed.