RESULTS

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SERUM THYMIDINE KINASE VALUES IN HEALTHY SUBJECTS IN RELATION TO AGE AND SEX

In order to determine the normal serum TK activity twenty sera from normal healthy children and adults were analysed.

Table (1) represents the serum (TK) values in different age and sex groups of healthy controls.

Among the pediatric cases: the (TK) ranged between 18 and 82 U/L with a mean ± standard deviation 41.2 ± 18 U/L for the females the range was between 18 and 42 U/L with a mean ±S.D. of 32 ± 9.3 U/L, and for the males it was between 25 and 82 U/L with a mean ± S.D. of 50.4 ± 25.8 U/L.

No statistical significant difference between male and female children cases was elicited.

In the adult age group, the serum (TK) level ranged between 2 and 43 U/L with a mean of 27.7 ± 13.9 S.D females had a range between 2 and 38 U/L with a mean of 21 ± 15.3 S.D. while the males had a range between 30 and 43 U/L with a mean of 36.3 ± 5.6 S.D., With no statistically significant sex variation.

It was also found that there is no significant difference between the mean (Tk) values in pediatric and adult age groups.

Pre-Treatment level in Acute Leukemia Cases

Analysis of the pre-treatment S-TK level for patients suffering from acute leukemia was carried out. The results showed that the pre-treatment S-TK level was significantly elevated in almost all patients with acute leukemia. Serum (TK) values in ALL and AML as compared to normal control are shown in table (2 and 3).

Among ALL cases, serum (TK) levels were elevated in 22 out of 23 children (95.7%) and 4 out of 5 adults (80%) with a mean ± S.D. 115.4 ± 11 U/L (range from 76-123 U/L) for children and 104.6 ± 19.1 U/L (range from 77-119 U/I) for adult.

In AML groups serum (TK) levels were elevated in 5 out of 6 children (83.3%) and 14 out of 15 adults (93.3%) with a mean ± S.D. (TK) levels of 99.3 ± 22.8 U/L (range from 61-120 U/L and in adult it was 106.6 ± 15.7 U/L (range from 67-120 U/L). The mean (TK) levels in all groups were significantly increased when they were compared to that of the control group ($P < 0.001$).

Fig. (I) and (II) shows the distribution of the pretreatment level of S-TK activity in pediatric and adult group among ALL and AML cases.

The cutoff value of (TK) being 80 U/L.

Results of (TK) level in relation to age group with ALL or AML are shown in table (4).

In ALL group the mean ± S.D. (TK) level in children < 10 years was 115.9 ± 8.0 U/L (range between 2.5-8 years) and > 10 years was 114.1 ±

16.9 U/L with no statistical significant difference between the two age groups. In adults range 19-35 years the mean ± S.D. of (TK) level was 104.6 ± 19.1 U/L. Also the difference between adulthood cases and childhood cases was not statistically significant

As regards AML cases the mean ± S.D. among the childhood cases was 99.3 ± 22.8 U/L and that for the adult was 106.6 ± 15.7 U/L with no statistical significant difference.

Table (5) shows the sex distribution in All and AML cases. ALL cases were characterized by male predominance. In childhood ALL 15 out of 23 (65.2%) were males, and 8 out of 23 (34.7%) were females with M/F ratio 1.88 and in adults 3 out of 5 (60%) were males an 2 out of 5 (40%) were females with M/F ratio 1.5.

The AML cases in our study were characterized by female predominance. In children 4 out of 6 (66.6%) were females and 2 out of 6 (33.3%) males with M/F ratio 0.5 and in adults 8 out of 15 (53.3) were females and 7 out of 15 (46.7%) were males with M/F ratio 0.88.

Common symptoms in ALL and AML are presented in table (6).

In ALL group hepatomegaly was encountered in 23 out of 28 patients (82.1%), splenomegaly in 24 out of 28 (85.7%) and lympadenopathy 25 out of 28 (89.3%).

In AML cases hepatomegaly was found in 8 out of 18 (44.4%), splenomegaly in 8 out 18 (44.4%) and lymphadenopathy in 8 out of 18 (44.4%).

(TK) level and hematological findings in acute leukemias are shown in table (7).

In ALL group the mean ± S.D. (TK) value for the cases that had hemoglobin level (< 7.0 gm/dl) was 112.9 ± 11.5 U/L and those (> 7.0 gm/dl) was 114.3 ± 12.9 U/L. The mean ± S.D. (TK) value for cases having total leucocytic count (< 50.000/ cmm) was 111.9 ± 13.2 U/L and those (> 50.000/cmm) was 112.5 ± 15.3 U/L, also with platelets count (< 50.000/cmm) (TK) value was 112.2 ± 13.2 ± U/L and with platelets (> 50.000/cmm) it was 115.4 ± 9.5 U/L as regards bone marrow infilteration if (< 70% blasts) (TK) value was 117.4 ± 4.0 U/L and If (> 70% blasts) (TK) value was 111.5 ± 15.1 U/L on the whole no significant difference was identified between S-TK value and hematological findings in ALL.

In AML the mean ± S.D. (TK) value for the cases that had hemoglobin (< 7.0 gm/dL) was 100.9 ± 21.8 U/L) and (> 7.0 gm /dL) was 109.9 ± 11.3 U/L., and for cases having total leucocytic count (< 50.000/cmm) was 101.1 ± 18.8 U/L and (> 50.000 / cmm) was 116.5 ± 7.0 U/L, also with platelet count (< 50.000/cmm) (TK) value was 103..8 ± 18.0 U/L and (> 50.000/cmm) was 105.0 ± 19.2 U/L and for bone marrow infilteration (with < 70% blasts) (TK) level was 104.2± 16.7 U/L and (> 70% blasts) 102.8 ± 22.9 U/L. No statistically significant difference between S-TK level and hematological parameter was found in AML cases.

Pre-Treatment S-TK Level
In Chronic Leukemia Cases

Analysis of the pre-treatment S-TK level for patients with CML and CLL was carried out. The results showed that S-TK value was elevated in all cases with chronic leukemias compared to the control cases, this is illustrated in table (2 and 3).

Among CML cases S-TK level were elevated 13 out of 13 adults (100%) with a mean ± S.D. was 120.5 ± 2.5 U/L (range from 116-124 U/L). There is statistically significant difference in CML group when compared to control group value ($P < 0.0001$).

Table (5) shows the sex distribution CML. CML cases was characterized by male predominance with 9 out of 13 (69.2%) was males and 4 out of 13 (30.8%) was females with M/F ratio 2.25.

Huge splenomegally was most common in CML 11 out of 11 (100%) ; hepatomegally was 6 out of 11 (54.6%) and lymphadenopathy was 3 out of 11 (27.3%). These results are illustrated in table (6).

In CLL the clinical and haematological finding of 8 patients are summarized in table (8). The mean age ± SD at presentation was 57.2 ± 6.6 years with a range from (49-70 y). This series comparised 5 out of 8 (62.5%) males and 2 out of 8 (37.5%) females with M/F ratio 5/3.

According to organomegaly spleen just palpable in 8 out of 8 (100%), lymphodenopathy 6 out of 8 (75%) and hepatomegaly 2 out of 8 (25%), all patients had normal liver enzymes at presentation. 2 out of 8 (25%) were anaemic on presentation (HB less than log/dl). Thrombocytopenia (platelets less than 100 x 10^9/L). was detected in 2 out of 8 (25%) of our

cases at presentation.

The patients were classified according to the *Rai staging system (1975)* 4 (50%) in stage II two in stage III (25%) and two in stage IV (25%) . Accordoing to the international clinical staging scheem for CLL cases *Binet et al., 1981* in each of which there is significantly differente prognosis making the classification useful in therapeutic decision. There was 4 out of 8 (50%) presented in stage (B) and 4 and of 8 cases (50%) in stage (C). The presence of most patients in stage B and C may be due to the fact that these are referred cases to the NCI (National cancer Institute) who did not seek medical advice until the disease become progressive.

Among CLL cases S-TK level was elevated 4 out of 8 (50%) with mean ± S.D was 98.5 ± 7.92 U/I and low in 4 out of 8 (50%) with mean ± S.D. was 55± 4.63 U/I. There is statistically significant difference in all group when compared to control group value ($P < 0.001$).

Fig. (I) shows the distribution of the pre-treatment S-TK level in CML and CLL cases. In CML we noted that there was no variability of the S-TK level while in CLL (TK) value was highly variable.

By analysis of variance (ANOVA) to our studied group we found that there was no significant statistically difference in S-TK level adult ALL and AML and between adult AML and CML. These are represented with symbol (A) in table (2).

On the contrary there was a significant difference between ALL (adult and childhood) and CLL which is represented with symbol (B) and between ALL and AML of the childhood.

Comparing our results achieved in all types of leukemias with the control cases, we found statistically significant difference between them

the control group was respresented in table (2) with symbol (C).

Serum (TK) Value in Relation to Leukemia Status:

Thymidne kinase level of the patients during reminssion is iillustrated in Fig. (3).

All cases (18 patients) that achieved complete remission showed rapid fall of (TK) to the normal level while the three cases that did not achieve complete remission at the time of our evaluation had their (TK) above normal value.

Cases that were evaluated during the maintenance period showed also a rapid fall of (TK) to normal level Fig. (4).

On the contrary, when S-TK level for cases that relapsed was compared to the level of (TK) pre-treatment did not show any difference Fig. (5).

Table (9) illustrates that the mean ± S.D. (S-TK) level in leukemia patients after complete remission was 58.2 ± 22 U/L this is compared to the pre-treatment S-TK level mean ± S.D. 112.1 ± 14.1 U/L and the difference between them was highly significant ($P < 0.0001$).

Evaluation of the S-TK level during the maintenance period after complete remission showed mean ± S.D. 49.6 ± 13.3 U/L which is also highly significant if compared to the pre-treatment value mean ± S.D. was 116. 1 ± 7.2 U/L ($P < 0.0001$).

On the contrary the patients with relapsed leukemia had elevated S-TK value mean ± S.D. 111.4 ± 8.1 U/L compared to the pre-treatment S-TK value mean ± S.D. 118.2 ±5.5 U/L. There is no statistically significant difference between the two groups ($P < 0.0338$).

S-TK level in longitudinal studies of leukemic patients related to remission, maintenance and relapse:

Representative examples of variation in S-TK level for 6 patients (3 ALL, 2AML and one ABC on top of CML) during remission-maintenance and relapse and 3 patients (2 ALL & one AML) during remission and manitenance we given in Fig (6) and (7). Which shows that a rapid fall in S-TK value was observed after complete remission followed by normalization S-TK level. This was continue during maintenance.

Progression and relapse of the disease was accompained by increase S-TK level nearly to the pre-treatment level. This is discrimination analysis was performed in order to find the S-TK level for distingushing the four stages of leukemia (pretreatment remission-maintenance-relapse).

Serum TK level in relation to ALL prognostic factors:

Serum TK value in relation to prognostic factors in ALL cases was illustrated in table (10) as comparing the S-TK level to the prognostic factors of All in pediatric age group we found there is borderline significant difference between the S-TK level and the total leucocytic count, but there is no significant between S-TK level and age, sex. Most of cases studied has organomegally (lymphadenopathy and splenomegally). So we cannot able to show the significant of S-TK level and cases who had orgnomegally or not.

For morphological typying to our studied group all cases has L_2 type except three cases had L_1so it is difficult to show the significant effect on the level of S-TK this could be due to the limited number of cases. C.N.S infilteration reported to worsen the prognosis, but in ALL studied group no C.N.S. leukemia was mainfested clinically and laboratory through C.S.F. examination.

Table 1. Serum TK level (U/L) in relation to age and sex of control group.

Group	No.	Mean±SD	Range
Adult			
Total	10	27.8±13.9	2-43
Male	4	36.3± 5.6	30-43
Female	5	21.0±15.3	2-38
Children			
Total	10	41.2±18.0	18-82
Male	5	50.4±20.8	25-82
Female	5	32.0± 9.3	18-42

Table 2. Pretreatment serum levels (U/L) of TK activity in different types of leukemia and controls.

Groups	Mean±SD	Range	ANOVA results[b]
Adult			
Controls	27.8±13.9	2-43	C
ALL	104.6±19.1	77-119	A
AML	106.6±15.7	67-120	A
CML	120.5± 2.5	116-124	A
CLL	71.7±24.1	45-108	B
P-value[a] = 0.0001			
Children			
Controls	41.2±18.0	18-82	C
ALL	115.4±11.1	76-123	A
AML	99.3±22.8	61-120	B
P-value[a] = 0.0001			

[a] P-value less than 0.05 is considered significant.
[b] ANOVA reults = Analysis of variance results
Means with same letter are not significantly different.

Table 3. Frequency of abnormal TK levels (U/L) in different types of leukemia.

Types	Total No.	TK < 80 UL	
		Number	Percent
Adult			
ALL	5	4	80.0
AML	15	14	93.3
CML	13	13	100.0
Children			
ALL	23	22	95.7
AML	6	5	83.3

Table 4. Serum TK level (U/L) in relation to age in patients with ALL and AML.

Factors	No.	Mean±SD
Childhood ALL		
2-10 yrs	16	115.9± 8.0
<2 and >10	7	114.1±16.9
Adulthood ALL	5	104.6±19.1
Childhood AML	6	99.3±22.8
Adulthood AML	15	106.6±15.7

Table 5. Sex distribution in studied groups.

Groups	Male N (%)	Female N (%)	Total N	M/F ratio
ALL				
Childhood	15(65.2)	8 (34.7)	23	1.88
Adulthood	3(60.0)	2 (40.0)	5	1.50
AML				
Childhood	2(33.3)	4 (66.6)	6	0.50
Adulthood	7(46.7)	8 (53.3)	15	0.88
CML	9(69.2)	4 (30.8)	13	2.25

Table 6. Frequency of organomegaly in studied groups.

Organomegaly	ALL (N=28) N (%)	AML (N=19) N (%)	CML (N=11) N (%)
Hepatomegaly	23(82.1)	8(44.4)	6(54.6)
Splenomegaly	24(85.7)	8(44.4)	11(100.0)
Lymphadenopathy	25(89.3)	8(44.4)	3(27.3)

Table 7: Serum TK level (U/L) in relation to hematologic findings in patients with ALL and AML.

Hematologic finding	ALL No.	ALL Mean±SD	ALL P-value[a]	AML No.	AML Mean±SD	AML P-value
Haemoglobin						
≤7.0g/dl	11	112.9±11.5		11	100.9±21.8	
>7.0g/dl	17	114.3±12.9	N.S.	7	109.9±11.3	N.S.
Total leucocytic count						
≤50,000/cmm	14	111.9±13.2		15	101.1±18.8	
>50,000/cmm	10	112.5±15.3	N.S.	4	116.5± 7.0	N.S.
Platelet count						
≤50,000/cmm	14	112.3±13.2		10	103.8±18.0	
>50,000/cmm	8	115.4± 9.5	N.S.	9	105.0±19.2	N.S.
Bone marrow infiltration						
≤70% blasts	8	117.4± 4.0		13	104.2±16.7	
>70% blasts	20	111.5±15.1	N.S.	6	102.8±22.9	N.S.

[a] P-value less than 0.05 is considered significant,
N.S. = Not significant

Table 8. Clinical and haematological finding in CLL cases.

Finding	Number	Percent
Total number of cases	6	75
Age		
Mean±SD(range)	57.2± 6.6	49.0-70.0
Organomegaly		
Lymphadenopathy	6	75
Splenomegaly	8	100
Hepatomegaly	2	25
Hematologic finding		
Lymphocytosis ($15x10^9/L$)	8	100
Haemoglobin (10gm/dL)	2	25
Platelets ($10x10^9/L$)	2	25

Table 9. Serum TK levels (U/L) before and after treatment in studied groups.

Time	Number	Mean±SD	P-value
Remission			
Before TX	21	112.1±14.1	
After TX		58.2±22.6	
Before-After		53.9±23.9	0.0001
After remission			
Before TX	9	116.1± 7.2	
After TX		49.6±13.3	
Before-After		66.6±16.6	0.0001
Relapse			
Before TX	9	118.2± 5.5	
After TX		111.4± 8.1	
Before-After		6.8± 7.9	0.0338

[a] P-value less than 0.05 is considered significant.

Table 10. Mean (± standard deviation) of TK levels (U/L) by different prognostic factors among ALL children.

Factors	Mean±SD	P-value
Age		
2-10 yrs	115.1± 8.0	
<2 and >10	114.1±16.9	0.8033
Sex		
Male	114.1±13.3	
Female	117.6± 4.5	0.3698
White blood count		
≤50	111.4±13.6	
>50	120.0± 2.0	0.0456

a P-value less than 0.05 is considered significant.

Figure 1. Serum levels of TK (U/L) activity in various types of leukemia among adults.

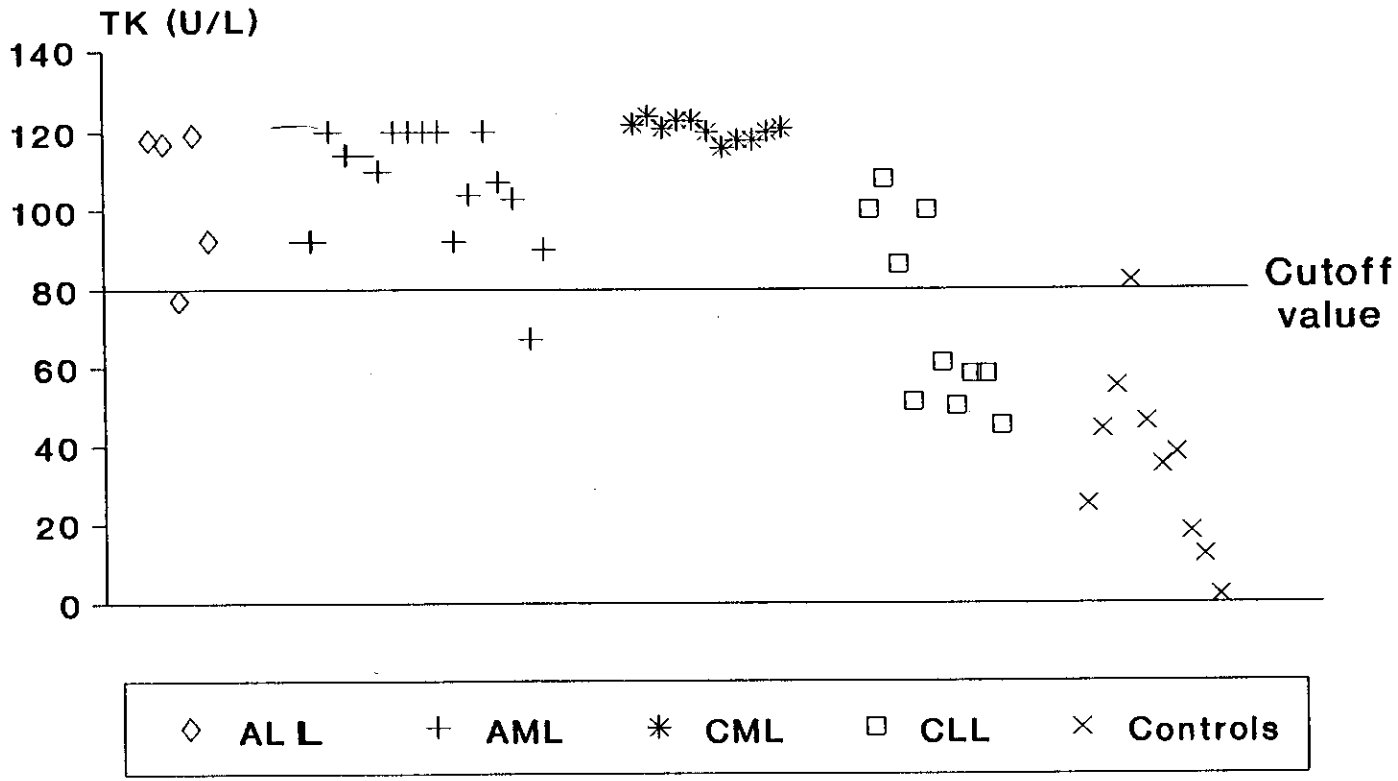

Figure 2. Pretreatment serum levels of TK (U/L) activity in various types of leukemia among children.

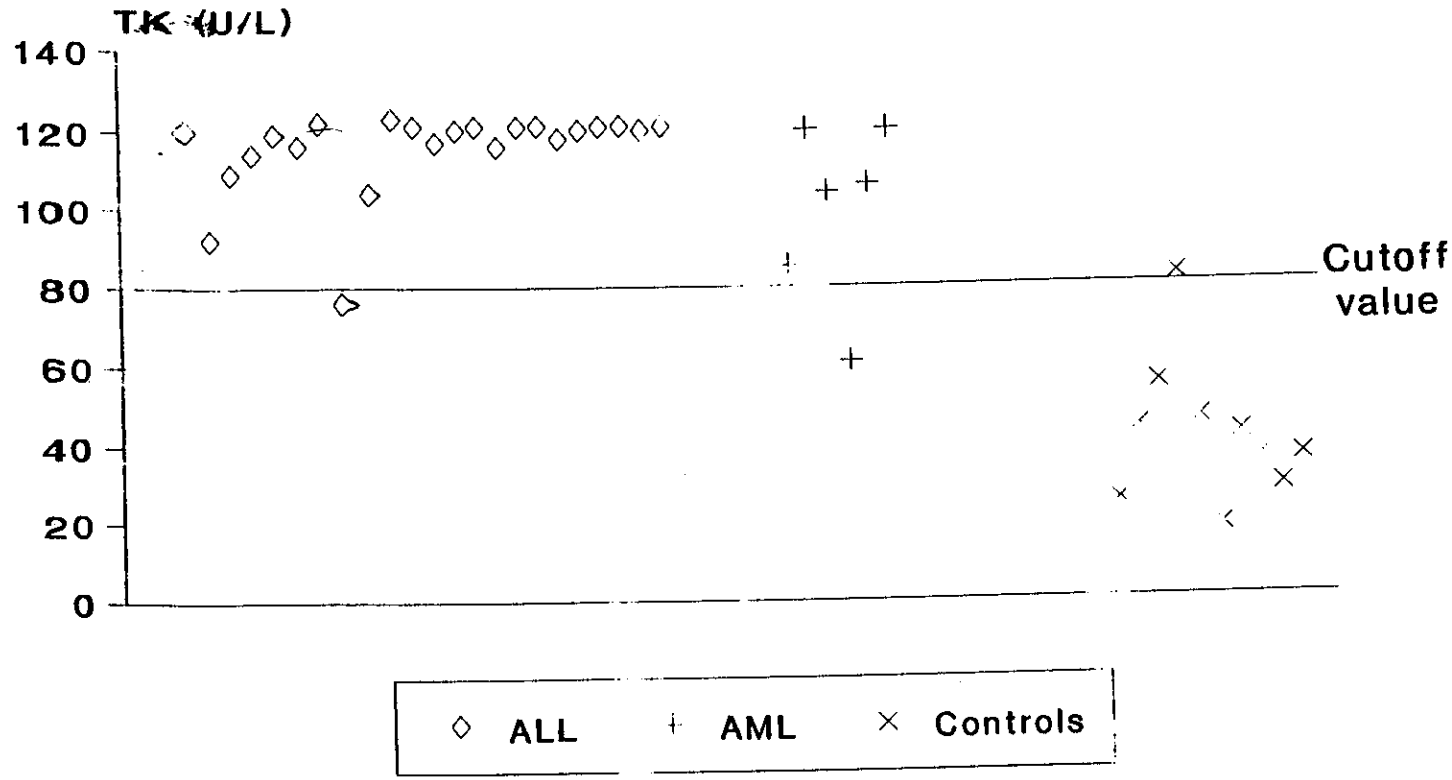

Figure 3. Pre treatment serum TK (U/L) and during remission

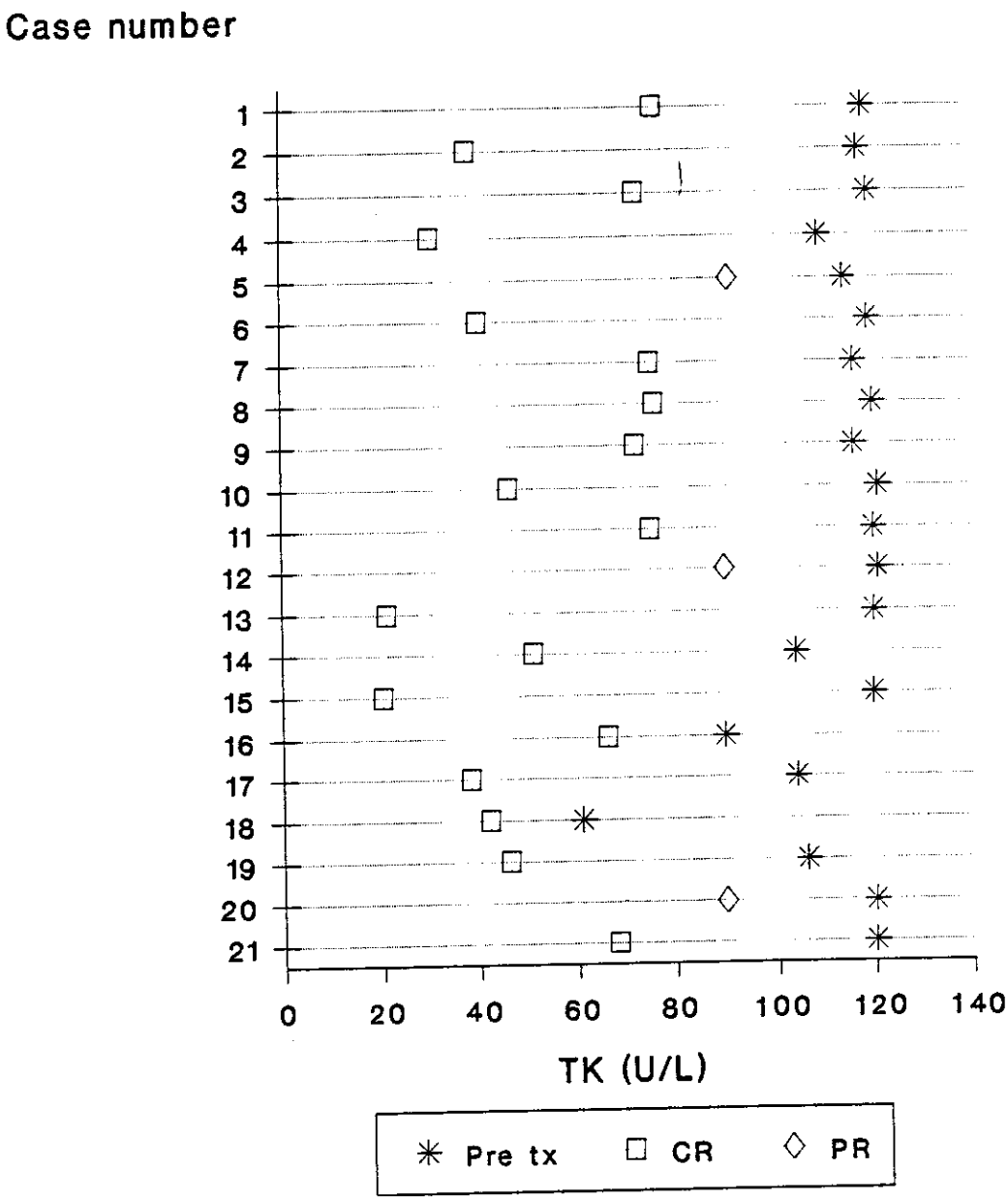

Figure 4. Pre treatment serum TK (U/L) and during maintenance

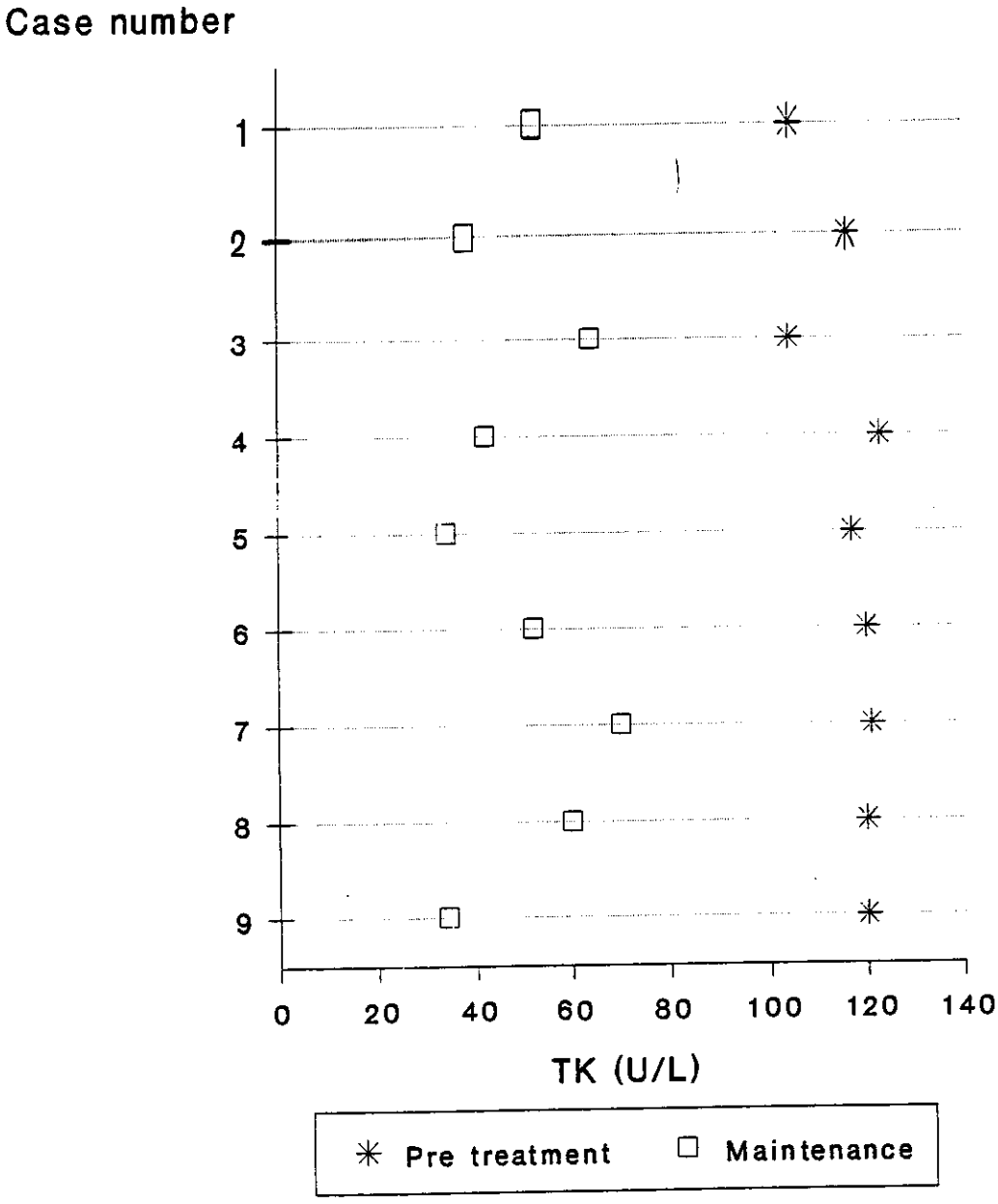

Figure 5. Pre treatment serum TK (U/L) and during relapse

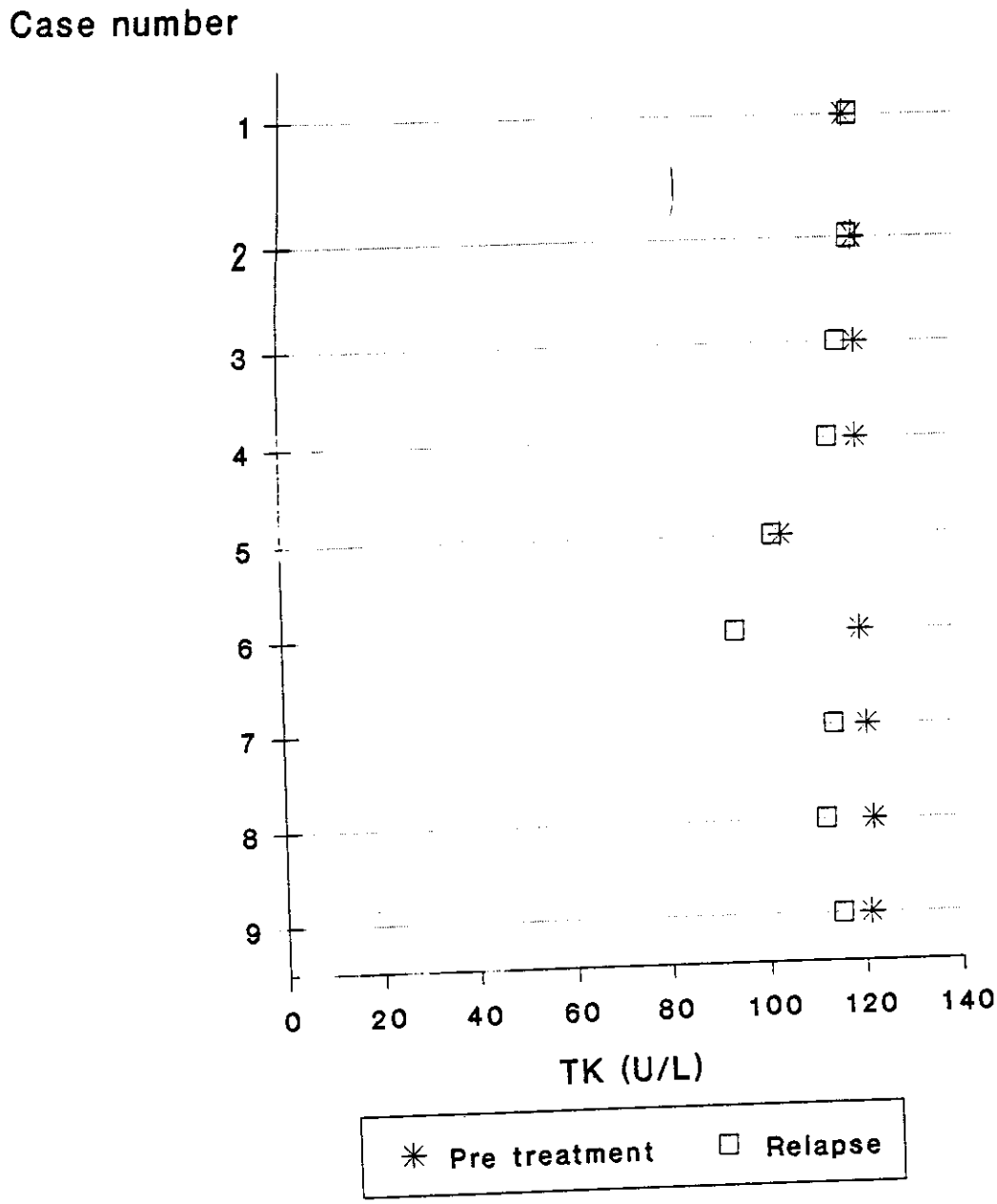

Figure 6. Serum TK (U/L) among cases who went to remission then maintencance and then relapsed.

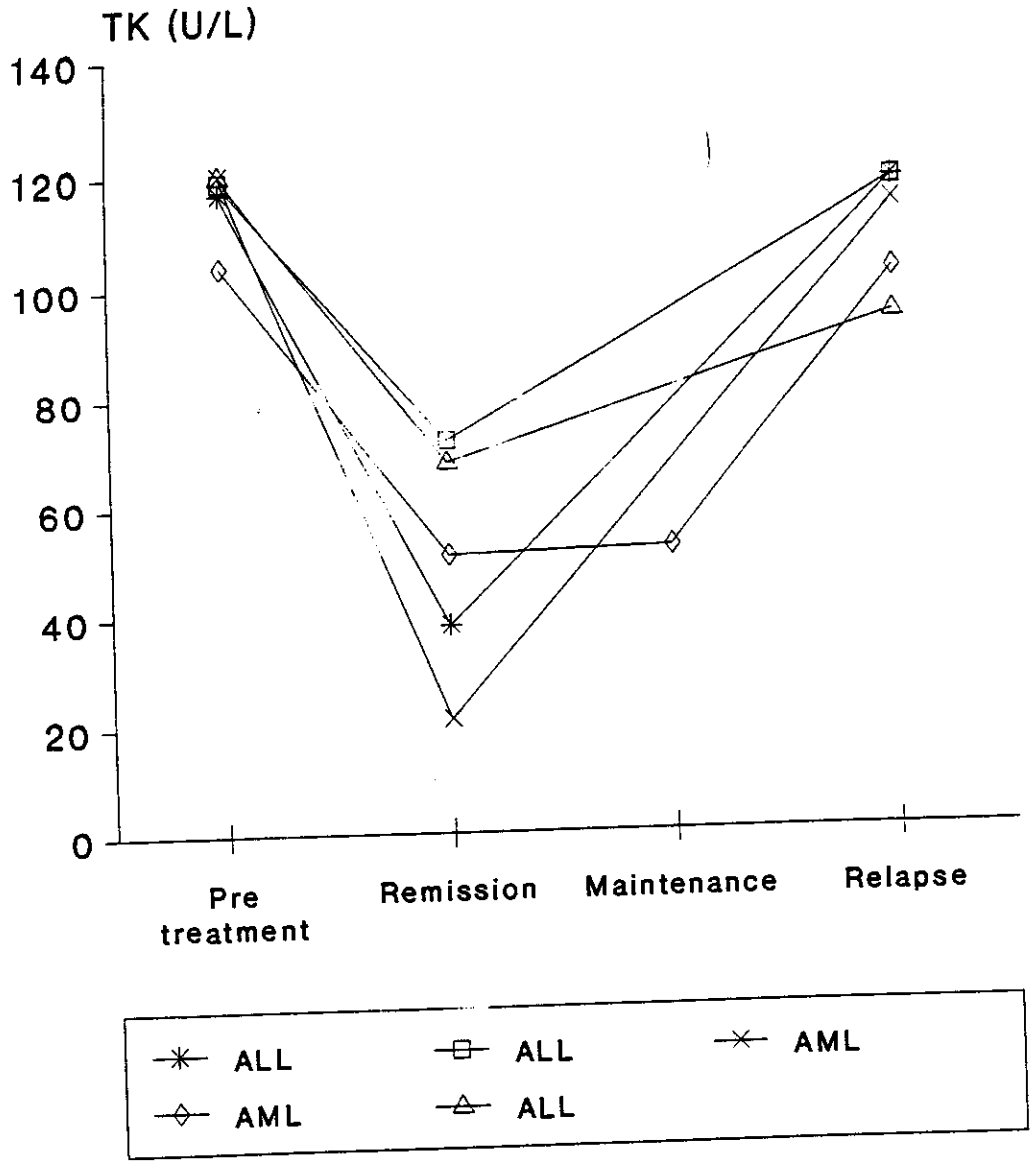

Figure 7. Serum TK (U/L) among cases who went to remission then maintencance.

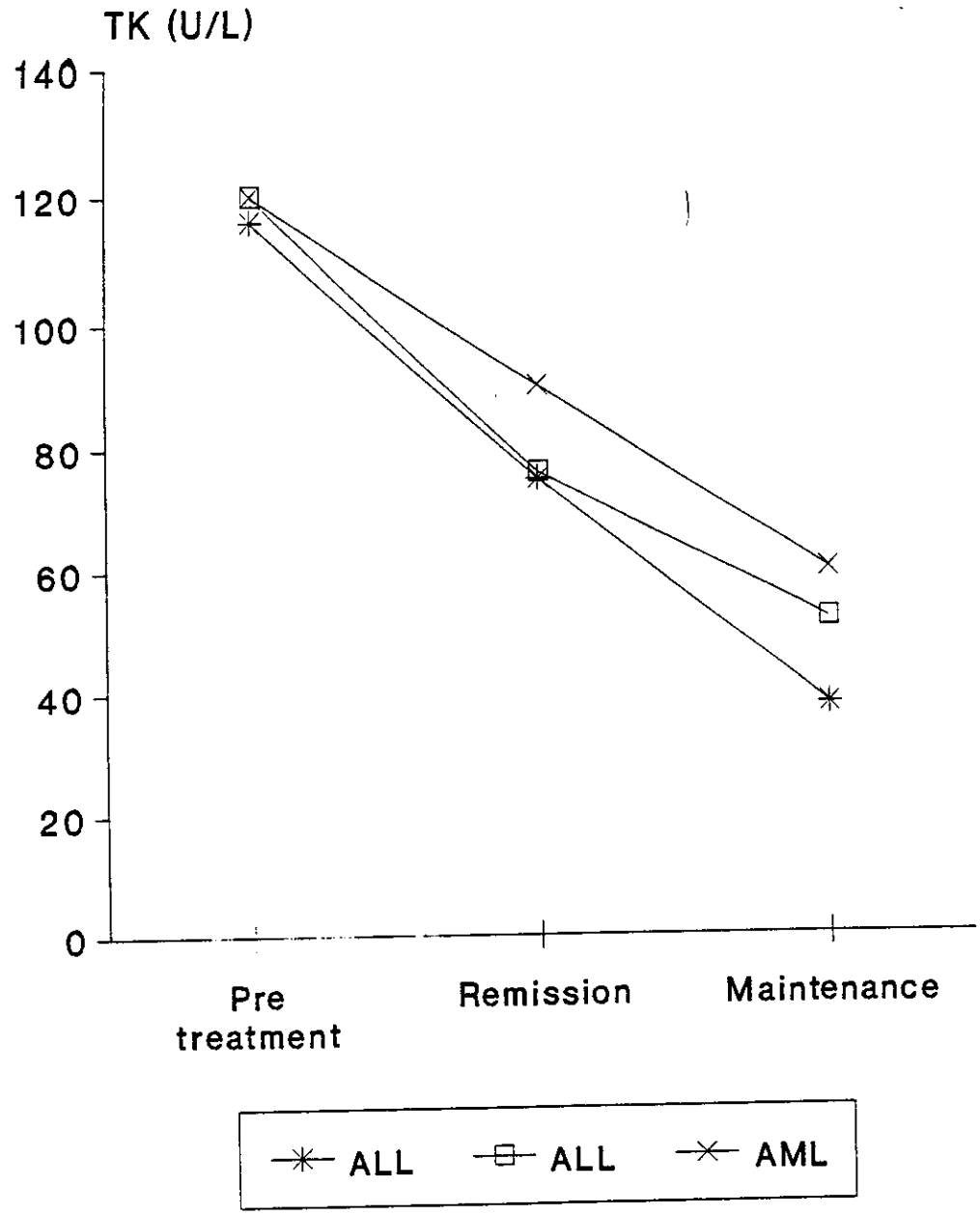

Table 11. Data collected from children ALL patients.

Case	Age	Sex	FAB	Hb	WBC	Plt	Blast	Pretx	Remis	Relapse	Maint
1	8	M	L2	8.38	3.87	140	79	120	.	.	.
2	7	M	L2	4.39	12.35	67	82	92	.	.	.
3	7	F	L2	8.00	4.00	25	56	109	30	.	.
4	3	F	L2	7.84	10.77	23	95	114	91	.	.
5	6	M	L2	8.50	63.60	48	91	119	40	.	.
6	8	M	L2	4.66	4.18	10	63	116	75	.	38
7	5	F	L2	9.33	25.36	24	97	122	.	112	.
8	16	M	L1	.	43.00	.	80	76	.	.	.
9	2	M	L1	5.43	8.08	24	93	104	.	.	64
10	15	M	L2	3.66	73.76	14	95	123	.	.	42
11	15	M	L2	.	.	.	98	121	.	.	.
12	13	F	L2	9.90	156.80	61	80	117	.	.	34
13	12	M	L2	4.33	92.22	14	99	120	76	.	52
14	11	M	L2	7.78	119.20	25	88	121	.	.	.
15	2	F	L2	4.33	8.42	24	60	116	72	.	.
16	6	M	L1	6.95	9.91	48	60	121	.	.	.
17	4	M	L2	7.99	18.70	.	61	121	46	.	.
18	6	M	L2	8.30	19.43	85	67	118	.	.	.
19	4	M	L2	6.00	208.00	75	94	120	.	.	.
20	2	F	L2	.	.	.	39	121	.	115	70
21	6	F	L2	.	.	.	91	121	.	.	.
22	5	M	L2	5.46	8.17	79	90	120	75	.	.
23	13	F	L2	.	.	.	86	121	90	.	.

Table 12. Data collected from children AML patients.

Case	Age	Sex	FAB	Hb	WBC	Plt	Blast	Pretx	Remis	Relapse	Maint
1	5	F	M5	5.40	5.06	6	46	85	.	.	.
2	8	F	M2	7.81	9.73	13	70	120	.	.	.
3	8	F	M2	5.07	22.00	70	34	104	38	.	.
4	15	M	M1	3.40	16.10	88	82	61	42	.	.
5	14	M	M2	8.05	89.87	95	62	106	46	.	.
6	12	F	M2	6.62	23.46	67	43	120	90	.	60

Table 13. Data collected from adult ALL patients.

Case	Age	Sex	FAB	Hb	WBC	Plt	Blast	Pretx	Remis	Relapse	Maint
1	35	F	L2	5.20	11.09	45	85	118	76	.	.
2	22	M	L2	.	60.21	59	60	117	38	118	.
3	28	M	L2	7.90	133.70	20	92	77	.	.	.
4	23	M	L2	8.72	87.90	57	93	119	72	118	.
5	19	F	L2	5.50	131.80	34	94	92	.	.	.
6	36	M		.	.	.	.	.	25	.	.
7	22	M		.	.	.	.	.	.	95	.

Table 14. Data collected from adult AML patients.

Case	Age	Sex	FAB	Hb	WBC	Plt	Blast	Pretx	Remis	Relapse	Maint
1	70	F	M2	3.50	19.00	25	33	92	.	.	.
2	37	M	M2	3.05	20.00	8	62	120	.	.	.
3	24	F	M2	4.81	8.51	52	89	114	.	.	.
4	30	M	M1	8.23	36.62	59	89	110	.	.	.
5	34	M	M4	9.09	87.52	86	.	120	.	116	.
6	18	M	M2	.	.	.	44	120	21	114	.
7	23	F	M1	4.57	3.47	15	86	120	.	.	.
8	54	M	M2	2.40	94.11	19	51	120	.	.	.
9	28	M	M5	.	.	.	84	92	.	.	.
10	28	F	M4	.	27.50	22	63	104	51	102	52
11	25	M	M1	7.56	103.30	68	89	120	20	.	.
12	35	F	M2	5.58	49.95	25	35	107	.	.	.
13	69	M	M2	7.17	16.50	13	.	103	.	.	.
14	37	F	M5	3.40	12.54	47	65	67	.	.	.
15	30	F	M2	9.94	6.98	101	70	90	66	.	.

Table 15. Data collected from adult CLL patients.

Case	Age	Sex	FAB	Hb	WBC	Plt	Blast	Pretx	Remis	Relapse	Maint
1	62	F		5.00	250.00	.	.	100	.	.	.
2	53	F		10.2	13.33	188	.	108	.	.	.
3	70	F		7.60	300.00	.	2	86	.	.	.
4	55	H		11.8	30.88	93	.	51	.	.	.
5	49	H		13.7	166.60	156	.	100	.	.	.
6	57	H		10.2	167.20	80	.	61	.	.	.
7	50	H		11.6	155.00	188	.	50	.	.	.
8	60	H		11.4	89.20	137	2	58	.	.	.

Table 16. Data collected from adult and children CML patients.

Case	Age	Sex	FAB	Hb	WBC	Plt	Blast	Pretx	Remis	Relapse	Maint
1	60	F		14.0	700.00	.	9	122	.	.	.
2	27	F		11.4	128.00	457	2	124	.	.	.
3	39	H		.	144.00	.	.	121	.	.	.
4	20	H		14.1	124.00	192	.	123	.	.	.
5	55	H		10.7	146.80	169	2	123	.	.	.
6	43	H		8.40	150.00	.	9	120	68	94	34
7	18	H		7.00	5.50	25	10	116	.	.	.
8	35	F		.	.	.	.	118	.	.	.
9	30	H		.	.	.	1	118	.	.	.
10	55	H		.	.	.	.	120	.	.	.
11	39	H		7.00	36.13	.	.	121	.	114	.
12	15	H		10.3	150.00	646	4	120	.	.	34
13	12	F		9.70	110.40	151	3	120	.	.	.