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CENTRAL NERVOUS SYSTEM RELAPSE IN CHILDREN WITH ACUTE LEUKEMIA

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SUMMARY

During 12 years, eight hundred and seventy patient with acute leukemia were treated and seen for follow up Central Teaching Hospital for children to study the incidence of CNS relapse and the relationship between CNS relapse with some prognostic factors, the ages of patients between 5 months and 15 years, the result shows the percentage of CNS relapse was 26.55% which include ALL and AML the percentage of relapse in ALL 29.8% & AML 11.18%. and the relapse more in male than female. Among the factors influencing the increase in incidence of CNS relapse are sex (male), high initial WBC count >10000/mm^3, initial organomegaly and low initial platelets count <100 000/mm^3. Also the result show the more relapse occur in first year of diagnosis 72.29% and also there is recurrence of CNS relapse and more in 3-6 months between first and second relapse. Also the prognosis of CNS relapse is poor and most of them die or loss of follow up during first year after relapse.

INTRODUCTION

Every patient with ALL and many patient with AML receive specific CNS therapy designed to prevent proliferation of leukemic cells within the CNS, nonetheless, CNS relapses continue to occur, albeit at low rate, despite widespread application of these preventive measures.

Definition

The definition of CNS leukemia at most centers specifies. The presence of at least 5 leukocyte per ml. of CSF plus leukemic blast cells in a cyto centrifuge sample of the fluid or the presence of cranial nerve palsies.

Incidence of CNS leukemia

Some study prove that meningeal leukemia used to occur in three of every four children during the first 4 years after diagnosis of leukemia and some said that 50-70 % children who don't receive CNS prophylaxis will develop CNS leukemia

Patho physiology CNS leukemia

Lymphoblast probably reach the CNS via haematogenous spread by migrating out of blood vessels into the meninges or by direct extension from cranial bone marrow in to the arachnoid.

Clinical picture of CNS leukemia

1. infiltration of brain substance with leukemic cells result in mass lesions with symptoms of increase intracranial pressure like (headache, vomiting, papilloedema, lethargy, diplopia, blurred of vision).
2. diffuse meningeal involvement: These children present with increase intracranial pressure, fever is usually absent, Other symptoms and sign of CNS leukemia is fascial nerve palsy

Prognosis of CNS leukemia

Children with a relapse confined to the CNS as the first site of relapse who are off therapy when they relapse have the best prognosis in those who have an isolated CNS relapse on therapy. The prognosis is best in those with longest interval to CNS relapse and particularly if the interval is more than 12 to 18 months.

Diagnosis of CNS leukemia

1. Lumber puncture and CSF examination.
2. Plain X- ray of skull if there is sign of increase ICP.
3. Magnetic resonance imaging.
4. Computerized tomography of brain before and after contrast administration.

Factors influencing CNS relapse

Age and sex

Some study said that there was a significant higher risk for boys than for girls to relapse in the CNS, and no significant effect of age on CNSL.

Initial W.B.C. count

High initial WBC count more than 10000/mm was associated positively with the incidence of CNS relapse.

Initial platelet count

The lower the initial platelets count the greater the incidence of CNS relapse.

Organ enlargement

It Mean hepatosplenomegaly, and lymphadenopathy, organomegaly was have effect at diagnosis on CNS relapse.

Differential diagnosis of CNS leukemia

1. Chemical meningitis.
2. May be there is isolated cranial nerve palsies.
3. Differentiate it from viral meningitis.
4. Aseptic meningitis.
5. Traumatic spinal lap.

Aim of the study

1. To evaluate the incidence of CNS relapse among patients with acute leukemia including ALL and AML treated and followed up
2. To study the relation between CNS relapse and various prognostic factors.
3. To study the incidence of CNS relapse at presentation of acute leukemia and recurrence with duration from diagnosis of acute leukemia to CNS relapse.
4. To study outcome of CNS relapse

Patients and methods

During 12 years, a recorder of eight hundred and seventy patient with acute leukemia including 718 ALL and 152 AML, were reviewed at Central Teaching Hospital for children to study the incidence of the CNS relapse, the age of these patient at the time of initial diagnosis of acute leukemia ranged from five months to fifteen years, those patients including 480 male and 390 females. Those patients were treated and then develop CNS relapse and some of them at beginning of diagnosis develop CNS relapse, the CNS relapse were analyzed with regard to clinical features at presentation, age, sex, WBC count, platelet count, Hb concentration and organ involvement.

The evidence of CNS leukemia was confirmed in each patient with lumber puncture by the presence of more than 5 leukocyte permililater of CSF plus leukemic blast cells after good centrifuging of the sample of CSF, we also find that the pressure of CSF is usually elevated and fluid show pleocytosis. Protein may be increased in CSF and sugar may be decreased.

Table (1): Incidence of ALL and AML and female and male in acute leukemia

	No.	%
Total No.	870	
ALL	718	82.52%
AML	152	17.48%
MALE	480	55.17%
Female	390	44.83%
CNS. Relapse	231	26.55%

$X^2 = 18$ p.value < 0.005

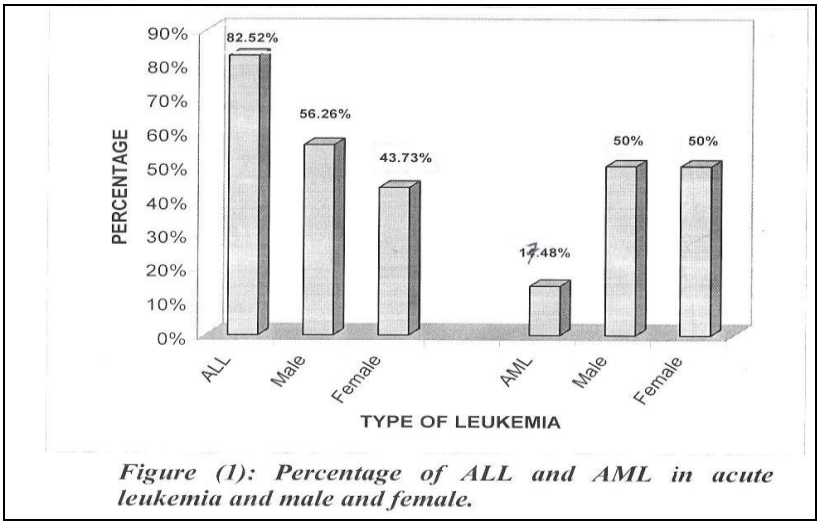

Figure (1): Percentage of ALL and AML in acute leukemia and male and female.

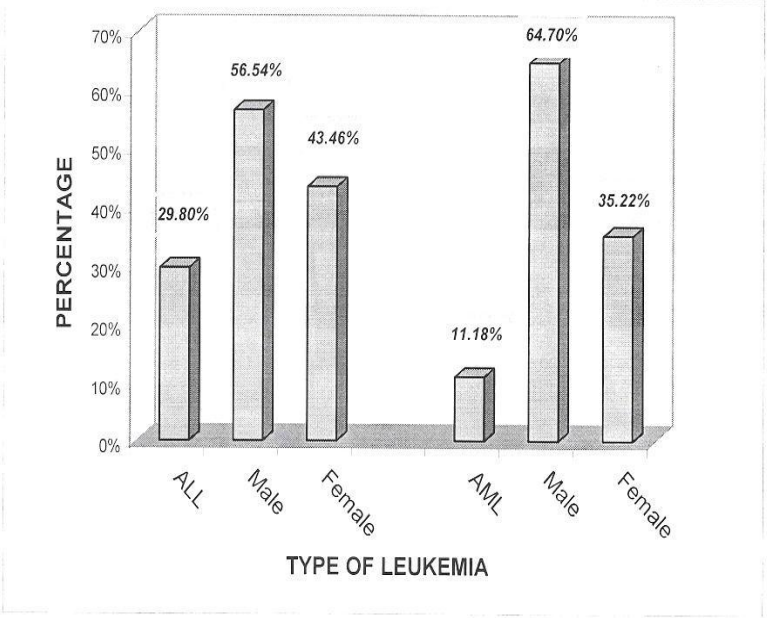

Figure 2: incidence of CNS relapse in ALL and AML and its relation to sex

Table(3):Frequency distribution of CNSL according to their age.

Age	Total n	%	CNS relap	%
<2 years	86	9.88%	18	20.93%
2 – 10 years	688	79.08%	190	27.61%
> 10 years	96	11.03%	23	23.95%

Table (4):The time from initial diagnosis of acute leukemia to onset of CNS relapse .

Time from diagnosis of CNS relapse	Number	%
1st year	167	72.29%
2ed year	31	13.41%
3rd year	14	6.06%
4th year	8	3.46%
total	231	100%

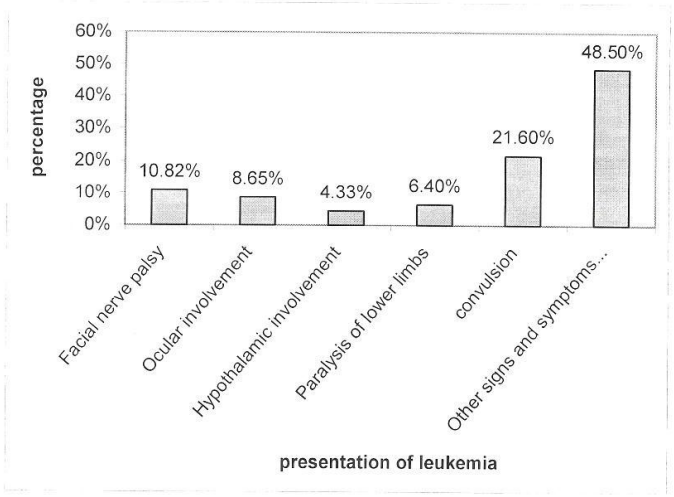

Figure 4: Incidence of different clinical presentation of CNS relapse.

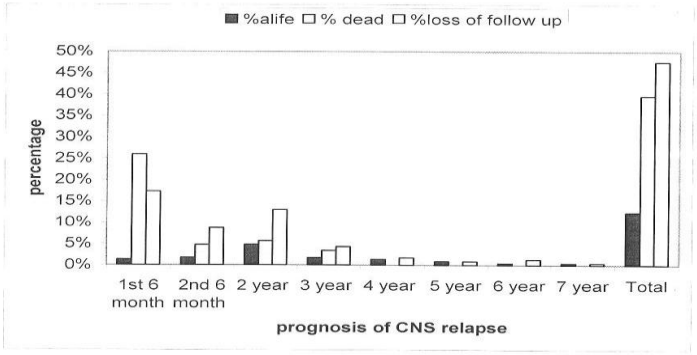

Figure 5: Outcome of CNS relapse according to the time from CNS relapse to last events.

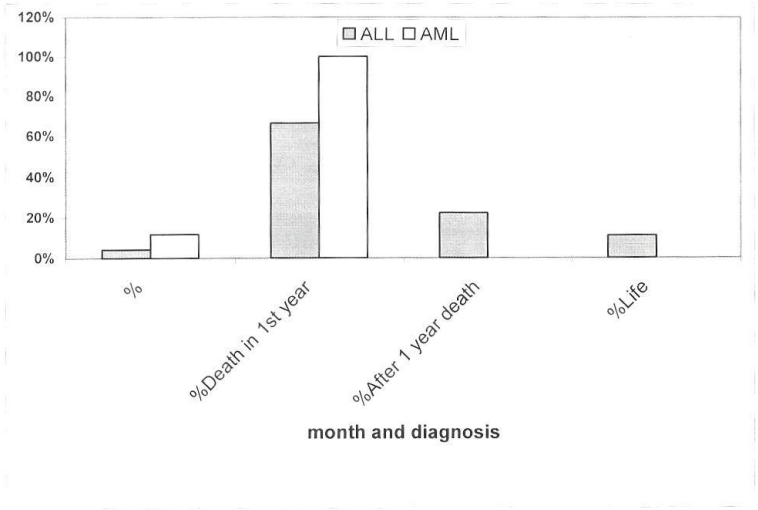

Figure 6: Incidence of CNS relapse at time of presentation and in first month of presentation.

Table 8A: The duration of recurrance of CNS relapse from first relapse to other

Time from first relapse to other	Number of patient	%
3-6 month	13	59.09%
6-12 month	6	27.27%
After 1 year	3	13.63%
Total	22	100%

Table 8B: Incidence of recurrance of CNS relapse in ALL and AML

Type of leukemia	Number of patient	%
ALL	21	9.81%
AML	1	5.88%

Table (9):Relation of initial WBC count to CNS relapse.

WBC count	No. which have CNS relapse	%
< 10 000	58	25.11%
>10 000	173	74.89%
>100 000	46	20%

$X^2 = 173$ *P. value <0.05*

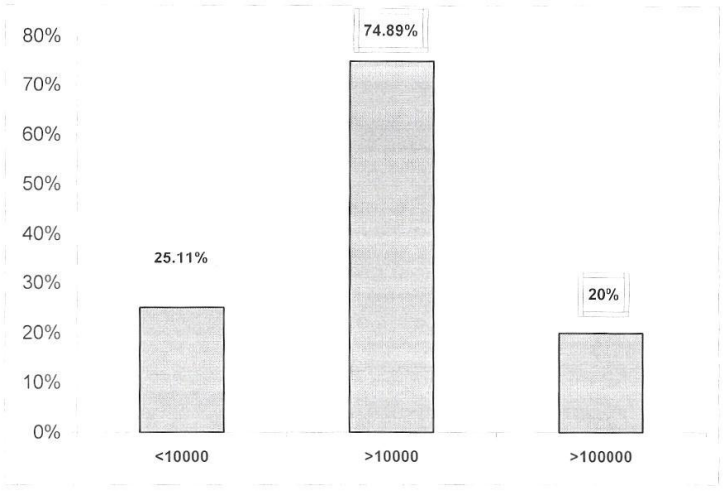

Figure 8: Relation of initial WBC to CNS relapse.

Table(10):Relation of initial Hb to CNS relapse.

Hb %	No. which have CNS relapse	%
< 7	128	55%
> 7	103	45%

Table (11): Relation of initial organomegaly to CNS relapse.

Organomegely	No. which have CNS relapse	%
+ve	196	85%
-ve	35	15%

$X^2 = 35$ *p. value <0.05*

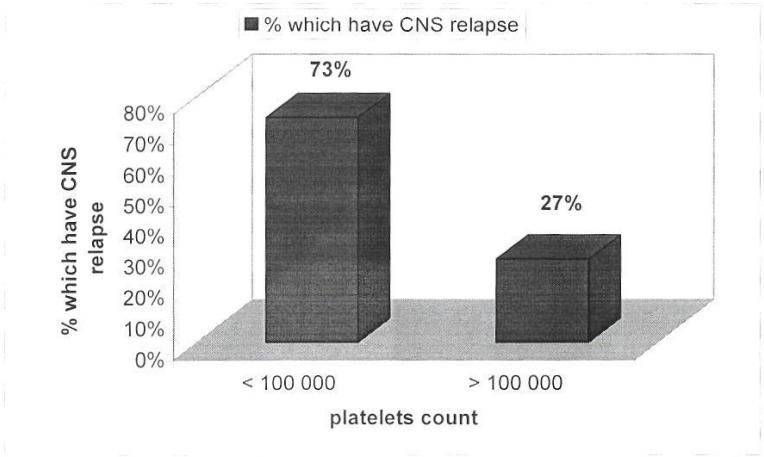

Figure 11: relation of initial platelet count to CNS relapse.

DISCUSSION

LDC Incidence of CNS relapse

The study has shown that the incidence of CNS relapse was 26.55%. This Figure included CNS relapse in ALL which was 29.8%. And CNS relapse in AML was 11.18%. The CNS relapse is highly significant in acute leukemia

The effect of sex and age on incidence of CNS leukemia:

The results in our work doesn't show any particular age group vulnerable to develop CNS relapse.

But according to the sex the Male incidence of developing CNS relapse more than female especially in AML.

Incidence of ALL and AML in acute leukemia and their CNS relapse in theme

Our study show that the ALL was 82.52% and AML was 17.48% from total acute leukemia, the CNS relapse in ALL 29.8% which is more than AML which is 11.18%,

The Time of CNS relapse from Diagnosis of acute leukemia to CNS relapse:

The time of CNS relapse was during the first year after Diagnosis of acute leukemia and highest percentage which was 72.29% during first year.

***The incidence of recurrence of CNS relapse*:**

Recurrence of CNS relapse is present mostly and highest between 3-6 months from first relapse to other after treatment of first relapse.

Outcome of CNSL

The high percentage of death during the first 6 months from Diagnosis and also the highest percentage of loss of follow up during this period, those who's loss of follow up either dead or go to other hospital or go to home and not received treatment.

Incidence of different clinical presentation of CNSL

The most clinical presentation which was found that with increasing intracranial pressure like headache, vomiting, irritability and lethargy with papilloedema.

Incidence of CNS relapse at time of presentation and in first month of presentation

The percentage of relapse at time in presentation was 4.2% in ALL and 11.76% in AML, which mean higher in AML than in ALL.

The effect of initial WBC count on CNDL

The 74.89% of patient with CNS relapse had initial high WBC count and there is 20% of patient with CNS relapse had initial WBC count more than 100 000 WBC/mm^3. There is significant relationship between WBC count and CNS relapse.

The effect of initial platelet count on CNSL
(the 73% patient of CNS relapse had initial platelet less than 100 000/mm^3. There is significant relationship between platelet count and CNS relapse.

The effect of initial organomegaly on CNSL:
85% of patient which had CNS relapse had initial organomegaly.

The effect of initial Hb to the CNSL:
No specific relationship between Hb at initial Diagnosis and between CNS relapse.

CONCLUSION

On the basis of our study and results we conclude that

1. The incidence of CNS relapse 26.55%.
2. The incidence of CNS relapse is higher in male than female.
3. There is no significant effect of age on the incidence of CNS relapse.
4. The highest incidence of CNS relapse occur within the first year after diagnosis of acute leukemia.
5. The highest incidence of recurrent of CNS relapse is between 3-6 months from diagnosis of first relapse to other.
6. There is different clinical presentation of CNSL and the highest incidence is increasing ICP.
7. Initial high WBC count and low platelet count and oraganomegaly have effect on the incidence of CNS relapse.
8. Initial Hb had no significant effect on CNS relapse.
9. CNS relapse is a poor prognostic factor especially if occur at presentation of acute leukemia or with frequent relapses.
10. The incidence of CNS relapse at time of presentation in AML was more than in ALL.

Recommendation

1. All patient with ALL and AML should have initial spinal tap done early in coarse of disease and prophylactic therapy should be prescribed early in induction phase of treatment of leukemia to eradicate the leukemic cells from the meninges.
2. We hope that in future we can use other methods which can diagnosis CNS relapse early and to differentiate it from other condition.

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