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Clinico Haematological Study of Acute Lymphoblasticleukemia

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Aims:

1. To know the relative incidence of Acute Lymphoblastic leukemia among the patients referred for complete haemogram at the department of pathology, JJMMC, Davangere.
2. To study the clinical manifestations and their correlation with various types of acute Lymphoblastic leukemia.
3. To study the haematological profiles in acute Lymphoblastic leukemia.

Settings and design: The study was a hospital based study conducted at haematology unit, Department of Pathology, JJM Medical college, Davangere.

Methods and material: The present study was done during the period of June 2006 to May 2008 at haematology unit department of Pathology, JJM Medical college, Davangere. Cases from chigateri general hospital, Bapuji hospital and other private hospitals situated in and around Davangere were included for the study.

Keywords: *leukemias, all, hospital-based study.*

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Statistics: The results were expressed in percentage.

Results and conclusion: A total of 1039 patients who were referred to the department of haematology out of which 13 patients were diagnosed as Acute Lymphoblastic Leukemia. The present study is to highlight that light microscopic features of peripheral smear and bone marrow will still remain mainstay in the diagnosis of acute Lymphoblastic leukemias.

Keywords: leukemias, all, hospital-based study.

I. Introduction

Acute lymphoblastic leukemia encompasses a group of neoplasms composed of immature, precursor(B- pre-B) or T (pre-T) lymphocytes re - ferred to as lymphoblast[1].

Although ALL affects all age groups, ALL has its highest incidence in children between ages, 1-5 years with a peak at 3-4 years[2]. In 1976, Bennet JM et al classified ALL into three sub types (L1, L2 and L3). According to

a) the occurance of individual cytological features
b) The degree of heterogeneity in the distribution among the leukemic population of some or all of these features. The features considered are cell size, nuclear chromatin, nuclear shape, nucleoli, amount and basophilia of the cytoplasm[3].

In the year 1985, the first MIC (morphologic, immunologic, cytogenetic cooperative study group) proposed a classification of ALL[4]. The children cancer study group (CCSG) has presented their own class - ification of ALL which borrows from FAB nomen - clature[5]. The latest WHO classification of the acute leukemias differs from the FAB classification in that greater than or equal to 20% blasts are used for the diagnosis of acute leukemias[6].

II. Objectives

1. To know the relative incidence of Acute lymphoblastic leukemia among the patients referred for complete haemogram at the department of pathology, JJMMC, Davangere.
2. To study the clinical manifestations and their correl- ation with various types of acute lymphoblastic leuk- emia.
3. To study the haematological profiles in acute lymph- oblastic leukemia.

III. Materials and Methods

The present study on "Clinico-Haematological study of Acute LymphoblasticLeukemias" was under- taken during the period of June 2006 to may 2008 at haematology unit, Department of Pathology, J J M Medical College, Davangere.

The cases from chigateri hospital, Bapuji hospital and other private hospitals situated in and around Davangere formed the material of the study. Case selection was based on clinical features and supported by laboratory evidences. Bone marrow aspiration was subsequently carried out after obtaining written consent from the patient or the guardian.

Inclusion criteria

- New cases of ALL

Exclusion criteria

- Treated cases of ALL

The following investigations were done:

1. Complete haemogram was performed and peripheral smear was stained by Leishman stain for all cases and examined in detail.

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2. Bone marrow aspiration and study was done in all cases and leishman stained smears were examined.

In all cases, the following cytochemical stains were employed for diagnosisand subtyping of leukemias.

- MPO – Myelo-peroxidase stain
- SBB – Sudan Black B
- PAS- Periodic Acid Schiff stain
- NSE- Non specific esterase stain

Acute lymphoblasticleukemias were classified based on FAB Criteria.

IV. Results

13 patients in this study were diagnosed as ALL. ALL patients were seen in the age range of 5months to 16 years with a mean age of 8.3 years. The mean ages for males and females were 9.2 years and 6.0 years respectively. Out of the 13 patients, 9 were males and 4 were females, with a male to female ratio of 2.2:1.

The main presenting symptoms were fever in 6 patients (46.1%), generalized weakness in 4 patients (30.8%) and backache in 3 patients (23%).

Physical examination showed pallor of varying degrees in all patients. Lymphadenopathy was present in 8 out of 13 patients constituting (61.5%). All the patients had localized lymphadenopathy among which cervical lymphadenopathy was common.

Mild to moderate Hepatomegaly was seen in 7 patients (53.8%).

Mild to moderate Splenomegaly was seen in 10 patients (76.9%).

Anemia of variable degree was seen an all patients of ALL. The Hb level ranged from 5.9-7.2gm/dl. The mean Hb level being 6.7gm/dl. TLC ranged from 16.9× 10^9/l to 210× 10^9/l. the mean TLC being 75.8× 10^9/l. 5 patients (38.4%) had count between 11-49× 10^9/l, 4 patients (30.7%) had counts between 50-100× 10^9/l, 4 (30.7%) patients had counts >100× 10^9/l.

All the 13 patients had thromobocytopenia at the time of diagnosis, 5 patients had counts from 11-49× 10^9/l, 4 patients had counts from 50-100× 10^9/l, 4 patients had counts >100× 10^9/l, with a mean platelet count of 82.3× 10^9/l.

10 out of 13 patients had an ESR of >50mm at the end of 1st hour and 3 patients between 20-50mm at the end of 1st hour.

Bone marrow aspiration was performed in all 13 patients. Lymphoblast was the predominant cell with an average of 85% blasts on differential count. All the patients had decreased megakaryocytes. All were subtyped on morphological basis using FAB criteria into 3 subtypes-L1, L2, and L3. The identification of lympho - blasts was mainly on morphological grounds as stated in the FAB proposals. MPO/SBB and PAS stains were performed. Most of the ALL patients were MPO/SBB negative, but characteristic block positivity on PAS was seen in 38.5% of the patients.

Table 1 : Haematological Parameters in FAB Subtypes of ALL

Haematological parameters	ALL (n=13)	L1	L2	L3
Hb (gm/dl) Range Mean	 5.9-7.2 6.7	 - -	 5.9-7.2 6.7	 - -
TLC (×10^9/L)				
Range	16.8-210	-	16.8-210	-
Mean	75.8	-	75.8	-
Platelets (×10^9/L)				
Range	0.46-145	-	0.46-145	-
Mean	82.3	-	82.3	-
Blast range (%)	60-90	-	60-90	-
Bone marrow decreased megakaryocytes	13	-	13	-
Blast mean	85%	-	85%	-

a) Acute Lymphoblastic Leukemia (L1)

No case of L1 was encountered in this study.

b) Acute Lymphoblastic Leukemia (L2)

All the 13 patients who were diagnosed as ALL were ALL-L2 in this study. The age range was 5 months to 16 years with a mean age of 8.3 years. The mean ages for males and females were 9.2 years and 6 years respectively. Out of the 13 patients, 9 were males and 4 were females, with a male to female ratio of 2.2:1.

The main presenting symptoms were fever in 6 patients (46.1%), generalized weakness in 4 patients (30.8%) and backache in 3patient (23%).

Physical examination showed pallor of varying degrees in all patients. Lymphadenopathy was present in 8 of the 13 patients constituting (61.5%). All the 8

patients had localized lymphadenopathy among which cervical lymphadenopathy was common.

Mild to moderate hepatomegaly was seen in 7 patients (53.8%).

Mild to moderate Splenomegaly was seen in 10 patients (76.9%).

Anemia of variable degree was seen an all patients of ALL. The Hb level ranged from 5.9-7.2gm/dl. The mean Hb level being 6.7gm/dl. TLC ranged from 16.9× 10^9/l to 210× 10^9/l. the mean TLC being 75.8× 10^9/l. 5 patients (38.4%) had count between 11-49× 10^9/l, 4 patients (30.7%) had counts between 50-100× 10^9/l, 4 (30.7%) patients had counts >100× 10^9/l.

All the 13 patients had thromobocytopenia at the time of diagnosis, 5 patients had counts from 11-49× 10^9/l, 4 patients had counts from 50-100× 109/l, 4 patients had counts >100× 10^9/l, with a mean platelet count of 82.3× 10^9/l.

10 out of 13 patients had an ESR of >50mm at the end of 1st hour and 3 patients between 20-50mm.

Bone marrow aspiration was done in all 13 patients. Marrow was hypercellular. Aspiration showed reduced erythropoiesis and megakaryopoiesis. Leucopoiesis showed a predominance of lymphoblasts which comprised of heterogenous population of both large and small lymphoblasts. The average blast count was 85%.

Cytochemical staining for MPO/SBB was negative and PAS positivity was seen in 38.5% of the patients.

c) Acute Lymphoblastic Leukemia (L3)

No case of L3 was encountered in this study.

V. Discussion

The mean age incidence in the present study was 8.3%. In studies conducted by Shome et al (1985)7 and Mathur (1993)8 et al, the mean age incidence was 15.6 and 29.7 respectively. This was more when compared to the present study.

The male female ratio in our study was 2.2:1. In studies done by Shome et al (1985) and Mathur (1993) et al, the male to female ratio was 3.4:1 and 2.4:1 respectively. This is more when compared to the present study.

The average figures for age incidences in the present study are less than the figures quoted in other Indian studies.

The main presenting symptoms were fever and generalized weakness in our study. The same was noted by Shome et al (1985) and Mathur (1993) et al. Bleeding manifestation as a presenting symptom was not noted in this study. Higher incidences of bleeding manifestations were noted by Shome et al (55%) and Mathur et al (47%). A high incidence of lymphad - enopathy was seen consistently in this study and also in other studies. Hepatosplenomegaly was also a prese - nting symptom in this study. Similar observation was noted by Shome et al (1985) and Mathur (1993) et al, but with a more frequency among patients. Backache was seen in 23% of the patients in this study. Backache was not seen in study done by Shome et al (1985) and Mathur (1993) et al.

Pallor was present in our study and it correlates well with a study done by Mathur (1993) et al.

Sternal tenderness was present in studies conducted by Shome et al (1985) and Mathur (1993) et al, but was not observed in the present study. CNS manifestations was present in study conducted by Sho - me et al (1985), but it was not observed in the present study.

Table 2 : Comparison of clinical features of ALL (in %)

Clinical features	Shome et al (1985)	Mathur et al (1993)	Present study (2008)
Fever	73	94	46.1
Generalized weakness	80	100	30.8
Bleeding	55	47	-
Pain abdomen	20	18	-
Pallor	87	100	100
Lymphadenopathy	80	88	61.5
Splenomegaly	77	75	76.9
Hepatomegaly	88	75	53.8
Sternal tenderness	39	53	-
Signs of haemorrhage	16	47	-
CNS manifestations	10	-	-
Back ache	-	-	23

Anemia was seen in all the cases of ALL in the present study. Similar finding was observed in study conducted by Mathur et al. Mean Hbpercent was 6.7gm/dl in the present study, and it was more compared to Mathur et al.

The mean TLC in the present study was 75.8×10^9/l. In the study done by Mathur et al, it was

35.8×10^9/l. This count was less when compared to the present study.

Thrombocytopenia was present in all the patients in the present study. The mean platelet count was 82.3×10^9/l in the present study. This was high when compared to the study conducted by Mathur et al, where it was 55.2×10^9/l.

Bone marrow examination was performed in all 13 cases.

The mean blast percentage was 85%. This was more when compared to Mathur et al where it was 57%.

Table 3 : Comparison of haematological parameters of ALL

Haematological parameters	Mathur et al (1993)	Present study (2008)
Hbgm/dl Range Mean	2-9.5 5.2	5.9-7.2 6.7
TLC ($\times10^9$/l) Range Mean	8-90 35.8	16.8-210 75.8
Platelets ($\times10^9$/l) Range Mean	20-150 55.2	0.46-145 82.3
Blasts (%) Range Mean	20-90 57	60-90 85

In the present study, all the patients, that were diagnosed as ALL were ALL-L2 (100%). In the study done by Mahendrakumar (1998)9 L2 was a predominant subtype. Shome et al (1985) reported an almost equal incidence of L1 and L2 (45.8% and 42.4%).

The mean age for L2 was 8.3 years in the present study. Shome et al (1985) reported a mean age of 17.7, whereas Mahendrakumar (1998) reported a mean age 13.6 for L2. In this study, the sex ratio showed a male predominance in L2 subtype (2.2:1). The Shome et al (1985) showed a sex ratio of 2.6:1 in L2 type, whereas the study of Mahendrakumar (1998) showed a sex ratio of 1.8:1 in L2 type.

The general pattern of clinical features varies with the findings of Shome et al (1985). Fever and generalized weakness were a common initial clinical presentation in the present study whereas in study done by Shome et al (1985) a higher percentage of fever and generalized weakness were noted. Lymphadenopathy was common in ALL-L2 in the present study (61.5%) and is less when compared to Shome et al (73%). Splenomegaly correlates well with study by Shome et al (1985). Hepatomegaly was seen in less frequency when compared to Shome et al (1985). Backache was seen in 23% of the patients in this study and was not seen in study conducted by byShome et al (1985).

The mean Hb levels in ALL-L2 subtype correlates with Shome et al study (1985). TLC also correlates with Shome et al series.

Thrombocytopenia was seen in all patients in this study. The mean platelet count was little less when compared to study done by Shome et al (1985).

Table 4 : Comparison of haematological parameters of in FAB subtypes of ALL

Haematological parameters	L1		L2		L3	
	PGI	PS	PGI	PS	PGI	PS
Hbgm/dl) Mean	6.6	-	6.8	6.7	8.4	-
TLC ($\times10^9$/l) Mean	39.10	-	77.6	75.8	29	-
Platelets ($\times10^9$/l) Mean	81	-	85	69.3	49.3	-
Bone marrow decreased megakaryocytes (in %)	96	-	90	100	100	-

In the present study PAS positivity was seen in only 38.5% of patients while study by Shome et al (1985) series reported PAS positivity in 20% of ALL patients. Mahendrakumar (1998) reported PAS positivity in 43.8% of ALL patients. Fayaz khan10 reported PAS positivity in 53.5% of ALL patients.

VI. Conclusion

ALL was diagnosed in 13 patients (20.63%). All the patients that were diagnosed with ALL were ALL-L2.

Lymphadenopathy was the most consistent feature with fever, generalised weakness, backache and

hepatomegaly. Anemia and thrombocytopenia were pre -sent in all the patients. TLC count ranged from 16.9 to 210×10^9 /l with a mean of 75.8×10^9 /. The mean blast percentage was 85%.

The present study is to highlight that light microscopic features of peripheral smear and bone marrow still remain mainstay in the diagnosis of acute leukemias, whereas immunotyping and cytogenetics are complimentary procedures at specialized centres.

However, with newer modalities of therapy and rewarding curative results in haematological malign - ancies, the use of cytochemistry, immunotyping and cytogenetics have become gold standards for arriving at a specific diagnosis.

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