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Haematological and Cytomorphological Study of Acute Lymphoblastic Leukemia (ALL)

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Objective: Acute lymphoblastic leukaemia (ALL) has long been recognized to be clinically and morphologically heterogeneous .We tried to study, analyze, and interpret the relationships between age, sex, clinical manifestations, FAB classification, and hematological investigations.

Methods: Over a period of 6 months, sixty-four, newly diagnosed (Sudan Black B –negative), cases had been included in this study, from different centers. Clinical study was conducted concentrating on the presence of fever, pallor, bleeding tendency, lymph node enlargement, spleen and liver enlargement, neurological and testicular manifestations, and the presence of mediastinal mass on chest x-rays. Hematological investigations included haemoglobin concentration, initial total white cell count, and platelets count. Bone marrow smears were stained with MGG stain and the FAB classification and the FAB scoring system had been used.

Results: Showed that children were 61% of total cases while adults were 39%, with the highest age incidence between 0-5 years. Male: female ratio was 2:1. Age incidence in males was higher than that for females for all age groups. Lymph node enlargement and hepatomegaly were the most common clinical findings. The presence of mediastinal mass on chest x-ray was more in male than female sex (39.5% Vs 9.5%). L2- morphological subtype was more common in both children and adults 87.2% & 92% respectively) than L1 morphological subtype (12.8% and 8% respectively). No L3 type had been found in our study.

Conclusion: ALL is a disease of children mainly with higher incidence in males than females and, unlike the internationally reported cases where L1 type is more prevalent, L2 type is more prevalent in Iraqi cases.

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INTRODUCTION

Acute lymphoblastic leukaemia (ALL) has been recognized to be clinically and morphologically heterogeneous[1]. Morphologically it has been classified according to the FAB (French, American and British) criteria into three subtypes, L1, L2 and L3[2-4]. This system of classification, which is still valid till now, had been proven to be clinically reproducible[4-,6]. In L1 subtype the cells are small, homogenous, the cytoplasm is little, the nuclei–cytoplasmic (N/C) ratio is high with inconspicuous nucleoli[7] .It is more common in children (about 74%) than in adults (about 66%)[4,7]. In L2 subtype, the cells are heterogeneous, larger in size with ample amount of cytoplasm and, thus low N/C ratio, and are usually associated with nuclear clefting, indentation and folding with 1-2 conspicuous nucleoli.

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It is less prevalent than L1 subtype but is more common in adults .The L3 cells are large with finely stippled nuclear chromatin and characteristically a deeply stained, basophilic and usually vacuolated cytoplasm, (Burkitt, s type). It is the least common subtype and there are no significant age differences in its incidence[1,3]. The current study is planned to verify the incidence of the three ALL subtypes and their relation to age, sex and clinical and haematological presentations in our society.

METHODS

Patients: Sixty-four newly diagnosed acute lymphoblastic leukaemic patients, regardless of the age had been included in this study.

Clinical study: Full history and physical examination have been done, concentrating on the presence of the following: fever, pallor, bleeding tendency, lymphadenopathy, spleenic or liver enlargement, neurological and testicular manifestation in males and any radiological evidence for the presence of mediastinal masses.

The following haematological investigations were done: Hb concentration, WBC and platelet count using standard manual methods.

Cytomorphological examination of bone marrow smear had been done, using May–Granwald-Giema's stain (MGG)[8]. The original FAB criteria and the FAB scoring system had been used to differentiate between L1 and L2 morphological subtypes[9].

Statistical analysis: A statistical survey had been done including the percentage, mean and standard deviation .To test the significance between the variables, the 2x2 contingency table had been constructed and the X^2 test done, the Fisher, s exact "p" value had been used when the number of the variables <20.

RESULTS

The age ranged between 4 months and 45 years; children (below 15 years) were 39 patients (61% of total), while adults (15-45 years) were 25 only. The peak age incidence was between 0-5 years (16 cases) and those between 6-10 years (15 cases) respectively.

Males constituted 43 cases and females 21 cases with male: female ratio =2:1. For males, the peak age incidence was between 6-10 years (11cases) and for females, it was between 0-5 years (6 cases). The age incidence of males was higher than that of females for all age groups and there was a gradual decline in the incidence with progress of age among both sexes (figure -1).

Figure 1

Lymph node enlargement and hepatomegaly were the two most common presenting features, (89 % for each), the next were pallor, fever, splenomegaly and bleeding tendency respectively (table -1). The presence of mediastinal mass on chest X-ray was in 29.7% of total cases (28% in adults and 30.7% in children), with marked and statistically significant sex difference (39.5% in male and 9.5% in female).

Table 1

The mean haemoglobin concentration was 8.2 ± 2.9, while the mean of WBC count 102 .6 $x10^9$/L ±174.9 and of platelet count was 55.5 $x10^9$ /L ± 63.4 (table -2).

Table 2

Using FAB criteria, 12. 8% of children and 8% of adults have been shown to have L1 morphology (Fig -2), while 87.2% of children and 92% of adults were found to have L2 morphology (Fig. 3). No case has been found to have L3 morphology .In total, 11% of cases were of L1 subtype while 89% were of L2 subtype (table –3).

Figure 2, 3 & Table 3

DISCUSSION

Acute leukemias usually appear with symptoms resulting from suppression of normal marrow function. These symptoms include anemia, with accompanying fatigue; fever, usually reflecting an infection; and/or bleeding, usually caused by thrombocytopenia. Acute leukemias are usually fatal within weeks if left untreated.

Acute lymphoblastic leukemia is most common in children under 10 years, constituting about 80% of childhood leukemia's[10,11] . It becomes increasing rare with advancing age .It has a higher male incidence[12]. The age distribution in this study (61% children and 39% adults) with the peak age incidence between 0-5 years and the male predominance (M: F = 2:1) have been well accepted with other observations[2,13.]

The modern era for classification of acute leukemia's dates to 1976 when two proposals appeared. One was published by a cooperative group of hematologists and hematopathologists from France, America, and Britain and was designated the French-American-British (FAB) classification[14]. Although the WHO classification was never widely used, the FAB proposal was adopted internationally. It provided long needed standard terminology for the acute leukemias and was quickly accepted by most of the multiinstitutional study groups. The major advantages of the FAB classification are the cytological criteria are well defined; they do not require high technology and can be applied in most laboratories; also are applicable to the majority of cases of acute leukemia, and they partially defined prognostic groups.

In the present study L2 morphological sub-type was highly prevalent in ALL cases, (both in children and adults), while L1 sub-type was quite less. No L3 case had been found. This fact contradicts with the well-established observations in childhood ALL, but agreed with those found by Bennett et al concerning adult ALL[9]. All other clinical and haematological findings were well accepted by other observations.

CONCLUSION

ALL is a disease of children mainly with higher incidence in males than females and, unlike the internationally reported cases where L1 type is more prevalent, L2 type is more prevalent in Iraqi cases.

REFERENCES

1. Hoffbrand AV, Lewis SM. Postgraduate hematology 4th edn, Heinemann medical books,1999:

Chapter 14 .
2. Bennett, JM, Catovsky D, Danial, MT, et al. Criteria for the diagnosis of acute leukaemia of megakaryocytic lineage (M7). a report of the French –American – British co- operative group. Ann Int Med 1985;103:460-2.
3. Harris NL, Laffe ES, Diebold J, et al. Lymphoma classification - from controversy to consensus: the REAL and WHO classification of lymphoid neoplasms. Annals of Oncol 2000;11:3-10.
4. Miller DR, Leikin S, Albo V, et al. Prognostic importance of morphology -FAB classification- in childhood acute lymphoblastic leukaemia –ALL. Br J Haematol 1981; 48:199-206.
5. Ching-Hon Pui. Acute lymphoblastic leukaemia; chap.97in William s Haematology; 6th edn. 2001:1141-61.
6. Viana MB, Maurer HS, Ferencec. Sub- classification of acute lymphoblastic leukaemia in children: Analysis of the reproducibility of morphological criteria and prognostic implication. Br J Haematol 1980;44:383-8.
7. Sultan C, lmbert M. Classification, morphology, cytochemistr Of acute leukaemia's; chapter 7 in Leukaemia. Ed Whihaker JA. Delamore LW. Blackwell scientific publications;1987:129-36.
8. John V, Dacie X, Lewis SM. Practical haematology, 9th edn, Churchill Livingstone.2001:19-64.
9. Bennett JM, Catovsky D, Daniel MT, et al. The morphological classification of acute lymphoplastic leukaemia: Concordance among observers and clinical correlation's; Br J Haematol 1981;47:553-61.
10. Burnett AK, Eden OB. The treatment of acute Leukaemia; Lancet 1997;349:270-5.
11. PuiC-H, EvansWE. Acute lymphoblastic leukaemia N Engl J Med 1998;339:605-15.
12. Kamps WA, Humphery B. Heterogeneity of childhood acute lymphoblastic leukaemia – impact on prognosis and therapy. Semi Oncol 1985;12:268-80.
13. Wintrobe MM, Clinical haematology. 8th edn. Lea fibiger- Philadelphia; 1982;60:1450.
14. Harris NL, Laffe ES, Diebold J, et al. Lymphoma classification - from controversy to consensus: the REAL and WHO classification of lymphoid neoplasm. Annals of Oncol 2000;11:3-10.