Original Article

Pattern of Haemotological Disorders Diagnosed by Bone Marrow Examination at a Paediatric Hospital in Larkana Pakistan

1. Raja Rahul Chand 2. Haresh Chand 3. Khurshid Ahmed Abbasi
4. Saeed Ahmed Shaikh 5. Amrita

1. Trainee and Medical Officer of Medicine 2. Asstt. Prof. of Pathology, 3. Prof. of Paediatrics 4. Asstt. Prof. of Community Medicine 5. House Officer, Chandka Medical College Hospital, Larkana

ABSTRACT

Background: Bone marrow examination is an integral part for establishing the diagnosis of haematological disorders in association with clinical and other routine laboratory tests.
Objective: To evaluate the frequency and pattern of haematological disorders in children at a tertiary care hospital in Larkana.
Study Design: Descriptive study.
Place and Duration: The study was conducted at children hospital and pathology department of Chandka Medical College Larkana from Jan: 2008 to Dec: 2010.
Patients and Methods: Marrow aspirates were collected from children under the age of 15 years as per guidelines recommended by international council for standardization in haematology (ICSH). Smears obtained were stained with Romanowsky stains and examined under light microscope.
Results: Bone marrow examination reports of 271 patients ranged from 2 months to 15 years, with male /female ratio of 1.6:1 were analyzed. Malignant disorders were seen in 36.5% and non malignant disorders in 59.8% of children. Amongst the malignant haematological disorders, acute lymphoblastic leukaemia (ALL) cases were 64 (23.6%) and was found to be most common disorder, followed by lymphoma 7 (2.6%) cases and acute myeloid leukaemia (AML) 6 cases (2.2%). In non malignant disorders aplastic anaemia was the most common 40 (14.8%) cases, followed by iron deficiency anaemia 30 (11%) cases. The megaloblastic anaemia was least common seen only in 8 (3.0%) cases. Other non malignant disorders were idiopathic thrombocytopenic purpura (ITP) 71 (26.2%) cases and malaria 4 (1.5%) cases.
Conclusion: Appropriate diagnosis can not be made in haemotological disorders of childhood without bone marrow examination.
Key Words: Bone marrow examination, diagnostic value, haematological disorders.

INTRODUCTION

Hematological diseases are quite common affecting both sexes and all ages including pediatric populations [1,2]. Wide range of common as well as rare hematological disorders can be seen in children[2]. Most of these can be diagnosed by thorough clinical examination and simple laboratory tests, but Bone Marrow examination is essentially required for confirmation of not only hematological but also for non hematological diseases [2,3,4,5,]. This is an invasive procedure [6] but usually safe if carried out by experienced medical personnel [5]. Occasionally infection, bleeding or embolism has been reported [7]. Most frequent indications for bone marrow examination are unexplained anemias and pancytopenia [4, 8]. It is commonly done for diagnosis and follow up of haematological malignancies like leukemia [2, 8] and continues to be gold standard test for diagnosis of multiple myeloma, [9] accurate staging of lymphoma [10], Neuroblastoma and investigation of bone marrow metastases[11]. So for none of the study has been carried out on the prevalence of haematological problems in children in upper part of Sindh as well as adjacent areas of Balochistan and Punjab, hence this study would correctly highlight the frequency of haematological diseases in children of this region, there by helping health managers and planners to formulate adequate future strategies for prevention and early diagnosis of these diseases.

PATIENTS AND METHODS

This is a retrospective descriptive study done with approval of ethical committee of Chandka Medical College, Larkana. A total of 271 children under 15 years of age, admitted in children hospital Chandka Medical College Larkana, who underwent bone marrow aspiration in pathology department of same institute, during the period from Jan: 2008 to Dec: 2010 were

included in this study. After reviewing clinical records and routine haematological tests, procedure was explained in details to the parents of patient, and informed consent was obtained. Bone marrow aspirate specimen were collected as per guidelines recommended by International Council for Standardization in Haematology (ICSH) [12]. Anatomic site selected for aspiration was posterior iliac crest or medial surface of tibia in infants under 6 months of age. 2% lignocaine injection was used as local anesthetic and injection diazepam, as a sedative. Lumber puncture 16 gauge needle (Nipro) was inserted and aspirate drawn in 10cc plastic syringe Becton Dickinson (B.D). Smears were prepared on glass slides either directly or after mixing the aspirate with Eythylenedinitrilo tetra acetic acid (EDTA) anticoagulant. Smears were air dried, stained with Romanowsky stain and examined in microscope under low power to look for the cellularity of particles and under oil immersion lens for the morphological assessment of cells. The aspirate slides were always reviewed in conjunction with peripheral blood smear. The reports were prepared by consultant pathologist and finalized after discussing the findings with fellow expert. Data was analyzed on SPSS version 13.

RESULTS

A total of two hundred seventy one bone marrow aspirates were examined during the study period. There were 167 males and 104 female, with a male/female ratio of 1.6:1. (Table No.1). The age ranged from 2 months to 15 years.

Table No.1: Frequency distribution according to sex.

Sex	Frequency	Percent	Valid percent	Cumulative
Male	167	61.6	61.6	61.6
Female	104	38.4	38.4	100.0
Total	271	100.0	100.0	

The majority of patients were in the 6-15years age, representing 62% of study group while ages of 38% patients were upto 5 years. (Table No.2).

Table No.2: Frequency distribution according to age.

Age	Frequency	Percent	Valid percent	Cumulative
0-5	103	38.0	38.0	38.0
6-15	168	62.0	62.0	100.0
Total	271	100.0	100.0	

The most frequent indication for BME was investigation of suspected leukaemia and remission assessment, followed by anaemia, thrombocytopenia and others as shown in table No.3.

Table No.3: Clinical indications for Bone Marrow Aspirates

Indication	No of Patients	Percentage
1. Suspected Leukaemia & remission assessment	90	33.2
2. Investigation of anaemia	78	28.8
3. Thrombocytopenia	71	26.2
4. Lymphoma and solid tumour investigation	09	3.3
5. Fever lasting for more than 02 weeks	23	8.5
Total	271	100

Non malignant haematological disorders were seen in 162 (59.8%) patients and 36.5% patients showed malignant disorders. Marrow findings were normal in 3.7% of cases (Table No.4).

Table-No.4: Frequency distribution of malignants and non malignant disorders.

	Frequency	%cent	Valid %cent	Cumulative
Malignant haemoto-logical disorder	99	36.5	36.5	36.5
Non-malignant haemoto-logical disorder	162	59.8	59.8	96.3
NAD	10	3.7	3.7	100.0
Total	271	100.0	100.0	

Table No.5: Diagnosis on the basis of Bone Marrow Examination in descending order of frequency.

	Frequency	%cent	Valid %cent	Cumulative
ITP	71	26.2	26.2	26.2
Aplastic anemia	40	14.8	14.8	41
Hypochromic Microcytic anemia	30	11.0	11.0	52.0
Megaloblastic anemia	8	3.0	3.0	55.0
ALL	64	23.6	23.6	78.6
ALL (Remission)	20	7.4	7.4	86.0
AML	6	2.2	2.2	88.2
Lymphoma	7	2.6	2.6	90.8
Metastatic	2	.7	.7	91.5
Malaria	4	1.5	1.5	93.0
Reactive	9	3.3	3.3	96.3
NAD	10	3.7	3.7	100
Total	271	100.0	100.0	

In non-malignant haematogical disorders, anaemias of various etiologies accounted for 28.9% cases. Of the anaemias, aplastic anaemia was most common and magaloblastic least common. Another frequent non malignant haematogical disorder was idiopathatic thrombocytopenic purpura, seen in 71 cases (26.2%). Amongst the malignant haematological disorders, acute lymphoblastic leukaemia was the most common, seen in 23.6% (64) of cases, followed by lymphoma and others (Table No.5).

DISCUSSION

Bone marrow examination (BME), being safer method in children is frequently used for the diagnosis of variety of haematological and non haematological disorders[2]. In the present study 90 cases (33.2%) of leukaemia were observed, while Rahim et al noted lower percentage (24.76) of leukaemia cases in children[2]. Acute lymphoblastic leukaemia (ALL) was found to be the commonest, seen in 23.6% of our cases and acute myeloid leukaemia (AML) was rare (2.2%). ALL to AML ratio was found to be 10.6:1, much higher than that of Githang'a and Dave (3.75:1)[4]. Our study was different from studies of kasili[13] and Mwangi[14] in which ALL to AML ratio was 1:2 and 1:17 respectively.

Bone marrow examination was performed for assessment of remission status of ALL during and at the end of chemotherapy in 20 (7.5%) cases. This indicates the improved survival of these patients. However some workers have suggested no diagnostic or prognostic value of this invasive procedure in such cases[15].

BME is also indicated in the evaluation of lymphoma and other solid tumours in children[4]. Involvement of bone marrow by malignant lymphoma indicates stage IV disease [10]. In this study bone marrow was involved in all seven cases. Variable percentage of bone marrow involvement ranging from 27.6 to 55% has been reported in the literature[10, 16]. Bone marrow involvement in all our cases is due to inadequate diagnostic facilities and lack of health awareness in the community so that patients consult the health experts at an advanced stage. Bone marrow involvement in two cases of solid tumours, one each in neuroblastoma and nephroblastoma was noted.

Anaemia affects 30% of world population[17]. In our study, cases of anaemia were on the top in non malignant disorders (28.8%). Of these, aplastic anaemia with picture of marrow failure was seen in 14.8% of cases, our results are almost similar to study of Rahim et al [2]. Higher frequency reported in our study & in developing world as compared to industrialized West [18, 19] may be due to common injudicious use of antibiotics like chloramphenicol etc in children with prolonged fever by unqualified quacks especially in the rural areas. In this study iron deficiency anaemia with the picture of hypochromia and microcytosis has been seen in 11% of cases. Our results are significantly higher as reported by Rahim et al (5%) [2], but comparable with studies of Githang'a & Dave[4] and Mwangi (12.7%) [14]**.** The higher number of cases of iron deficiency anemia may be due to economic starved population of this region who can not afford the iron rich fruit and food items. Megaloblastic anaemia is commonly caused by folate deficiency in paediatric age groups[20]. In our study megaloblastic anemia cases are merely 3%. Our results are different as various studies have shown these, ranging from 24% to as high as 68%[2,21,22]. The lowest percentage of cases of megaloblastic anaemia are possibly due to frequent supplementation of vitamin A, E and Folic acid in the prescription of children attending the paediatric clinics.

The ITP is common in childhood as compared to adults[4]. Though bone marrow is not needed for diagnosis of ITP,[23] but it is noted in 26.2% of cases. Our results are different and higher than reported by Bashawari[5], Rehman et al[6] and Al-Ghazaly et al[24], who reported its frequency 9.5%, 7.6% and 3.7% respectively. However Mohammad [25] has reported higher percentage of cases (48%). Such a large number of cases seen in the present study could be due to an exaggerated altered immune response in children of this region.

Reactive marrow findings due to recurrent and chronic infection were seen in 13 (4.8%) cases. One and half percent of our cases had evidence of malaria, which are comparable to study conducted by Githang'a and Dave[4]. Normal active marrow was found in 10 (3.7%) cases which might have been seen because cases may have been referred without proper indications or just on the basis of doubt about the diagnosis.

CONCLUSION

Appropriate diagnosis can not be made in haemotological disorders of childhood without bone marrow examination.

Acknowledgement

The authors are thankful to Mr. Mukhtiar Ali Kalhoro Computer Operator, for typing the manuscript.

REFERENCES

1. Kusum A, Negi G, Gaur DS, Kishore S, Meena H, Sharma A, Verma SK. Heamatological Malignancies diagnosed by bone marrow examination in a tertiary hospital at Uttarakhand, India. Indian J Hematol. Blood Transfus 2008; 24 (1): 7-11.
2. Rahim F, Ahmad I, Islam S, Hussain M, Khatak TAK, Bano Q. Spectrum of hematological

disorders in children observed in 424 consecutive bone marrow aspirations/biopsy. Pak J Med Sci 2005; 21 (4): 423-436.
3. Tahlan A, Bansal C, Palta A, Chauhan S. Spectrum and analysis of bone marrow findings in anemic cases. Indian J Med Sci 2008; 62:336-9.
4. Githang'a J.N, Dave P. Bone marrow examination at a pediatric hospital in Kenya. East African Medical Journal 2001; 78 (Supplement): 537-539.
5. Bashawari L.A. Bone marrow examination. Indications and diagnostic value. Saudi Medical Journal 2002; 23(2): 191-196.
6. Rahman MM, Khan MA, Afrose S, Ara T, Islam S, Biswas AR. Bone marrow examinations: Findings from four year retrospective Single Centre Review. J Medicine 2010; 11:115-118.
7. Onal IK, Sumer H, Tufan A, Shorbagi A. Bone marrow embolism after bone marrow aspiration and biopsy. Am J Hematol 2005 28; 78 (2):158.
8. Mirzai AZ, Hosseini N, Sadeghipour A. Indications and diagnostic Utility of Bone marrow examination in different bone marrow disorders in Iran. Laboratory Hematology 2009; 15 (4): 38-44.
9. Subramanian R, Basu D, Dutta TK. Prognostic significance of bone marrow histology in multiple myeloma. Indian J Cancer 2009; 46:40-5.
10. Kumar S, Rau A R, Naik R,Kini H, Mathai AM, Pai MR, Khadilkar UN. Bone marrow biopsy in non-Hodgkin lymphoma: A morphological study. Indian J Pathol Microbiol 2009; 52:332-8.
11. Krishnan C, Twist CJ, Fu T, Arber DA. Detection of isolated Tumor Cells in Neuroblastoma by Immunohistochemical Analysis in Bone Marrow Biopsy Specimens. Am J Clin Pathol 2009; 131:49-57.
12. Lee SH, Erber WN, Porwit A, Tomonaga M, Peterson LC & International council for Standardization in Hematology. ICSH guidelines for the standardization for bone marrow specimens and reports. International J Lab Hematol 2008; 30 (5): 349-364.
13. Kasili E.G. M.D. Thesis, University of Nairobi, 1979.
14. Mwangi J. Bone marrow aspiration and cytology-two year analysis. East Afr J Hosp Med 1999; 14:15-19.
15. Hatt PJ H, Gilchrist GS, O'Brien C. Childhood acute lymphoblastic leukemia; are routine end of therapy bone marrow and cerebrospinal fluid examination necessary? Mayo Clin. Proc. 1996; 71:8545-6.
16. Arber DA, George TI. Bone marrow biopsy involvement by non-Hodgkin's lymphoma: frequency of lymphoma types, patterns, blood involvement, and discordance with other sites in 450 specimens. Am J Surg Pathol 2005; 29:1549.57.
17. Huang J, Means R. The frequency and significance of iron deficiency anemia in patients with selected concurrent illness. The internet journal of internal Medicine 2009; 8:1.
18. Neal S, Young, JL, Abkowitz, Luzzatto L. New insights into the pathophysiology of acquired Cytopenias. Hematology 2000; 18-38.
19. Issaragrisil S, Leaverton PE, Chansung K, Thamprasit T, Porapakham Y, Young NS. The Aplastic Anemia Study Group: The incidence of aplastic anaemia in Thailand. Am J Hematol 1999; 61: 164-8.
20. Modood-ul-Mannan, Anwar M, Saleem M, Wigar A, Ahmad MA. Study of serum vitamin B12 and folate levels in patients of megaloblastic anemia in northern Pakistan. J Pak Med Assoc 1995; 45: 187.
21. Mussarat N, Raziq F. The incidence of underlying pathology in pancytopenia. An experience 0f 89 cases. J postgr Med Inst 2004; 18(1):76-9.
22. Ng SC, Kuperan P, Chan KS, Bosco J, Chan GL. Megaloblastic Anemia- a review from University Hospital, Kuala Lumpur. Ann Acad Med Sing 1988; 17:261.
23. British committee for standards in Haematology task force. Guidelines for the investigation and management of idiopathic thrombocytopenic purpura in adults, children and in pregnancy. Br J Haematol 2003; 120:574-596.
24. Al-Ghazaly J, Al-Selwi AH, Abdullah M, Al-Jahafi AK, Al-Dubai W, Al-Hashdi A. pattern of hematological diseases diagnosed by bone marrow examination in Yemen: a developing country experience. Clin lab Haematol. 2006; 28 (6): 376-381.
25. Mohammad AJ. Thyrombocytopenia in children. J Postgr Med Inst 2004;18(3):353-8.

Address for Corresponding Author:
Dr. Haresh Chand
Assistant Professor of Pathology
Chandka Medical College, Larkana
Mobile: 0333-7541954, 0312-2111954