FREQUENCY OF COMMON HEMATOLOGICAL DISEASES IN PAEDIATRIC PATIENTS PRESENTING WITH CLINICAL FEATURES INDICATIVE OF BONE MARROW EXAMINATION

Huma Riaz[1], Munawar Ali Shah[2], Rashid Azeem[3]

ABSTRACT

Objective: The objective of the study was to find the frequency of common hematological diseases diagnosed on bone marrow examination in our pediatric age group of patients.

Material and Methods: This study was conducted in the haematology unit, department of pathology, past medical graduate institute(PGMI), Hayatabad Medical Complex Peshawar (HMC)from March 1st 2012 to Jan 23rd 2013. Children admitted with bleeding, lymphadenopathy, Splenomegaly, Hepatomegaly, isolated or pancytopenia on peripheral blood smear was included in this study. The data was statistically analyzed by SPSS version 10.

Results: One hundred and sixty three cases were included in this study. The age range was from >1 month to15 years with a mean age of 6.56 years and standard deviation of + 4.668. Majority 82 (50.3%) of the children were in the age range of 1to 5 years. Male to female ratio was1.39:1. The commonest disorder was leukemia present in 65(39.9%)of the cases followed by megaloblastic anemia present in 25(15.3%)cases, idiopathic thrombocytopenic purpura(ITP) present in 18(11%) cases and aplastic anemia present in 11(6.7%) cases.

Conclusion: leukemia followed by megaloblastic anemia were the common most haematological disorders, most commonly found in males of age group 1year to 5 years.

Key Words: Bone marrow Examination, Leukemia, Megaloblastic anemia, Aplastic Anemia, Idiopathic Thrombocytopenic Purpura (ITP)

INTRODUCTION

Haematological disorders are quite common in children. These vary from simple conditions like iron deficiency anemia to congenital hypo plastic anemia and physiological anemia of infancy to acquired red cell aplasia.[1] And Bone marrow examination is a very important investigation for the diagnosis of many haematological and non-haematological diseases.[2]

An important indication for bone marrow investigation is the presence of bone marrow failure, which manifests itself as pancytopenia[3]. This may be a transient event secondary to viral infection or something grave like congenital bone marrow aplasia. This can also result from either a failure of production of haemopoitic progenitor cells, called aplastic anemia or peripheral destruction of cellular elements either due to infection, immune mediated damage or Hypersplenism.[4]

[1] FCPS (Hemat), DCP (Clinical Pathologies) Molvi Ameer Shah Govt, Hospital Peshawar
[2] Lecturar Anotomy Department KGMC
[3] Assistant Professor North West School of Medicine

Address for correspondence:
Dr. Huma Riaz
FCPS (Hemat), DCP (Clinical Pathologies) Molvi Ameer Shah Govt, Hospital Peshawar
Cell: 0320-9013328
E-mail: humariaz82@yahoo.com

Pancytopenia is a common occurrence in paediatric patients.[5] The etiology of bicytopenia/pancytopenias varies widely in children, ranging from transient marrow viral suppression to marrow infiltration by fatal malignancy. Depending on the etiology, the clinical presentation can be with fever, pallor or infection. Knowing the exact etiology is important for specific treatment and prognostication.[6] Cytopenias e.g.; bicytopenia and pancytopenias are common findings in megaloblastic anemia of the childhood. Megaloblastic anemia is common in pediatric population of developing countries. It is a macrocytic anemia caused by the deficiency of folic acid, vitamin B12 or both.[7]

Aplastic anemia is a hematological disorder characterized by pancytopenias resulting from early stem cell deficiency. Chemical exposure, medicines, viral infections and immunodeficiency are the etiological factors responsible.[8]

Clinically a child presenting with pancytopenias should be evaluated for the possibility of either a bone marrow failure syndrome or acute malignancy, particularly when associated with lymphadenopathy or visceromegaly.[11,12]

There is a wide variety of disorders in pediatric patients where bone marrow examination provides diagnostically important information.[13] liquid bone marrow is aspirated from the tibia or posterior iliac crest under local anesthesia with little discomfort to the patient. Trephine biopsy is usually performed when there is

hypoplasia or aplasia on aspiraton.[14]

There is a long list of diseases which reveal bone marrow changes. A large number of these disorders presents with vague clinical symptoms and create a diagnostic problem which cannot be solved without resorting to bone marrow aspiration and examination. Furthermore the spectrum of haematological disorders is relatively different in the developing world than the developed countries[2,15]. A study conducted in Khyber Teaching Hospital in 2005 showing frequency of Megaloblastic anemia 24%, Aplastic anemia 14%, Leukemias 26% and ITP 9% in paediatric patients[16]. While another study conducted at Gomal Medical College D I Khan shows frequencies as Megaloblastic anemia 57.7%, Aplastic anemia 20%, Leukemias 15%, ITP 15 %.[17]

Therefore, this study is designed with the view to know the etiological pattern of disorders diagnosed on bone marrow in the pediatric population of a tertiary care hospital.

MATERIAL AND METHODS

This study was conducted at the Department of pathology, Post Graduate Medical Institute (PGMI), Hayatabad Medical Complex, Peshawar (HMC) over a period 11 months. It was a cross sectional descriptive study with non-probability convenient sampling. Total of 163 patients were included using 9% proportion of Immune thrombocytopenic purpura, 95% confidence level and 4.4% margin of error under WHO software for sample size determination.

All the patients with Age >1 month and <15 years with signs and symptoms having Pallor, Bleeding, Lymphadenopathy, Peripheral Cytopenias, Pyrexia of unknoworigin, Hepatosplenomegaly Were included in the study. All patients having Hemorrhagic disorders such as Congenital coagulation factor deficiencies like Hemophilia, Disseminated intravascular coagulation, Taking anticoagulant drug therapy, Skin infection or recent radiation therapy at the sampling site, Bone disorders such as Osteomyelitis or Osteogesis imperfecta were excluded from the study. The data was statistically analyzed by SPSS version 10 for variables.

RESULTS

The study was conducted in Department of Hematology Hayatabad Medical Complex, Peshawar. A total of 163 children were included in the study.

In Majority of children 82(50.3%), the age was ranged from 0-5 years, while the rest 81 (49.7 %) children were in the range of 6-15 years. Minimum age in this study was 1 year, while maximum age was 15 years, with mean age of 6.56 years standard deviation $\pm$ 4.668 years. (Table No. 1)

Out of these 163 children 95 (58.3 %) were males while 68 (41.7%) were females. The overall male to female ratio was 1.39: 1. (Table No. 2)

Out of these 163 children 25 (15.3%) were having megaloblastic anemia, 11 (6.7%) were having aplastic anemia, 65 (39.9 %) were having acute leukemia, 18 (11.0%) were having ITP, while 44 (27%) of children were having pathologies other than these common haematological disorders. (Table No. 3)

Out of 163 children those 25 children having megaloblastic anemia 16 children were having age between 0-5 years while 09 children were between 6-15 years of age, those11 children having aplastic anemia 01 child was having age from 0-5 years while 10 children were

Table: 1 Age distribution (n=163)

Age	Frequency	Percent
0-5 years	82	50.3
6-15 years	81	49.7
	163	100.0

Mean age 6.56 with SD + 4.668 year

Table: 2 Sex distribution frequency table (N= 163)

	Frequency	Percent
Male	95	58.3
Female	68	41.7
Total	163	100.0

Table 3 Disease distribution (N= 163)

Disease	Frequency	Percent
Megaloblastic anemia	25	15.3
aplastic anemia	11	6.7
Leukemia	65	39.9
ITP	18	11.0
Others	44	27.0
Total	163	100.0

Table 4 Stratification of Disease in age distribution (N= 163)

Disease	Age 0-5 year	Age 6-15 years	Total
Mega-loblastic A	16	09	25
Aplastic anemia	01	10	11
Leukemia	27	38	65
ITP	12	06	18
Others	26	18	44

Chi square test was applied in which P value was 0.046

Table 5 Stratification of Disease in gender distribution (N= 163)

		Sex		Total
		Male	Female	
Disease	megaloblastic anemia	9	16	25
	aplastic anemia	8	3	11
	Leukemia	39	26	65
	ITP	13	5	18
	Others	26	18	44
Total		95	68	163

Chi square test was applied in which P value was 0.108

having age between 6-15 years, in those 65 children having leukemia 27 children were in age between 0-5 years while 38 children were from 6-15 years, in those 18 children having ITP 12 children were in age between 0-5 years while 06 children were having age from 6-15 years. Chi square test was applied with P value 0.046. (Table No. 4)

Out of 163 children among those 25 children having megaloblastic anemia 09 children were male and 16 children were female, in 11 children with aplastic anemia 08 children were male and 03 were female, of 39 children with acute leukemia 39 were male and 26 were female and among 18 children with ITP, 13 were male while 05 were female. Chi square test was applied in which P value was 1.108.(table No.5)

DISCUSSION

Haematological disorders are very frequently encountered in general paediatric practice and in investigation of such patients, bone marrow examination is proved to be an important investigation to reach a conclusive diagnoses. In our study the frequencies of four most common haematological disorders, i.e; megaloblastic anemia, aplastic anemia, leukemia and idiopathic thrombocytopenic purpura (ITP) were considered in paediatric population of age from >1 month to 15 years. Leukemia was found to be the commonest entity, present in 39.9% of the total cases, followed by megaloblastic anemia, present in 15.3% of the total cases. Similar results have been reported in a recent study from Peshawar, [16] though the margin of frequency of leukemia is much higher in our study compared to that study conducted.

Leukemia was the most common disorder found to be present in 39.9% of these cases. Similar results were reported in a study conducted in P eshawar[15] While conflicting results have been reported in a study from Peshawar and another study from Islamabad[2,84], in which aplastic anemia was the commonest reported disorder about 20.2% of the total cases followed by ITP,15.7% of the total cases[2]. Worldwide leukemia is the most commonly found malignancy of children, accounting for about 41% of all types of malignant disorders that encounter the paediatric age group having age less than 15 years,[85] in USA the annual incidence of 4.5 cases per 100000 children, out of which acute lymphoblastic leukemia (ALL) is the most common type of malignancy and leukemia.[59] The exact incidence is not known in our country due to lack of studies conducted on large scale, however this is the commonest malignancy in this part of the world too.[84] the exact etiology of ALL is not known however exposure to radiation, viral infections and toxic chemical substances like herbicides, pesticides, chemical solvents and ground water chemical contamination are thought to play a role in etiology of acute leukemia. Fortunatetely over the last few decades, there has been a great improvement in the survival rate of children with leukemia .i.e; 80% at five years from diagnoses.[86]

The second most common haematological disorder in this study was megaloblastic anemia found to be in 15.3% of all the cases. Similar results have been published in a few other national studies.[15] While the frequency of megaloblastic anemia was recorded to be very high in a study conducted in DI Khan in 2006 as 57.7% of the total cases. This is considered to be one of the main causes of nutritional deficiency anemia in the developing world where it reflects the poor socioeconomic status of the society. Nutritional Megaloblastic anemia is one of the leading causes of pancytopenia among younger paediatric age group.[87] our country is rich in green leafy vegetables, which is a prime source of folic acid, however factors like chronic diarrhea, worms infestation, malabsorption and poor eating habits may be contributing to the micro nutritional deficiency.[2]

Idiopathic Thrombocytopenic Purpura (ITP) was 3 rd commonest haematological disorders found in our study, found to be 11% of the total cases. While ITP was reported as a least common disorder the studies conducted in Peshawar found to be 9 % and DI Khan found as 15% of the total cases,[15,17] it is one of the commonest cause of purpura. The common presenting feature is more often Epistaxis, haematuria and in very rare cases intracranial bleed which is fatal.[73]

The least common hematological disorder in our study was aplastic anemia, found as 6.7% of the total cases. In a similar local study conducted in 2007, aplastic anemia was found as the commonest hematological disorder in children, reported as 20.2% of the total cases.[2] no accurate prospective data available regarding the incidence of aplastic anemia worldwide.[57] Aplastic anemia is thought to be more common in Asia than in West.[58] The patients are mostly presented with unexplained pallor, prolonged pyrexia and bleeding tendencies. Its exact etiology is still not known, but autoimmune mechanism have been considered to have an important role in the Pathophysiology. Studied con-

ducted worldwide have confirmed the role of exposure to toxic chemical substances and radiation in causing bone marrow failure.[53]

CONCLUSION

It is concluded from the results of our study that Leukemia was the commonest haematological disorder followed by megaloblastic anemia and ITP, Aplastic anemia being lowest in frequency. The commonest age group affected was between 0-5 year among whom males were affected more than females.

REFERENCES

1. Khan A, Aqeel M, Khan TA, Munir A. Patterns of haematological diseases hospitalized pediatric patients based on bone marrow examination. J Post Graduate Med Institute 2008 Jul-Sep; 22(3); 196-200.
2. Neal S, Young JL, Abkowitz, Luzzatto L. New insight into the pathophysiology of acquired Cytopenias. Haematology 2000; 18-38.
3. Lequit RJ, Van-den-Tweel JG. The pathology of bone marrow failure. Histopathol 2010 Nov;57(5);655-0.
4. Listernick R. A 14- years old girl with pancytopenias. Ped Ann 2006; 35: 76-8.
5. Memon S, Shaikh S, Nizamani A. Etiological spectrum of pancytopenia based on bone marrow examination in children. J Coll Physicians Surg Pak 2008 Mar;18 (3):163-7.
6. Naseem S, Varma N, Das R, Ahluwalia J, Sachdeva MU, Marwaha RK. Pediatric patients with bicytopenia/ pancytopenias: Review of etiologies and clinico-hematological profile at a tertiary care centre. Indian j pathol micribiol. 2011 Jan-Mar; 54(1): 75-80.
7. Ayub T, Khan FR. Prevalence of megaloblastic anemia in a pediatric unit. Gomal J Med Sci 2009 Jan- June; 7(1): 62-4.
8. Kazi MY, Iftikhar S, Khan HI. Aplastic anemia in children. Pak Paed J 1998; 22(2); 71-4. revised March 2007.
9. Wen JQ, Feng HL, Wang XQ, Pang JP. Hemogram and bone marrow morphology in children with chronic aplastic anemia and myelodysplastic syndrome. World J Peditr. 2008 Feb; 4(1); 36-40.
10. Gupta V, Tilak V, Bhatia BD. Immune thrombocytopenic purpura. Indian J Pediatr. 2008 July; 75(7); 723-8
11. Syed NN, Moiz B, Adil SN, Khurshid M. Diagnostic importance of bone marrow examination in non-hematological disorders. J Pak Med Assoc. 2007 March;57 (3);123-5.
12. Agarwal S, Narayan S, Sharma S, Kahkashan D, Patwari AK. Haemophagocytic syndrome associated with visceral Leishmaniasis. Indian J Pediatr. 2006; 73; 445-6.
13. Ozyurek E, Ozcay F, Yelmaz B, Ozbek N. Hemophagocytic lymphohistiocytosis associated with Visceral Leishmaniasis: A case report. Pediatr Hematol Oncol 2007; 22; 409-14.
14. Afzal S, Ahmad M, Mubarik A, Khan SA, Zafar L, Khan DA. Significance of bone marrow trephine biopsy in the diagnosis of hematological and non-hematological disorders. Pak J Pathol 2006; 17; 10-5.
15. Rahim F, Ahmad I, Islam S, Hussain M, Khattak TA, Bano Q. Spectrum of hematological disorders in children observed in 424 consecutive bone marrow aspirations/biopsies. Pak J Med Sci 2007; 21; 433- 6.
16. Neal S, Young JL, Abkowitz, Luzzatto L. New insights into the pathophysiology of acquired cytopenias. Hematol 2006; 18-38.
17. Rahman F. Ahmad I, Islam S, Hussain M, Khattak TA, Bano Q. spectrum of hematological disorders in children n 424 consecutive bone marrow aspirations/biopsies. Pak J Med Sci 2007 Oct – Dec; 21(4); 433-6.
18. Ayub T, Khan FR. Prevalence of megaloblastic anemia in a paediatric unit", Gomal Journal of Med Sci 2009 Jan – Jun;7(1). 62–4.
19. ParapiaLA. Trepanning or trephines: a history of bone marrow biopsy. Br J Haematolo. Oct 2007;139(1):14-9.
20. Fend F, Tzankov A, Bink K, et al. modern techniques for the diagnostic evaluation of the trephine bone marrow biopsy:methodological aspects of applications. Prog Histochem Cytochem. 2008; 42 (4): 203-52.
21. Grace F D'costa, Seema R Dua Yoganand V Patil. Spectrum of Paediatric bone marrow trephine biopsies.Lancet Neurol. 2007; 6: 201.
22. Fauzia Shafi Khan, Rabiya Fayyaz Hasan Bone marrow examination of pancytopenic children. J Pakistan Med Assoc. 2012; 62: 660
23. Rubin R, David S. Strayer. Rubin's Pathology; clinicopathologic Foundations of Medicine. Lippincott Williams &Wilkins; 2007; 90.
24. Bain BJ. Bone marrow trephine biopsy. J Clin Pathol. Oct 2001; 54(10): 737-42.
25. Bain BJ. Bone marrow aspiration. J Clin Pathol. Sep 2001; 54(9); 657-63.
26. Oussama Abla MD, Jeremy friedman, John Doyle",Performing bone marrow aspiration and biopsy in children; Recommended guidelines,"-PAEDIATR Child health Vol13 no 6 (498-501), july/ august 2008.
27. Riley RS, Hogan TF, Pavot DR, et al., a pathologist's perspective on bone marrow aspiration and biopsy;I, performing a bone marrow examination. j Clin Lab. Anal 2004;18; 70-90.
28. Rahim F, Ahmad I, Islam S, Hussain M, Khattak TA, Bano Q," Spectrum of haematological disorders in children observed in 424 consecutive bone marrow aspiration/biopsies." Pak J Med Sci.2005; 21: 433-6.
29. Bashawri LA. Bonemarrow examination, indications and diagnostic value, Saudi Med J 2002; 23; 191-6.

30. Sokolowska B, Skomra D, Czartoryska B et al. gaucher disease diagnosed after bone marrow trephine biopsy- a report of two cases. Folia histochem Cytobiol. 2011; 49(2): 352-6.

31. Trewhittt KG. Bone marrow aspiration and biopsy; collection and interpretation. Oncol Nurs Forum. Oct 2001;28(9): 1409-15; quiz 1416-7.

32. WilkinsBS. "Pitfalls in bone marrow pathology; avoiding errors in bone marrow trephine biopsy diagnosis". J Clin Pathol. May 2011; 64(5); 380-6.

33. Bain BJ. Morbidity associated with bone marrow aspiration and trephine biopsy- a review of UK data for 2004, haematologica. Sep 2006; 91(9): 1293-4.

34. Antony AC, Hoffman R, Benz EJ, Shattil SJ, et al 'Megaloblastic anemia'. Hematology. Basic principles and practice.4th ed. Edinburgh:Churchill Livingstone; 2005: 519–56

35. Harmening DM. Clinical Hematology and Fundamentals of Hemostasis. 4th Ed. 2001.

36. Carmel R. Greer JP, Foerster J, Lukens JN, Rodgers GM, Paraskevas F, Glader B (eds). "Megaloblastic anemias: Disorders of impaired DNA synthesis". In: Wintrobe's clinical hematology. 11th ed. Philadelphia: Lippincott Williams and Wilkins; 2004: 1367–95

37. Braunwald E, et al., eds., Harrison's principles of Internal Medicine. 15th ed. New York, McGraw-Hill. 2001; 674-680.

38. Antony AC. Vegetarianism and vitamin B-12 (cobalamin) deficiency. Am J Clin Nutr; 2003; 78: 3–6.

39. Clarke R, Grimley. Evans J, Schneede J, Nexo E, Bates C et al 'Vitamin B12 and Folate deficiency in later life. Age ageing 2004; 33. 34-41.

40. Hoffman R, Benz EJ, Furie B, Shattil SJ. Haematology; Basic principles and practice. Philadelphia, Pa; Churchill Livingstone; 2009; 271-281.

41. Von Castel-Dunwoody, K.M., Kauwell, G.P., Shelnutt, K.P,et al, 'Transcobalamin 776C fi G polymorphism negatively affects vitamin B-12 metabolism. American Journal of Clinical Nutrition (2005), 81, 1436–1441.

42. Wang YH, Yan F, Zhang WB, Ye G, Zheng XH, et al, An investigation of vit B12 deficiency in elderly patients in neurology dept. Neurosci Bull. 2009; 25(4); 209-15.

43. Dali Youcef N, Anres E. An update on cobalamine deficiency in adults. QJM. Jan 2009; 102(1) ; 17-28.

44. Olsen BS, Hahnemann JM, Schwartz M, et al. 'THIAMINE RESPONSIVE MEGALOIBLASTIC ANEMIA; A CAUSE OF SYNDROMIC DIABETES IN CHILDHOOD' pediatr Diabetes Aug. 2007; 8(4); 239-41.

45. Tariq Ayub and Fazal Ur Rahman KhanDepartment of Paediatrics, Gomal Medical College D.I.Khan, Pakistan' PREVALENCE OF MEGALOBLASTIC ANAEMIA IN A PAEDIATRIC UNIT'. Gomal Journal of Medical Sciences January-June 2009, Vol. 7, No.1; 62-64.

46. Iqbal SP, Kakepoto GN, Iqbal SP.,'Vitamin B12 deficiency--a major cause of megaloblastic anaemia in patients attending a tertiary care hospital', J. Ayub Med Coll Abbottabad. 2009 Jul-Sep; 21(3): 92-4

47. Khanduri U, Sharma A Department of Haematology, St Stephen's Hospital, Tis Hazari, Delhi, India,' Megaloblastic anaemia: prevalence and causative factors',Nati Med J India 2007 Jul-Aug; 20(4): 172-5.

48. Young NS.' Patho physiologic mechanisms in acquired aplastic anemia', Hematology Am Soc Hematol Educ Program. 2006; 72-74..

49. Wu Y, Yu J, Zhang L, Luo Q, Xiao JW, Liu XM, et al. [Hematopoiesis support of mesenchymal stem cells in children with aplastic anemia. Aug 2008; 10(4): 455-9.

50. Young NS. Patho physiologic mechanisms in acquired aplastic anemia. Hematology Am Soc Hematol Educ Program. 2006; 72-7.

51. Liu H, Mihara K, Kimura A, Tanaka K, Kamada N.' Induction of apoptosis in CD34+ cells by sera from patients with aplastic anemia'. Hiroshima J Med Sci. Jun 2003; 48(2): 57-63.

52. Passweg JR, Pérez WS, Eapen M, Camitta BM, Gluckman E, Hinterberger W, et al."Bone marrow transplants from mismatched related and unrelated donors for severe aplastic anemia'. Bone Marrow Transplant. Apr 2006; 37(7): 641-9.

53. Rosti V. "The molecular basis of paroxysmal nocturnal hemoglobinuria", Haematologica. Jan 2000;85(1):82-7.