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Original Research Article

Clinico hematological profile of pancytopenia in pediatric patients: an institutional experience in North Himalayan region of India

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ABSTRACT

Background: Pancytopenia is a common clinical pattern with an extensive differential diagnosis, but literature search shows only limited studies of pancytopenia in Pediatrics patients in Uttarakhand state of India. The present study was therefore conducted to study the spectrum of pancytopenia with bone marrow and haematological profile in Pediatrics patients in this north Himalayan state of India.
Methods: Prospective observational study was conducted in the Department of Pediatrics in the teaching institute situated in Uttarakhand state of India over a period of 12 months. The study included all the patients of pancytopenia below 18 years of age who underwent bone marrow examination after written informed consent.
Results: The study included total 50 pediatrics patients of pancytopenia with male to female ratio of 1.38:1. The mean age of patients was 10.58±4.94 with median age of 12 years. Mean hemoglobin was 5.31±2.09 g/dl, total leukocyte count was 2492.68±941.76/mm3, platelet count was 34724±26423/mm3, mean corpuscular volume was 90.95±16.65 fl, mean corpuscular hemoglobin was 30.11±6.07 pg, mean corpuscular hemoglobin concentration was 33.06±1.65% and reticulocyte count was 1.21±1.10%. Nutritional deficiency (28%) was the most common cause for pancytopenia followed by aplastic anemia (24%). Megaloblastic anemia was the commonest cause of nutritional deficiency anemia (71.42%) with pancytopenia.
Conclusions: Pancytopenia is an important presentation in Pediatrics population with the most common cause being nutritional anemia and aplastic anemia. Megaloblastic anemia is the commonest cause of nutritional anemia with pancytopenia. The clinicians should be aware of spectrum of pancytopenia with clinical and haematological presentation in Pediatrics patients of this region so as to avoid unnecessary work ups and delay in treatment.

Keywords: Clinical, Haematological, Pancytopenia, Pediatrics

INTRODUCTION

Pancytopenia refers to a reduction below normal values of all the three peripheral blood lineages including leukocytes, platelets and erythrocytes.[1] The spectrum of pancytopenia is different in children in comparison to adults and it also varies from developing world to developed countries.[2] The mechanisms contributing to pancytopenia include decrease in hematopoietic cell production, marrow replacement by abnormal cells, suppression of marrow growth and differentiation, ineffective hematopoiesis with cell death, defective cell formation, antibody mediated sequestration or destruction of cells in a hypertrophied and overactive reticuloendothelial system.[3] The presenting symptoms are often attributable either to the anemia or thrombocytopenia. while leucopenia is often seen in the subsequent course of the disorder.[3] Pancytopenia may

present with some benign or other serious conditions like bone marrow failure and acute malignancy cases specially associated with hepatosplenomegaly with varying differential diagnosis and usual clinical presentation of pancytopenia, we find limited studies in pediatric patients in Uttarakhand state of India.

The present study was therefore conducted to study the spectrum of pancytopenia with bone marrow and haematological profile in Pediatrics patients in this north Himalayan state of India.

METHODS

The study was conducted in the department of Pediatrics over a period of one year from October 2012 to October 2013. Subjects were recruited from patients presenting with a primary diagnosis of pancytopenia and after obtaining written informed consent. This is the observational type of the study. 50 consecutive patients presenting with pancytopenia in OPD/IPD were recruited for the study

Inclusion criteria

- Age <18 years
- Pancytopenia measured by automated cell counter and confirmed via general blood picture, defined as
  - Anemia : hemoglobin <10 gm /dL.
  - Leukopenia : total white cell count <4 x 10^9/L.
  - Thrombocytopenia : platelet count <100×10^9/L.[2]

Exclusion criteria

- Age ≥18 years
- Exposure to myelotoxic drugs
- Recent history of blood transfusion
- Patients not consenting for bone marrow examination

Study tools

Case recording form, routine blood counts, Abbott Cell-Dyn 3700, bone marrow examination, Jamshidi needle.

Study protocol

Patients presenting with the diagnosis of pancytopenia and signs and symptoms of fever, pallor, petechial rash, bleeding, bone pain, hepatomegaly, splenomegaly, lymphadenopathy were taken into the study.

Baseline characteristics

Details were recorded in subject proforma that included age, sex, address.

Relevant medical history were taken involving present illness, past illness, personal and family history. Complete clinical examination was done.

Routine blood examination were sent to measure various blood indices viz. hemoglobin, red blood cell count, total leukocyte count, differential leukocyte count, platelet count, mean corpuscular volume (MCV), mean corpuscular hemoglobin (MCH), mean corpuscular hemoglobin concentration (MCHC), packed cell volume (PCV), Mean Platelet Volume (MPV).

Confirmation was done by peripheral smear stained by Leishman stain for all the cases. Bone marrow aspiration was subsequently carried out under aseptic precaution after obtaining written consent from the patient or guardian.

Data management and statistical analysis

Interpretation and statistical analysis of obtained results was done using SPSS version 22.

RESULTS

The study included total 50 pediatrics patients of pancytopenia with male to female ratio of 1.38:1. The mean age of patients was 10.58±4.94 with median age of 12 years. Maximum numbers of cases were seen in 11-18 years group (56%). Majority of children (64%) were completely immunized for age and no un-immunized child was seen in the study. Maximum number of cases belonged to upper lower class (44%) and 64% were vegetarian in their dietary habits. Common presenting symptom of patients was fever (86%) followed by generalized weakness, abdominal pain, vomiting and bleeding manifestations. Table 1 shows the clinical presentation of the cases. It shows that pallor was present in all the cases while hepato-splenomegaly was observed in 40% of cases. Equal no (24%) of subjects had skin bleeds and lymphadenopathy.

Table 1: Clinical presentation of the cases.

Clinical presentation	Number of cases (% of total cases)
Pallor	50 (100%)
Tachycardia	34 (68%)
Tachypnea	11 (22%)
Skin Bleeds (Petechiae, Purpura, Ecchymosis)	12 (24%)
Lymphadenopathy	12 (24%)
Hyper Pigmented Knuckles	6 (12%)
Bony Tenderness	3 (6%)
Hepatomegaly	11 (22%)
Splenomegaly	1 (2%)
Hepatosplenomegaly	20 (40%)

According to WHO grading the anemia was severe in 86% while moderate in 14% cases. Mean haemoglobin was 5.31±2.09 g/dl, total leukocyte count was 2492.68±941.76/mm^3, platelet count was 34724±26423/mm^3, mean corpuscular volume was 90.95±16.65 fl, mean corpuscular haemoglobin was

30.11±6.07 pg, mean corpuscular haemoglobin concentration was 33.06±1.65% and reticulocyte count was 1.21±1.10%. The general blood picture of the majority of patients was normocytic (42%) followed by microcytic (32%) and macrocytic (24%). Single case showed dimorphic blood picture. Bone Marrow examination revealed normocellularity in 42% cases, hypercellularity in 30% cases and hypocellularity in 28% cases. Table 2 shows the different causes of pancytopenia observed in the present study. It shows that nutritional deficiency (28%) was the most common cause for pancytopenia followed by aplastic anemia (24%). Cases of nutritional deficiency anemia along with pancytopenia were further analysed and the commonest cause (71.42) found to be megaloblastic anemia. Leukemic patients presented predominantly with pallor (100%), lymphadenopathy (80%), hepatosplenomegaly (80%) and tachycardia (60%). Acute lymphoblastic leukemia (ALL) was the most common type of leukemia identified in the study in 70% cases whereas acute myeloid leukemia (AML) was identified in 10% of the cases. In 20% of cases definite opinion on type of leukemia was not possible on morphology. Visceral leishmaniasis (72.72%) was the most common infectious etiology causing pancytopenia observed in this study followed by one case each of enteric Fever, malaria with scrub typhus and tuberculosis with staphylococcal sepsis.

Table 2: Different causes of pancytopenia observed in the study.

Causes	No. of cases (%)
Nutritional deficiency anemia	14 (28%)
Aplastic anemia	12 (24%)
Infections	11 (22%)
Leukemia	10 (20%)
Others (Hypersplenism, anemia of chronic disease)	3 (6%)

Table 3 shows the comparison of haematological indices in various aetiologies of pancytopenia. It shows that mean Hb was lowest in megaloblastic anemia while mean TLC and platelet count was lowest in acute leukemia and aplastic anemia patients respectively.

Table 3: Comparison of hematological indices in various aetiologies of pancytopenia.

Indices	Megaloblastic anemia	Aplastic anemia	Acute Leukemia	Infection
Hemoglobin (g/dl)	4.44±1.63	4.55±2.01	6.61±2.21	5.73±1.68
TLC (/mm^3)	2561±974.53	2525±836.27	2149.40±1134.02	2391.81±919.42
MCV (fl)	112.95±12.08	91.55±8.87	85.49±5.65	77.98±13.13
MCH (pg)	37.59±4.79	30.87±3.11	28.49±1.73	25.37±4.90
MCHC (%)	33.52±1.71	33.68±1.03	33.47±1.45	32.45±1.33
Platelet Count (/mm^3)	45920±24380.17	16791.66±9917.88	30010±23283.53	35900±23105.45
Retic (%)	1.7±1.45	0.49±0.29	1.21±0.89	1.02±0.85

DISCUSSION

More no of male children in the present study is in harmony with other studies from Indian sub-continent.[4-6] The reason for this may be the deep rooted mind set of this society toward concern and care of male children. In this study median age of presentation of 12 years was higher in comparison to other studies where pancytopenia children presented at median age of 6-8 years.[7,8] The main presenting features of children with pancytopenia were progressive pallor (100%) and fever (86%). Memon et al, also reported pallor (87%) and fever (65%) as the main presentations of pancytopenia.[9] The most common cause of pancytopenia in this study was nutritional anemia (28%) followed by aplastic anemia (24%). This is in contrast to previous study which reported megaloblastic anemia and leukemias as a cause of pancytopenia in only 13% of children.[9] Pine et al, observed that infectious etiology (64%) (including bacterial sepsis, non-EBV viral infections and sepsis syndrome) and aplastic anemia (11%) were two important causes of pancytopenia.[8] Lack of vitamin B12 or folic acid in cases of megaloblastic anemia may accelerate the early death of hematopoietic stem cells; leading to ineffective erythropoiesis, leucopoiesis, thrombopoiesis and may incriminate pancytopenia.[10] There were two cases (4%) of combined nutritional deficiency anemia in this series. Memon et al, reported 8.06% cases of mixed nutritional deficiency anemias in their study which was more than the present study.[9]

In this study, out of 11 subjects with infections, kala- azar accounted for 7(63.63%) patients. Kala-azar in itself is not a common cause of pancytopenia but isolated cytopenias in form of anemia, leucopenia, thrombocytopenia or bicytopenia, are encountered frequently.[11] Although visceral leishmaniasis (VL) is endemic in various parts of India but is rarely reported from the hilly areas of India.[12] A good number of cases in the pediatric age group highlights the fact that Garhwal region should be considered as an endemic region of VL. The hematological changes were reversed after the

institution of appropriate therapy with parenteral sodium stibogluconate in 6 patients and amphotericin B in 1 patient which was contrary to recent reports of refractoriness of sodium stibogluconate in treating VL thereby reinforcing the fact that VL of Garhwal region is sodium stibogluconate sensitive.[13] One patient in this study had disseminated Koch's coexisting with Staphylococcal septicemia. Pancytopenia can be a rare presentation of disseminated TB and occasionally it can be appreciated in pulmonary tuberculosis as well.[14] However, pancytopenia as the presenting feature of disseminated tuberculosis is extremely rare both in children and adults.[15,16] In this study 10 patients of pancytopenia had the eventual diagnosis of acute leukemia comprising 20% of all cases. This is reported less than the studies which previously observed 23% and 26.6% cases of acute leukemia in their series of pancytopenia patients.[4,7]

Important limitation of this study were small sample size which may not be representative of the population. In addition, as the study was carried out in the tertiary care centre so the exact prediction of pancytopenia in this region may have not been predicted.

CONCLUSION

Pancytopenia is an important presentation in pediatric population with the most common cause being nutritional anemia and aplastic anemia. The commonest cause of nutritional deficiency anemia with pancytopenia is megaloblastic anemia. Leishmaniasis which is considered to be non-endemic in this north Himalayan region constituted an important cause of pancytopenia in children of this region. The clinicians should be aware of spectrum of pancytopenia with clinical and hematological presentation in pediatric patients of this region so as to avoid unnecessary work ups and delay in treatment.

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REFERENCES

1. Freedman MH. The Inherited Pancytopenias. In: Kliegman RM, Stanton BF, St. Geme III JW, Schor NF, Behrman RE, eds. Nelson Textbook of Pediatrics. 19th ed. New Delhi (India): Saunders-Elsevier; 2011: 1684.
2. Young NS, Abkowitz JL, Luzzatto L. New insights into the pathophysiology of acquired cytopenias. ASH Edu Progr Book. 2000 Jan;2000(1):18-38.
3. Jha A, Sayami G, Adhikari RC, Panta AD, Jha R. Bone marrow examination in cases of pancytopenia. J Nepal Med Assoc. 2008 Jan 1;47(169):12-7.
4. Naseem S, Varma N, Das R, Ahluwalia J, Sachdeva MU, Marwaha RK. Pediatric patients with bicytopenia/pancytopenia: review of etiologies and clinico-hematological profile at a tertiary center. İndian J Pathol Microbiol. 2011 Jan 1;54(1):75.
5. Tilak V, Jain R. Pancytopenia-a clinico-hematologic analysis of 77 cases. Ind J Pathol Microbiol. 1999 Oct;42(4):399-404.
6. Gupta V, Tripathi S, Tilak V, Bhatia BD. A study of clinico-haematological profiles of pancytopenia in children. Trop Dr. 2008 Oct;38(4):241-3.
7. Bhatnagar SK, Chandra J, Narayan S, Sharma S, Singh V, Dutta AK. Pancytopenia in children: etiological profile. J Trop Pediatr. 2005 Aug 1;51(4):236-9.
8. Pine M, Walter AW. Pancytopenia in hospitalized children: a five-year review. J Pediatr Hematol/Oncol. 2010 Jul 1;32(5):e192-4.
9. Memon S, Shaikh S, Nizamani MA. Etiological spectrum of pancytopenia based on bone marrow examination in children. J Coll Physi Surg Pak. 2008 Mar 1;18(3):163-7.
10. Whitehead MV, Rosenblatt DS, Cooper BA. Megaloblastic Anemia. In: Nathan DG and Orkin SH. Eds. Nathan And Oski's Hematology of Infancy and Childhood. 5th ed. WB: Saunders-Philadelphia; 1989; 385-422.
11. Chandra J, Anand V, Patwari AK, Mandal RN, Aneja S, Sharma D. Kala-azar: experience from a non-endemic area in India. J Trop Pediatr. 1995 Oct 1;41(5):298-300.
12. Verma SK, Ahmad S, Shirazi N, Kusum A, Kaushik RM, Barthwal SP. Sodium stibogluconate-sensitive visceral leishmaniasis in the non-endemic hilly region of Uttarakhand, India. Transact Royal Soci Trop Medi Hygi. 2007 Jul 1;101(7):730-2.
13. Dube A, Singh N, Sundar S, Singh N. Refractoriness to the treatment of sodium stibogluconate in Indian kala-azar field isolates persist in in vitro and in vivo experimental models. Parasitol Res. 2005 Jun 1;96(4):216-23.
14. Luamerer KM, Kissane JM. Pancytopenia and hepatosplenomegaly in a 69-year-old woman. The American J Medi. 1991 Jun 1;90(6):740-9.
15. Maartens G, Willcox PA, Benatar SR. Miliary tuberculosis: rapid diagnosis, hematologic abnormalities, and outcome in 109 treated adults. Am J Medicine. 1990 Sep 1;89(3):291-6.
16. Chandra J, Marwaha RK, Marwaha N, Kumar A, Mohanty D. Pancytopenia and leukemoid reactions in tuberculosis. Ind J Pediatr. 1986 Sep 1;53(5):665-7.

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