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Clinical, etiological and hematological profile of pancytopenic childern admitted in balchikitsalaya of RNT medical college, Udaipur Rajasthan

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ABSTRACT

Introduction: To study the Clinical, Etiological and Hematological profile of Pancytopenic Children age group from 1 month to 18 years admitted in BalChikitsalay of MBGH, RNT Medical college, Udaipur.
Material and Methods: A Hospital based prospective study on children age group from 1month to 18 years admitted having pancytopenia and consenting for study were enrolled in study. Children who had received blood transfusion in previous 3 months, not consenting for study and known case of acute leukemia, aplastic anemia were excluded from study. Study was conducted in Balchikitsalay, MBGH, RNT Medical college, Udaipur, Rajasthan for a period of 1 year.
Result: 42 children were enrolled in this study among this 22 were male and 20 were female. Most of the children presented with pallor (100%) fever (88%), bleeding manifestations (78.5%), pain abdomen (35.7%). On examination all these were anemic (100%), had splenomegaly(64.2%) ,hepatomegaly(59.5%) and bleeding manifestation in the form of hematemesis(21.4%) ,petechiae(26.1%) ,bleeding gums(21.4%) . Hematological findings in majority of children were anemia 4 to 7mg/dl, WBC count 2000to 4000/mm^3 and Platelet count20,000 to 50,000/mm^3. Peripheral Blood smear revealed blast cells in 11patients, megaloblasts in 8 patients and malarial parasite in 3 children. Serum Vitamin B12 levels were <200 pg/ml in 20 children and <100 pg/ml in12 children. Bone marrow examination was performed in 36 children which revealed hypercellular marrow (28),normocellular marrow (5), hypocellular marrow(3). Most common cause of pancytopenia was vitamin B12 deficiency (40.4%). Other common causes were ALL (21.4%), Aplastic anemia (7.1%), Scrub typhus (7.1%), falciparum malaria (7.1%), CLD (7.1%), AML two patient Dengue & SLE one patient each.
Conclusion: Vitamin B 12 deficiency is the commonest cause of pancytopenia, followed by ALL (21.4%) & Aplastic anemia (7.1%).

1. Introduction

Pancytopenia is a hematological entity in which all blood cell lineages i.e. leukocytes, erythrocytes and platelets are reduced in blood.[1] Pancytopenia is defined as Hb less than 10 gm%, Leucocyte count <4000/mm and Platelet count less than 1lac/mm.[2] The causes of pancytopenia varies from viral infections that causes a self limiting bone marrow suppression to hematological malignancies and storage disorders causes bone marrow replacements with malignant and storage cells.[3] Among children clinical manifestations of disease leading to bone marrow suppression include fever, pallor, mucocutaneous bleed, hepatosplenomegaly and lymphadenopathy.[4] Timely diagnosis on the basis of suspected clinical features required for early institution of therapy and avoidance of complications.[5] Many of

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the cases of pancytopenia in pediatric age group such as malaria, enteric fever, sepsis and certain malignancies (ALL)are treatable.[6] Peripheral smear study becomes essential if cause of pancytopenia was not apparent from clinical history and examination. If this didn't reveal the cause bone marrow aspiration or biopsy is needed.[6] Clinically anemia leads to fatigue, breathlessness and cardiac symptoms. Thrombocytopenia leads to bruising and mucosal bleeding, and leucopenia leads to increased susceptibility to infection.[7]

Etiology of Pancytopenia includes Viruses (Dengue virus, HIV, Hepatitis B, C, seronegative hepatitis, parvo virus infection, cytomegalovirus, Epstein Barr virus, herpes simplex infection, adeno virus). Parasitic diseases (malaria, kala azar). Bacterial infections (enteric fever, shigella, septicemia).Nutritional causes includes vitamin B12/folate deficiency. Hematological causes include Leukemia (ALL, MDS, NHL, LGL), PNH. Autoimmune diseases like SLE eosinophilic fascitis, thymoma, hypoglobulinemia. Drugs (chloramphenicol)chemicals(benzene), radiation. Inherited causes like Fanconi anemia,dyskeratosis congenita.[8]

2. Material and Methods

The present study was an observational hospital basedstudy carried out at Department of Pediatrics of MBGH, RNT MEDICAL COLLEGE, UDAIPUR (RAJASTHAN) for one year from Aug 2018 to July 2019. Written approval from the institutional ethical committee was obtained before this study. After written and informed consent from the parents, total 42 children of either gender who were admitted in balchikatsalaya and fulfilling the inclusion criteria, were enrolled for the study. Inclusion criteriaof this study were all the children in age group of 1 month to 18 years admitted with Pancytopenia in Bal-Chikitsalaya, MBGH RNT Medical College, Udaipur.

Exclusion criteria were all those children who had received blood transfusion in previous 3 months. Patient not consenting for participation in the study. Known acute leukemia and lymphoma, aplastic anemia, malaria patients who were diagnosed before the study period and on regular treatment in our institute during the study period were excluded from the study.

Patients were subjected to detailed history, physical examination and dietary habits. Complete hemogram was performed using the Sysmax automated analyzer. Peripheral smears were examined by pathologist for morphology of RBC, macro ovalocytes, degree of anisocytosis, poikilocytosis, atypical cells, hemoparasites and blast cells. Bone marrow aspiration cytology was done in based on clinical assessment. Bone marrow is evaluated for features of cellularity, myeloid: erythroid ratio, megaloblast, dysplastic cells, proportion of cells and fat spaces, abnormal fibrosis and blast cells. It was done in children who had atypical cells or blast cells in peripheral smear. The diagnosis was established by morphological examination of bone marrow smears or biopsy. Immunohistochemistry and cytogenetic analysis were alsodonewherever required. Vit B12 and folic acid levels were measured using chemiluminescence method. Normal levels of Vit B12 and folic acid were defined as 211–911 pg/ml and >5.38 ng/ml respectively.[9] Some of relevant investigation also done like antibody titer for SLE, ELISA Dengue and scrub typhus were done whenever required.

3. Results

During the study period, 42 children of age group 1 month to 18 years who presented with pancytopenia were studied. They consisted of 22 males and 20 females with a male to female ratio of 1.2:1. (Table 1)

Table 1: Age and gender wise distribution

Age group	Males	Females	Total no.
1 Month - 1 years	4	0	4 (9.52%)
1 year -5 years	8	6	14 (33.3%)
6 years- 12 years	7	11	18 (42.8%)
>12 years	3	3	6 (14.2%)
Total	22	20	42 (100%)

Fever was (88%) was the commonest symptom at presentation followed by bleeding manifestations (78.5%), abdominal pain (35.7%) and weight loss (43.3%). All children with pancytopenia had pallor 42 (100%). Other findings were splenomegaly (64.2%), hepatomegaly (59.5%), lymphadenopathy and hyperpigmented knuckles (38%). (Table 2)

Table 2: Presenting complaints and physical findings in pancytopenia

Presenting symptoms and signs	Number of patients of pancytopenia
Fever	37 (88%)
Bleeding manifestations	35 (78.5%)
Petechial rashes	11
Hematemesis	09
Bleeding from gums	09
Malena	06
Pain Abdomen	15 (35.7%)
Pallor	42 (100%)
Splenomegaly	27 (64.2%)
Hepatomegaly	25 (59.5%)
Lymphadenopathy	16 (38%)
Hyperpigmented knuckles	16 (38%)
Petechial rashes	11(26.1%)
Bleeding gums	09 (21.4%)

19 children (45.2%) had Hb levels of 4 to 7gm/dl. Lowest level of hemoglobin was 1.2gm/dl, this child had aplastic anemia. Majority of children (69%) had Leucocyte counts in range of 2000- 4000/mm^3. Lowest level was noted in case

Table 3: Hematological parameters in three subgroups of pancytopenia

Parameters	Megaloblastic anaemia	Leukemia	Aplastic anaemia
Hb(gm/dl)	2.1-8	3-7.2	1.2-7.8
TLC(mm^3)	900-3900	500-3800	700-3000
Platelets(mm^3)	15,000-20,000	10,000-98,000	15,000-50,000

of leukemia which was 500/mm^3. 16 children (38%) had platelets value of 20,000 to 50,000. (Table 3)

Table 4: Bone marrowcellularity in cases of pancytopenia

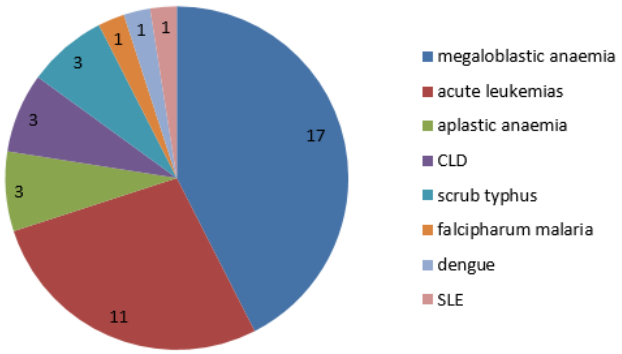
Bone marrow findings	No. of patients
Normocellular marrow	5 (11.9%)
Hyper cellular marrow	28 (66.6%)
Hypocellular marrow	3 (7.1%)
Total	36

We found hypercellular marrow in 28 (66.6%) cases and megaloblastic anemia (40.4%) was the most common cause of hypercellularity. The most common cause of hypo cellularity was aplastic anemia, all 3 (7.1%) children had hypocellular bone marrow.

Table 5: Etiological profile of pancytopenia

S. No.	Etiology	N (%)
1.	Megaloblastic anemia	17 (40.4%)
2.	ALL	9 (21.4%)
3.	Aplastic anemia	3(7.1%)
4.	AML	2 (4.7%)
5.	Scrub typhus	3(7.1%)
6.	Falciparum malaria	3(7.1%)
7.	CLD with PHTN	3(7.1%)
8.	Dengue	1(2.3%)
9.	SLE	1(2.3%)
	Total	42

Most common condition causing pancytopenia in our study was megaloblastic anemia 17 (40.4%), followed by acute lymphoblastic leukemia 9 (21.4%), 3^{rd} were aplastic anemia 3 (7.1%). In this study infectious cause of pancytopenia was, scrub typhus (7.1%) and falciparum malaria (7.1%) dengue 1(2.3%). Other causes were portal hypertension and SLE.



4. Discussion

A limited number of studies have been published in literature for evaluation of spectrum of Pancytopenia in children. Pancytopenia is the feature of many transient illness and serious life threatening diseases. The frequency of pattern of disease varies in different population groups and has been attributed to differences in nutritional status, prevalence of infections and varying exposure to myelotoxic drugs.[10]

In the present study a total of 42 cases of pancytopenia were studied. Age -gender wise distribution, clinical feature and various causes of pancytopenia were studied and observation were compared with other published studies.

Across the globe, many studies have been conducted on spectrum of pancytopenia. A study from Zimbabwe comprising 134 patients with pancytopenia, megaloblastic anemia was the most frequent cause, followed by aplastic anemia and acute leukemia in their cohort of pancytopenic patients.[9]

This study concluded that wide variety of disease can present with pancytopenia in pediatrics population in our country.

A limited number of studies has been conducted in India and has shown variable etiologies depending on demographic profile and nutritional status of study population. Clinico-hematological analysis on pancytopenic adult and children was studied by tilak et al. and khungr et al.,[11] they concluded megaloblastic anemia was the most important cause of pancytopenia in adults. Bhatnagar et al. and Gupta et al. have evaluated causes of pancytopenia exclusively in children.[9–16]

A retrospective study done by Bhatnagar et al. in 2015 on 109 pediatric patients presenting with pancytopenia, found megaloblastic anemia (28.4%) is the most common etiological factor causing pancytopenia in children followed by acute leukemia (21%) and infections (20%) {9}. Gupta et al. in 2010 reviewed 105 childern with pancytopenia at BHU found aplastic anaemia (43%) followed by acute leukemia (25%) and infections (most common kala azar).

Table 6: Age gender distribution compared to those in other studies of pancytopenia

S. no	Authors	No of cases	Age range (years)	M:f ratio
1	Khunger et al	200	2-70y	1.2:1
2	Tilak et al	77	5-70y	1.1:1
3	Bhatnagar et al	200	0-14y	1.7:1
4	Gaythri et al	104	2-80y	1.2:1
5	Present study	42	0-18y	1.1:1

Table 7: Reviews of studies on pancytopenia

S. no	Author	Year	place	Study population	No of patients	Most common cause	2^{nd} most common	Most common finding
1	Tilak et al.	1999	india	Children and adults	77	Megaloblastic anaemia	Aplastic anaemia	pallor
2	Bhatnagar et al.	2005	india	Children	109	Megaloblastic anaemia	Aplastic anemia	bleeding
3	Gayathri et al.	2007	india	Children and adults	104	Megaloblastic anaemia	Aplastic anaemia	pallor
4	Naseem et al.	2010	india	Children	139	Aplastic anaemia	Acute leukemia	Fever
5	Gupta et al.	2010	india	Children	105	Aplastic anaemia	Acute leukemia	Fever
6	Memon et al.	2008	pakistan	Children	230	Aplastic anaemia	Megaloblastic anaemia	pallor
7	Sharrif et al.	2012	pakistan	Children	105	Megaloblastic anemia	infections	Fever
8	Present study	2019	india	Children	42	Megaloblastic anaemia	Acute leukemia	Fever

Megaloblastic anaemia was seen only in 6.7% children.[10] In present study, the most common underlying etiology causing pancytopenia was Megaloblastic anaemia (40.4%) followed by acute leukemia (28.5%), aplastic anaemia (7.1%). In the present study, infectious causes of pancytopenia were scrub typhus (7.1%), malaria (7.1%) and dengue (2.3%). In the present study the most common presenting symptom in children with pancytopenia was fever in 37 (88%) cases followed by bleeding manifestations in 35 (78.5%) cases. In the present study all children with pancytopenia had pallor 42 (100%). Other findings were splenomegaly 27(64.2%), hepatomegaly 25 (59.5%). Fever and bleeding were the most common presenting complain in children studied by Gupta et al. and Bhatnagar et al. respectively.[9,10] The most common examination finding of pancytopenic children was pallor in various studies. Thus, the commonest etiologies of pancytopenia, concluded by various studies across the world have been megaloblastic anaemia, aplastic anaemia and acute leukemia. Table 5 demonstrates the most common causes and findings of pancytopenic patients of various studies.

5. Conclusion

Though aplastic anemia and leukemia are believed to be common causes of pancytopenia megaloblastic anemia was found to be single most common cause of pancytopenia in this series. Many of these patients may present in emergency room with pancytopenia and with severe bleeding due to thrombocytopenia. Emergency treatment with vit b 12 and folic acid will immediately improve the affected bone marrow and halt the associated complications. Early recognition of these conditions will certainly have impact on the morbidity and mortality in vulnerable pediatric patient. Moreover in developing countries infections such as enteric fever, malaria and fulminant sepsis need careful evaluation since these conditions may unnecessarily boggle the mind of attending physicians.

6. Source of Funding

None.

7. Conflict of Interest

None.

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