International Journal of Contemporary Pediatrics
Panda P et al. Int J Contemp Pediatr. 2023 Nov;10(11):1658-1663
http://www.ijpediatrics.com
pISSN 2349-3283 | eISSN 2349-3291

DOI: https://dx.doi.org/10.18203/2349-3291.ijcp20233234

Original Research Article

A study of etiological and clinico-hematological profile of pancytopenia in children in a tertiary care hospital

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Received: 08 September 2023
Revised: 04 October 2023
Accepted: 06 October 2023

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ABSTRACT

Background: Pancytopenia is a disorder in which all three major formed elements of blood are reduced below the lower limit of normal for the age and sex. Pancytopenia is a striking feature of many serious life-threatening illnesses ranging from simple drug-induced bone marrow hypoplasia, and megaloblastic anemia to fatal bone marrow aplasia and leukemias. In India, pancytopenia causes vary and still are more varied among the pediatric population. So, the present study was carried out to evaluate the various causes and clinic-hematological factors of pancytopenia in the pediatric age group.
Methods: It was a hospital-based analytical cross-sectional study conducted in the department of pediatrics, SVPPGIP & SCB Medical College, Cuttack from September 2016 to October 2018. A total of 106 children between 6 months to 18 years with Pancytopenia were enrolled in our study. Bone marrow aspiration was conclusive in most of the cases. All data were analyzed using SPSS. Chi-square test was used to analyze any association and a p-value of <0.05 was considered significant.
Results: Out of 106 patients, the majority were 10-14 years old. Female to male ratio was 1.4:1. The most common etiological factors were ALL (58.5%), Aplastic Anemia (19.8%), and others. Fever and Weight loss were the most common presenting symptoms. The most common signs were Pallor and Hepatomegaly.
Conclusions: The present study concludes that detailed primary hematological investigations along with bone marrow aspiration are really helpful for understanding the disease process, diagnosing the etiology of pancytopenia, and helpful in planning further investigations and management of pancytopenia patients.

Keywords: Pancytopenia, Children, Etiological, Clinico-hematological, ALL, Aplastic anemia

INTRODUCTION

Pancytopenia is a disorder in which all three major formed elements of blood (red blood cells, white blood cells, and platelets) are reduced below the lower limit of the normal range for age and sex. It is a triad of findings that may result from several disease processes-primarily or secondarily involving the bone marrow. The presenting symptoms are usually due to anemia, leucopenia, and thrombocytopenia. Pancytopenia is a striking feature of many serious life-threatening illnesses ranging from simple drug-induced bone marrow hypoplasia, megaloblastic marrow to fatal bone marrow aplasia and leukemias. The pattern of diseases leading to pancytopenia is expected to vary in different population groups with

their difference in age patterns, nutritional status, and prevalence of infective disorder. Careful assessment of blood elements is often the first step in the assessment of hematological function and diagnosis of disease. Physical findings and peripheral blood pictures provide valuable information in the workup of pancytopenia patients and help in planning further investigations on bone marrow. The severity of pancytopenia and the underlying pathology determine the management and prognosis of these patients. In India, pancytopenia causes vary and still more varied among the pediatric population. Previous studies in India are mostly based on the adult population with megaloblastic anemia as the major cause of pancytopenia.[1-3] So, the present study has been undertaken to evaluate the various causes of pancytopenia in the pediatric age group and to correlate the peripheral blood findings with bone marrow aspirate. Thereby, this data would help in planning the diagnostic and therapeutic approach in patients with pancytopenia.

Objectives

Objectives of current study were to enlist the etiology, peripheral blood smear findings, and bone marrow studies of patients presenting with pancytopenia and to analyze the hematological parameters and clinical findings in differentiating causes of pancytopenia.

METHODS

It was a hospital-based analytical cross-sectional study conducted in the department of Pediatrics of SVPPGIP & SCB Medical College, Cuttack from September 2016 to October 2018.

Inclusion criteria

Children with Pancytopenia with the following blood counts were included; haemoglobin <10gm%**,** total leucocyte count <4,000/mm^3, total platelet count <1 lac/mm^3 and reticulocyte count <1%.

Exclusion criteria

Children admitted who were on Myelotoxic chemotherapy, and already diagnosed cases of pancytopenia were excluded from the study.

Sample size

All patients of age 6months-14years admitted during the study period to the Department of Pediatrics at SVPPGIP and SCB MCH, Cuttack with features of Pancytopenia were included in the study. A total of 106 cases were enrolled, who were followed till diagnosis was established.

Data collection

After obtaining consent from the parents, various investigations were done in the present study, which includes; a complete hemogram done on an automated hematology analyzer (Beckman coulter-LH-750) either at SVPPGIP or at the department of clinical hematology, SCB MCH, Cuttack. The Peripheral blood smear examination was confirmed at the Department of Pathology, SCB MCH, Cuttack. Bone marrow aspiration and biopsy were carried out as per the clinical indication at the Department of Pathology and Department of Clinical Hematology, SCB MCH, Cuttack. The bone marrow procedure and further staining were carried out by standard methods.

Statistical analysis

All observational data were entered in an Excel sheet, tabulated, and analyzed using IBM SPSS version 21 to draw the final inference. All categorical variables were described as percentages. Chi-square test was performed to find any association between categorical variables. A p value <0.05 was taken as a statistically significant finding.

RESULTS

The study was carried out taking a total of 106 children with pancytopenia out of which 1/3rd were less than 6 years old. Maximum children belong to the age group of 10-14 years (36%). Female to male ratio was 1.4:1 (Table 1).

Table 1: Socio-demographic profile of study participants (n=106).

Variables		N (%)
Age	6 month-3 years	11 (10.4)
	3-6 years	24 (22.6)
	6-10 years	33 (31)
	10-14 years	38 (36)
Sex	Male	44 (41.5)
	Female	62 (58.5)

When we look for etiological factors, among malignant causes, acute lymphocytic leukemia (ALL) was most commonly associated with pancytopenia (58.5%) followed by Acute Myeloid Leukemia (AML- 4.8%). Among the non-malignant causes aplastic anemia (AA) was most common (19.8%) followed by megaloblastic anaemia (10.5%). rest causes were myelofibrosis, myelodysplastic syndrome (MDS), systemic lupus erythematosus (SLE), hemophagocytic lymphohistiocytosis (HLH), and disseminated tuberculosis (Figure 1). The most common presenting symptom was fever (91.5%) followed by weight loss (80.2%), bleeding (43.4%), and malaise (41.5%). Pallor was the most common clinical sign (90.6%) followed by hepatomegaly (70.6%). More than 50% of patients had lymphadenopathy and splenomegaly. Around 74.6% of patients had severe anemia (Hb <7 gm%). The majority of the patients (36.8%) had Total leukocyte count (TLC) of 3000-4000/mm^3. About 32% of patients had severe thrombocytopenia (Platelet count <20,000) (Table 2).

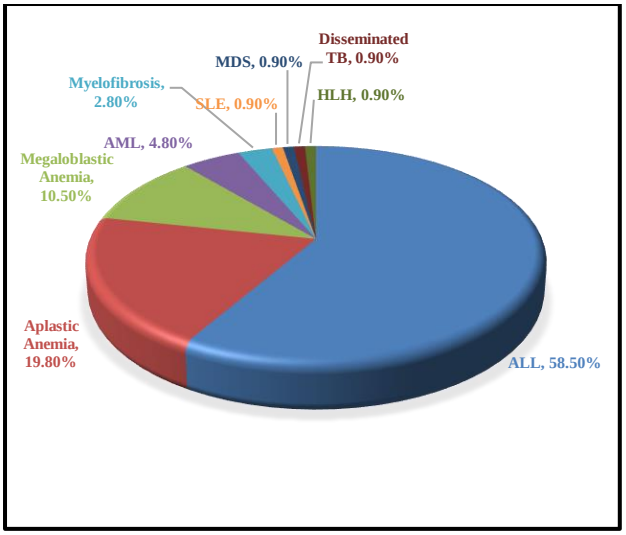

Figure 1: Final diagnosis among children with pancytopenia.

Table 2: Clinico-hematological profile in pancytopenia (n=106).

Variables		N (%)
Symptoms	Fever	97 (91.5)
	Weight loss	85 (80.2)
	Bleeding	46 (43.4)
	Malaise	44 (41.5)
	Abdominal distension	31 (29.2)
Signs	Pallor	96 (90.6)
	Hepatomegaly	77 (72.6)
	Lymphadenopathy	60 (56.6)
	Splenomegaly	59 (55.7)
	Sternal tenderness	21 (19.8)
Hematological parameters	**Hemoglobin (gm%)**	
	3.1-5	29 (27.4)
	5.1-7	50 (47.2)
	7.1-10	27 (25.4)
	Total Leucocyte Count (per mm^3)	
	500-1000	13 (12.3)
	1000-2000	28 (26.4)
	2000-3000	26 (24.5)
	3000-4000	39 (36.8)
	Total platelet count (per mm^3)	
	<10,000	3 (2.8)
	10,000-20,000	31 (29.2)
	20,000-50,000	18 (17)
	50,000-75,000	27 (25.5)
	75,000-1,00,000	27 (25.5)

The peripheral smear finding among pancytopenia children showed Blast cells in maximum number i.e., 56 out of 106 followed by pancytopenia (27), macrocytic hypochromic cells (11), hypocellular (6), microcytic hypochromic (4) and normocytic normochromic cells (2) (Figure 2). On aspiration, bone marrow showed lymphoblast in a majority of the cases (58.5%) followed by hypocellular (24.5%), megaloblast (10.3%), myeloid (4.7%), myelodysplastic (0.9%) and erythroid cells (0.9%) (Table 3).

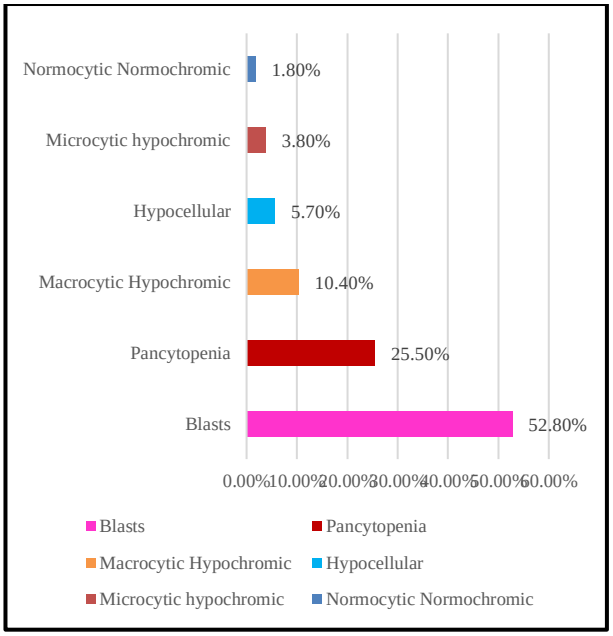

Figure 2: Peripheral smear finding of children with pancytopenia (n=106).

Table 3: Bone marrow aspiration findings in pancytopenia (n=106).

Findings	N (%)
ALL	62 (58.5)
Hypocellular	26 (24.5)
Megaloblastic	11 (10.3)
AML	5 (4.7)
MDS	1 (0.9)
Erythroid Hyperplasia	1 (0.9)

As ALL and AA were the most common etiological finding among the malignant and non-malignant causes of pancytopenia in our study, we analyzed the association between the respective diseases and the clinico-hematological parameters.

All the patients suffering from ALL presented with fever (100%) and about 71.6% had weight loss as a significant clinical symptom ($p<0.05$). Among significant clinical signs, 95.2% of ALL patients had hepatomegaly, 74.2% had splenomegaly, 72.6% had Lymphadenopathy and 30.6% had sternal tenderness. Pallor was present in about 88.7% of ALL patients however it was not statistically significant ($p>0.05$) (Table 4). Among the hematological parameters, TLC and CPS findings were significantly associated with ALL where 30.6% had TLC between 1000-2000/mm^3 followed by 29% having a count of 2000-3000/mm^3. About 83.9% showed blast cells in peripheral smear and the rest showed pancytopenia (Table 4). Bleeding was the most common significant presenting symptom among patients with AA i.e., 66.7%.

Table 4: Association between ALL and Clinico-hematological parameters (n=62).

ALL	**Symptom**	**Fever**		**Abdominal distension**	**Malaise**		**Bleeding**	**Weight loss**	
	N (%)	62 (100)		22 (35.5)	23 (37.1)		27 (43.5)	44 (71.6)	
	P value	0.000		0.09	0.27		0.97	0.005	
	Sign	**Pallor**		**Lymphadenopathy**	**Hepatomegaly**		**Splenomegaly**	**Sternal Tenderness**	
	N (%)	55 (88.7)		45 (72.6)	59 (95.2)		46 (74.2)	19 (30.6)	
	P value	0.51		0.000	0.000		0.000	0.001	
	Hemato-logical Parameter N (%)	**Hb (gm%)**		**TLC (10^3/ mm^3)**		**TPC (10^3/mm^3)**		**CPS**	
		3.1-5	18 (29)	0.5-1	10 (16.1)	<10	1 (1.6)	Blast	52 (83.9)
		5.1-7	28 (45.2)	1-2	19 (30.6)	10-20	21 (33.9)	Pancyto-penia	10 (16.1)
		7.1-10	16 (25.8)	2-3	18 (29)	20-50	9 (14.5)		
		-	-	3-4	15 (24.2)	50-75	18 (29)	-	-
		-	-	-	-	75-100	13 (21)		
		-	-	-	-	-	-		
	P value	0.86		0.01		0.37		0.000	

Table 5: Association between AA and clinico-hematological parameters (n=21).

AA	**Symptom**	**Fever**		**Abdominal distension**	**Malaise**		**Bleeding**	**Weight loss**	
	N (%)	17 (81)		4 (19)	7 (33.3)		14 (66.7)	19 (90.7)	
	P value	0.07		0.25	0.39		0.01	0.23	
	Sign	**Pallor**		**Lymphadenopathy**	**Hepatomegaly**		**Splenomegaly**	**Sternal Tenderness**	
	N (%)	18 (85.7)		5 (23.8)	4 (19)		3 (14.3)	0 (0)	
	P value	0.41		0.001	0.000		0.000	0.01	
	Hemato-logical Parameter N (%)	**Hb (gm%)**		**TLC (10^3/ mm^3)**		**TPC (10^3/mm^3)**		**CPS**	
		3.1-5	4 (19)	0.5-1	2 (9.5)	<10	1 (4.8)	Pancyto-penia	16 (76.2)
		5.1-7	14 (66.7)	1-2	4 (19)	10-20	5 (23.8)	Hypo-cellular	5 (23.8)
		7.1-10	3 (14.3)	2-3	6 (28.6)	20-50	5 (23.8)		
		-	-	3-4	9 (42.9)	50-75	7 (33.3)	-	-
		-	-	-	-	75-100	3 (14.3)		
		-	-	-	-	-	-		
	P value	0.13		0.79		0.53		0.000	

Other common symptoms were weight loss (90.7%), fever (81%), malaise, and abdominal distension in descending order, however, we could not find any significant association between them. The most common clinical sign was pallor (85.7%), but it was not a significant finding (p=0.41). The most common significant findings were Lymphadenopathy (23.8%), Hepatomegaly (19%), and Splenomegaly (14.3%) with p<0.05 (Table 5). If we look at the hematological parameters, maximum patients with AA had Hb between 5.1-7 gm% (66.7%), TLC 3000-4000/mm^3 (42.9%), TPC 50,000-75,000/mm^3 (33.3%). However, none of these findings were statistically significant. In the peripheral blood picture, Pancytopenia (76.2%) and Hypocellularity (23.8%) were the two only findings and were associated significantly (p=0.000) (Table 5).

DISCUSSION

Most patients in our study were between 10-14 years. Females dominated over males which is opposite to a study done by Chand et al and Gupta et al where the male-to-female ratio was 1.47:1 and 2.6:1 respectively.[4,5] In our study, the most common cause of pancytopenia came out to be Acute Lymphocytic Leukemia (58.5%) followed by Aplastic Anemia (19.8%) and Megaloblastic anemia (10.5%). Acute leukemia was the commonest cause which indicates a high prevalence of both genetic and

environmental factors at play in the pathogenesis of the disease. The other common causes were myelofibrosis, systemic lupus erythematosus, myelodysplastic syndrome, hemophagocytic lymphohistiocytosis, and disseminated tuberculosis.

A study done by Chand et al and Bhatnagar et al among children revealed Megaloblastic anemia as the most common cause of pancytopenia with a prevalence of 19.4% and 28.4% respectively.[4,6] The second most common cause among both the above studies was acute leukemia (14.2% & 21% respectively). A study done by Tilak et al and Barik et al among children and adults, also found Megaloblastic anemia to be the most common finding (68% & 66% respectively) followed by Aplastic anemia (7.7% & 18% respectively), the second most common cause.[7,8] Studies done in India by Kumar et al, Gupta et al, Naseem et al, predicted Aplastic Anemia as the most common cause of pancytopenia contributing 29.5%, 43%, and 33.8% of the total cases.[9,5,10] The second most common cause was megaloblastic anemia (22.2%), acute leukemia (25%), and acute leukemia (26.6%) respectively among all the above studies. A study conducted in Pakistan by Memon et al also found AA as the 1st and megaloblastic anemia as the 2nd most common cause of pancytopenia among pediatric age group.[11] However, a five-year review study by Pine M et al., among hospitalized children in the USA revealed Infections (64%) as the most common culprit followed by Hematologic causes (28%).[12] In contrast, our study could not establish a good amount of infectious causes of pancytopenia except for one case of disseminated tuberculosis.

Fever, weight loss, and bleeding were the three most common symptoms present among the children in our study. Pallor and hepatomegaly were the most common clinical signs detected. A study done by Rathod et al among 200 children found fever to be the most common presenting symptom (65%) and pallor as the most common sign (81.5%).[13] Similarly, Jan et al conducted a study among 205 children, concluding that Fever (62.8%) and Pallor (82.9%) were the most common presenting clinical findings.[14] In a study among all age groups, found generalized weakness and dyspnoea as the most common presenting symptom. Pallor was present universally among all the patients in their study followed by splenomegaly.[15] About 74.6% of patients had severe anemia (Hb <7 mg%), 36.8% had TLC between 3000-4000 and 32% had severe thrombocytopenia (TPC <20,000) in our study. Peripheral smear showed Blast cells in the majority followed by pancytopenia. Bone marrow (BM) aspiration findings were conclusive in most of the cases. Most of the BM slides showed blast cells followed by hypoplastic features. We analyzed the association between the two most common etiology of pancytopenia i.e., ALL and AA with various clinico-hematological features. As per the results, fever and weight loss were significantly associated with ALL as the most common presenting symptom, whereas in AA, bleeding was the most common significant presenting complaint among hospitalized children. Lymphadenopathy, hepatosplenomegaly, and sternal tenderness were the significant clinical signs among ALL patients, however, AA patients showed signs of lymphadenopathy and hepatosplenomegaly in majority of the cases. None of the AA cases had sternal tenderness. Pallor was almost universal among all patients, so we could not establish any significant difference between the individual diseases in terms of pallor as the significant sign. TLC was as low as 1000-2000 cells/mm^3 among 30.6% of the candidates and it was significant among ALL patients. About 85.7% (Hb=3.1-7) patients had severe anemia, at the time of presentation among AA patients which is nearly similar to a finding (Hb=2-8.6gm%).[15] The peripheral smear finding among ALL children showed blasts (83.9%) in the majority and the rest revealed pancytopenia (16.1%) and it was a significant finding. While in about 76.2% of patients suffering from AA showed significant pancytopenia in peripheral smear followed by hypocellularity (23.8%).

Strength and limitations

Strength; current study discovered the association between the most common etiological factor of pancytopenia and the clinico-hematological parameters. We could establish the most common cause of pancytopenia including a broad range of pediatric population. Limitations were; This study was limited by the detailed investigation into the exact causes of pancytopenia in patients with aplastic anemia and megaloblastic anemia. Delayed referral to our hospital might have increased the number of complications in subjects included in the study. Bone marrow biopsy procedures were performed in selective cases for diagnosis. Immunocytochemical staining of peripheral blood smears was not done. Patients were not followed up after diagnosis for morbidity and mortality.

CONCLUSION

Pancytopenia is not an uncommon hematological problem encountered in clinical practice and should be suspected on clinical grounds when a patient presents with unexplained pallor, prolonged fever, and a tendency to bleed. The physical findings and peripheral blood picture provide valuable information in the workup of pancytopenia patients. Evaluation of peripheral blood film reveals the most probable cause of Pancytopenia. The importance of peripheral blood smear examination in cases of Pancytopenia cannot be overemphasized. The presence of immature cells, megaloblast, erythroid precursors, and scanty cells of all lineage may suggest the primary hematologic disorder. Bone marrow aspiration is an important diagnostic tool that helps to evaluate various causes of pancytopenia. Bone marrow examination is an accurate, reproducible information at an economic cost with minimal discomfort to patients. Bone marrow aspiration is sufficient to make a diagnosis in the majority of cases.

Recommendations

Blood counts and peripheral blood smear examination should be done at the earliest for children presenting with prolonged fever and bleeding manifestations. Early and prompt referral to tertiary care hospitals of pancytopenic children for prompt diagnosis and institution of therapy. Use of all available investigation means to establish the etiology and diagnosis. Having a liberal transfusion policy and anti-microbial use at treatment centers which maintains the benefit of avoiding complications and the hazards associated thereof.

ACKNOWLEDGEMENTS

We are grateful to the parents of our study participant for their constant cooperation throughout the study period. Authors are also grateful to the department of pathology, SCBMCH, Cuttack for their immense help in carrying out various investigations like bone marrow examination and peripheral smears.

Funding: No funding sources
Conflict of interest: None declared
Ethical approval: The study was approved by the Institutional Ethics Committee

REFERENCES

1. Sharma DA, Maheep DB. Pancytopenia- A clinicopathological analysis of 132 cases. Int J Med Res Rev. 2016;4(8):1376-86.
2. Pooja A, Asbah S, Prashant P, Harendra K, Ashwini N. Evaluation of pancytopenia in adults through haematological parameters and bone marrow studies . Indian J Pathol Oncol. 2018;2018:781-7.
3. Goli N, Koguru S, Wadia R, Agarwal S, Patel P, Reddy P, et al. Etiological profile of pancytopenia in a tertiary care hospital. Int J Adv Med. 2016;3(3): 533-7.
4. Chand R, Singh N. Clinic-etiological profile of pancytopenia in children: a tertiary care center based study of Kumaun region, India. Int J Contemp Pediatr. 2018;5(6):2173.
5. Gupta V, Tripathi S, Tilak V, Bhatia BD. A study of clinico-haematological profiles of pancytopenia in children. Trop Doct. 2008;38(4):241-3.
6. Bhatnagar SK, Chandra J, Narayan S, Sharma S, Singh V, Dutta AK. Pancytopenia in children: etiological profile. J Trop Pediatr. 2005;51(4):236-9.
7. Tilak V, Jain R. Pancytopenia--a clinico-hematologic analysis of 77 cases. Indian J Pathol Microbiol. 1999; 42(4):399-404.
8. Barik S, Chandoke R, Verma A, Sweta. A prospective clinico-hematological study in 100 cases of pancytopenia in capital city of India. J Appl Hematol. 2014;5(2):45.
9. Kumar R, Kalra SP, Kumar H, Anand AC, Madan H. Pancytopenia--a six year study. J Assoc Physicians India. 2001;49:1078-81.
10. Naseem S, Varma N, Das R, Ahluwalia J, Sachdeva MUS, Marwaha RK. Pediatric patients with bicytopenia/pancytopenia: review of etiologies and clinico-hematological profile at a tertiary center. Indian J Pathol Microbiol. 2011;54(1):75-80.
11. Memon S, Shaikh S, Nizamani MAA. Etiological spectrum of pancytopenia based on bone marrow examination in children. J Coll Physicians Surg Pak. 2008 Mar;18(3):163-7.
12. Pine M, Walter AW. Pancytopenia in hospitalized children: a five-year review. J Pediatr Hematol Oncol. 2010;32(5):e192-4.
13. Rathod GB, Alwani M, Patel H, Jain A. Clinico-hematological Analysis of Pancytopenia in Pediatric Patients of Tertiary Care Hospital. Int Arch Integr Med. 2015;2(11):15-9.
14. Jan AZ, Zahid B, Ahmad S, Gul Z. Pancytopenia in children: A 6-year spectrum of patients admitted to Pediatric Department of Rehman Medical Institute, Peshawar. Pakistan J Med Sci. 2013;29(5):1153-7.
15. Rao KS. Pancytopenia: A Clinico Hematological Study. J Lab Physic. 2011;3(01):15-20.

Cite this article as: Panda P, Behera J, Nanda CR. A study of etiological and clinico-hematological profile of pancytopenia in children in a tertiary care hospital. Int J Contemp Pediatr 2023;10:1658-63.