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Etiology & Clinical Pattern of Pancytopenia in Adults in a Tertiary-level Hospital

*MZ Huq[1], AA Faroque[2], K Nahar[3], KS Parvez[4], MS Rahman[5], MF Islam[6], F Khaliduzzaman[7], MN Kabir[8]

Abstract

Background: Pancytopenia is a hematological condition characterized by the simultaneous reduction of red blood cells, white blood cells and platelets, presenting a wide differential diagnosis. **Objective:** This study aimed to analyze the clinical profile and etiological spectrum of pancytopenia patients admitted to the Medicine department of Khulna Medical College Hospital. **Methods:** This observational study was conducted in the Department of Medicine at Khulna Medical College Hospital (KMCH), Khulna, Bangladesh, from December 2013 to May 2014. A total of 50 patients with pancytopenia were enrolled through purposive sampling. Patients underwent thorough evaluations including clinical assessments, laboratory investigations and bone marrow examinations. All Statistical analyses were performed using the Statistical Package for the Social Sciences (SPSS) software (version 17). **Results:** In this study, aplastic anemia emerged as the most prevalent cause, affecting 56% of patients, followed by megaloblastic anemia (18%), hypersplenism (10%), and malaria (8%). Clinical manifestations primarily included pallor, fatigue, fever and bleeding with significant variations in hematological parameters. Statistical analyses revealed significant differences in absolute neutrophil count (p-value<0.05) and mean corpuscular volume (p-value<0.05) among the various cases. **Conclusion:** This study underscores the importance of a comprehensive diagnostic approach to pancytopenia, highlighting regional variations in its etiologies and calling for further investigations to delineate local factors influencing this condition.

Keywords: Pancytopenia, Aplastic Anemia, Megaloblastic Anemia

Introduction

Pancytopenia is a condition characterized by the simultaneous presence of three blood cell deficiencies: anemia, which involves low red blood cells; leukopenia, marked by low white blood cells; and thrombocytopenia, indicating low platelet levels. These deficiencies can lead to symptoms such as fatigue, increased susceptibility to infections, and a higher risk of bleeding. When these three conditions occur together, they often signal a more serious underlying issue affecting blood cell production, highlighting the need for thorough evaluation and treatment.[1]

Usually, the blood picture shows the hemoglobin level is less than 10g/dL, total leukocyte count is less than 4×109/L, and platelet count is less than 150×109/L.[2] Pancytopenia develops when the bone marrow, responsible for producing blood cells, is damaged or impaired. This can occur due to various diseases, environmental factors, or treatments. Cancers that affect the bone marrow, including leukemia, multiple myeloma, Hodgkin's and non-Hodgkin's lymphoma, and myelodysplastic syndromes, are common causes. Blood disorders such as megaloblastic anemia, which results in abnormal red blood cells, and aplastic anemia, where blood cell production in the bone marrow is severely reduced, can also lead to pancytopenia.[3]

Additionally, rare conditions like paroxysmal nocturnal

1. Dr. Md. Zahirul Huq, Assistant Professor, Department of Medicine, Khulna Medical College Hospital, Khulna, Bangladesh. Email: zahirul77.zh@gmail.com ORCID: https://orcid.org/0009-0003-0377-7560
2. Dr. Abdullah Al Faroque, Associate Professor, Department of Pathology, Gazi Medical College, Khulna, Bangladesh.
3. Dr. Kamrun Nahar, Junior Consultant of Medicine, Dumuria Upazila Health Complex, Khulna, Bangladesh.
4. Dr. Kazi Samim Parvez, Junior Consultant, Department of Cardiology, Khulna Specialized Hospital, Khulna, Bangladesh.
5. Dr. Md. Sayfur Rahman, Junior Consultant of Medicine, Phultala Upazila Health Complex, Khulna, Bangladesh.
6. Dr. Md. Forhadul Islam, Registrar, Department of Medicine, Khulna Medical College Hospital, Khulna, Bangladesh.
7. Dr. Fakir Khaliduzzaman, Assistant Professor, Department of Pathology, Gazi Medical College, Khulna, Bangladesh.
8. Dr. Md. Nazmul Kabir, Assistant Professor, Department of Medicine, Khulna Medical College Hospital, Khulna, Bangladesh.

hemoglobinuria, which causes red blood cell destruction, may contribute. Infections like Epstein-Barr virus, cytomegalovirus, HIV, hepatitis, malaria, and sepsis can also damage bone marrow. Other contributing factors include chemotherapy, radiation, exposure to toxins like arsenic or benzene, inherited bone marrow disorders, vitamin B-12 or folate deficiencies, splenomegaly (an enlarged spleen), liver disease, excessive alcohol consumption, and autoimmune diseases like lupus. In approximately half of pancytopenia cases, the cause remains unknown, which is referred to as idiopathic pancytopenia. Early and accurate diagnosis is key to managing the condition and improving the patient's prognosis.[4]

A review of the available literature indicates that comprehensive studies on pancytopenia as a unified condition are relatively scarce, particularly in the developed world. Despite this, there has been significant research focused on its causes, such as aplastic anemia, megaloblastic anemia, leukemia, and myelodysplastic syndromes. These specific conditions are well-studied, yet broader investigations that address pancytopenia in its entirety, including all potential causes and variations, remain limited. This gap in research underscores the need for more in-depth studies, especially in regions with different clinical manifestations and environmental influences, to better understand the disorder as a whole.[5]

To effectively explore the varying trends in clinical patterns, hematological changes, treatment approaches, and outcomes associated with pancytopenia, a detailed study is imperative. Hematological investigations are fundamental to the management of patients with this condition, providing crucial insights for thorough research. Therefore, this study was designed with two primary objectives: to identify the underlying causes of pancytopenia and to examine its clinical presentation in adult patients.

Materials and methods

Study Design and Setting:

This observational study was conducted in the Department of Medicine at Khulna Medical College Hospital, Khulna, Bangladesh, from December 2013 to May 2014. The study focused on hospitalized patients diagnosed with pancytopenia.

Study Population:

The study included adult patients meeting the specified inclusion criteria. A total of 50 patients were selected through purposive sampling, ensuring that they provided informed consent to participate in the study.

Inclusion Criteria:

Patients eligible for the study had to meet the following criteria:

- Diagnosis of pancytopenia is characterized by hemoglobin levels <10 g/dL, total leukocyte count $<4\times10^9$/L, and platelet count $<150\times10^9$/L.
- Voluntary provision of informed consent.

Exclusion Criteria:

Patients were excluded from the study based on the following conditions:

- Refusal to give informed consent.
- Pregnancy-related pancytopenia.
- Patients aged 18 years or younger.

Data Collection Instruments:

Data were collected using a combination of observation, structured questionnaires, and key informant interviews. Patients were interviewed to obtain socio-demographic information and clinical history.

Data Analysis:

Data were presented in suitable tables and graphs for clarity. Continuous parameters were expressed as mean ± standard deviation (SD), while categorical parameters were reported as frequency and percentage. Statistical analyses were performed using the Statistical Package for the Social Sciences (SPSS) software (version 17). Comparisons between continuous parameters were made using the Student's t-test, and categorical parameters were analyzed using the Chi-Square test. A confidence interval of 95% and a p-value of <0.05 were considered statistically significant.

Ethical Considerations:

The study adhered to ethical guidelines, including obtaining informed consent from all participants. Confidentiality of the participants' information was maintained throughout the study. Ethical clearance was granted by the ethical review committee of Khulna Medical College Hospital, and financial assistance was provided for investigations of economically disadvantaged patients.

Results

The study analyzes the clinical and hematological characteristics of 50 patients diagnosed with pancytopenia, focusing on various demographic factors, causes, clinical manifestations, hematological parameters, and severity.

Table 01 indicates a male predominance in the patient cohort, with 37 males (74%) and 13 females (26%).

Table 01: Frequency of Male and Female

Male		Female	
Frequency (n)	Percentage (%)	Frequency (n)	Percentage (%)
37	74	13	26

Table 02 reveals that pancytopenia was most common in the 31-40 age group, accounting for 34% of the cases, while older age groups (51 years and above) had fewer instances.

Table 02: Distribution of patients according to age and sex

Age group (Years)	Frequency (n)	Percentage (%)
18 -20	7	14
21-30	10	20
31-40	17	34
41-50	7	14
51-60	2	4
61-70	5	10
71-80	2	4
Total	50	100

Table 03 illustrates the occupational distribution, identifying peasants as the most affected group (28%), followed by the unemployed (20%) and garment workers (16%), with aplastic anemia being the most frequent diagnosis.

Table 03: Occupational distribution

Occupation	AA (n=23)	HS (n=5)	MDS (n=06)	MA (n=09)	Malaria (n=4)	AL (n=2)	SLE (n=1)	Total
Peasant	5	3	3	3	0	0	0	14
								28%
Laborer	4	0	0	0	1	1	1	7
								14%
Garment worker	2	1	2	1	2	0	0	8
								16%
Housewife	5	1	1	0	0	0	0	7
								14%
Unemployed	4	0	0	5	1	0	0	10
								20%
Student	3	3	0	0	0	1	0	7
								14%

AA: Aplastic anemia. AL: Acute leukemia. ANC: Absolute neutrophil count. Hb: Hemoglobin. HS: Hypersplenism. IDA: Iron deficiency anemia. MA: Megaloblastic anemia. MCV: Mean corpuscular volume. MDS: Myelodysplastic syndrome. No: Number of patients

Table 04 categorizes the causes of pancytopenia by age, highlighting aplastic anemia (AA) as the leading cause, impacting 23 (46%) patients with a mean age of 36.6 years, primarily in the younger demographic (18-40 years). In contrast, megaloblastic anemia (MA) predominantly affected older patients (mean age of 56.43 years), while myelodysplastic syndrome (MDS) was most common among the oldest participants (mean age of 64.6 years).

Table 04: Causes of pancytopenia according to age group

Sl No.	Causes	Age group (years)						Total	Percentage (%)
		18-30	31-40	41-50	51-60	61-70	71-80		
1	AA	5	9	5	2	2	0	23	46
2	MA	0	0	1	4	3	1	9	18
3	HS	2	2	1	0	0	0	5	10
4	MDS	0	0	0	2	5	0	6	12
5	Malaria	2	1	1	0	0	0	4	8
6	AL	0	1	0	1	0	0	2	4
7	SLE	0	0	1	0	0	0	1	2
	Total	15	17	11	2	3	2	50	100

AA: Aplastic anemia. AL: Acute leukemia. ANC: Absolute neutrophil count. Hb: Hemoglobin. HS: Hypersplenism. IDA: Iron deficiency anemia. MA: Megaloblastic anemia. MCV: Mean corpuscular volume. MDS: Myelodysplastic syndrome. No: Number of patients

Table 05 details the causes of pancytopenia by gender, reaffirming that AA was the most prevalent cause among both genders.

Table 05: Causes of pancytopenia according to gender

Causes	Male (n=37)		Female(n=13)	
	No.	%	No.	%
AA	16	43.24	7	53.84
Malaria	2	5.41	2	15.39
MA	8	21.62	1	7.69
HS	4	10.81	1	7.69
AL	1	2.7	1	7.69
MDS	5	13.51	1	7.69
SLE	1	2.7	0	0
Total	37		13	

AA: Aplastic anemia. AL: Acute leukemia. ANC: Absolute neutrophil count. Hb: Hemoglobin. HS: Hypersplenism. IDA: Iron deficiency anemia. MA: Megaloblastic anemia. MCV: Mean corpuscular volume. MDS: Myelodysplastic syndrome. No: Number of patients

In **Table 06**, clinical manifestations indicate that fever and fatigue were the most frequent symptoms, with aplastic anemia patients exhibiting the highest rates. Notably, all patients displayed pallor, while significant bleeding was observed in 60% of cases.

Table 06: Clinical manifestations according to the causes of pancytopenia

Clinical Features	HS	Malaria	MA	AA	AL	MDS	Others	Total No.	%	
Symptoms										
Fever	5	4	6	23	1	4	2	45	90	>0.05 (NS)
Fatigue	4	2	9	18	2	5	1	41	82	
Dizziness	2	1	0	9	1	4	1	18	36	
Weight loss	2	0	0	16	0	2	0	20	40	
Anorexia	3	2	0	5	1	3	0	14	28	
Night sweat	3	0	0	3	0	2	0	8	16	
Signs										
Pallor	5	5	9	23	2	4	2	50	100	>0.05 (NS)
Splenomegaly	4	1	0	11	0	3	1	20	40	
Bleeding	3	2	3	15	1	4	2	30	60	
Hepatomegaly	1	0	1	1	0	1	1	5	10	
Lymphadenopathy	3	1	0	2	1	1	0	8	16	
NS: Not significant										
AA: Aplastic anemia. AL: Acute leukemia. HS: Hypersplenism. IDA: Iron deficiency anemia. MA: Megaloblastic anemia. No: Number of patients										

Table 07 discusses the severity of pancytopenia with bone marrow cellularity, indicating that 90% of patients with severe anemia fell into the severe category for hemoglobin levels, while total leukocyte counts were primarily moderate in 70% of patients.

Table 07: The severity of pancytopenia with bone marrow cellularity

Bone marrow cellularity and parameters	Frequency (%)		
	Mild	Moderate	Severe
Hypocellular (n = 50)			
↓ Hb%	-	5 (10%)	45 (90%)
↓ TLC	8(16%)	35 (70%)	7 (14%)
↓ Platelet count	14 (28%)	22 (44%)	14 (28%)
Hb: Hemoglobin; TLC: Total Leucocyte Count			

Table 08 presents the hematological parameters, revealing that systemic lupus erythematosus (SLE) patients had the highest mean hemoglobin levels, while MDS patients had the lowest. Moreover, significant differences were noted in absolute neutrophil count (ANC) and mean corpuscular volume (MCV) between different conditions.

Table 08: Hematological parameters in pancytopenic patients

Diagnosis	Hb (g/dl)	TLC/mm^3	ANC/mm^3	Platelet (1000/mm^3)	MCV (fl)
	Mean±SD	Mean±SD	Mean±SD	Mean±SD	Mean±SD
HS	6.4±1.9	2154.8±712.4	673.9±448.4	61.8±25.8	83.5±7.7
Malaria	6.4±2.0	2030.8±808	757.6±401.4	60.3±30.7	80.8±15.4
MA	5.5±1.7	2318.2±686.8	1080.5±335.9	60.±31.9	101.2±11.9
AA	5.5±2.2	1805.0±968.5	468.4±584.5	46.4±33.0	88.4±3.9
AL	5.5±1.4	1795.0±1064.2	244.2±354.0	38.6±26.1	86.1±9.8
MDS	4.7±2.4	2558.5±586.9	946.5±788.1	53.7±16.8	94.0±7.2
SLE	6.8±2.1	1766.7±1026.3	806.7±524.7	45.7±28.7	82.2±1.5
Total	5.4±1.9	2168.6±820.9	767.4±530.1	59.9±28.6	84.7±11.9
p-value*	0.3 (NS)	0.4 (NS)	0.002 (S)	0.3 (NS)	0.0001 (S)
NS: Not significant					
S: Significant					
Statistical analysis was calculated by Student's t-test.					
AA: Aplastic anemia. AL: Acute leukemia. ANC: Absolute neutrophil count. Hb: Hemoglobin. HS: Hypersplenism. IDA: Iron deficiency anemia. MA: Megaloblastic anemia. MCV: Mean corpuscular volume. MDS: Myelodysplastic syndrome. SLE: Systemic Lupus Erythematosus. SD: Standard deviation. TLC: Total leukocyte count.					

Discussion

Pancytopenia, a hematological condition characterized by the simultaneous decrease of red blood cells, white blood cells, and platelets, poses diagnostic challenges due to its diverse etiologies. This prospective cross-sectional study was conducted at Khulna Medical College Hospital over six months, involving 50 patients with diagnosed pancytopenia, selected through purposive sampling. The primary objective was to explore the causes and clinical profiles associated with pancytopenia. Findings revealed aplastic anemia (AA) as the predominant cause, affecting 56% of the patients, a statistic that aligns with global patterns showing higher incidences of AA in developing countries compared to the West.[6,7]

Notably, while previous studies indicated a male predominance in AA cases due to occupational exposures to chemicals, our study observed a higher prevalence among females, potentially linked to their exposure to arsenic in household water and chemicals in garment factories.[8,9] Megaloblastic anemia was the second most common cause, identified in 18% of cases, highlighting its association with vitamin B12 and folate deficiencies.[10] This condition often presents with symptoms such as pallor and bleeding, with nutritional deficiencies being a concern in Bangladesh,

exacerbated by chronic gastrointestinal disorders and malnutrition.[11] Interestingly, the expected high incidence of iron deficiency anemia was not observed in this hospital-based study, possibly due to the typical outpatient management of such cases.[12]

Hypersplenism emerged as the fourth common cause, identified in 10% of patients, primarily linked to cirrhosis and portal hypertension.[13] Malaria was noted in 8% of cases, indicating a region-specific prevalence that correlates with local epidemiological factors. Moreover, while myelofibrosis is often documented in adult patients with pancytopenia, it was rarely found in this cohort, which included only one case of systemic lupus erythematosus (SLE) associated with hypocellular bone marrow.[14,15]

Clinical manifestations such as fever, bleeding, and splenomegaly were common, reflecting the immunocompromised state due to reduced blood components. Notably, the study underscores the complexity of diagnosing and managing pancytopenia, emphasizing the need for comprehensive investigations, including history taking, physical examination, and various laboratory tests, including bone marrow examinations. The findings from this study contribute valuable insights into the etiological spectrum of pancytopenia in Bangladesh, supporting existing literature while highlighting the necessity for targeted diagnostic approaches to effectively manage this hematological condition.[16]

Limitations of the study

Every hospital-based study has some limitations, and the present study is no exception to this fact. The limitations of the present study are mentioned. The results of the present study may not be representative of the whole of the country or the world at large. The number of patients included in the present study was less in comparison to other studies. Because the trial was short, it was difficult to remark on complications and mortality.

Conclusion and recommendations

The study identifies aplastic anemia as the most common cause of pancytopenia, followed by subleukemic leukemia, myelodysplastic syndrome, and megaloblastic anemia. Symptoms predominantly included pallor, weakness, fever, and bleeding manifestations. Hematological parameters, including hemoglobin, total white blood cell count, platelet count, and bone marrow studies, were analyzed, revealing significant associations between bleeding history and platelet count. The findings emphasize the necessity of thorough investigations for all pancytopenia cases to ensure accurate diagnosis and effective management.

The study highlights a lack of kala-azar cases and notes discrepancies in anemia and erythrocyte sedimentation rate among aplastic anemia patients. Future extensive studies with larger sample sizes are recommended to explore these unresolved factors and provide insights specific to the region.

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References

1. Singh MK. Evaluation of Pancytopenia in Adults. Indian Journal of Public Health Research & Development. 2024 Jan 1;15(1).
2. Rehman HU, Mohammad F, Faiz Mohammad K. The etiology pattern of pancytopenia in children up to 15 years. 2003
3. Singh S, Sachdev L. Pancytopenia and Its Evolution Profile of Patients: A Study. International Journal on Recent Trends in Life Science and Mathematics. 2017 Dec 31;4(12):01-3.
4. Sankar V, Villa A. Hematologic diseases. Burket's Oral Medicine. 2021 Aug 30:627-64.
5. Ishtiaq O, Baqai HZ, Anwer F, Hussain N. Patterns of pancytopenia patients in a general medical ward and a proposed diagnostic approach. Journal of Ayub Medical College Abbottabad. 2004;16(1).
6. Issaragrisil S, Leaverton PE, Chansung K, Thamprasit T, Porapakham Y, Vannasaeng S, Piankijagum A, Kaufman DW, Anderson TE, Shapiro S, Young NS. Regional patterns in the incidence of aplastic anemia in Thailand. American journal of hematology. 1999 Jul;61(3):164-8.
7. Young NS. Acquired aplastic anemia. Annals of Internal Medicine. 2002 Apr 2;136(7):534-46.
8. Stanislas P, Driss F, Devergie A, Brechot C, Berthelot P, Gluckman E. Is hepatitis C virus involved in hepatitis-associated aplastic anemia? Annals of Internal Medicine. 1990 Sep 15;113(6):435-7.
9. Bhatnagar SK, Chandra J, Narayan S, Sharma S, Singh V, Dutta AK. Pancytopenia in children: etiological profile. Journal of tropical pediatrics. 2005 Aug 1;51(4):236-9.
10. Chandra J, Jain V, Narayan S, Sharma S, Singh V, Kapoor AK, Batra S. Folate and cobalamin deficiency in megaloblastic anemia in children. Indian Pediatr. 2002 May;39(5):453-7. PMID: 12037276.

11. Hussain M, Khattak TA, Bano Q. Spectrum of hematological disorders in children observed in 424 consecutive bone marrow aspirations/ biopsies. Pak J Med Sci. 2005 Oct;21(4):433-6.
12. Zlotkin S. A New Approach to Control of Anemia in "At Risk" Infants and Children Around the World 2004 Ryley-Jeffs Memorial Lecture. Canadian Journal of Dietetic Practice and Research. 2004 Sep;65(3):136-8.
13. Govindaraj T. Bone marrow study in adults with pancytopenia (Doctoral dissertation, Rajiv Gandhi University of Health Sciences (India)).
14. Imbert M, Scoazec JY, Mary JY, Jouzult H, Rochant H, Sultan C. Adult patients presenting with pancytopenia: a reappraisal of underlying pathology and diagnostic procedures in 213 cases. Hematologic pathology. 1989 Jan 1;3(4):159-67.
15. Pereira RM, Velloso ER, Menezes Y, Gualandro S, Vassalo J, Yoshinari NH. Bone marrow findings in systemic lupus erythematosus patients with peripheral cytopenias. Clinical rheumatology. 1998 May; 17:219-22.
16. Santra G, Das BK. A cross-sectional study of the clinical profile and aetiological spectrum of pancytopenia in a tertiary care centre. Singapore Medical Journal. 2010 Oct 1;51(10):806.