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Aplastic Anemia in Southern Odisha: An Institutional Study of Clinical and Hematological Features

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Abstract

Introduction: Aplastic anemia is a potentially life-threatening failure of hematopoiesis, characterized by pancytopenia and hypocellular bone marrow. Aplastic anemia if untreated results in very high mortality. Early diagnosis of aplastic anemias is essential for appropriate management of the patient. ***Aims and Objectives:*** The aim of the study was to assess the prevalence of the condition in southern Odisha admitted to this institute and to study the clinico-hematological profile for the assessment of severity by using the modified Camitta criteria aiding in their management protocol. ***Materials and Methods:*** This study was carried out prospectively in the Department of Pathology, MKCG Medical College & Hospital during the period of June 2017 to May 2019. A detailed clinical history, physical examination, Complete Blood Count, CPS, Reticulocyte count, Bone marrow aspiration and Biopsy were performed in each case and the observations were evaluated using simple and basic statistical tools. ***Results:*** There are 63 diagnosed cases of aplastic anemia during the study period. Out of 63 cases 36 cases are male (57.1%) and 27 cases are female (42.8 %) indicating a male preponderance of this disease and male to female ratio is1.3:1. We also found that, aplastic anemia has a bimodal age distribution. Fever, generalized weakness and bleeding due to thrombocytopenia are commonest clinical manifestations. All 63 cases are subcategorized into 38 Non severe cases (60.3%), 17 severe cases (26.9%) and 8 cases are very severe (12.7 %). ***Conclusion:*** A good knowledge on clinical and hematological parameters will certainly aid in early diagnosis of aplastic anemia and sub-categorization for treatment. But in a developing country financial constraints and lack of awareness forms a major drawback in patient management. So early diagnosis of aplastic anemia reduces the treatment cost as well as will decrease mortality.

Keywords: ***Hematologic Diseases, Aplastic anemia, Hematopoiesis, Pancytopenia.***

Introduction

Aplastic anemia represents a potentially life-threatening hematopoetic failure characterized by pancytopenia and hypo cellular bone marrow, resulting from injury to or loss of pluripotent hematopoietic stem cells in the absence of marrow-infiltrating disease [1].

Aplastic anemia affects individuals of all ages and races, with a slight male predominance [2]. The age distribution is bimodal, peaking in young adults (15-25 years) and older adults (over 60 years) [3,4]. Hospital-based studies in Asian countries report a two- to threefold higher frequency of aplastic anemia compared to Western countries. The overall incidence in the general population is estimated at three to six per million, encompassing both inherited and acquired forms [5]. While the incidence has been increasing in recent decades, potentially due to factors such as environmental exposures, genetic background, diagnostic criteria, drug and chemical use, and study designs, over 70% of acquired aplastic anemia cases are idiopathic, meaning the cause remains undetermined [4,6]. Identifiable etiological factors in the remaining cases include ionizing radiation, chemicals like benzene, certain viruses (e.g., parvovirus B19), and various drugs (e.g., chloramphenicol, gold, sulfonamides, and cytotoxic drugs). Pregnancy is also a recognized risk factor, although spontaneous recovery often occurs postpartum [3,7]. Data specific to India are limited due to a scarcity of dedicated studies. Our study was conducted to describe the Clinico-heamatological profile of 63 aplastic anemia cases diagnosed at our centre during the study period.

Materials and methods

This prospective study was conducted in the Department of Pathology, MKCG Medical College & Hospital, between June 2017 and May 2019. Prior to commencing the study, approval was obtained from the Institutional Ethics Committee. A total of 63 cases of aplastic anemia, meeting the inclusion criteria, were diagnosed. The inclusion criteria were based on the International agranulocytosis and aplastic anemia study group criteria of 1987, defined as follows:

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1. Peripheral blood showing at least two out of three of the followings:
   a) Hemoglobin less than 10 g/dl or hematocrit less than 30%.
   b) A total leukocyte count (white blood cell count) less than 3.5 x 10^9/L or a granulocyte count less than 1.5 x 10^9/L
   c) Platelet count less than 50×10^9/L.
2. Bone marrow biopsy showing the following:
   a) Decrease in cellularity with absence or depletion of all hematopoietic cells <25%.
   b) Absence of significant fibrosis or neoplastic infiltration.

Patients who did not consent to the procedure, those with pancytopenia and acellular marrow on bone marrow aspiration or biopsy, and those with pancytopenia and hypocellular marrow but with neoplastic infiltration were excluded from the study. Informed consent was obtained from patients and their guardians if they were minors.

The following laboratory investigations were carried out in all patients:

1. A detailed clinical history, physical examination and available previous investigations were recorded.
2. Complete blood count, including reticulocyte count.
3. Peripheral blood film examination.
4. Bone marrow aspiration and biopsy.

Bone marrow aspiration was performed in the department's procedure rooms under sterile conditions after administering local anesthetic over the right posterior superior iliac spine. Pediatric patients received intravenous ketamine. Approximately 0.5 ml of bone marrow aspirate was collected and smeared in each case. Trephine biopsies were taken from a site slightly distant from the aspiration site, with attempts made to obtain a biopsy core of at least 2.5 cm in length. The core biopsies were fixed in 10% formalin for 24 hours and decalcified in 20% EDTA for 12 hours. Subsequently, paraffin blocks were prepared, and slides were made. All peripheral blood and bone marrow aspirate smears were air-dried and stained with Leishman stain. The biopsy slides were stained with hematoxylin and eosin. Finally, the severity of each patient's condition was assessed using the modified Camitta criteria.

I. Severe AA: Marrow cellularity <25% (or 25-50% with < 30% residual hematopoietic cells), plus at least 2 of:

a) Neutrophils <0.5 x 10^9/l;
b) Platelets < 20 x 10^9/l;
c) Reticulocyte count < 20 x 10^9/l.

II. Very Severe AA; As for Severe AA but neutrophils < 0.2 x 10^9/L

III. Non severe AA; AA not fulfilling the criteria for severe or very severe AA.

Results

During the study period, 63 cases of aplastic anemia meeting the inclusion criteria were diagnosed. Of these, 36 (57.1%) were male and 27 (42.9%) were female, demonstrating a male predominance with a male-to-female ratio of 1.33:1 [**Table1**].

Table1: Sex wise distribution of aplastic anemia cases.

Gender	No	%
Male	**36**	**57.1%**
Female	**27**	**42.8%**
Total	**63**	**100%**

Our findings corroborated the established bimodal age distribution of aplastic anemia, with peaks observed in adolescence and the elderly [**Table2**].

Table2: Age distribution of the patients

Age groups (years)	No	%
0–15	10	15.87%
16–30	18	28.57%
31–45	09	14.28%
46–60	11	17.46%
>60	15	23.82%

The most frequent clinical manifestations included fever (42 cases), generalized weakness (34 cases), and bleeding manifestations (14 cases), followed by easy fatigability (12 cases) and breathlessness (4 cases). Purpura, vaginal bleeding, rectal bleeding, and gingival bleeding constituted the most common bleeding manifestations [**Table 3**].

Table3: Clinical manifestations of aplastic anemia cases.

Clinical features	No	%
Fever	42	66%
Generalized weakness	34	54%
Bleeding manifestations	14	22.2%
Easy fatigability	12	19%
Breathlessness	04	6.3%

Febrile patients demonstrated total leukocyte counts ranging from 440/µl to 3200/µl (mean: ~1200/µl) and absolute neutrophil counts ranging from 112/µl to 1480/µl (mean: ~660/µl) [**Table 4**].

Table 4: Correlation between fever and leukocyte count and absolute neutrophil count

Clinical presentation	Leukocyte count(/µl)		Absolute Neutrophil count(/µl)	
Fever	Range	Mean	Range	Mean
	440-3200	1820	112-1480	660

Purpura represented a micro hemorrhagic manifestation, while bleeding per vagina, rectal bleeding, and gingival bleeding constituted macro hemorrhagic manifestations. Patients exhibiting micro hemorrhage demonstrated platelet counts ranging from 11,000/µl to 41,000/µl (mean: ~23,000/µl). In contrast, patients presenting with macro hemorrhage had platelet counts between 4,000/µl and 35,000/µl (mean: ~16,000/µl) [**Table5**].

Table 5: Correlation between bleeding manifestations and platelet count.

Bleeding manifestations	No	Platelet range/µl	Mean
Minute bleeding manifestation	3	11,000-41,000/µl	23,000/µl
Gross bleeding manifestations	11	4,000-35,000/µl	16,000/µl

Of the 63 cases, 38 (60.32%) were classified as non-severe, 17 (26.98%) as severe, and 8 (12.70%) as very severe [**Table 6**].

Table 6

Severity	Male	Female	Total cases =N (%)
Very severe	5	3	8 (12.7)
Severe	11	6	17 (26.9)
Non severe	22	16	38 (60.3)

During bone marrow sample collection, no serious complications (e.g., bleeding, needle breakage, or local anesthetic reaction) were observed. Minor complications included local hematoma formation in six patients (9.52%) and a "dry tap" (blood tap) during aspiration in nine patients (14.2%). No complications were reported during the two-week post-procedure follow-up period.

Discussion

Sixty-three patients with a diagnosis of aplastic anemia meeting the inclusion criteria were identified during the study period. Patient ages ranged from 6 to 78 years. Of these, 36 (57.1%) were male and 27 (42.8%) were female, demonstrating a male predominance with a male-to-female ratio of 1.33:1. This aligns with prior Indian studies, one of which reported an age range of 12-63 years and a male-to-female ratio of 1.4:1, while another reported an age range of 1.5-70 years (median age 17 years) and a ratio of 1.3:1 [2,9]. The observed biphasic age distribution, peaking between 10-25 years and over 60 years, is consistent with findings reported by Montane *et al.*[4].

Fever (66%, n=42) was the most frequently observed clinical manifestation, followed by generalized weakness (54%, n=34). While anemia can contribute to fatigue, neutropenia increases susceptibility to infections, often resulting in fever. These findings are consistent with previous reports, although the specific prevalence of individual features varies. For example, one study reported pallor and generalized weakness as common (98%), while another identified fever as the most frequent symptom (51.8%) [10,11].

In this study, hemoglobin concentrations ranged from 2.0 to 9.8 g/dL, total leukocyte counts (TLC) from 530 to 3200/µL, and platelet counts from 4,000 to 57,000/µL. These findings are broadly consistent with previous reports of hemoglobin ranging from 2.9 to 5.0 g/dL and 1.3 to 8.0 g/dL, TLC from 200 to 3800/µL, and platelets from 1,000 to 136,000/µL and 8,000 to 86,000/µL [2,9]. In the present study, normocytic normochromic erythrocytes were observed in 68.2% of patients, and 86.3% exhibited relative lymphocytosis. Bone marrow cellularity in aplastic anemia was typically reduced, ranging from hypocellular to acellular, with a relative increase in lymphocytes and plasma cells. Prior studies have reported anisocytosis in 33.3% of patients, relative lymphocytosis in 50%, normocytic normochromic erythrocytes in 64%, and macrocytic normochromic blood picture in 20% [12,13]. Their study analysis of 50 cases revealed hypocellular marrow in 74%, normocellular marrow (progressing to hypocellularity) in 16%, and acellular marrow in 10%. In the present study, all patients exhibited hypocellular bone marrow aspirates composed primarily of fat cells, with a relative increase in plasma cells and lymphocytes [**Fig-1(A)**]. Trephine biopsy confirmed hypocellularity in 92% of cases [**Fig-1(B)**], with the remaining 8% exhibiting acellular marrow replaced by fat cells.

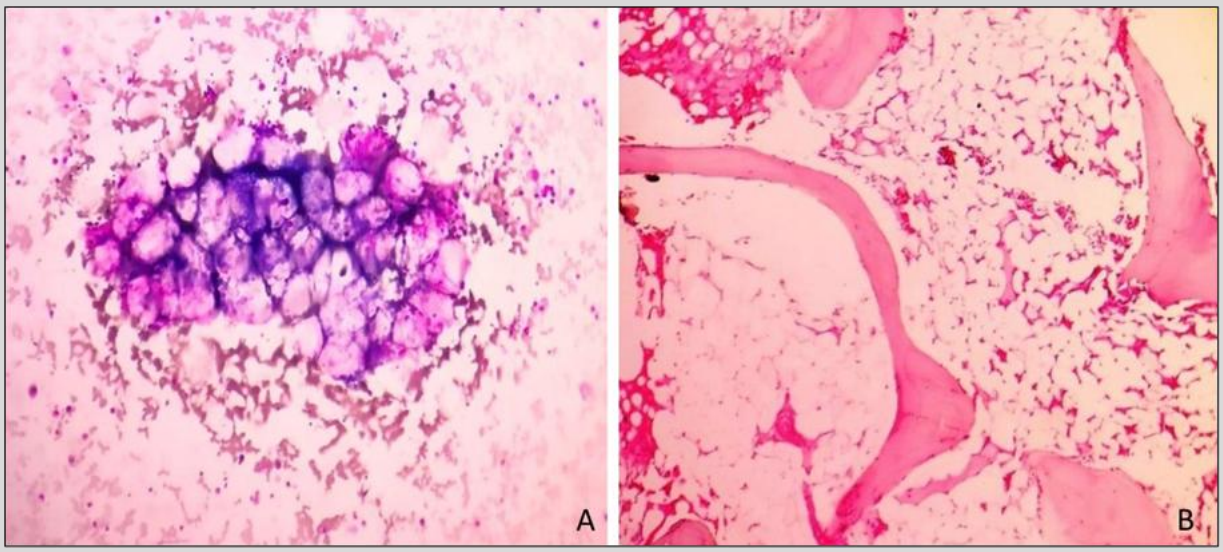

Figure 1: (A) Bone marrow aspiration showing hypocellular marrow particles. Particle shows only fat cells. (B) Bone marrow biosy showing hypo cellular marrow.

While several studies have reported a higher prevalence of severe and very severe aplastic anemia compared to non-severe forms, our study observed a predominance of non-severe cases, potentially attributable to the referral-based nature of the comparative data. Accurate disease severity assessment is crucial for guiding treatment strategies. Bone marrow biopsies were performed on all 63 diagnosed aplastic anemia patients. Despite repeated attempts, bone marrow aspiration yielded a "bloody tap" in 9 (14.28%) patients. No significant adverse events, such as bleeding, needle breakage, local anesthetic reaction, or mortality, were encountered; only localized hematoma formation was observed in 6 (9.52%) patients. Post-procedure follow-up for up to two weeks revealed no infectious complications. In a large study of 54,890 biopsies, adverse events were rare (0.047%), primarily consisting of hemorrhage (0.028%), needle-related incidents (0.014%), and infection (0.006%) [14]. Notably, none of the patients experiencing hemorrhage had aplastic anemia. Six of the 14 hemorrhage cases required transfusion, with one resulting in mortality. Our findings are consistent with this prior report, which also noted the absence of bleeding complications in aplastic anemia patients [14].

Of the bone marrow aspirates, nine were classified as "bloody taps." Forty-four cases exhibited hypocellular marrow particles, while the remaining ten showed a few normocellular particles interspersed within a predominantly hypocellular background. Bone marrow biopsies confirmed the diagnosis of aplastic anemia in all patients. In cases exhibiting normocellular particles within a predominantly hypocellular background, accurate assessment of overall marrow cellularity from aspirate smears alone proved challenging, potentially due to localized sampling from areas of relatively preserved hematopoiesis. In these instances, biopsy proved crucial for definitive evaluation [15].

Bone marrow biopsy provided definitive assessment of marrow cellularity and the relative proportions of cellular elements, mitigating potential bias introduced by normocellular particles in marrow aspirate smears [15,16]. Biopsy resolved challenges in cellularity assessment arising from hemodilution or hypocellularity in aspirate smears. Final diagnoses were established by integrating biopsy findings with data from peripheral blood analysis and bone marrow aspirates. While bone marrow biopsy represents the gold standard for diagnosing marrow suppression in aplastic anemia, cellular morphology is often better assessed in aspirates. In critically ill patients, the combination of clinical presentation, peripheral blood pancytopenia, and hypocellular marrow aspirate findings can facilitate rapid and reliable aplastic anemia diagnosis, potentially allowing for prompt treatment initiation before biopsy results are available.

Conclusion

Aplastic anemia, a potentially life-threatening condition, can manifest at any age, though it predominantly affects adolescents and the elderly. Clinical presentation reflects hematopoietic suppression, including fever (often associated with neutropenia), generalized weakness, fatigue, pallor, and purpura, with bleeding severity correlating with thrombocytopenia. While bone marrow aspiration suggests marrow aplasia or hypoplasia, definitive diagnosis requires bone marrow biopsy, providing superior assessment of cellularity and excluding other causes of hypocellularity, such as hypocellular myelodysplastic syndrome and myelofibrosis. Although biopsy is crucial for diagnosis, hematological parameters remain essential for severity classification and treatment guidance. In developing countries like India, financial constraints and limited awareness pose challenges to patient management. Therefore, early diagnosis of aplastic anemia is critical for reducing treatment costs and improving patient outcomes.

Declarations

Ethical Approval and Consent to participate

Yes, approved and obtained

Consent for publication

Yes obtained

Availability of supporting data

Upon request to the corresponding author

Competing interests

Nil

Funding Statement

Nil

Authors ‘contributions

B. B. B., A. K. B., & S.M. design the concept; B. B. B., involved in the recruitment of cases; A.K.B., examined the histopathological slides, B. B. B, A. K. B., S. M., D. R. R. R., and S. D., were involved in the data acquisition; B. B. B., A. K. B., S. M., were involved in the data analysis; B. B. B, A. K. B., S. M., D. R. R. R., and S. D., were involved in the manuscript preparation. All the authors have reviewed the manuscript.

References

[1] Schoettler ML, Nathan DG. The Pathophysiology of Acquired Aplastic Anemia: Current Concepts Revisited. Hematol Oncol Clin North Am. 2018 Aug; 32(4):581-594.

[2] Jha SC, Singh A, Mazuffar MA *et al.* Acquired idiopathic aplastic anemia; Study of 20 cases and review of literature. Inter J Bio Adv Res.2015; 6:569-73.

[3] Furlong E, Carter T. Aplastic anaemia: Current concepts in diagnosis and management. J Paediatr Child Health. 2020;56(7):1023-1028.

[4] Montané E, Ibáñez L, Vidal X, *et al.* Epidemiology of aplastic anemia: a prospective multicenter study. Haematologica. 2008; 93(4):518-523.

[5] Ahmed P, Chaudhry QUN, Satti TM, *et al.* Epidemiology of aplastic anemia: a study of 1324 cases. Hematology. 2020;25(1):48-54.

[6] Issaragrisil S, Kaufman DW, Anderson T, *et al.* The epidemiology of aplastic anemia in Thailand. Blood. 2006; 107(4):1299-1307.

[7] McCahon E, Tang K, Rogers PC, McBride ML, Schultz KR. The impact of Asian descent on the incidence of acquired severe aplastic anaemia in children. Br J Haematol. 2003; 121(1):170-172.

[8] Mahapatra M, Singh PK, Agarwal M, *et al.* Epidemiology, Clinico-Haematological Profile and Management of Aplastic Anaemia: AIIMS Experience. J Assoc Physicians India. 2015;63(3 Suppl):30-35.

[9] Gupta V, Kumar A, Saini I, Saxena AK. Cytogenetic profile of aplastic anaemia in Indian children. Indian J Med Res. 2013; 137(3):502-506.

[10] Aziz T, Ali L, Ansari T, Liaquat HB, Shah S, Ara J. Pancytopenia: megaloblastic anemia is still the commonest cause. Pak J Med Sci. 20101; 26(1):132-6.

[11] 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. Indian J Pathol Microbiol. 2011; 54(1):75-80.

[12] Gayathri BN, Rao KS. Pancytopenia: a clinico hematological study. J Lab Physicians. 2011 Jan;3(1):15-20.

[13] Vaht K, Göransson M, Carlson K, *et al.* Incidence and outcome of acquired aplastic anemia: real-world data from patients diagnosed in Sweden from 2000-2011. Haematologica. 2017 Oct;102(10):1683-1690.

[14] Bain BJ. Bone marrow trephine biopsy. J Clin Pathol. 2001;54(10):737-742.

[15] Bulduk T. Aplastic anemia from past to the present: A bibliometric analysis with research trends and global productivity during 1980 to 2022. Medicine (Baltimore). 2023;102(36): e34862.

[16] Parapia LA. Trepanning or trephines: a history of bone marrow biopsy. Br J Haematol. 2007;139(1):14-19.