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**Original Research Article**

# Pattern of clinico-haematological presentation of newly diagnosed adult aplastic anaemia in Bangladesh

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## ABSTRACT

**Background:** Aplastic anaemia (AA) is characterized by pancytopenia and a hypocellular bone marrow without abnormal infiltrates. While commonly seen in young adults, there is a secondary peak of incidence in the fifth and sixth decades of life. This study aimed to assess the clinical presentation and haematological profiles of adult AA patients in Bangladesh.
**Methods:** A cross-sectional study was conducted on 49 newly diagnosed adult AA patients at the Department of Haematology in Bangabandhu Sheikh Mujib Medical University (BSMMU) from September 2014 to March 2015.
**Results:** The average age of patients was 36 years (±15), with a range of 18 to 77 years. Nearly half (45%) were aged 18-30 years, and the male-to-female ratio was 2.8:1. Anaemia (100%), fatigue (92%), fever (84%), and respiratory distress (73.5%) were the most frequent symptoms. Bleeding was present in 65%, with petechiae (49.2%) and ecchymosis (29.2%) being the most common. Among 19 patients who were tested for hepatitis, 36.8% were positive for hepatitis B virus. All patients had pancytopenia, hypocellular bone marrow, and decreased megakaryopoiesis. Reduced erythropoiesis was observed in 83.7%. Haemoglobin, total WBC, absolute neutrophil, and platelet counts were reduced, while lymphocyte counts were elevated.
**Conclusions:** Aplastic anaemia is a significant cause of pancytopenia. Accurate diagnosis requires comprehensive clinical evaluation and haematological testing. Differentiation from inherited bone marrow failure syndromes, such as Fanconi anaemia, necessitates advanced tests like chromosomal breakage studies and karyotyping.

**Keywords:** Aplastic anaemia, Bangladesh, Clinical presentation, Haematological pattern, Hypocellular bone marrow, Pancytopenia

## INTRODUCTION

Aplastic anemia is a rare, life-threatening condition characterized by pancytopenia and a hypocellular bone marrow, leading to a deficiency in red blood cells, white blood cells, and platelets. This condition can result from a variety of aetiologies, including immune-mediated destruction of haematopoietic stem cells, environmental exposures, infections, and genetic predispositions.[1] Although aplastic anemia can occur at any age, it is most commonly diagnosed in young adults and the elderly, presenting significant challenges in diagnosis and management.[2] The clinical presentation of aplastic anemia is often non-specific, with symptoms such as fatigue,

dyspnea, recurrent infections, and bleeding tendencies being common due to cytopenia.[3]

Haematological abnormalities are the central to the diagnosis, with laboratory findings typically revealing pancytopenia without any apparent cause, normocytic or macrocytic anemia, reticulocytopenia, and severe neutropenia.[4] Bone marrow biopsy is essential for diagnosis, revealing a markedly hypocellular marrow, devoid of haematopoietic cells, which is replaced by fat.[5] The pathophysiology of aplastic anemia involves immune-mediated destruction of haematopoietic stem cells, often triggered by environmental factors such as drugs, chemicals, or viruses.[6] In idiopathic cases, which constitute the majority, the precise trigger remains unidentified.[7] Despite advancements in the understanding of its pathogenesis, the disease remains to be a clinical challenge due to its heterogeneous presentation and the need for individualized treatment approaches.[8]

Epidemiologically, the incidence of aplastic anemia varies geographically, with higher rates reported in Asia compared to Western countries.[9] This variation suggests a possible role of environmental or genetic factors unique to different populations.[10] The prognosis of aplastic anemia has improved over the past few decades with the advent of immunosuppressive therapy (IST) and haematopoietic stem cell transplantation (HSCT).[11] However, the disease remains associated with significant morbidity and mortality, particularly in patients who are unresponsive to initial treatment or who relapse.[12]

Given the rarity of aplastic anemia and its variable clinical course, it is crucial to study the pattern of clinico-haematological presentations in newly diagnosed adult patients to enhance understanding of the disease and improve diagnostic and therapeutic strategies.[13]

This study aims to characterize the clinical features, haematological parameters, and outcomes in adults presenting with newly diagnosed aplastic anemia, thereby contributing to the growing body of literature on this complex condition.[14] The findings are expected to provide insights into the diagnostic challenges and management strategies in the context of a developing country, where resources and access to advanced treatments may be limited.[15] This study aimed to find out the patterns of clinical presentation and haematological parameters of newly diagnosed adult aplastic anaemia patients in Bangladesh. Also, to ascertain the risk factors of newly diagnosed adult aplastic anaemia patients in Bangladesh. Moreover, to find out the presence of co-morbidity of adult aplastic anaemia patients in Bangladesh.

## METHODS

### *Study design*

This study was a cross-sectional descriptive study conducted over a period of six months, from September 2014 to March 2015. The research was carried out at the department of Haematology of Bangabandhu Sheikh Mujib Medical University (BSMMU), Shahbag, Dhaka. The study population included all newly diagnosed adult patients with aplastic anaemia who presented at the department of haematology during the study period. Sampling was done using a convenient sampling method.

### *Inclusion criteria*

Participants were included in the study based on specific criteria to ensure the accurate identification of aplastic anaemia (AA) cases. At first they must have hypocellular bone marrow, a hallmark of AA. They were also required to exhibit cytopenia, defined by meeting at least two of the following: haemoglobin levels below 10 g/dl, platelet count less than $100\times10^9$/L, and neutrophil count below $1.5\times10^9$/L. Only newly diagnosed cases of AA were included, focusing on adults aged 18-77 years. Patients suspected of having inherited bone marrow failure syndromes were excluded, as these conditions require additional diagnostic testing, such as chromosomal breakage studies, for differentiation.

### *Exclusion criteria*

Patients who refused to provide informed consent, the presence of blasts in the peripheral blood, suggestive of a malignant process, were excluded from the study. Furthermore, patients with inevitable cytopenia, including chemotherapy-induced cytopenia or cytopenia with hypercellular marrow like myelodysplastic syndromes, were excluded to maintain a focus on true AA cases.

### *Data collection procedure*

Data were collected using a semi-structured questionnaire developed after pre-testing. This questionnaire was designed to collect the patient profile, including socio demographic characteristics, clinical presentation, and pathological findings. Data were gathered through patient interviews, physical examinations, and review of laboratory reports. A pre-designed data sheet was used to systematically record all collected data.

### *Statistical analysis*

The collected data were compiled, tabulated on a master sheet, and analyzed using standard statistical methods. The IBM SPSS Statistics for Windows, version 17.0 (Armonk, NY: IBM Corp.) software was utilized for data analysis. Results were presented in the form of tables and graphs to facilitate interpretation.

### *Ethical implication*

The study's aims, objectives, procedures, methods, potential risks, and benefits were thoroughly explained to all participants in easily understandable local language. Informed consent was obtained from each participant, with

assurances given regarding the confidentiality of their information and records. Participants were informed that the findings of the study would contribute to better case management for both physicians and patients.

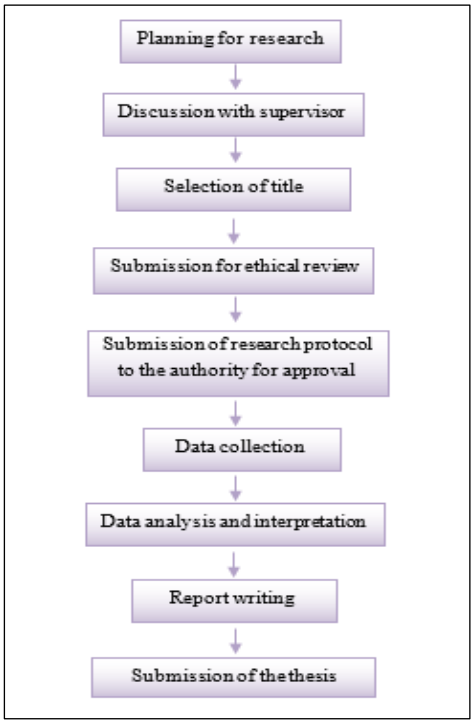


**Figure 1: Flow chart.**

## RESULTS

Table 1 presents a comprehensive overview of the demographic characteristics of the study population. The age distribution shows that the majority of participants (44.9%) are in the 18-30 age group, with smaller percentages in the older age groups. The gender distribution reveals a predominance of male participants (73%) compared to females (27%). Most participants are married (84%), and the most common occupation is service (30.62%), followed by business and housewife, each representing 22.44% of the population. Farmers make up 18.36%, while a small fraction (6.12%) are categorized under "Others."

Figure 2 depicts the age distribution of the patients. The age range was 18-77 years. The mean age was 35.57 (±SD 14.576) 15 years. The age roughly followed a normal distribution.

Table 2 shows the socio-economic status of the patients. On the basis of monthly family income they were stratified into lower class (earning less than 10000 BDT per month) and middle class (earning 10000-20000 BDT per month). Sixty percent of the patients were thus classified as middle class and the rest 40% as lower class.

**Table 1: Demographic characteristics of the study population.**

| Characteristics | Frequency (N) | Percentage (%) |
|---|---|---|
| **Age group (yrs.)** | | |
| 18-30 | 22 | 44.9 |
| 31-40 | 13 | 26.5 |
| 41-50 | 6 | 12.2 |
| 51-60 | 4 | 8.2 |
| 61-77 | 4 | 8.2 |
| **Gender** | | |
| Male | 36 | 73 |
| Female | 13 | 27 |
| **Marital status** | | |
| Married | 41 | 84 |
| Unmarried | 08 | 16 |
| **Type of occupation** | | |
| Services | 15 | 30.62 |
| Business | 11 | 22.44 |
| Farmer | 09 | 18.36 |
| House wife | 11 | 22.44 |
| Others | 03 | 6.12 |

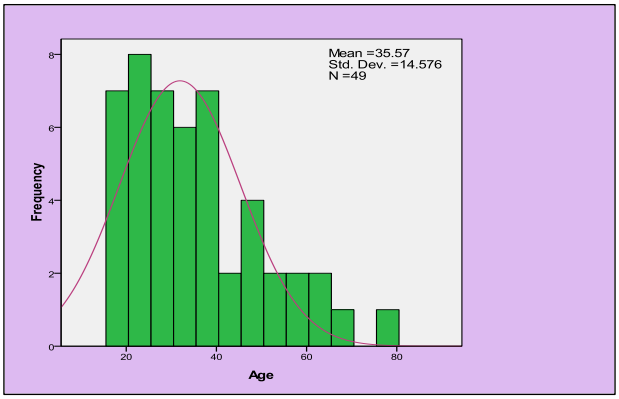


**Figure 2: Histogram showing age distribution of the patients.**

**Table 2: Distribution of socio-economic status of the patients.**

| Socio-economic status | Percentage of cases |
|---|---|
| **Middle class (10000-20000)** | 60 |
| **Lower class <10000** | 40 |
| **Total** | 100 |

Table 3 shows the types of bleeding experienced by the patients. Petechiae was the leading bleeding manifestation complained by more than 65% of the patients. Second leading type was ecchymosis (39%). Rash was present in about 16% cases.

Table 4 shows the causative agents of hepatitis among the patients. In 30 cases tests were not carried out. In tested 19 patients HBV emerged the leading cause (36.8%) followed

by HAV and HCV (about 15.8% each). Six patients found to be negative in this regard.

**Table 3: Types of bleeding experienced by the patients.**

| Types of bleeding | Frequency (N) | Percentages of cases |
|---|---|---|
| **Petechiae** | 32 | 65.3 |
| **Ecchymosis** | 19 | 38.8 |
| **Rash** | 8 | 16.3 |
| **Other** | 6 | 12.2 |
| **Total** | 65 | 132.7 |

**Table 4: Distribution of the patients by types of hepatitis virus (n=19).**

| Types of hepatitis virus | Frequency (N) | Percentages of cases |
|---|---|---|
| **HAV+ve** | 3 | 15.8 |
| **HBV+ve** | 7 | 36.8 |
| **HCV+ve** | 3 | 15.8 |
| **Negative** | 6 | 31.6 |

**Table 5: Some signs elicited by the patients.**

| Anemia signs | Frequency (N) | Percentages of cases |
|---|---|---|
| **Mild** | 5 | 10.2 |
| **Moderate** | 24 | 49.0 |
| **Severe** | 20 | 40.8 |
| **Overt infection** | 41 | 83.7 |
| **Hepato-splenomegaly** | 17 | 34.7 |
| **Rhonchi** | 14 | 28.6 |
| **Jaundice** | 12 | 24.5 |
| **Lymphadenopathy** | 3 | 6.1 |

Table 5 shows the distribution of the patients by signs. All the patients had anaemia. About half of the patients (24) had moderate type of anaemia while around 40.8% (20/49) showed severe form of anaemia. Most of the patients (41/49) exhibited signs of overt infection. Rhonchi was present in 14 patients. Hepato-splenomegaly was the finding in about 34.7% of patients. Everyone in all the four patients were suffering from jaundice.

Table 6 shows the clinical features of the patients. About Fatigue (91.8%) was the leading symptoms experienced by the patients. In about 83.7% cases fever was the main complaint. Respiratory distress was reported by 36 (73.5%) cases. H/O hepatitis was reported in 14 (28.6%) cases and bone pain was mentioned by 4 (8.2%) patients.

Table 7 shows the blood tests findings are presented in the above table. It is evident from the table that Hb%, total WBC, absolute neutrophil count and platelet counts were reduced in the study population while lymphocyte count is increased.

**Table 6: Clinical features of the study population.**

| Symptoms | Frequency (N) | Percentages (%) |
|---|---|---|
| **Fatigue** | 45 | 91.8 |
| **Fever** | 41 | 83.7 |
| **Respiratory distress** | 36 | 73.5 |
| **H/O hepatitis** | 14 | 28.6 |
| **Bone pain** | 4 | 8.2 |
| **H/O chemical exposure** | 4 | 8.2 |
| **H/O radiation exposure** | 4 | 8.2 |
| **H/O similar family disease** | 3 | 6.1 |

**Table 7: Blood tests (CBC with PBF) findings.**

| Blood test | Minimum | Maximum | Mean | Std. Deviation |
|---|---|---|---|---|
| **Hb% (gm/dL)** | 2.6 | 11.3 | 7.073 | 1.9 |
| **Total WBC count (per cumm)** | 530 | 3600 | 1983.67 | 811.2 |
| **Neutrophil (%)** | 3 | 55 | 21.61 | 11.8 |
| **Lymphocyte (%)** | 40 | 96 | 75.51 | 12.5 |
| **Monocyte (%)** | 0 | 6 | 1.92 | 1.3 |
| **Platelet (per cumm)** | 2000 | 50000 | 14806 | 11772 |

**Table 8: Investigations (bone marrow aspiration, trephine & others) findings.**

| Findings | Frequency (N) | Percent |
|---|---|---|
| **Pancytopenia** | 49 | 100.0 |
| **Hypocellularity** | 49 | 100.0 |
| **Decreased megakaryopoiesis** | 49 | 100.0 |
| **Decreased erythropoiesis** | 41 | 83.7 |
| **Decreased ME ratio** | 23 | 46.9 |
| **Abnormal RFT result** | 10 | 20.4 |

Continued.

| Findings | Frequency (N) | Percent |
|---|---|---|
| **Abnormal LFT result** | 9 | 18.4 |
| **Abnormal abdominal USG result** | 9 | 18.4 |
| **Abnormal cytogenetic result** | 2 | 4.1 |
| **Abnormal flow-cytometry result** | 2 | 4.1 |

Table 8 shows the hallmarks of aplastic anaemia i.e. pancytopenia, hypocellularity and decreased megakaryopoiesis were present in all cases. Decreased erythropoiesis was noted in most of the cases (83.7%). Decreased ME ratio was found in 23 patients (46.9%). In about one-fifths cases abnormal RFT, LFT and abdominal USG findings were found.

## DISCUSSION

The results of our study highlight several key aspects of adult aplastic anemia and its associated features. The demographic profile revealed that the majority of participants were in the 18-30 age group (44.9%), with a notable predominance of males (73%) and a high proportion of married individuals (84%). This finding is consistent with other studies that reported a higher prevalence of aplastic anemia in younger adults and a male predominance.[16,17] The mean age of 35.57 years in our study aligns with previously documented trends where aplastic anemia often presents in young adults but can vary across different populations.[18] Socio-economic analysis indicated that 60% of patients belonged to the middle class, which is reflective of broader socio-economic patterns seen in other study of aplastic anaemia. Similar findings have been observed in studies where socio-economic status was shown to impact disease outcomes and access to care.[19,20] The stratification into lower and middle classes provides a useful context for understanding the economic challenges faced by patients with aplastic anemia. In terms of bleeding manifestations, petechiae were was the most common, affecting over 65% of patients, followed by ecchymosis and rash. This distribution is consistent with the classic presentation of aplastic anemia, where skin manifestations are prominent due to thrombocytopenia and impaired platelet function.[21,22] The predominance of petechiae aligns with findings from other studies that highlight this symptom as a primary indicator of the condition.[23]

The causative agents of hepatitis among patients showed HBV as the leading cause (36.8%), followed by HAV and HCV. This result is notable given the established links between viral hepatitis and aplastic anemia.[24,25] The fact that 30 cases were not tested highlights the need for more comprehensive diagnostic protocols in similar studies for better understanding the etiology of aplastic anemia.

Regarding clinical features, our study found that 91.8% of patients experienced fever, and 73.5% had respiratory distress, which are common in aplastic anemia due to infections and anemia-related complications.[26,27] The presence of overt infection and signs such as rhonchi and hepatosplenomegaly is in line with the literature that describes these as common clinical findings in patients with aplastic anemia.[28,29] Blood test findings revealed reduced levels of Hb%, total WBC, absolute neutrophil count, and platelet counts, while lymphocyte counts were elevated. This haematological profile is characteristic of aplastic anemia, which is marked by pancytopenia and dysregulation of blood cell production.[30,31]

This study has few limitations. Like all other research work the current study was also not without flaw. The study included only a single centre with a relatively small sample size which limits generalizability. This descriptive type of study design was also weak to extract underlying information. Multi-centre studies with larger sample and sound study design could bring more insight regarding this issue. Reticulocyte was not done.

## CONCLUSION

Pancytopenia should be suspected on clinical grounds when a patient present with unexplained anemia, prolonged fever and tendency to bleed. One of the common causes of pancytopenia is aplastic anaemia. An increasing use of chemicals in agriculture might be the responsible factor for the development of AA. The present study concludes that detailed primary haematological investigations along with bone marrow examination in severely anaemic patients is helpful for understanding disease process, to diagnose or to rule out the presence of aplastic anaemia. It is also useful in planning further investigations and management.

### *Recommendations*

Aplastic anaemia (AA) is a major non-malignant haematological disease in this part of the world. Adult patients diagnosed with AA are a unique patient population that requires added attention to both diagnosis and treatment. Long-term follow-up for the development of late complications of the disease and treatment is mandatory. Larger population based study is suggested in this regard.

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