

Research Article

## Clinicohaematological profile of aplastic anaemia in BRIMS, Teaching Hospital, Bidar

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### Abstract

**Objectives:** There is a scarcity of clinical data in the field of aplastic anaemia from rural India. Present study was conducted in BRIMS, Teaching Hospital, Bidar to find out the clinicohaematological profile and the possible aetiological factors in patients with aplastic anaemia.

**Methodology:** The study population (n=100) included 25 children with male to female ratio 4.93:1. Weakness was present in all cases and pallor was present in 74.70% cases. Fever, bleeding episodes and localized infection were found in 55.42%, 48.19% and 27.71% cases respectively. There was no difference in clinical manifestation between children and adult except occurrence of fever (p=0.0365).

**Results:** We identified possible aetiological factors in 32.53% cases as relevant drug intake in 10.84%, exposure of chemicals in 13.25% and hepatitis in 8.43% cases. We found low mean haemoglobin (3.81±1.71g/dl), leucocyte and platelet (3.05±1.3 and 37.30±35X10<sup>3</sup>/cmm, neutrophil (30.28±21.76%) and high lymphocyte (67.27±22.50%) in peripheral blood. At the time of presentation, aplastic anaemia was moderate in 59.04% cases, severe in 48.19% cases and mild cases. We estimated the prevalence of aplastic anaemia in 4 district of Karnataka including tea garden areas was 2.98/ million population per year.

**Keywords:** Aplastic Anaemic, rural population, Bidar District, Clinical profile haematological profile, aetiological factor.

### 1. Introduction

Chronic Apalsic anemia (AA) is a disorder of haemopoietic stem cells, sometimes induced by a variety of environmental factors such as drugs, chemicals and infection. Although in many cases the precise aetiology cannot be obtained, a search for aetiology is necessary for better management and prevention. Wide clinical and geographical variations in the prevalences and presentations of AA have been reported<sup>1</sup>. AA is a relatively common haematological disease in the east<sup>2,3</sup>. The reported incidence is as high as 7.2 per million in the age group of 15 to 24 years<sup>2</sup>. Among the various aetiological factors, the role of insecticides is significant in the less developed countries<sup>4</sup>. The diagnosis of AA relies on the finding of peripheral blood pancytopenia and hypocellular marrow with increased fat spaces in the absence of any other disease<sup>3</sup>.

However, diagnosis is sometimes difficult due to the presence of residual hypercellular areas (hot pocket) of haemopoiesis<sup>5</sup>. Very few studies have been carried out regarding the incidence and clinicohaematological features of AA in India<sup>6,7</sup>.

BRIMS, Teaching Hospital caters patients from rural areas of Bidar District and Rural areas of Medak dist Telangana (state) as the blood bank of this institute has the facilities of component separation, almost all patients with haematological disorders are referred to this institution. The present study was undertaken to find out the clinicohaematological pattern of AA; to identify the possible aetiological factors, to compare the clinicohaematological patterns of AA between adult and children, and to estimate the approximate prevalence of disease in the rural areas of Bidar district.

### 2. Material and method

The present study was undertaken in BRIMS during the period of 2 years. All cases diagnosed at or referred to this institution with AA were included in the study.

All cases, except those not willing to give written informed consent, were subjected to a detail clinical history to assess the severity and complication of diseases like history suggestive of local or systemic infection, bleeding manifestations and symptoms due to anaemia (weakness); and to identify the possible aetiological factors that included present past drug intake, exposure to insecticides, fungicides, herbicides and fertilizers, exposure to radiation, past or present history of jaundice, suggestive family history etc., The probability of congenital AA was evaluated in children as per International Fanconi Anemia Registry scoring<sup>8</sup>. All cases were then undergone details clinical examination with special emphasis on degree of anemia, presence of infection, purpura or bleeding manifestations, enlargement of liver, spleen or lymph node, sternal tenderness, gum hypertrophy and liver disease. Investigations included complete blood count (CBC) including reticulocyte count, and the changes of different parameters were compared against the standard normal values<sup>9</sup>. Bone marrow examination was done from two different sites. Aspiration was done and smears were stained by Leishman's and Prussian blue stain (for iron content). For the histological sections, marrow particle were concentrated, fixed in equal amount 15% formalin and absolute alcohol solution and stained with haematoxylin and eosin (H&E) and Prussian blue technique<sup>1</sup>. Trephe biopsy was done by Jamshidi's needle and fixed in formal saline, stained by H&E and reticulin stain. Biochemical examinations including liver function test (LFT), serum urea and creatinine, fasting blood sugar, and hepatitis B surface antigen (HBsAg) and antihepatitis C virus (anti HCV) done in all cases.

The cases were classified at presentation as moderate AA when bone marrow cellularity was less than 50% and 2 or 3 cytopneias noted: absolute neutrophil count (ANC) below 1,500/cmm, absolute reticulocyte count (ARC) below 40,000/ cmm and platelet count less than 100,000/cmm; without meeting the criteria of severe AA (bone marrow cellularity <30% and 2 or 2 cytopneias: ANC< 500/cmm, ARC,

20,000/cmm, platelet count, 20,000/cmm). Rest of the cases were classified as mild AA when bone marrow hypocellularity and two or three cytopenias persisted for more than 6 weeks, but not so severe to fulfill the criteria for moderate AA<sup>11,12</sup>. Standard statistical methods were used for analysis of data.

### 3. Observations

100 cases of AA consisting of 83 males (83.13%) and 17 females (16.87%) were included in this study. The male to female ratio was 4.93:1 children (less than 15 years of age) accounted for 25 cases (25.30%) (Table 1).

**Table 1: Showing the Demographic Pattern of the Study population**

Parameter	Adults (n=75)	Children's (n=25)	Total (n=100)
Sex (male: female)	52.10 (5.2:1)	17.4(4.25:1)	69.14 (4.93:1)
Age Range (years)	18 to 65	6 to 14.5	6 to 65
Mean age (years)	31.64 (±12.39)	11.36 (±2.83)	26.46(±13.95)

**Table 2: Distribution of Cases according Clinical Manifestations**

Clinical manifestations	No. of cases (%)		
	Adults (n=75)	Children's (n=25)	Total (n=100)
Insidious onset	70 (93.55%)	21 (85.71%)	91 (91.57%)
Weakness	75 (100%)	25 (100%)	100 (100%)
Pallor	50 (66.13%)	25 (100%)	75 (75%)
Fever	38 (48.39%)	17 (76.19%)	55 (55.42%)
Bleeding	38 (48.39%)	10 (47.62%)	48 (48.19%)
Infection	22 (29.03%)	6 (23.81%)	28 (27.71%)
Hepatomegaly	5 (6.45%)	3 (14.28%)	8 (8.43%)

**Table 3: peripheral Blood Parameters in the study population**

Parameters	Adult (n=75)		Children (n=21)		Total (n=100)	
	Range	Mean (Standard deviation)	Range	Mean (Standard deviation)	Range	Mean (Standard deviation)
Haemoglobin 9g/dl)	1.35-9.40	30.72 (±1.73)	2.2-8.5	4.15(±1.65)	1.35-9.40	3.81(±1.71)
Total leucocytes (X10 <sup>3</sup> /cmm)	0.80-9.70	2.99 (±1.47)	1.5-4.8	3.238(±0.985)	0.80-9.70	3.05 (±1.3)
Platelets (X10 <sup>3</sup> /cmm)	8.00-9.00	4.52 (±39.28)	10.0-68.00	27.95(±17.27)	1.00-1900.00	37.30(±35)
Neutrophils (%)	3-84	32.26 (±22.92)	2-75	24.5 (±17.1)	3-84	30.25(±21.76)
Lymphocytes (%)	14-97	6530 (±23.82)	23-98	73(±1.74)	14-97	67.27(±22.50)

History of drug intake (chloramphenicol, Chloroquine ibuprofen and other drugs known to cause marrow depression) was present in 11 cases (10.84%), exposure to insecticides, fungicides and fertilizers was found in 13 cases (13.25%) and history of hepatitis was noted in 8 cases (8.43%). However the role of fertilizers and insecticides could not be analysed with appropriate pharmacological and biological study for the detection of traces of chemical compounds due to the lack of such laboratory facility in this institution. The onset was insidious in 92 cases (91.57%). The significant clinical manifestations were weakness (found in all cases), pallor in 74 cases (74.70%), fever in 55 cases (55.42%), history of bleeding episodes form at least one site in 48 cases (48.19%) and localized infection (in skin, mucus membrane, throat, lungs and gut) in 25 cases (25.43%), (table 2). Hepatomegaly was observed in 8 cases (8.43%), and none of them had lymphadenopathy or splenomegaly.

Peripheral blood showed anemia in all cases, leucopenia in 90 cases (90.36%), thrombocytopenia (in 94 cases, 93.98%) and neutropenia below corpuscles (RBC) were predominantly normocytic but mild anisocytosis was noted in 27 cases (27.1%). The mean differential neutrophil and lymphocyte counts in peripheral blood were 30.28 and 67.27 per mm<sup>3</sup> respectively (Table 3). The average reticulocyte count was 0.3%. Stainable iron (indicating adequate iron store) was normal or increased in all cases. We did not estimated Hb-F or other abnormal haemoglobin as some of patients had already received blood transfusion on an emergency basis at presentation.

**Table 4: Showing the grade Aplastic Anaemia and Average count of Different peripheral blood parameters**

Degree of aplastic anemia	Bone marrow cellularity (%)	Absolute neutrophil count (%)	Platelet count (%)	Absolute reticulocyte count (%)
Severe	31 (37.35%)	33 (39.76%)	34 (40.96%)	41 (49.40%)
Moderate	49 (59.04%)	40 (48.19%)	45 (54.22%)	38 (45.78%)
Mild or no reduction	3 (3.6%)	10 (12.05%)	4 (4.82%)	4 (4.82%)

Bone marrow examination revealed adequate sampling with decreased cellularity in all cases. Histological section of the aspirated marrow particles revealed better architectural relationship between the cellular and fat components. Bone marrow in aspirated smears (Leishman x100) and trephine biopsy revealed increased reduction of cellularity (<30%) was noted in 37 cases (37.35%). An absence of cell trail in aspirated material was noted in 78 cases (78.31%). Presence of hot spots ie. Focal areas of hypercellular marrow (H&E x50) were observed in 23 cases (22.89%) and mild dyserythropoietic changes were noticed in 23 cases (22.89%).

Abnormalities in LFT (raised liver enzymes and /or hypoproteinaemia) were detected in 6 cases (6.02%), while normal renal function was noted in all cases. HBsAg was positive in 2 cases (2.41%) and anti-HCV was not detected in any case. Moderate AA was most prevalent at the time of presentation (n=59 cases, 59.04%), and that was followed by severe AA (n=37:37.35%). Mild AA at the time of presentation was least frequent and was noted in 4 cases (3.61%) (Table 4).

### 4. Discussion

Children accounted for 25.30% of the total cases of AA in this study, while in the west this age group accounts for 16.4% of the total cases of AA<sup>13</sup>. However different studies showed that AA is more common in children in Asia, accounting for up to 30% cases<sup>14</sup>. A study at Mumbai (Bombay) India reported 29% cases occurred under the age of 10 year<sup>6</sup>. In this study, the male to female ratio was 4.93, which was higher compared to other studies conducted in the orient<sup>3</sup> (1.4 to 4.1) and India (1.31)<sup>6</sup>.

The increased ratio of fat to cellular areas as well as architectural pattern of fat spaces confirms the diagnosis of AA. However, bone marrow aspiration may be inconclusive due to presence of hypercellular foci, and bone marrow biopsy is helpful to exclude proliferative and infiltrative marrow disease and thereby establishes the diagnosis of AA. In the present study, the clinical features along with peripheral blood picture suggested and bone marrow examination confirmed the diagnosis of all cases. We observed that the marrow yield was satisfactory with plenty of hypocellular particle obtained in all cases, and focal hypercellularity in 23 cases (22.89%). According to Zhang *et al*<sup>15</sup>, the confirmation of AA requires correlation of different diagnosis techniques, and trephine biopsy alone can detect 93.6% of cases. We have used different techniques (bone marrow aspiration smears, histological section of aspirated particle and trephine biopsy) to increase the diagnostic accuracy. Normal or raised marrow iron found in this study might reflect decreased iron utilization by the marrow and occasional areas of active erythropoiesis.

The probable aetiology was identified in 33 cases (32.53%) in this series. Among them 13 (13.25%) had a history of exposure to insecticides and fertilizers, 11 (10.84%) had suggestive drug history of hepatitis before the onset of symptoms AA. However we could not definitely establish the aetiological factors as the role of fertilizer and insecticides could not be analysed by detecting traces of organ phosphorus and other compounds due to lack of sophisticated laboratory facility in this institution. An escalating use of insecticides and fertilizer, particularly in the tea plantation area, might be a contributing factor of AA. There are some reported cases of AA due to insecticides from the South East Asia<sup>14</sup>. We did not find any case of congenital AA which is in contrast to the 10.81% of cases as reported by Mehta *et al*<sup>6</sup>. However in that study the diagnosis of congenital AA was done solely on clinical basis. We have observed similar clinical features of children with AA with that of adult. However the occurrence of fever indicating local or systemic infection were found to be significantly higher ( $p=0.0365$ ) when compared with the adult patients. Associate malnutrition might be a contributory factor in children for increased susceptibility of infection.

BRIMS Teaching Hospital, is the only referral center in 4 rural northern districts of west Bengal with a modern blood bank, and this area does not have private set-up with blood component separation unit. It can be assumed that patients of AA attending this institute approximately reflect the occurrence of AA in that area, was 9,929,208 according to that data of census 2001 of India<sup>9</sup>. So, the estimated prevalence of AA (total 74 cases from these districts in 2.5 years) was 2.98/million population per year. However a population-based study is required to ascertain the true incidence of AA in the area.

It was found that AA was major non-malignant haematological disorder of northern rural districts of West Bengal. The clinical manifestations and bone marrow morphology were almost identical in adults and children. We noted that concurrent examination of smears and histological sections of particles obtained after bone marrow aspiration played a very important role in the diagnosis of AA. We identified the use of insecticide and fertilizers as a possible aetiological factor in rural and tea plantation areas.

## 5. Conclusion

It was concluded that aplastic anaemia is a major non-malignant haematological disease in this part of India and, and an increasing use of chemicals in agricultural and tea garden areas might be the responsible factor. Larger population bases study is suggested.

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