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January 2001

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Recommended Citation

Adil, S., Kakepoto, G., Khurshid, M., Burney, I. (2001). Epidemiological features of aplastic anaemia in Pakistan. *Journal of Pakistan Medical Association*, 51, 443.

Available at: http://ecommons.aku.edu/pakistan_fhs_mc_pathol_microbiol/568

Epidemiological Features of Aplastic Anaemia in Pakistan

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Abstract

Objective: To complete the data on the demographic features of patients diagnosed to have aplastic anemia at a single institution over a 7.5 years period.

Methods: Demographic information was retrieved from the patients medical records retrospectively as well as prospectively of those patients who presented with features of aplastic anaemia. Their diagnosis was confirmed by performing a complete blood count and bone marrow trephine.

Results: One hundred and forty four patients were diagnosed to have aplastic anemia; there were 106 males and 38 females. Their ages ranged from 2 to 75 years, with a median of 17 years, 112 (77.7%) patients were below the age of 30 years. Severe aplastic anemia (SAA) was seen in 74 (51.4%), very severe (VSAA) in 24 (16.7%) and non-severe aplastic anemia (NSAA) in 46(31.9%) patients. No obvious cause could be established for 74.3%. Thirteen patients admitted using drugs known to cause AA and one was a radiographer (9%). Out of 44 patients tested, 7 (15.9%) were found to have either hepatitis B virus markers or antibody to hepatitis C at the time of diagnosis of AA. However it was difficult to establish a cause and effect relationship with either drugs or viruses.

Conclusion: Aplastic anaemia is found to occur mostly severe aplastic anaemia (JPMA 51:443,2001).

Introduction

Epidemiological studies have shown that the presentation of aplastic anemia (AA) in the orient is different from the west¹⁻³. Studies from the far east also show that the disorder mainly affects the younger population and there is a male preponderance^{2,4}. Geographical variation in epidemiological features of AA is thought mainly to be due to environmental rather than genetic factors^{1,5}. However, etiology largely remains unknown. Most studies describe idiopathic aplastic anemia as the largest group⁶. While information regarding the presenting data on AA is available from the west as well as the far east, data from south Asia are scarce. Since environmental factors are thought to play a major role in etiology of AA, it is conceivable that the presentation of the disease in south east Asia might be different compared to what has been reported from elsewhere. The following is a compilation of clinico pathological features of patients in young males. The most common type was idiopathic diagnosed to have AA at a tertiary referral center in Southern Pakistan.

Patients and Method

The data were collected both retrospectively as well, as prospectively. The medical records of patients diagnosed to have AA between January 1990 and December 1993 were traced from the Medical Records section. The section uses International classification of diseases (ICD 9.0 version) database. The attending physicians logged the diagnosis on to the face sheet. Between January 1994 and June 1996, the data were collected prospectively. Records were maintained for every patient diagnosed to have AA in the laboratory, whether the patient was admitted to the hospital for management, or the patient was only referred from elsewhere else for a bone marrow examination.

All patients had a complete blood count done on Coulter S-IV (Coulter Electronics, Florida, USA) absolute neutrophil count (ANC) and reticulocyte count. The diagnosis of AA was established on the

basis of cellularity observed on bone trephine. Standard criteria of Cammita was employed to stage AA into severe (SAA) and very severe aplastic anemia (VSAA)⁷.

Bone marrow smear was available in 73 of 144 cases in addition to bone trephine. Serology for hepatitis B and C viruses (HBsAg and anti-HCV) was also checked in several patients. Acid hemolysis (Ham's) test, carried out routinely was available for analysis. Cytogenetic studies were not performed in any case.

Results

Over a 7.5 year period, 144 patients were diagnosed to have AA. Their ages ranged between 2 to 75 years (Median 17 years). One hundred and twelve (77.7%) were less than 30-years and 13 (9%) were above 50 years. The peak incidence (45.8%) was in 11-20 years age group (Figure).

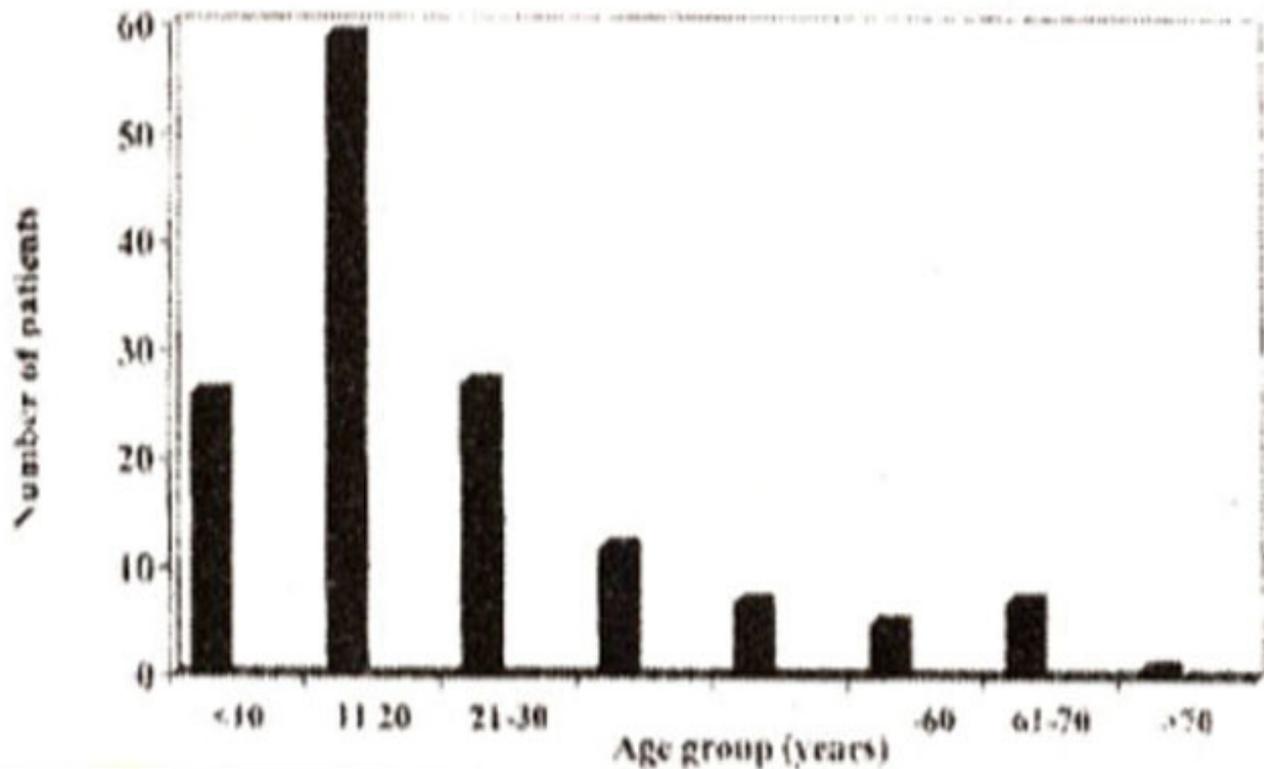


Figure. Age groups in Aplastic Anaemia.

There were 106 males and 38 females. One hundred and two patients belonged to Karachi and 42 were residents of rural Sindh, Baluchistan, Punjab and the Frontier province.

Figure Age groups in Aplastic Anaemia

The major reason to seek medical attention was a non-remitting fever. Sixty five (45.1%) patients had more than one episode of fever. Forty four (30.6%) patients presented with bleeding; 17 bled from gums 11 had epistaxis, 8 presented with purpura, per rectal bleeding occurred in 2 and 3 bled from other sites. Nine patients had life-threatening bleeding. Thirty (20.8%) patients had symptomatic anemia i.e. tiredness, shortness of breath and increasing pallor. Eight (5.5%) were diagnosed either incidentally or during check up for unrelated medical problems. The duration of symptoms ranged from 2 to 360 days with a median of 60 days. As many as 30 (20.8%) patients had received transfusion on more than one occasion before the diagnosis was established.

At the time of diagnosis the patients were also classified into prognostic groups using the standard criteria. Forty six (31.9%) patients had NSAA, 74 (51.4%) had SAA and 24 (16.7%) were diagnosed to

have VSAA. The mean haemoglobin (Hb), total leukocyte count (TLC), ANC and platelet count for the groups SAA and VSAA are shown in table 1.

Table 1. Laboratory Features at Presentation.

	SAA*	VSAA+
Hemoglobin (gm/dl)	6.0	5.7
Total Leucocyte Count ($\times 10^9/L$)	2.9	2.3
Absolute Neutrophil Count ($\times 10^9/L$)	0.413	0.166
Platelets ($\times 10^9/L$)	15	10

* Severe aplastic anaemia,
+Very severe aplastic anaemia

It was difficult to define an etiology in each case. In 74.3% of the patients, no cause could be established or suspected. Eight patients had a prior history of taking sulpha drugs. One patient had anti tuberculous therapy (ATT) one year prior to diagnosis, 2 had a history of chloramphenicol use and 2 took unconventional medicines. One patient worked as a radiographer for more than three months prior to the onset of symptoms. However, the vast majority of the subjects had symptomatic treatment by the general practitioners before a final diagnosis of AA was established, and hence it was difficult to establish a cause and effect relationship.

Viral serology was checked on 44 patients, 3 were found to be positive for Hepatitis B surface antigen and four had antibody to hepatitis C virus. All these cases had been transfused before the diagnosis and no direct cause and effect relationship could be established.

Discussion

In our study, AA was seen to affect mainly the children, adolescent and young adults. One hundred twelve (77.7%) patients were less than 30 years of age. In comparison with western studies, the median age at the time of diagnosis was 17 years^{3,5,6}. A bimodal peak was not observed in our patients as has been reported in some studies from the West⁶. The results of our study are however consistent with studies from Thailand^{2,4}, Korea⁸ and China⁹ where 60-70% of the patients presented at less than 20 years of age. A small study from Northern Pakistan also suggested a higher frequency of AA in young adults¹⁰. It remains unclear as to why there is such a marked geographical difference in age frequency in AA.

The male to female ratio of 2.8:1 observed in our study is also at variance with reports from the West^{6,11}.

However, the ratio is comparable to data from Asian countries, particularly those from China⁹ and Bangkok² and to earlier studies from Pakistan¹⁰. The age and sex distribution of patients from Japan and Hong Kong is closer to Western patients¹². The Japanese immigrants in Hawaii have pattern of AA similar to that of Americans¹³.

In this study, we could not establish an etiological correlation with environmental factors. The largest group was composed of the "idiopathic" entity, which comprised more than 74.3% of our cases. It is

possible that like other studies^{6,14,15} “idiopathic” group is actually a major group, however some points merit discussion. It is plausible to think that the free availability of non-steroidal anti inflammatory drugs, antibiotics, anticonvulsants, and anti malarials without prescriptions, may have played a bigger role than has been discussed. Additionally, “traditional remedies” which are much more widely available and are also cheaper may have had a positive etiologic role. Another explanation could be that the patients generally have no record of their illnesses; a problem inherent to our social and cultural circumstances and hence a correct estimate of various drugs causing AA could not be made. Only 9% of patients gave a definite history of taking suspected drugs.

Hepatitis-associated AA typically occurs within six months of an acute attack of hepatitis^{16,17} of our patients were detected to have viruses associated with hepatitis. 4 were positive for hepatitis B surface antigen and 3 to hepatitis C antibody. All of these cases had received at least one blood transfusion prior to presentation. We believe that at least in some patients this reactivity was secondary to transfusions given to them for symptomatic anemia or bleeding. Studies from Taiwan and Thailand also reveal a high incidence of hepatitis associated AA^{17,18}. We however, did not screen our patients for hepatitis A, a water-borne virus which has also been incriminated in the causation of AA¹⁹.

There are several limitations of the study. Firstly, the data were collected retrospectively for a period of time, and although the medical charts were the source of information, it is possible that the relevant drug history could not be obtained from every case. Also, since this part of the study dealt with patients admitted to the hospital, the total number of patients diagnosed to have AA is actually an underestimate. Another limitation of this study was the lack of availability of cytogenetic data.

Hypoplastic myelodysplastic study above the age of 50 years, when hypoplastic MDS is syndrome (MDS) constitutes 20% of all the MDS in our country²⁰. At times it is impossible to differentiate AA from hypoplastic MDS on morphological grounds. However, there were only a few patients in this seen more commonly²⁰. If some of the patients were diagnosed to have AA erroneously, because of a lack of availability of cytogenetic studies, the age incidence would likely to be even lower.

In conclusion these data show that AA is not an uncommon problem in our country. It usually affects young males and majority have SAA. The etiology of AA remains uncertain.

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