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ORIGINAL ARTICLE / RESEARCH

Incidence of Aplastic Anaemia in Khuzestan Province, Iran: A Retrospective Single-Centre Study

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ABSTRACT

Introduction: Aplastic anaemia (AA) is a rare but serious disorder with high mortality and morbidity rates. The incidence of AA worldwide is 2–5 patients/million/year. There is paucity of studies on this disorder from Iran. The aim of the study is to find out the incidence of AA in Khuzestan province, Iran.

Patients, Materials, and Methods: The study was conducted at the Research Center of Thalassemia and Hemoglobinopathies (PCTH), Khuzestan province, Iran, from 21 March 2002 through 21 March 2005. This centre covers the 4.3 million population of Khuzestan province (~20% of Iran's population). All the haematological findings and bone marrow biopsy specimens were studied at Shafa Hospital, Jondishapur University of Medical Sciences, which is the only oncology centre in Khuzestan province. Patients were diagnosed as having AA if they satisfy two or more of the following criteria: (1) leukocytes <3500/mm3, (2) platelets <50,000/mm3, and (3) haemoglobin <10.0 g/dl or haematocrit <30%, in addition to bone marrow features compatible with AA.

Results: A total of 1753 patients were examined during the study period. Of them, 257 (14.6%, 95% CI: 13.1–16.4%) satisfied AA criteria, giving an incidence of 20 (95% CI: 13–29) cases/million individuals/year in Khuzestan province, Iran. The age distribution of AA showed a bi-modal pattern; males and females aged 15–30 years, the majority of patients falling under this category, were affected equally. There was a gradual decline in the incidence over the studied years.

Conclusion: The incidence established in this study is less than incidences from other parts of the world. This may reflect the role of environmental factors in aetiology of bone marrow suppression.

Keywords: Anaemia, aplastic anaemia, incidence, Khuzestan, Iran

Introduction

Aplastic anaemia (AA) is a low-incidence disease, ranging from 0.5 to 4 cases/million individuals/year [1–3]. However, its clinical evolution is more severe, involving higher case fatality and requiring more complex therapeutic interventions [4–8]. AA is a rare but life-threatening haematopoietic stem cell disorder, which is characterised by near-total to complete loss of blood-forming cells. The result is more than just anaemia; there is severe reduction in other blood components such as white blood cells (WBCs) and platelets, which results in bleeding and infections as well as anaemia [9].

So far, no study on this disorder has been carried

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out in Iran, and our practice is based on the studies from other parts of the world. The problem of AA in Khuzestan province has not been previously investigated, and no current report is available on the incidence of this disorder.

We undertook a systematic epidemiologic study of AA in Khuzestan province of Iran to determine its precise incidence rate. Despite the fact that most of the cases are idiopathic, this disease has been clearly linked to a variety of chemical or toxic exposures such as drugs, radiation, environmental toxins, and insecticides and is also autoimmune. Laboratory and clinical observations have factors, reasoning that etiologic environmental exposures could be more implicated than immunologic pathophysiology.

The incidence of AA in selected countries is shown in [Table/Fig 1]. Marrow failure is reported to be severe in Europe and Israel [19],[20]; clusters of AA have been reported [10],[21]. Early Western observers were struck by large numbers of cases they observed in Asian clinics [22]. The disorder is more prevalent in Asia than in the Western world [23]. There were also a few cases attributed to the use of medication [24].

[Table/Fig 1] Incidence of aplastic anaemia in selected countries

Country	Incidence/million/year
UK [10]	2.3
France [11]	1.4
Japan [12]	31–48
Thailand [13]	5.7
China [14],[15]	19–21
Turkey [16]	1.14
USA [17]	2.5
Brazil [17]	2.4
Mexico City [18]	3.9

Patients, Materials, and Methods

In this study, we have focused retrospectively on the patients whose haematological findings and bone marrow biopsy specimens were studied in Shafa Hospital, Ahwaz Jondishapur University of Medical Sciences and Research Center of Thalassemia and Hemoglobinopathies, during 21 March 2002 to 21 March 2005.

For the purpose of this study, we focused on the patients of a single medical institution: the Research Center of Thalassemia and Hemoglobinopathies (PCTH), which covers the 4.3 million population of Khuzestan province (around 20% of Iran's population). These two centres are the only organisations in Khuzestan that work in haematology and oncology fields.

Patients were diagnosed as having AA if they satisfy two or more of the following criteria: (1) leukocytes $<3500/mm^3$, (2) platelets $<50{,}000/mm^3$, and (3) haemoglobin <10.0 g/dl or haematocrit <30%. Additionally, the bone marrow evaluation had to comply with the diagnosis, demonstrating hypocellularity, but excluding fibrosis, lymhosomatous or carcinomatous leukaemic infiltration, or hypocellular myelodysplasia. The bone marrow evaluation by biopsy was recommended for all patients in our study.

A total of 1753 patients were examined during the study period. We divided all patients into four categories based on World Health Organisation (WHO) age division scale: 0–11 years old patients as group 1, 12–30 years as group 2, 31–50 years as group 3, and >51 years as group 4.

Data Management

Data were collected by the study coordinators who were nurses or pharmacists. All study coordinators underwent a standard training programme in the study coordination office.

Data entry was performed through electronic capture via the Internet, which consisted of a form, using HTML resources, that was similar in appearance to the manual filing form but had the advantage of giving the possibility of selecting data coded in available lists. A few fields were restrictive, such that values outside of pre-established limits could not be entered, and some fields were interlinked, such that divergent information was not allowed.

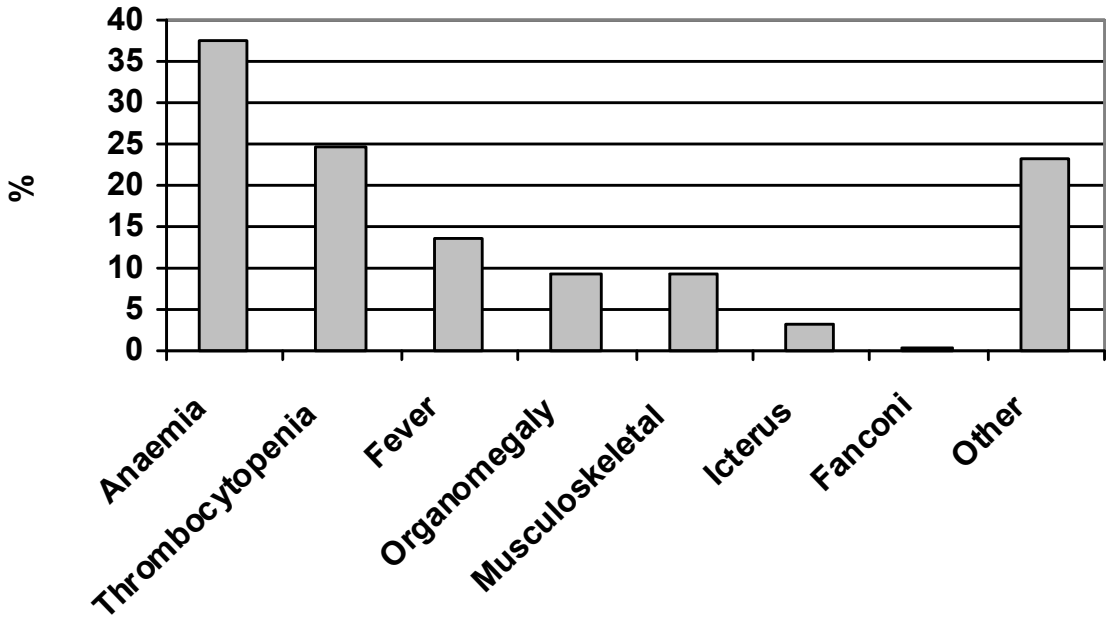
Data Analysis

The quantitative variables were described through means and standard deviations or medians and quartiles; the categorical variables were expressed as absolute and relative frequencies. To determine the incidence, the total population of the regions where active search was carried out was used as the

denominator (Khuzestan province population was 4.3 million).

Results

There were 1753 bone marrow biopsy reports from 21 March 2002 through 21 March 2005, 257 (14.6%, 95% CI: 13.1–16.4%) of whom either were aplastic or had hypocellular marrows. The most common clinical findings in these patients were anaemia (37.0%), thrombocytopenia (24.5%), and fever (13.6%). Eight patients had jaundice, and one patient had features of Fanconi syndrome [Table/Fig 2]. Twenty-four (9.3%) patients had hepatomegaly or splenomegaly; 179 (69.6%) patients did not report any significant past medical history. The most common reported medical histories were lymphoma and AA in nine (0.3%) and six (0.2%) patients, respectively. The distribution was bi-modal: males and females aged 15–30 years were affected equally, and males showed a higher frequency above 51 years of age [Table/Fig 3]. Annual rate of AA in Khuzestan province, Iran, with a population of 4.3 million, was 20 (95% CI: 13–29) cases/million individuals/year.

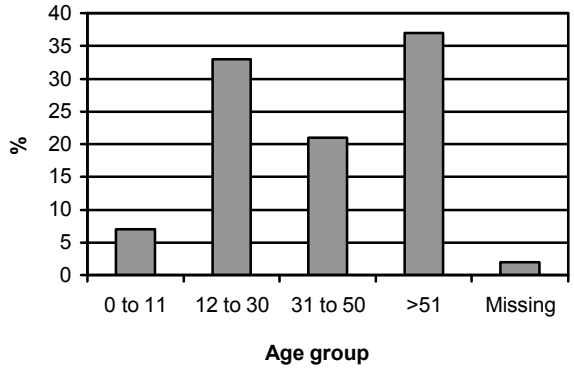


[Table/Fig 2] The prevalence of sign and symptoms of aplastic anaemia in the study groups.

Discussion

The incidence of AA in Europe and Israel between 1980 and 1984 was two cases per million, based on case–control studies [25]. The incidence seems to be two or three times higher in South-East Asia. In Thailand and China, the rate is 5–7 cases per million [26]. The analysis of the data generated during the study enabled us to obtain preliminary values for the incidence of AA. The incidence of AA observed in the present study is 20 (95% CI: 13–29) cases/million individuals/year in Khuzestan province, Iran. The incidence of AA reported from different countries was pretty low ([Table/Fig 1]). In different series, the highest incidences are from Japan, Sweden, and Iran [10–16],[18]. This series demonstrates different geographic characteristics, diet, lifestyle, education, and occupational exposure characteristics.

Our study population demonstrated a bimodal age distribution: 15–30 and over 51 years of age. Additionally, our population had a higher incidence above 51 years of age (37%) compared to that at 12–30 years of age (33%) in the other series. Only one study from France showed a peak incidence above 60 years of age. In most studies the male-to-female ratio was 1:1. One study from Iraq, between 1975 and 1978, showed a male-to-female ratio of 3:1.



[Table/Fig 3] Age distribution of the study group.

In our study, observations along with the higher incidence of AA in middle-aged men may raise the suspicion about the role of ammunitions and chemicals, used over 8 years of Iran–Iraq war, in pathogenesis of this disease.

The major complications of these patients are infection and bleeding. It has been shown that with a thorough supportive care approximately one-fifth of these patients will recover from the aplastic phase. In older patients, incidence of paroxysmal nocturnal haemoglobinuria, myelodysplastic syndrome, and graft versus host disease is higher. Also bone marrow transplant outcome and overall prognoses are poor.

Early diagnosis and a thorough supportive care may improve the prognosis. However, detection of the possible aetiology factor, especially preventable environmental exposures and early management of this fatal disease, may also help in improving the prognosis of the disease.

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