

# Frequency of Meeting and Causes of Development of Aplastic Anemia in the Republic of Uzbekistan

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**Abstract** It is proved that in the population of patients with aplastic anemia, among the inhabitants of Uzbekistan, men prevail in their frequency of occurrence, but in the elderly and senile age there are 2.5 times more women than men. The provocateurs of aplastic anemia can be drugs, certain diseases of viral etiology in the acute period, metabolic diseases and endocrine pathology, unfavorable working conditions. Among the causes of impaired hematopoietic function of the bone marrow should be considered autoimmune diseases, in which the immune mechanisms are aimed at destroying not only disease-causing agents, but also damage to their own cells.

**Keywords** Aplastic anemia, Prevalence and incidence

## 1. Introduction

Aplastic anemia (AA) is one of the most difficult and insufficiently studied problems in modern hematology. This is a rare and serious disease of the blood system with a high percentage of disability and patient mortality. 5-year patient survival is up to 20%. The main characteristic of aplasia is the cessation of bone marrow and its replacement with adipose or connective tissue. The destruction of associative connections and the disappearance of the normal microenvironment of stem cells leads to a global triple-hematopoietic deficiency - in particular, erythrocytes, platelets and leukocytes. AA is characterized by bone marrow hypocellularity and peripheral blood pancytopenia [3]. In adults, the disease develops acutely with relapses and complications.

In the diagnosis of aplastic anemia, it is important to know that it is characterized by pancytopenia of peripheral blood and reduction of bone marrow cellularity. The diagnosis of acquired AA requires the exclusion of other conditions associated with pancytopenia, in particular, Fanconi anemia (hereditary bone marrow failure) and myelodysplastic syndrome (MDS) [1]. MDS can be excluded by conducting appropriate cytohistological and cytogenetic analysis. It is very important to differentiate these three pathological conditions, since the treatment of each of them has its own

characteristics.

It is important to know that normal hemopoiesis depends on the complex interaction of several types of cells, including hematopoietic stem cells and microenvironment cells. In recent years, evidence has been obtained that the functions of the cells and their environment are disturbed in AA [1].

Despite the undeniable progress in understanding the mechanisms of development of aplastic anemia, the question of a unified and generally accepted theory of the pathogenesis of the disease cannot be considered solved. One of the leading mechanisms of damage to blood formation in aplastic anemia is considered to be immune aggression, aimed at cells - the predecessor of hematopoiesis [1]. It is proved that bone marrow insufficiency in aplastic anemia develops because of suppression of the proliferation of hematopoietic precursors by activated T-lymphocytes and natural killers. Activation of T-lymphocytes, expansion of cytotoxic T-clones and release of mediators of immune suppression of hematopoiesis (interferon  $\gamma$ , tumor necrosis factor  $\alpha$ ) or stimulating the proliferation and activation of T-lymphocytes (interleukin 2), lead to disruption of proliferation processes and to stimulation of apoptosis of precursors, resulting in a significant decrease in the pool of hematopoietic cells and the development of bone marrow aplasia [2, 4].

The disease is characterized by the following symptoms [5]:

1. Pancytopenia - that is, low blood levels of red blood cells, white blood cells and platelets, and a simultaneous increase in the concentration of lymphocytes;

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Published online at <http://journal.sapub.org/ajmms>

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2. Myelogram records a decrease in the concentration and production of myelokaryocytes, an absolute reduction in neutrophils and elements of erythropoiesis, a relative increase in the number of lymphocytes;
3. In the biopsy with iliac, there is a predominant amount of fatty bone marrow, while in the remaining active, the bone marrow is mostly lymphocytes, erythro and normoblasts, sometimes containing iron granules;
4. Erythrocyte destruction during intracellular hyperhemolysis, mainly in the spleen, is diagnosed in 90% of cases of aplastic anemia.

Aplastic anemias, according to epidemiological studies, occur with varying frequency in regions such as Europe, North America, the Far and Middle East), while according to the International Study of agranulocytosis and aplastic anemia, in European countries, the prevalence of aplastic anemia is 2 per 1 million population per year, with this indicator varying from country to country from 0.6 to 3 or more per 1 million people per year [6]. Data to establish any patterns and causes of aplastic anemia of blood is currently not enough. In a number of US states, in particular in California, the incidence of such diseases ranges from 1 to 300-500 thousand patients. There is also no direct link between racial or gender affiliation and incidence rates [7, 8].

To date, the criteria for the diagnosis of aplastic anemia are data confirming the low cellularity level of the bone marrow from the general blood test: the number of granulocytes is less than  $0.5 \times 10^9 / l$ ; platelets less than  $20 \times 10^9 / l$ ; hemoglobin is below  $80g / l$ , as well as studies of the cytokine status of peripheral blood including erythropoietin, tumor necrosis factor, interleukins I, II, IV, VI, VIII, and immunoglobulins A, G, M. [7, 8].

## 2. Main Body

### 2.1. The Purpose of Our Research

**Objective:** To determine the prevalence of aplastic anemia among the inhabitants of Uzbekistan and to establish the cause of its occurrence.

### 2.2. Material and Methods of Study

Researchers from the Scientific Research Institute of Hematology and Blood Transfusion carried out a statistical analysis and found out that 567 adult patients and 199 children under 14 years old are registered in the Republic of Uzbekistan by 2018. In contrast to the data of 2017 and 2016, the situation is worsening, as there is a significant increase, so in 2016 there were 281 adult patients and 114 children, and in 2017, 427 and 171, respectively. A retrospective analysis of 416 case histories of patients with aplastic anemia treated in the clinical departments of the institute for the period 2016-2017 was conducted.

### 2.3. Results of the Study

According to the data of the case histories, 191 (46%) patients were primary, 225 (54%) - the same, re-hospitalized for the studied period of time. Among the primary AA patients, males were 111 (58%), female - 80 (42%). Sex ratio M: W = 1.4: 1. Among the re-hospitalized AA patients, there were 44 men (39.6%) among the primary patients, and 29 women (36.3%) among women. Sex ratio M: W = 1.5: 1. The bulk of the patients in the studied population consisted of representatives of the indigenous nation - Uzbeks (88%). The distribution of patients of other nationalities: Kazakhs, Russians, Koreans, Tatars and others looked like 3.1%, 2.6%, 4.7% and 1.6%, respectively, in percentage terms. 45.8% of the surveyed were residents of the city of Tashkent and the Tashkent region, the remaining 54.2% were from other regions of the Republic: Surkhan-Darya region - 8.9%, Fergana region. - 7.3%, Kashkadarya region - 6.8%, Namangan and Andijan regions - 5.2% each, Khorezm, Navoiy and Samarkand regions - 3.7% each, Bukhara region - 3.1%, Syrdarya and Andijan regions - 2.6%, Republic Karakalpakstan - 1.4%. The age of patients ranged from 1 year to 74 years.

In the overwhelming majority of cases (50-75%), it is not possible to find out the cause of the development of aplastic anemias. So, for the period of 2016, we studied 136 questionnaire cards, which included 52 (38.2%) men and 84 (61.8%) women (average age was  $33.8 \pm 5.7$ ). It was found that 67 (49%) patients do not know, and do not suggest the cause of their disease. 18 (13.2%) patients associate the cause of their illness with the ARVI "on their feet". Also, with recent flu or a cold with a high fever, another 15 (11%) patients who received antiviral and antibacterial drugs for treatment noted. Angina has recently had 28 (20%) patients. In 11 (8%) patients, among which there were only women, thyroid gland diseases in the form of thyroiditis were detected. 32 patients out of 136 suffer from the chronic form of rheumatoid arthritis, 12 of them have received inpatient treatment with steroid and anti-inflammatory drugs for the last 6 months. Not long before the diagnosis of AA, the presence of a herpes virus infection, in the form of the usual rashes on the red border of the lips and nose wings, 15 (11%) people complained. Also 6 (4.5%) people with type II diabetes were identified. 11 (8%) patients with AA regularly receive drugs for hypertension, hypertension, and 3 of them for myocardial infarction, these patients receive drugs from the group of statins, antihypertensives,  $\beta$ -blockers and anticoagulants. 20% of patients (26 people) had a history of iron deficiency anemia, which they suffered for a long time. 28 (20.5%) AA patients spoke about the harsh working conditions associated with heavy physical exertion, and 17 (12.5%) patients also work with the use of chemical pollinators. Frequent stress and increased nervousness in the workplace were noted by 23 patients (17%). When examining and interviewing patients, 5 patients were identified with a body mass index below 16, which indicates cachexia, and 16 (11.7%) patients reported

irregular and inadequate nutrition. Obesity II - III degree suffer 7 patients with aplastic anemia.

Mortality without treatment in the first 6 months with severe forms of AA reached 70% or more. The causes of death of patients are the progression of the disease and the development of hemorrhagic and severe infectious complications [7, 8].

### 3. Conclusions

In the population of patients with aplastic anemia, the frequency of occurrence is dominated by men. In adolescence, men are 2 times more than women. In adulthood, gender does not significantly affect the incidence of aplastic anemia. In elderly and senile age, women are 2.5 times more than men, which, apparently, is due to the fact that men with aplastic anemia do not live to be elderly or old.

We noted that aplastic anemia often acts as an adverse reaction from the use of certain groups of drugs, and its occurrence does not depend on the dose or on the duration of taking this drug. The role of adverse working conditions among residents of Uzbekistan who work in agricultural production has also been revealed. In addition, certain acute viral etiology diseases, metabolic diseases and endocrine pathology can also become provocateurs of aplastic anemia. Among the causes of impaired hematopoietic function of the bone marrow should be considered autoimmune diseases, in which the immune mechanisms are aimed at destroying not only disease-causing agents, but also damage their own cells.

Despite the great scientific breakthrough in determining the causes of the development of the disease, a unified theory of the pathogenesis of the disease has not yet been developed, there is no consensus about the factors causing damage to the stem cell and its microenvironment. The relationship between cytokine and immune status disorders and the severity of hematopoiesis depression has not been elucidated, and, therefore, their significance and place in the mechanism of the development of the disease has not been determined.

The data of our studies confirm the need for further more in-depth study of the causes and causes of such a high increase in this pathology among the people of Uzbekistan, as well as the global increase in this pathology. More data from diagnostic and clinical research will lead to a more improved and high-quality diagnosis of aplasia, which will shorten the patient's stay in the clinic and significantly improve the quality of the therapy, help to eliminate provoking factors, and improve patient survival. In general, future prospective randomized and multi-center studies will be the basis for early diagnosis and objective treatment.

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