

# ETIOLOGICAL FACTORS FOR ACQUIRED APLASTIC ANEMIA IN PATIENTS ADMITTED TO KHYBER TEACHING HOSPITAL, PESHAWAR

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## ABSTRACT

**Background:** Aplastic anemia is a rare but serious disorder. More than 70% cases of anemia are idiopathic. This study was conducted to find out the possible etiological factors in our set up.

**Methodology:** This descriptive study was carried out in Department of Medicine, Khyber Teaching Hospital, Peshawar from January, 2005 to December, 2009. One hundred patients with acquired aplastic anemia were studied. Patients above age 11 and below 65 years having pancytopenia and empty bone marrow or marrow replaced by fatty cells were included. Patients with pancytopenia due to bone marrow infiltration with abnormal cells or fibrosis were excluded from the study. After a thorough history and clinical examination all patients were subjected to a list of investigations. All the findings were recorded on proforma devised for this study and analyzed.

**Results:** One hundred patients with 72% male and 28% female were included in this study. Majority of the patients were in age group 11-45 years. In 48% of patients there was no etiological factor for aplastic anemia. Thirteen (13%) patients had megaloblastic anemia. Other risk factors identified were interferon therapy 6%, cytotoxic drugs 7%, heroin 6%, kushtas 2%, systemic lupus erythematosus 2%, paroxysmal nocturnal hemoglobinuria 2%, Anti-malarials containing sulpha group 2% and pregnancy 1%, hepatitis B 8% and hepatitis C 3%.

**Conclusion:** Acquired aplastic anemia is more prevalent in young males. In the majority of cases it is idiopathic but in many cases the cause can be searched out and prevented or treated.

**KEY WORDS:** Aplastic anemia, Pancytopenia, Etiological factors.

## INTRODUCTION

Aplastic anemia is a rare but serious disorder with a high morbidity and mortality rate. It is characterized by peripheral pancytopenia and bone marrow aplasia.<sup>1</sup> The pathophysiologic characteristic of this disorder is injury to or loss of pluripotent hematopoietic stem cells in the absence of infiltrative disease of the bone marrow.<sup>2</sup>

Its incidence in United States is 0.6–6.1 cases per million population and in Europe 2 cases per million population. It is more common in Asia and is as high as 14 cases per million population in Japan. The high incidence may be related to environmental rather than genetic factors because this increase is not observed in Asian people living in the West.<sup>3</sup>

More than 70% patients with acquired aplastic anemia are idiopathic i.e. no cause can be determined.<sup>1,4</sup> In the rest of the cases, the major identifiable etiological factors are exposure to ionizing

radiations, chemicals, some viruses and a number of drugs. Exposure to frequent and large doses of external radiation produces a dose dependent acute hematopoietic direct radiation injury.<sup>5,6</sup>

A variety of drugs like chloramphenicol, gold, sulphonamides, certain anti-epileptics, nifedipine and cytotoxic drugs can be the precipitating agents.<sup>4,5,7,17</sup> Other chemicals like prolonged exposure to benzene are known to induce aplastic anemia.<sup>8-10</sup>

Infectious agents like bacterial or viral infections sometimes induce pancytopenia in some patients. It is usually transient and multi-factorial but certain viruses like Parvovirus B19 can directly damage the stem cells and induce aplastic anemia.<sup>11,12</sup>

Approximately 5-10% of aplastic anemia occurs after an episode of hepatitis in which no known viral pathogen or relation with a drug can be identified.<sup>13</sup> Up to 15% of patients with seronegative

acute liver failure are prone to develop aplastic anemia.<sup>14</sup> Patients who receive liver transplantation for hepatic failure caused by such a seronegative fulminant hepatitis are at a high risk of developing aplastic anemia. It occurs in about 25% of these patients.<sup>18</sup>

Pregnancy is also a risk factor for aplastic anemia but in most of the pregnant ladies it recovers by itself when pregnancy is over.<sup>15,16</sup>

Clinical features of aplastic anaemia result from pancytopenia. Bleeding tendency leading to excessive bruising, petechial rash or epistaxis is often the first manifestation for which the patient seeks help.<sup>19</sup> Infection may also be the presenting feature. It exacerbate the effect of thrombocytopenia particularly mouth ulcers.<sup>20,21</sup>

This study was conducted to find out the possible etiological factors of aplastic anemia in our set up.

### MATERIAL AND MATHODS

This descriptive, retrospective, single center study of 100 patients of acquired aplastic anemia was carried out in Department of Medicine, Khyber Teaching Hospital Peshawar, from January, 2005 to December, 2009.

Patients of either sex above 11 and below 65 years of age with acquired anemia admitted in Medical Units of Khyber Teaching Hospital, Peshawar, were included in the study.

Patients whose bone marrow were empty or showed fatty infiltration while trephine biopsy showed no infiltration by abnormal cells were included. Patients with congenital aplastic anemia i.e. Fanconi's Anemia were excluded from the study. Patients with bone marrow infiltration with abnormal cells or fibrosis were also excluded from the study.

Detailed history was taken including history of present illness, past history including hepatitis, arthralgias and myalgias, fever, rash or drugs prescribed for any illness either by doctors, quacks or self medication. History of blood transfusion was also sorted out.

Each patient was examined in detail including general physical and systemic examination. All patients underwent investigations including full blood count, peripheral smear, bone marrow aspiration/trephine, blood urea, glucose, electrolytes and serum creatinine, x-ray chest, liver function tests, HBsAg and anti-HCV antibodies, AntiDs (Double stranded) DNA antibodies, anti-nuclear factor, pregnancy test (in females) and CD59 and CD55.

All the findings were recorded on a proforma devised for this study and then analyzed.

### RESULTS

It was observed that out of 100 patients, male were 72% while female were 28%. The minimum age of the patients was 11 years and maximum age was 65 years.

Majority of the patients (44) were in age range of 12-25 years, 20 patients in 26-35 years, 16 in 36-45 years, 14 in 46-55 and only 6 patients 56-65 years. (Table 1)

**Table 1: Age wise distribution of patients.**

Age Group (years)	Number of Patients
11-25	44
26-35	20
36-45	16
46-55	14
56-65	6

No cause could be determined in 48 patients (48%) with aplastic anemia and were labeled as idiopathic. Thirteen patients (13%) had megaloblastic anemia. Cytotoxic drugs caused aplastic anemia in 7 patients (7%). Interferon therapy and heroin and cocaine abuse led to plastic anemia in 6 patients (6%) each. HBs Ag was reactive in 8 patients (8%) while HCV Ab was present in 3 patients (3%). SLE in 2 patients (2%) while PNH, anti

**Table 2: Clinical presentation of patients with acquired aplastic anemia and their frequencies.**

Symptoms & signs	Percentage
Pallor	36%
Epistaxis	34%
Fever	30%
Petechial rash	24%
Palpitations	23%
Dyspnea	23%
Easy fatigability	20%
Menorrhagia	14%
Haemetemesis	8%
Malaena	6%

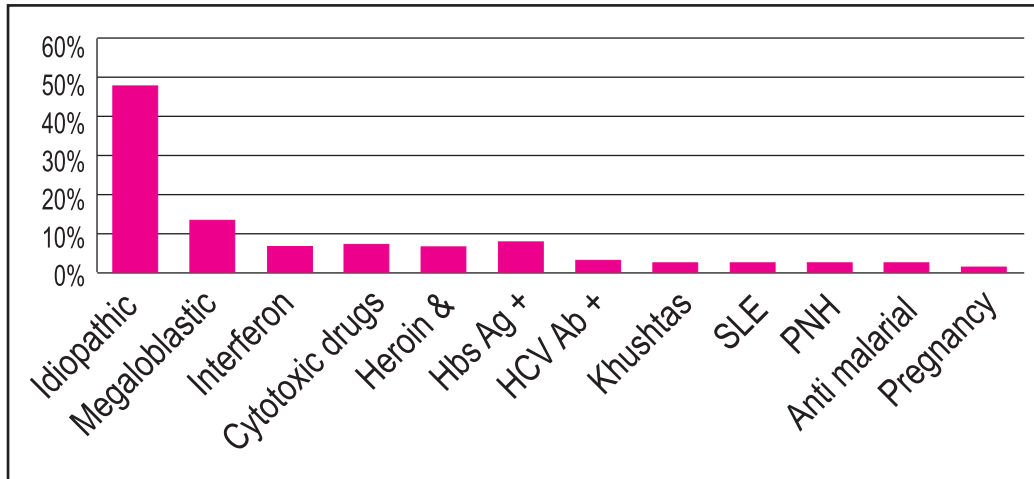


Figure: Frequency of aetiological factors in acquired aplastic anemia.

malarials, and kushtas (A mixture of unknown ingredients prepared by hakims and quacks to be used for many diseases) caused aplastic anemia in 2 patients (2%) each. Pregnancy was culprit in 1 patient (1%). All these results are shown in the Figure

Most of the patients with aplastic anemia presented pallor and epistaxis followed by fever and petechial rash. The results are shown in Table 2.

**DISCUSSION**

Aplastic anemia is a hematologic condition characterized by bone marrow hypoplasia or aplasia resulting in pancytopenia. It is a serious disease and its etiology has been attributed to medications,<sup>22</sup> chemicals,<sup>22,23</sup> and environmental factors.<sup>24</sup>

Various risk factors of aplastic anemia are identified with the help of clinical examination and investigations. In our study, 72% were males and 28% were females and thus males outnumbered females. This fact was also revealed by other local studies conducted by Malik S, et al<sup>19</sup> and Adil SN, et al<sup>20</sup> who also showed male predominance while a study conducted by Montane E, et al<sup>25</sup> in Barcelona showed equal sex distribution which contradicts our study. This male predominance may be due to many factors like in our society males move outside homes more frequently and are exposed to environmental factors like insecticides and external radiations.

Age of the patients in our study ranged between 11 and 65. Majority of the patients (44%) were between age group 11-25 years, showing that acquired aplastic anemia is more prevalent in younger population. This fact has also been proved by two local studies, Malik S, et al<sup>19</sup> and Adil SN,

et al<sup>20</sup> and one international study by Maluf EM et al.<sup>22</sup>

The most common presenting feature of acquired aplastic anemia was pallor and epistaxis followed by fever while in study conducted by Malik S, et al<sup>19</sup>, fever was the most common presentation followed by pallor and epistaxis.

In our study, no cause of aplastic anemia could be determined in 48% of patients and were labeled as idiopathic. In international literature, more than 70% of patients of aplastic anemia are idiopathic. In our study, less cases of idiopathic aplastic anemia were observed which may be due to small sample size. In the study conducted by Malik S, et al<sup>19</sup>, no cause was found in 70% of patients. A study conducted in India also showed that a specific cause could not be determined in most of the cases.<sup>26</sup>

Out of the known causes, drugs were the most common cause of acquired aplastic anemia contributing 17%. The most common culprit was interferon (6%) followed by cytotoxic drugs like methotrexate, cyclosporine and hydroxyurea. *Kushtas* are mixture of many drugs used by hakims and quacks for different illnesses causing acquired aplastic anemia in 2% patients in our series. No data is available on *kushtas* but these are used by hakims in our region. Anti-malarials containing sulpha group caused aplastic anemia in 2% of patients. Malik S, et al showed that drugs caused aplastic anemia in 30% and was the second most common cause of acquired aplastic anemia which resembles our study. These results are also supported by international studies.<sup>27, 28</sup>

Megaloblastic anemia caused aplastic anemia in 13% of patients in our study and was the 3<sup>rd</sup> leading cause of acquired aplastic anemia. A study

conducted by Qazi RA, et al<sup>29</sup> found megaloblastic anemia as the most common cause 28% of aplastic anemia. It was the second most common cause of pancytopenia in a study conducted by Khan MN, et al<sup>33</sup> in 16.7% of patients which correlate with our study. The most common cause is nutritional deficiency of these vitamins.

Viral hepatitis is an important cause of aplastic anemia. It caused aplastic anemia in 11% of our patients. This fact is shown by two other studies as well.<sup>30,31</sup> A study conducted by Gupta V, et al<sup>26</sup> showed that viral hepatitis caused aplastic anemia in 2% of patients.

PNH was the cause of aplastic anemia in 2% patients in this study. It also caused aplastic anemia in 2% of patients in a study conducted by Gupta V, et al.<sup>26</sup> There are many international studies which have shown variable incidence of PNH with aplastic anemia.<sup>20, 32</sup>

SLE caused aplastic anemia in 2% patients. In the study conducted by Khan MN, et al<sup>33</sup> showed that SLE caused aplastic anemia in 3.3% patient.

## CONCLUSION

Acquired aplastic anemia is more prevalent in young males. In the majority of cases it is idiopathic but in many cases the cause can be searched out and prevented or treated.

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