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Evaluation of Risk Factors in Patients with Acquired Aplastic Anemia

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Abstract
Introduction: *Aplastic anemia is a very rare and serious disease. Despite its low incidence rates in recent years due to medical advancements, it still has a high morbidity and mortality rate. It is a disease of multiple etiologies and is normally identified by pancytopenia and hypo-cellular bone marrow. Aplastic anemia can be divided into inherited and acquired types. Acquired aplastic anemia is more common than inherited aplastic anemia, and often has autoimmune etiology. The incidence of aplastic anemia varies depending on many factors, including geographical differences. The present study aimed to observe and evaluate the common risk factors of acquired aplastic anemia in our demographic.The aim of the study was to evaluate the risk factors of acquired aplastic anemia patients.*
Methods: *This cross-sectional departmental study was conducted at the Department of Medicine, Rangpur Medical college Hospital, Rangpur, Bangladesh during the period from January 2016 to December 2016 with a total of 80 participants. Hemoglobin levels, platelet counts, neutrophils counts, and absolute reticulocyte counts were used to diagnose and determine the severity of the aplastic anemia. Participants were selected following the inclusion and exclusion criteria.*
Result: *A total of 80 participants were selected for the present study. Among them, the majority of the participants belonged to the age group of 11-30 years. The male: female ratio was 2.3:1. Use of or contact with pesticides was the biggest risk factor, present in 90% of the participants, followed by smoking in 50%. All aplastic anemia cases were accompanied by weakness as a clinical manifestation, and fever and bleeding were also common presentations. The majority of the participants had the non-severe type of aplastic anemia, with only 10% having severe aplastic anemia.*
Conclusion: *Aplastic anemia, despite its rarity, is a serious disease with high morbidity and mortality rates. Males were more affected than females, and a majority of the participants belonged to the age group of 11-30 years. Contact with pesticides was the largest risk factor, followed by smoking and tobacco consumption. Moderate or non-severe aplastic anemia was the predominant type of aplastic anemia in the present study. Weakness, accompanied with fever or bleeding was the primary clinical manifestation.*

Keywords: *Anemia, Aplastic, Chemical, Bone Marrow*

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I. Introduction

Anemia is a disease in which your body does not have enough healthy red blood cells to transport enough oxygen to your tissues. Anemia, commonly known as low hemoglobin, can cause fatigue and weakness. There are several types of anemia, each with its unique set of causes. Iron deficiency anemia, vitamin deficiency anemia, aplastic anemia, and other forms of anemia are prevalent.[1] Aplastic anemia is a disease in which your body can not produce enough new blood cells. The disease causes tiredness and makes you more susceptible to

infections and uncontrollable bleeding. Although Aplastic Anemia (AA) is recognized as a rare blood disorder, it is also recognized as a bone marrow failure syndrome, as it is recognized by the inability of the bone marrow and stem cells in producing enough blood cells for the body.[2] This suppression of bone marrow results in progressive pancytopenia.[3]Aplastic Anemia is, despite its rarity, is recognized as a life-threatening disease globally. It can occur in people of all ages and gender, and the incidence rate can differ depending on geography and other factors. The incidence of aplastic anemia ranges from 1.5 per million to 7 per million cases.[4]Aplastic anemia can be divided into two types, Inherited Aplastic Anemia and Acquired Aplastic Anemia.[5] Inherited aplastic anemia is generally caused by a genetic mutation, and has a higher prevalence among children and young adults.[6] Acquired Aplastic Anemia, on the other hand, occurs due to problems in the immune system. The pathogenesis of aplastic anemia is currently thought to be immune-mediated, with lymphocytes actively destroying blood-forming cells. Environmental exposures, such as chemicals and medications, or viral infections, as well as endogenous antigens produced by genetically altered bone marrow cells, may cause an abnormal immune response.[7]Acquired aplastic anemia can occur in people of any and all ages. Depending on the number of blood cells present in the blood tests and in the bone marrow biopsy, Aplastic Anemia (AA) can be divided into three groups, non-severe or moderate (MAA), severe (SAA), and very severe (VSAA).[8] Aplastic Anemia has a wide variety of symptoms, making it harder to diagnose based simply on the presenting symptoms. This is why the quantity of each of the three blood cell types is tested and monitored when a physician suspects aplastic anemia.[8]Although AA can be diagnosed with precision based on specific blood test results, aplastic anemia remains as a diagnosis of exclusion to date. No single test can reliably diagnose aplastic anemia.[9]Although aplastic anemia is an extremely rare disease, the incidence rate of AA is 2 to 3 times higher than compared to the western countries.[10] Acquired AA can increase the risk of infections and blood-related problems, and the only cure for the disease is either a bone marrow transplant or immunosuppressive therapy.[11],[12] But initially, the ailment can be managed by improving the individual causes of low blood counts. Oftentimes, patients are given blood transfusions to manage the anemia. The present study was carried out with the goal of observing the risk factors present in acquired aplastic anemia in our demographic.

II. Objective

General Objective

- To determine the risk factors of acquired aplastic anemia patients

Specific Objectives

- To observe the clinical factors of acquired aplastic anemia patients

III. Methods

This cross-sectional departmental study was conducted at the Department of Medicine, Rangpur Medical college Hospital, Rangpur, Bangladesh during the period from January 2016 to December 2016. The total sample size of the study was determined as 80, and the participants were selected according to a convenient sampling method. All the participants were selected following the inclusion and exclusion criteria. Hemoglobin levels, platelet counts, neutrophils counts, and absolute reticulocyte counts were used to diagnose and determine the severity of the aplastic anemia. The aim and requirements of the study were explained to the participants prior to the admission into the study and informed written consent was obtained from each participant or their legal guardians. Ethical approval was obtained from the institutional ethics review board. Data was collected and recorded in a pre-acquired form, and statistical analysis was done using SPSS software

Inclusion Criteria

- Age ≥10 years
- Patients who had given consent to participate in the study.
- Patients of both gender

Exclusion Criteria

- Age <10 years
- Mentally ill.
- Unable to answer the criteria question.
- Inherited Aplastic Anemia Cases
- Pregnant women
- Exclude those affected with other chronic diseases etc.

IV. Results

A total of 80 participants were selected for the present study. Among them, the majority of the participants belonged to the age group of 11-30 years. In the present study, 67% of the participants were male

and 33% were female. The male: female ratio was 2.3:1. The use of pesticides was the biggest risk factor, present in 90% of the participants, followed by smoking in 50%. All aplastic anemia cases were accompanied by weakness as a clinical manifestation, and fever and bleeding were also common presentations. Majority of the participants had the non-severe type of aplastic anemia, with only 10% having severe aplastic anemia.

Table 1: Age distribution of the participants (n=80)

Age Group	Frequency	Percentage
11-30	40	50.00%
31-45	23	28.75%
46-60	14	17.50%
>60	3	3.75%

The participants were divided into 4 age groups. The majority of the participants belonged to the age group of 11-30 years. 28.75% of the participants belonged to the age group of 31-45, and 17.50% belonged to the age group of 46-60, and the remaining 3.75% were older than 60 years. The age range of the participants was from 13 years to 72 years.

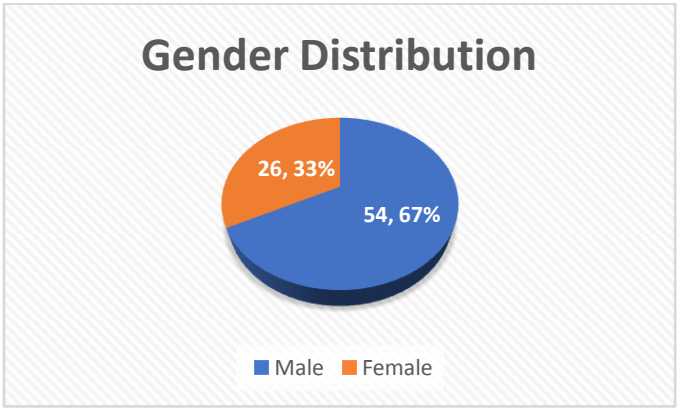

Figure 1: Gender Distribution of the participants (n=80)

Among the 80 participants, the majority (67%) were male, and 33% were female. The male: female ratio was 2.33:1

Table 2: Risk factor Distribution of the participants (n=80)

Risk Factors	Frequency	Percentage
Smoking and Tobacco	40	50.00%
Pesticides	72	90.00%
History of HBV infection	5	6.25%
Exposure to toxic chemicals	10	12.50%

The biggest risk factor present in the participants was the use and exposure to pesticides, which was the case for 90% of the participants. Smoking and tobacco consumption was the second biggest risk factor of acquired aplastic anemia, present in 50% of the participants. Exposure to different toxic chemicals was also a risk factor present in 12.50% of the participants, and a history of the Hepatitis-B virus was present in 6.25% of the participants as a risk factor.

Table 3: Clinical Presentations of the participants (n=80)

Clinical Presentation	Frequency	Percentage
Fever	45	56.25%
Bleeding	51	63.75%
Weakness	80	100.00%

All 80 participants had a weakness as a common clinical presentation. Among the other clinical presentations, bleeding was present in 63.75% of cases, and fever was present in 56.25% of cases.

Table 4: Distribution of the participants according to severity of Aplastic Anemia (AA) (n=80)

Severity	Frequency	Percentage
Non-Severe AA	40	50.00%
Severe AA	32	40.00%
Very Severe AA	8	10.00%

Most of the participants (50%) had moderate or non-severe cases of aplastic anemia, while 40% had severe aplastic anemia. The remaining 10% of the participants were very severe aplastic anemia cases.

V. Discussion

Aplastic anemia, despite its rarity, is of extreme interest for many researchersdue to the larger consequence of its association. The pathogenesis of aplastic anemia is currently thought to be immune-mediated, with lymphocytes actively destroying blood-forming cells. Environmental exposures, such as chemicals and medications, or viral infections, as well as endogenous antigens produced by genetically altered bone marrow cells, may cause an abnormal immune response.[7]Bone marrow failure is caused by immunologically induced, tissue-specific organ damage in the majority of individuals with acquired aplastic anemia. The disease's progression can be divided into various phases. After being exposed to an inciting antigen, immune system cells and cytokines act destructively on stem cells in the marrow, decreasing their number to the point that normal levels of circulating leukocytes, erythrocytes, and platelets are not maintained.[13]Aplastic anemia's lengthy history, beginning with Ehrlich's description at the end of the 19th century,[14] and the simplicity of its pathophysiology, an empty bone marrow, have made it the model of hematopoietic failure disorders. Aplastic anemia is increasingly being identified as being linked to other hematologic disorders. Aplastic anemia severely impairs hematopoiesis by any standard. By definition, there is pancytopenia, andNeutrophil levels of fewer than 200 per cubic millimeter, platelet counts of less than 20,000 per cubic millimeter, and reticulocyte counts of less than 60,000 per cubic millimeter are found in the most seriously afflicted individuals. Most of the cells observed in a histologic preparation of bone marrow are the progenitors of these circulating cells.[13]The most frequent kind of aplastic anemia is iatrogenic, defined as temporary marrow loss following cytotoxic treatment or radiation. Certain chemical or physical agents directly harm both proliferating and dormant hematopoietic cells, causing DNA damage and, eventually, apoptosis. Patients with community-acquired aplastic anemia, on the other hand, seldom have a history of exposure to any harmful chemical to the bone marrow, and even benzene is now infrequently linked with aplastic anemia in industrialized nations.[15] The present study was conducted to observe and evaluate the common risk factors of acquired aplastic anemia in a local demographic. In the present study, the majority of the participants were between the age group of 11-30 years. Half of the participants belonged to this group. This was in line with the common conception that acquired aplastic anemia affects people of all ages including young adults. But the findings of the present study were contradictory to the findings of a 1998 study.[12]The prevalence of participants saw a steady decrease with higher age groups in the present study. This might be due to the lack of willingness to visit hospitals and go through various tests among the older population of society. Although the prevalence of acquired aplastic anemia (AAA) is common among participants of all ages and gender, the present study saw a much higher prevalence of AAA among the male population. The male: female ratio was 2.33:1, which was somewhat similar to another study.[16]The biggest risk factor among the participants of the present study was the use of pesticides and insecticides. 90% of the present study participants had pesticide use as a common risk factor. This might be due to the demographic of the study, where pesticides are often used in farming. The use of pesticides as a risk factor was much higher in our study compared to various other studies with a risk factor prevalence of <%.[16],[17]Another common risk factor was smoking and tobacco consumption, present in 50% of the participants. Exposure to other toxic chemicals was present as a risk factor for 12.50% of the participants, which was much lower compared to another study.[17] This low prevalence might also be affected by the select demographic of this study. Weakness was a common clinical presentation in all 100% of the participants, along with bleeding in 63.75% of cases and fever in 56.25% of cases. This was in line with the findings of other studies.[10],[12]Among the participants of the present study, 50% were of moderate or non-severe aplastic anemia cases. Among the remaining participants, 40% had severe AA, and the remaining 10% had very severe AA. The prevalence of non-severe AA cases in our study was different from the findings of few other studies.[10],[12]

Limitations of The Study

The study was conducted in a single hospital with a small sample size. So, the results may not represent the whole community.

VI. Conclusion

Aplastic anemia, despite its rarity, is a serious disease with high morbidity and mortality rates. Males were more affected than females, and a majority of the participants belonged to the age group of 11-30 years. Contact with pesticides was the largest risk factor, followed by smoking and tobacco consumption. Moderate or non-severe aplastic anemia was the predominant type of aplastic anemia in the present study. Weakness, accompanied with fever or bleeding was the primary clinical manifestation.

VII. Recommendation

The study was carried out with a small sample size over a short period. A long-term comprehensive study is necessary to better understand the incidence and effects of acquired aplastic anemia.

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