ASSOCIATION OF DIFFERENT ETIOLOGICAL FACTORS AMONG PATIENTS WITH IDIOPATHIC ACQUIRED APLASTIC ANEMIA

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Abstract: A descriptive study was conducted at multiple centers, including Rashid Latif Medical College and Mayo Hospital in Lahore, from September 2022 to September 2023. The study aimed to determine the potential causes associated with idiopathic acquired aplastic anemia. The study included 55 patients with idiopathic acquired aplastic anemia. The patients were mainly between 18 and 35, with male patients being more prevalent. The etiological factors of aplastic anemia were assessed, and the results indicated that chronic liver disease affected 3 (5.5%) patients, drugs affected 2 (3.6%) patients, tuberculosis affected 3 (5.5%) patients, and pregnancy affected 1 (1.8%) patient. In conclusion, the study found that the most common etiological factors of idiopathic acquired aplastic anemia were chronic liver disease, drugs, tuberculosis, and pregnancy.

Keywords: Idiopathic Aplastic Anemia, Pallor, Risk Factors

Introduction

Idiopathic Acquired Aplastic Anemia (IAAA) is a rare and potentially life-threatening hematological disorder characterized by a marked reduction in blood-forming cells in the bone marrow, leading to pancytopenia (Luzzatto and Risitano, 2018). The term “idiopathic” suggests that the exact cause of this condition is unknown, making it a complex and enigmatic disease. While many cases of acquired aplastic anemia remain idiopathic, extensive research has revealed that various etiological factors may contribute to developing this condition (Nakao and Gale, 2016; Schoettler and Nathan, 2018; Solimando et al., 2022).

Immune System Dysregulation is one of the prominent hypotheses regarding the pathogenesis of IAAA, which involves the immune system's role (Liu et al., 2019). It is believed that, in some cases, an aberrant immune response, particularly the activation of cytotoxic T cells, plays a pivotal role in attacking hematopoietic stem cells in the bone marrow. Research has highlighted the presence of autoantibodies against blood cell precursors and elevated levels of inflammatory cytokines as potential markers of immune system dysregulation in IAAA patients (Javan et al., 2021; Liu et al., 2020).

Exposure to various environmental toxins and chemicals has been suggested as a possible contributing factor to the development of IAAA. Benzene, a known carcinogen, is one such substance that has been linked to aplastic anemia. Occupational exposure to benzene and other chemicals in industries such as petrochemicals and agriculture may increase the risk of developing this condition. Viral infections have been implicated in the pathogenesis of IAAA, although the exact mechanisms remain elusive (Belingheri et al., 2019; Loomis et al., 2017).

The hepatitis viruses, especially hepatitis-associated aplastic anemia, have been studied extensively. Parvovirus B19 is another viral agent linked to transient aplastic crises in individuals with underlying genetic predispositions (dos Santos Brito Silva Furtado et al., 2016). Although IAAA is not considered a hereditary disease, there is evidence to suggest that some individuals may have genetic predispositions that make them more susceptible to developing the condition when exposed to certain triggers.

Studies have identified specific polymorphisms and genetic variations associated with an increased risk of aplastic anemia, suggesting a genetic component to the disease's pathogenesis (Keel et al., 2016; Shimamura, 2016). Advancements in genetic and immunological research and an improved understanding of environmental factors have offered promising insights into the mechanisms underlying IAAA. As we unravel the mysteries surrounding this rare hematological disorder, identifying these etiological factors and their interplay will be essential for early diagnosis, targeted therapies, and improved outcomes for those affected by IAAA. This comprehensive exploration of potential associations sets the stage for further research, clinical management, and a deeper understanding of this complex and enigmatic disease.

Methodology

This retrospective study involving 55 patients diagnosed with acquired aplastic anemia was conducted at multiple...
centers, including Rashid Latif Medical College, Lahore, and Mayo Hospital, Lahore, from September 2022 to September 2023. The inclusion criteria encompassed patients of any gender aged 18 to 60 years with acquired anemia admitted to the Medical Units of ABC Hospital. Specifically, patients with bone marrow that was either empty or exhibited fatty infiltration, as confirmed by trephine biopsy indicating no abnormal cell infiltration, were included in the study. The patient’s history, along with clinical presentations, was recorded.

This comprehensive study design and thorough examination of patients, coupled with an extensive array of investigations, aimed to provide a detailed understanding of acquired aplastic anemia in the specified population over the specified timeframe. The study's findings were to determine the etiological factors of idiopathic acquired aplastic anemia.

For data analysis, we used SPSS version 20. The Chi-Square test assessed the association, keeping a P value < 0.05 as significant.

Results

Our study was conducted on 55 patients. The mean age of the patients was 33.71±12.47 years. Patients were higher in number in the age group of 18 to 30 years (58.2%). Male patients were 36 (65.5%), while female patients were 19 (34.5%). Nonsevere aplastic anemia was the most frequently observed type of aplastic anemia seen in 37 (67.3%) patients, severe aplastic anemia was the second most frequently observed type of aplastic anemia in 15 (27.3%), while very severe aplastic anemia was the least frequently observed type of aplastic anemia seen in 3 (5.5%) patients.

Regarding the clinical presentation, fever was seen in 29.9% of patients, pallor in 45 (81.8%) patients, bleeding in 11 (20%), and epistaxis in 14 (25.5%) patients (Table 2). We could not identify the etiological factors in 46 (83.6%) patients; chronic liver disease was seen in 3 (5.5%) patients, drugs 2 (3.6%) patients, tuberculosis in 3 (5.5%) patients, and pregnancy 1 (1.8%). Gender was significantly associated with the etiological factors (P = 0.03 and P = 0.001).

Discussion

The phrase "bone marrow failure" refers to various illnesses and syndromes marked by abnormalities in one or more blood cell lineages (erythroid, myelomonocytic, and megakaryocytic) that can be qualitative or quantitative. The pathogenesis of these illnesses was mostly unknown until a few years ago. Our understanding of these disorders has increased over time, which has resulted in the creation of novel treatment choices and better patient outcomes (Peffault de Latour et al., 2022). Myelodysplastic syndromes (MDS), aplastic anemia, paroxysmal nocturnal hemoglobinuria, idiopathic neutropenia, and significant granular leukemia are examples of acquired bone marrow failure syndromes. The pathogenesis and standard features of these syndromes are similar. One important consideration

Table 1 Type of anemia

<table>
<thead>
<tr>
<th>Type of anemia</th>
<th>Frequency</th>
<th>Percent</th>
</tr>
</thead>
<tbody>
<tr>
<td>Non severe aplastic anemia</td>
<td>37</td>
<td>67.3</td>
</tr>
<tr>
<td>Severe aplastic anemia</td>
<td>15</td>
<td>27.3</td>
</tr>
<tr>
<td>Very severe aplastic anemia</td>
<td>3</td>
<td>5.5</td>
</tr>
<tr>
<td>Total</td>
<td>55</td>
<td>100.0</td>
</tr>
</tbody>
</table>

Table 2 Etiological factors

<table>
<thead>
<tr>
<th>Etiological Factors</th>
<th>Frequency</th>
<th>Percent</th>
</tr>
</thead>
<tbody>
<tr>
<td>Factor not identified</td>
<td>46</td>
<td>83.6</td>
</tr>
<tr>
<td>Chronic Liver Disease</td>
<td>3</td>
<td>5.5</td>
</tr>
<tr>
<td>Drugs</td>
<td>2</td>
<td>3.6</td>
</tr>
<tr>
<td>Pregnancy</td>
<td>1</td>
<td>1.8</td>
</tr>
<tr>
<td>Tuberculosis</td>
<td>3</td>
<td>5.5</td>
</tr>
<tr>
<td>Total</td>
<td>55</td>
<td>100.0</td>
</tr>
</tbody>
</table>

Table 3 Association of gender with etiological factors of aplastic anemia

<table>
<thead>
<tr>
<th>Gender</th>
<th>Total</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Male</td>
<td>36</td>
<td>65.5%</td>
</tr>
<tr>
<td>Female</td>
<td>19</td>
<td>34.5%</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Factors</td>
<td>Male</td>
<td>Female</td>
</tr>
<tr>
<td>------------------------</td>
<td>------</td>
<td>--------</td>
</tr>
<tr>
<td>Factor not identified</td>
<td>31</td>
<td>15</td>
</tr>
<tr>
<td>Chronic Liver Disease</td>
<td>3</td>
<td>0</td>
</tr>
<tr>
<td>Drugs</td>
<td>2</td>
<td>0</td>
</tr>
<tr>
<td>Pregnancy</td>
<td>0</td>
<td>1</td>
</tr>
<tr>
<td>Tuberculosis</td>
<td>0</td>
<td>3</td>
</tr>
<tr>
<td>Total</td>
<td>36</td>
<td>19</td>
</tr>
</tbody>
</table>

is the possibility of clonal development leading to acute myelogenous leukemia; there are still unanswered problems about how to prevent this evolution in patients who are impacted (Killick et al., 2016). Hematopoietic cells are destroyed by T lymphocytes in aplastic anemia, a hematological condition. Non-severe aplastic anemia was the most common clinical stage of the illness in the current investigation (Adil et al., 2001). Patients with very severe aplastic anemia have a terrible prognosis, even though severe aplastic anemia is usually present in most cases (Gupta et al., 2008). Pallor, hemorrhage, fever, and epistaxis were common clinical characteristics in this investigation. Similar results were found in another study that identified common clinical characteristics such as epistaxis, petechiae, bleeding from the gums, pallor, and respiratory tract infections (Gonzalez-Casas et al., 2009).

Cases of aplastic anemia that cannot be linked to a specific etiology are frequently classified as idiopathic. Nonetheless, several international studies have linked specific variables to a higher chance of the illness. Eighteen acquired aplastic anemia linked to environmental causes is higher in Southeast Asia, where industrial and agricultural operations expose a large population to chemicals, poisons, fertilizers, and pesticides. Acquired aplastic anemia linked to autoimmune disorders and infections is more prevalent in highly populated urban regions with few tertiary healthcare services (Killick et al., 2016). A higher frequency of drug-associated acquired aplasia anemia is linked to the over-the-counter availability of antibiotics and analgesics without a prescription in undeveloped rural areas with inadequate primary health services (Ehsan et al., 2011; Killick et al., 2016).

Southeast Asian countries have higher rates of environmental pollution since fewer eco-friendly cars are on the road and industrial waste is poorly handled (Rathore et al., 2014). This causes the ozone layer to thin and exposes people to more UV radiation, which is linked to acquired aplastic anemia. Ionizing radiation from nuclear power plant waste is improperly disposed of, contaminating crops and water and raising the risk of acquired aplastic anemia in the area (Arber et al., 2016). Acquired aplastic anemia associated with pregnancy may be related to the high rate of population expansion. In this study, most patients (83.6%) had no known etiological variables. Drug use and viral hepatitis were frequent risk factors, which is in line with prior research that has reported occurrences of aplastic anemia with no known cause. Acquired aplastic anemia has been linked to drugs and hepatitis B&C infections in several studies (Ehsan et al., 2011; Killick et al., 2016).

**Conclusion**

From our study, we conclude that idiopathic aplastic anemia was more common in male patients. We found pallor, fever, bleeding, and epistaxis as common presentations of idiopathic acquired aplastic anemia. At the same time, the etiological factors observed in our study were chronic liver disease, drugs, tuberculosis, and pregnancy.

**Declarations**

**Data Availability statement**

All data generated or analyzed during the study are included in the manuscript.

**Ethics approval and consent to participate**

Approved by the department concerned.

**Consent for publication**

Approved

**Funding**

Not applicable

**Conflict of interest**

The authors declared absence of conflict of interest.

**Author Contribution**

**HEFSA QAMAR**

Data entry and Data analysis, drafting article

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Conception of Study, Final approval of manuscript

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Conception of Study, Development of Research Methodology Design, Study Design, Review of manuscript, final approval of manuscript

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Study Design, Review of Literature

**TANWEER AHMED SHAIKH**

Conception of Study, Final approval of manuscript

**MAHESH KUMAR LUNHANO**

Study Design, Review of Literature

**References**


