

**Clinical and hematological profile of bicytopenia in patients attending a tertiary hospital in north India.**

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**Abstract**

**Background:** Bicytopenia refers to the decrease in any two of three peripheral blood lineages, i.e., erythro cytes, leukocytes or platelets. Many studies are done on pancytopenia but very few studies exist in the literature evaluating the spectrum of a etiologies of bicytopenia.

**Methods:** We studied the clinical-hematological profile of patients with bicytopenia and investigated the different a etiologies of bicytopenia. 81 patients in the age group of 18-80 years with bi-cytopenia admitted to SMHS Hospital Govt. Medical College Srinagar was selected using systematic random sampling and included in the study. Their clinical profiles and hematological parameters were evaluated.

**Results:** The most common bicytopenia observed was anemia with thrombo cytopenia (55.5%) followed by anemia with leukopenia (22.2%) and leukopenia with thrombo cytopenia (22.2%). The most common etiology of bicytopenia was found to be infectious (20.9%). Megaloblastic anemia was the second predominant etiology (16.4%), followed by hematological malignancy (11%) and iron deficiency anemia (9.8%), and chronic liver disease (8.6%). The most common clinical feature

in our study was pallor (77.7%) followed by fever (33.3%) and dyspnea (25.9%).

**Conclusion:** It is concluded that infections (20.9%) and megaloblastic anemia (16.4%) were major causes of bicytopenia. Pallor (77.7%), fever (33.3%), and dyspnea (43.6%) were major clinical features.

**Keywords:** Bicytopenia, Pancytopenia, Anemia

**Introduction**

Pancytopenia is diagnosed when the hemoglobin (Hb) < 100 x 10<sup>9</sup>/L. Bicytopenia is a reduction in any two of the three peripheral blood cell lineages. It is labeled severe if the patient has two or more of the following: Hb < 7gm % ANC < 20 x 10<sup>9</sup>/L. <sup>1</sup> The likely causes of bicytopenia and pancytopenia are similar, ranging from bone marrow failure to peripheral destruction of Hema to poetic cells. Identification of the correct cause is mandatory as it will help to treat the patient appropriately and assess the prognosis.<sup>2</sup>

Etiological classification of bicytopenia can be done into three groups- failure of production (implying intrinsic bone marrow disease), sequestration (hypersplenism), and increased peripheral destruction.<sup>3</sup> Failure of bone marrow can be due to primary production defects.

inherited causes include Fanconi anemia, dyskeratosis congenita, Shwachmann Diamond syndrome, and a megakaryocytic thrombocytopenia.<sup>4</sup> The production of the hemopoietic cell can also be effected in the bone marrow either by infections, toxins, and malignant cell infiltration leading to hypocellular marrow.<sup>5</sup> If associated organomegaly and lymphadenopathy are present, the possibility of malignancies or bone marrow failure syndromes is considered. There are a number of other causes which can present in a similar way.<sup>6</sup> Acquired causes of bicytopenia can be nutritional deficiencies, idiopathic or secondary to exposure to radiation, drugs, and chemicals (Chemotherapy, chloramphenicol, sulfa drugs, antiepileptics, gold, etc.), viral infections (cytomegalovirus, Epstein-Barr virus, hepatitis B or C, HIV, etc.), autoimmune, paroxysmal nocturnal hemoglobinuria, and marrow replacement disorders (leukemia, myelodysplasia, myelofibrosis).<sup>7</sup>

Megaloblastic anemia and infections such as enteric fever, malaria, kala-azar, and bacterial infections are the common causes of bicytopenia in developing countries.<sup>8</sup> Hypersplenism causes bicytopenia by splenic sequestration and in some cases by hemolysis.<sup>9</sup> The common causes of hypersplenism include cirrhosis, congestive heart failure, and malignancies like leukemia/lymphoma, hemoglobinopathies, and infections. Autoimmune-mediated disorders like systemic lupus erythematosus (SLE) can present with bicytopenia when all three cell lines are affected.

Patients with connective tissue disorders like rheumatoid arthritis, psoriasis, and SLE are at increased risk for lymphoproliferative disorders and it is important to exclude underlying malignancies like lymphoma while evaluating these patients.<sup>10-12</sup> Autoimmune cytopenias are also seen in autoimmune lymphoproliferative syndrome (ALPS) and common variable immunodeficiency

disease (CVID). Paroxysmal nocturnal hemoglobinuria and hemophagocytic lymphohistiocytosis can cause both impaired production and increased peripheral destruction of blood cells. The aim of this study is to describe the different etiologies of bicytopenia in adult patients based on clinical and hematological profiles including peripheral blood and bone marrow examination.

### Materials and methods

The present study was hospital-based observational in nature conducted at the Department of Medicine, Government Medical College Srinagar over a period of one year from February 2022 to February 2023. Patients admitted to the Department of Medicine, SMHS, Srinagar who were suffering from bicytopenia were included in the present study.

### Inclusion and exclusion criteria

Patients with bicytopenia of any etiology who were aged between 18-80 years were included in this study. Known cases of hematological malignancy and patients receiving myelosuppressive drugs were excluded. A total of 81 patients were included.

Data collection and procedure Detailed clinical history and thorough physical examination were done for each patient. Laboratory investigations included complete blood count, reticulocyte count, bleeding profile, peripheral smear examination, liver function tests, and bone marrow examination to ascertain the cause. Bicytopenia was defined as hemoglobin (Hb)  $\leq 10$  g/dL, absolute neutrophil count  $\leq 1500/\mu\text{l}$ , and platelet count  $\leq 100000/\mu\text{l}$ . Bicytopenia was defined as any two of these cytopenias. Pretested proforma was used for data collection.

### Data analysis

Data was entered in Microsoft Excel 2007 and analyzed using SPSS v 16.0. Appropriate statistical tests were done. p value of  $\leq 0.05$  was considered to be statistically

significant. Informed consent was taken from patients.

**Results and observations**

All the records were kept confidential.

Table 1: Type of bicytopenia

Type of bicytopenia	Number of patients	Percentage
Anemia with thrombocytopenia	45	55.5%
Anemia with leucopenia	18	22.2%
Leucopenia with thrombocytopenia	18	22.2%

Table 2: Clinical features

Clinical features	Number	Percentage
Pallor	63`	77.7%
Fever	27	33.3%
Dyspnea	21	25.9%
Splenomegaly	18	22.2%
Hepatomegaly	15	18.5%
Hepatosplenomegaly	12	14.8%
Lymphadenopathy	9	11.1%

Table 3: Etiology.

Cause	Number of patients	Percentage
Megaloblastic anemia	13	16.04%
Chronic liver disease	7	8.6%
ITP	5	6.1%
CLL	2	2.4%
NHL	4	4.9%
Iron deficiency anemia	8	9.8%
ALL	3	3.7%
Drug	7	8.6%
Infectious	17	20.9%
Others	15	18.5%

## Discussion

Among the 81 patients included in the present study, 55.5% of the patients were males and 44.4% were females. Dubey et al found that there were 47% males and 53% females, with a male: female ratio of 0.88:1. However, Chhabra et al found that 60.4% of patients were males. The present study assessed all cases of bicytopenia in the 18-80year age group.

In the majority of the cases, the cause was infectious (20.9%). In the remaining cases, it was due to megaloblastic anemia (16.04%), leukemia (11%), iron deficiency anemia (9.8%), chronic liver disease (8.6%), drug induced (8.6%) and other causes (18.5%). Singh et al<sup>13</sup> observed that in 81.8% of cases, the cause was non-malignant in nature. Chhabra et al<sup>14</sup> found that megaloblastic anemia was responsible for 31.8% of cases. Malignancies were seen in 25.2% of cases which included acute lymphoblastic leukemia, acute myeloid leukemia, non-Hodgkin's lymphoma, Langerhans cell histiocytosis, and myelodysplastic syndrome. Infections (19.7%) such as kala-azar, malaria, enteric fever, and bacterial septicemia were other causes of pancytopenia. Similar observations were made by Bhatnagar et al<sup>15</sup> with megaloblastic anemia in 28.4% of cases, acute leukemia in 21% of cases, infections in 21% of cases and aplastic anemia in 20% of cases. However, Naseem et al<sup>16</sup> found that acute leukemia was the most common etiology (66.9%) in cytopenia children and aplastic anemia (33.8%) in pancytopenia children.

In the present study, most of the patients presented with pallor (77.7%). Other clinical features were fever (33.3%), dyspnea (25.9%), splenomegaly (22.2%), hepato megaly (18.5%), and lymphadenopathy (11.1%). Chhabra et al found that the commonest clinical feature was bleeding manifestations in the form of petechiae, bruises, and ecchymosis seen in malignancies and aplastic

anemia. Mucosal bleeds like epistaxis, gum bleeds, and Malena were commonly associated with megaloblastic anemia. 51.7% of cases of megaloblastic anemia had hepato megaly and 44.8% had splenomegaly. Similar observations were made by Naseem et al who found that the main presenting features in patients with cytopenia and pancytopenia were fever and pallor, other common ones being petechial rash, bleeding manifestations, and bone pains. Bhatnagar et al observed that skin bleeds in the form of petechiae, bruises, and ecchymosis were the commonest bleeding manifestations. Dubey et al<sup>17</sup> have reported that more than half of the cases had pallor, fever, and petechial hemorrhages at presentation. Other features included Hepato megaly, splenomegaly, lymphadenopathy, and bony tenderness. It is seen that many patients had illnesses due to causes that can be either treated easily or can be managed if detected in the early stages.

## Conclusion

It is concluded that infectious (20.9%) and megaloblastic anemia (16.04%) were major causes of bicytopenia. Leukemia was responsible for 11% of cases. Pallor (77.7%), fever (33.3%), and dyspnea (25.9%) were major clinical features.

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