INTRODUCTION

Pancytopenia is characterized by a decrease in all the three cellular elements of the peripheral blood, red blood cells, white blood cells, and platelets [1]. Usually caused by bone marrow failure pancytopenia is not a disease entity, but rather a triad of anemia with hemoglobin <13.5 g/dl in males and <11.5 g/dl in females, leukopenia with total leucocyte count <4000/mm³, and thrombocytopenia with platelet count <1.5 lakh/mm² [2-4]. Pancytopenia may be associated with a hypocellular bone marrow, hypercellular marrow, or bone marrow infiltration. Pancytopenia with a hypocellular bone marrow may be caused by aplastic anemia, drugs, viruses, radiation, toxins, autoimmune disease, malignancy, and paroxysmal nocturnal hemoglobinuria (PNH). In cases of pancytopenia with hypercellular bone marrow, the causative factor maybe hypersplenism, megaloblastic anemia, myelodysplastic syndrome, infections such as human immunodeficiency virus (HIV), and tuberculosis. Malignancies, granulomas, and fibrosis are causes of pancytopenia with bone marrow infiltration. The etiology of pancytopenia differs from one geographical area to another and varies in different population groups with their differences in nutritional status and prevalence of ineffective disorders. In India, cause of pancytopenia is not well defined which is a major cause for diagnostic dilemma. The present study was undertaken to evaluate the various causes of pancytopenia.

METHODS

This was a descriptive cross-sectional study done in the Department of General Medicine, Government Medical College, Kottayam, for a period of 12 months from the Institutional Review Board approval. Ethics committee clearance was obtained vide IRB No.28/2020 dated September 29, 2021. Patients with pancytopenia presenting to the Department of General Medicine, Government Medical College Kottayam, satisfying the inclusion criteria of hemoglobin level <13.5 g/dl in males or <11.5 g/dl in females, leucocyte count <4000 cells/mm³, and platelet count <1.5 lakhs/cu mm were recruited after obtaining their informed consent. Those with age <12 years and those on cancer chemotherapy or radiation therapy were excluded from the study. A sample size of 85 was calculated based on the prevalence of megaloblastic anemia 54% in a study by Yadav et al. [3]. Consecutive sampling was done.

RESULTS

The most common age group was 21–30 years, 29 (34.1%) of the 85 patients. 48 (56.5%) were males and 37 (43.5%) were females. Megaloblastic anemia was the most common etiology constituting 60 (70.6%). The most common presenting complaint was generalized weakness in 74 patients (87.1%). The mean hemoglobin level was 6.81±1.51 g/dl, the mean total WBC count was 2768.39±791.2, and the mean platelet count was 0.87±0.43. Macrocytic anemia was the predominant blood picture in cytopenic patients. Hypercellular marrow was the most common marrow finding in 78.1%.

Conclusion: Megaloblastic anemia was the most common cause of pancytopenia followed by aplastic anemia in the present study. Clinical alertness and suspicion can assure early diagnosis and treatment.

Keywords: Pancytopenia, Anemia, Bone marrow, Megaloblastic anemia.

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77 (90.6%), splenomegaly in 28 (32.9%), hepatomegaly in 21 (24.7%), jaundice in 13 (15.3%), lymphadenopathy in 9 (10.6%), Purpura in 11 (12.9%), and edema in 10 (11.8%) in this study, as shown in Table 2.

As shown in Fig. 2, the peripheral blood picture showed that macrocytosis was present in majority 69 (81.2%) of patients with pancytopenia. Microcytic anemia was the least common type and was present in 2 (2.4%). Bone marrow study was performed in 73 patients.

As shown in Fig. 3, the majority of them had a hypercellular marrow picture 57 (78.1%). Among them, most common cause was megaloblastic anemia.

As shown in Table 2, the mean hemoglobin level was 6.81±1.51 g/dl, mean WBC count was 2768±791.2, and the mean count of platelet was 0.87±0.43 lakhs.

Out of the 85 patients with 29 (34.1%) in the age group of 21–30 years had pancytopenia, of which 17 were males and 12 females. The number of patients above the age of 50 was 10 (11.8%) and those less than 20 were 6 (7.1%) (Table 3).

Megaloblastic anemia was the most common etiology constituting 60 cases (70.6%). Aplastic anemia was present in 7 cases (8.2%), cirrhosis of liver in 4 cases (4.7%), leukemia in 4 cases (4.7%), dengue in 3 cases (3.5%), sepsis in 3 cases (3.5%), myelodysplastic syndrome in 2 cases (2.4%), AIDS was present in a single case (1.2%), and one case (1.2%) was post-COVID (Table 4).

**DISCUSSION**

The present study was conducted in patients with pancytopenia who presented to the Department of General Medicine, Government Medical College, Kottayam. A total of 85 patients were included in this study. The mean age in the present study was 34.78 ± 10.95 years with the age range of 13–60 years. In the study by Khunger et al., in 200 cases of pancytopenia, the age group ranged from 2 to 70 years [5]. In a study by Kumar et al., the age group was 12–73 years, while in Khokde et al., it was 3–69 years, and in Tilak, it was 5–70 years V et al.[6-8].

In this study, 48 (56.6%) were males and 37 (43.5 %) were females. The male-to-female ratio was 1.3:1. The male: female ratio was comparable to that of Khunger et al. and Khokde Tilak et al., while Kumar et al. showed a further higher ratio of 2:1 [5-8]. There was a male preponderance in the present study as seen with the other studies.

The most common presenting complaint in the present study was generalized weakness (87.1%), followed by bleeding (32.9%), dyspnea (25.9%), and fever (23.5%). In the study by Gayathri et al., generalized weakness was present in all cases and dyspnea in 48.25% cases [9]. Physical findings such as pallor, icterus, hepatomegaly, splenomegaly, and lymphadenopathy were comparable with the study by Gayathri et al. [9]. Similarly, Pallor and splenomegaly were also the most common signs observed by Niazi et al.; however, generalized weakness was the most common symptom (68.2%) followed by fever (47.7%) and bleeding manifestations (33.33%) [10].

In a study by Agarwal et al., the most common presenting symptom was fever with 64.28%, followed by pain in legs in 34.28% [12]. Similar results were found by Khokde et al., who also found fever to be the most common symptom [7]. In the present study, fever was present in 23.5% of the cases.

<table>
<thead>
<tr>
<th>Table 2: Vital hematological parameters</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>N</strong></td>
</tr>
<tr>
<td>--------</td>
</tr>
<tr>
<td>Hb (g/dl)</td>
</tr>
<tr>
<td>Total count (/m(^3))</td>
</tr>
<tr>
<td>Platelet/lakh</td>
</tr>
</tbody>
</table>
Table 3: Age-wise and sex-wise distribution of pancytopenia in the present study

<table>
<thead>
<tr>
<th>Age in years</th>
<th>Male</th>
<th>Female</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>n</td>
<td>%</td>
<td>n</td>
<td>%</td>
</tr>
<tr>
<td>≤20</td>
<td>4</td>
<td>83</td>
<td>2</td>
</tr>
<tr>
<td>21–30</td>
<td>17</td>
<td>35.4</td>
<td>12</td>
</tr>
<tr>
<td>31–40</td>
<td>13</td>
<td>27.1</td>
<td>11</td>
</tr>
<tr>
<td>41–50</td>
<td>5</td>
<td>10.4</td>
<td>11</td>
</tr>
<tr>
<td>&gt;50</td>
<td>9</td>
<td>18.8</td>
<td>1</td>
</tr>
<tr>
<td>Total</td>
<td>48</td>
<td>100</td>
<td>37</td>
</tr>
</tbody>
</table>

Table 4: Etiology of pancytopenia

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>Frequency</th>
<th>Percent</th>
</tr>
</thead>
<tbody>
<tr>
<td>Megaloblastic anemia</td>
<td>60</td>
<td>70.6</td>
</tr>
<tr>
<td>Aplastic anemia</td>
<td>7</td>
<td>8.2</td>
</tr>
<tr>
<td>Cirrhosis of liver</td>
<td>4</td>
<td>4.7</td>
</tr>
<tr>
<td>Leukemia</td>
<td>4</td>
<td>4.7</td>
</tr>
<tr>
<td>Dengue</td>
<td>3</td>
<td>3.5</td>
</tr>
<tr>
<td>Sepsis</td>
<td>3</td>
<td>3.5</td>
</tr>
<tr>
<td>Myelodysplastic syndrome</td>
<td>2</td>
<td>2.4</td>
</tr>
<tr>
<td>Post-COVID</td>
<td>1</td>
<td>1.2</td>
</tr>
<tr>
<td>AIDS</td>
<td>1</td>
<td>1.2</td>
</tr>
<tr>
<td>Total</td>
<td>85</td>
<td>100</td>
</tr>
</tbody>
</table>

Megaloblastic anemia was the most common cause of pancytopenia in the study. The incidence of megaloblastic anemia is said to vary from 0.8 to 32.26%. However, in the present study, this incidence was higher with 70.6%. Yadav et al. found an incidence of megaloblastic anemia to be 35.84% [11]. A very high incidence of 68% of megaloblastic anemia was reported by Tilak et al. in their study, while only 1.43% was observed by Agarwal et al. [8,12].

In a study by Khunger et al. and Khodke et al., megaloblastic anemia was the most common cause for pancytopenia accounting for 72% and 44%, respectively [5,7]. In the study by Kumar et al., also megaloblastic anemia was the most common cause [6]. The second most common cause of pancytopenia in the present study was aplastic anemia, which accounted for 8.2% of the cases. The incidence of aplastic anemia worldwide is said to vary between 10% and 52.7%. In the study by Agarwal et al., Kumar et al., and Khodke et al., aplastic anemia was the second most common cause of pancytopenia accounting for 14.28%, 14%, and 29.5%, respectively [6,7,12]. It was much more comparable with Tilak et al. where its incidence was 7.8% [8]. Aplastic anemia was the most common cause of pancytopenia in several other studies [10,13,14]. Aplastic anemia is the most common cause of pancytopenia reported from various studies throughout the world and it shows a higher frequency in the developing world than in industrialized Western countries [15,16]. The more incidence of megaloblastic anemia as compared to aplastic anemia in this study in concurrence with other Indian studies reflects the higher prevalence of nutritional anemia in Indian subjects.

According to Prem Kumar et al. in developing countries, pancytopenia is mostly attributed to infectious diseases such as tuberculosis and HIV, which poorly correlates with the present study [17]. Cirrhosis of liver accounted for 4.7% of the cases which was not a notable cause in the other studies. Leukemia also accounted for 4.7% of cases. It was comparable to Khunger et al.’s study where leukemia was present in 5% of the cases [5]. A higher incidence of 12.1% was seen with Kumar et al.[6]. In Khodke et al., 2% of cases were due to leukemia, and in Tilak et al., 1.3% cases were due to leukemia [7,8]. Nazi et al. have reported 13.6% cases of acute leukemia as a cause for pancytopenia [10]. Acute leukemia was found to be the major cause, especially in children by Nazeem et al. in his study [18]. Dengue accounted for 3.5% of the cases in the present study, which was not a cause in the other studies mentioned so far. Myelodysplastic syndrome (MDS) was present in 2.4%. In Khunger et al., 4 cases (2%), Khodke et al., 1 case (2%), and Kumar et al., 6 cases (3.6%) were due to MDS [5,6].

The present study had a single case of each of AIDS and Post-COVID which accounted for only 1.2% of the cases. Khodke et al. have reported 1 case of AIDS (2%) [7].

The variation in the frequency of the causes of pancytopenia has been attributed to the differences in methodology and stringency of diagnostic criteria, period of observation, varying exposure to myelotoxic agents apart from the geographical area and genetic mutations [19,20]. Screening programs at community level will help in diagnosis and benefit avoiding further complications by offering adequate patient counseling, especially for anemia [21].

The limitations of this study are that it is a single-center study. A study with longer duration and better sample size might provide more insights into the etiology.

CONCLUSION
The most common presenting complaint was generalized weakness and clinical finding was pallor. Megaloblastic anemia was the most common cause of cytopenia, followed by aplastic anemia. Macrocytic anemia was predominant blood picture in cytopenic patients. Hypercellular marrow was the most common marrow finding and the most common cause was megaloblastic anemia.

AUTHORS’ CONTRIBUTION
Athsra Surendran: Project idea, protocol preparation, literature review, data collection, data analysis, manuscript preparation. Padmakumar N: Project idea, protocol review, manuscript review. Anoop Kumar N: Project idea, protocol review, manuscript preparation, manuscript editing, corresponding author.

CONFLICTS OF INTEREST
None.

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REFERENCES