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Etiological Spectrum and Clinical Profile of Pancytopenia in Adults: A Prospective Study at a Tertiary Care Hospital

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Abstract

Pancytopenia is a haematological condition, characterized by a simultaneous reduction of erythrocytes, leukocytes, and platelets in the peripheral circulation. It manifests a wide spectrum of primary disorders, including nutritional deficiencies and bone marrow failure syndromes, hematologic malignancies, thereby highlighting its heterogeneous aetiology. The diagnosis of underlying cause paramount importance, as several possible aetiologies potentially reversed. The aim of the present study was to delineate the clinical profile, etiologic distribution, and demographic features related to pancytopenia. A prospective observational design was used, in which included fifty adult participants with pancytopenia during the period of twelve months. Inclusion criteria required laboratory confirmation of pancytopenia on haematological evidence. Detailed clinical history, comprehensive physical examination and laboratory tests performed; including serum vitamin B12 levels and bone marrow evaluation through aspirate or biopsy. Participants younger than 30 years, majority of the cohort at 52 % and males accounted 64%. The most frequently reported clinical manifestation were fatigue (96%) and dyspnoea (94%), and followed by fever in 42% of cases. Pallor was presented among all the participants, with additional clinical features of knuckle hyperpigmentation (20%), hepato-splenomegaly (16%), and jaundice (14%). Etiologic analysis revealed that megaloblastic anemia (48%) was the most significant cause of pancytopenia, followed by infectious processes, hypersplenism, acute leukaemia, and aplastic anemia. Notably, 62.5% of megaloblastic anemia was found to have serum vitamin B12 deficiency. The findings underscore that megaloblastic anemia as the predominant aetiology of pancytopenia. Consequently, clinical evaluation combined with targeted lab investigations is essential for accurate diagnosis. Such a method allows early identification of reversible causes, which eventually enabling timely intervention and enhances patient outcomes.

KEYWORDS: Pancytopenia; Megaloblastic anemia; Bone marrow disorders; Hematological profile.

Introduction

Pancytopenia is defined as the simultaneous reduction in haemoglobin concentration, total leukocyte count, and platelet count in the peripheral blood. It is not a disease entity in itself but rather a haematological manifestation of a wide spectrum of underlying disorders that affect the production or survival of blood cells [1]. The condition usually results from impaired bone marrow function, bone marrow infiltration, or increased peripheral destruction and sequestration of blood cells [2]. Clinically, patients with pancytopenia commonly present with nonspecific symptoms such as generalized weakness, fatigue, pallor, recurrent infections, fever, and bleeding manifestations including petechiae, ecchymosis, or mucosal bleeding [3]. These symptoms correspond to anemia, leukopenia, and thrombocytopenia respectively and may vary depending on the severity and duration of the cytopenias.

Pancytopenia is a relatively common hematological abnormality encountered in routine clinical practice and may be associated with several potentially life-threatening conditions such as aplastic anemia, acute leukemia, myelodysplastic

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syndromes, megaloblastic anemia, and severe infections [4]. Among these, nutritional deficiencies and bone marrow failure syndromes are among the most frequently reported causes [5]. Globally, aplastic anemia, a major cause of pancytopenia, has an estimated incidence of approximately 2–5 cases per million populations per year [6]. Epidemiological studies have shown that the incidence is significantly higher in Asian countries compared to Western populations, possibly due to environmental, genetic, and socioeconomic factors [7].

The management of pancytopenia largely depends on the identification of the underlying cause. The interventions may include the use of vitamin substitution therapy in cases of nutritional deficiencies, antimicrobial therapy of infectious aetiologies, immunosuppressive therapy in aplastic anaemia, and chemotherapeutic therapy of hematologic malignancies [8]. The treatment of Hematopoietic stem cell transplantation remains a conclusive treatment modality [9]. Pancytopenia, which occurs due to a range of nutritional deficiencies or extreme marrow pathology, will require early diagnosis and specific management in order to reduce morbidity and mortality [10]. It is therefore of utmost importance to elucidate the clinical phenotypes and etiologic milieu of pancytopenia within the demographic cohort of various populations. The etiologic architecture is often dampened by geographic location and present healthcare infrastructure condition [11]. The shortages of vitamin B12 and folic acid are conspicuously found in low-resource areas, and malignancies of the haematology and myeloid neoplasms have a disproportionate incidence in more prosperous areas [12]. In this regard, investigative researches that outline the clinical and etiologic spectrum of pancytopenia provide the most crucial information in timely diagnosis, influence the choice of research instruments and the ability to provide a timely response in therapy [13].

Materials and Methods

This research was conducted as a prospective observational study at the Department of General Medicine at a teaching hospital that has a tertiary level environment in a period of twelve months. The would-be framework eased orderly acquisitions and evaluations of both clinical and laboratory information that related to adult patients diagnosed with pancytopenia all within the time limits that were provided. The population served by the institution is substantial, and there is a mixture of both city and countryside referrals, which means that the study will focus on a heterogeneous group of people. In its turn, this provides a thorough description of the clinical picture and etiologic spectrum of pancytopenia.

Sample Size Calculation: The sample size was calculated using the formula:n=Z^2 P(1-P)/ d^2. Based on this calculation, the minimum sample size was estimated to be approximately 50 patients.

Study population: The sample included patients aged 18 years and older with a clinical diagnosis of pancytopenia by the results of a complete blood count (CBC) and informed consent to take part in the study. Patients receiving chemotherapy and radiotherapy as well as those with a pre-existing hematological malignancy previously treated were excluded; incomplete clinical records were also avoided. The collection of clinical data was made with the help of a structured proforma containing the demographic data, clinical presentation, or laboratory investigations. Laboratory tests included peripheral smear, CBC, and in some cases, bone marrow aspiration and biopsy. The etiologic diagnosis was made with the help of systematic consideration of the clinical and laboratory evidence. Statistical analysis: all data that was collected was tabulated and analyzed using the Microsoft excel in association with other statistical packages SPSS. Descriptive statistics presented the findings and were in the form of frequencies, thus describing the clinical and etiologic profile of pancytopenia in the study population.

Results

Table 1. Etiological distribution in patients of pancytopenia (n=50)

Aetiology	n=50	%
Megaloblastic anemia	24	48
Infections	15	30
Hypersplenism	5	10
Acute leukemia	3	6
Aplastic anemia	2	4
Pure red cell aplasia	1	2

In the etiologic distribution of pancytopenia, our result showed that megaloblastic anaemia became the major cause with 48% of the cases and infected aetiologies with 30%. Other contributory causes were hypersplenism (10 %), acute leukaemia (6%), aplastic anemia (4 %) and pure red cell aplasia (2 %). Such findings highlight the long-term importance of nutritional deficiency and infectious mechanisms as the main causes of pancytopenia in the cohort of the study (Table 1).

The age- and gender-wise distribution showed that the majority of patients belonged to the <30 years age group (52%), followed by 30–49 years (26%) and ≥50 years (22%). Male patients constituted 64% (32 cases) of the study population, while females accounted for 36% (18 cases), indicating

a male predominance among patients with pancytopenia (Table 2).

Table 2. Age and gender-wise distribution of pancytopenia cases

Age (years)	Male n (%)		Female n (%)	
<30	14	28	12	24
30–49	8	16	5	10
≥50	10	20	1	2
Total	32	64	18	36

Table 3. Clinical features in patients of pancytopenia (n=50)

Clinical Symptoms	cases (n)	%
Fatigue	48	96
Dyspnea	47	94
Fever	21	42
Bleeding manifestation	7	14
Diarrhea/ other GI symptoms	6	12
Weight loss	4	8
Physical findings		
Pallor	50	100
Knuckle pigmentation	10	20
Hepatomegaly	08	16
Splenomegaly	08	16
Jaundice	07	14
Peripheral neuropathy	01	02

Fatigue (96%) and dyspnea (94) were the most frequent clinical manifestations and reflect the degree of anemia observed in pancytopenia. The frequency of fever was observed to be 42% and bleeding symptoms (14%), gastrointestinal symptoms (12 %) and weight loss (8%), were relatively low. Pallor was observed in all patients (100%) and, therefore, can be considered the most consistent clinical manifestation. Knuckle pigmentation was found in 20% of the cases, which indicates vitamin B12 deficiency in a subgroup of subjects. Hepatomegaly and splenomegaly were observed in 16 and 16 % respectively and jaundice (14%) and peripheral neuropathy (2%) were minor findings (Table 3).

Haemoglobin analysis indicated that 64% of the patients were severely anaemic, with a haemoglobin range ≤6 g/dL. 26% of cases (6.1-8.0 g/dl) was moderate anemia, and only a tenth of the patients had haemoglobin reading greater than 8.0g/dl. This set of results show that the most prevalent haematological abnormality was severe anemia amongst the study population. Analysis of leukocyte count revealed that most patients (84 %) were in the range of 2100-4000 cells/cumm, which is a moderate case of leukopenia. Extreme leukopenia (≤2000 cells/cumm) and almost normal (>4000 cells/cumm) counts were seen in 8 % in each case, indicating that the intermediate level of reduction in leukocyte count had been the most widespread. Platelet count evaluation showed that 44% of patients had platelet counts between 51,000–100,000 cells/mm^3, making it the most common category. Severe thrombocytopenia (≤25,000 cells/mm^3 was observed in 26% of patients, while 22% had counts between 26,000–50,000 cells/mm^3. Only 8% of patients had platelet counts above 100,000/cumm, indicating that moderate thrombocytopenia was the most frequent finding (Table 4).

Table 4. Range of haemoglobin, complete blood picture in patients with pancytopenia (n=50)

Hb Range (g/dL)	Cases (n)	%
≤6.0	32	64
6.1 – 8.0	13	26
>8.0	5	10
Leukocyte Count (cells/cumm)		
12%	6	
2001 – 3000	18	36
3001 – 4000	26	52
Platelet Count (cells/mm^3)		
≤25,000	13	26
26,000 – 50,000	11	22
51,000 – 100,000	22	44
>100,000	4	8
R.B.C morphology		
Normocytic	18	36
Macrocytosis	31	62
Microcytosis	1	2

Peripheral smear examination revealed that macrocytosis was the predominant RBC morphology (62%), followed by normocytic morphology (36%), while microcytosis was observed in only 2% of cases. The predominance of macrocytosis supports megaloblastic anemia as a major etiological factor in pancytopenia (Table 4).

Serum vitamin B12 analysis showed that 46% of patients had low B12 levels, while 48% had normal levels and 4% had elevated levels. Low B12 levels were predominantly associated with megaloblastic anemia, supporting the role of vitamin B12 deficiency in the pathogenesis of pancytopenia (fig 1).

Bone marrow examination was performed in 39 patients, while 11 patients were excluded due to contraindications or lack of consent. Bone marrow examination revealed that hypercellular marrow was the most common finding (89.75%),

followed by hypocellular marrow (7.69%) and normocellular marrow (2.56%). These findings suggesting increased marrow activity in response to peripheral cytopenia (Table 5).

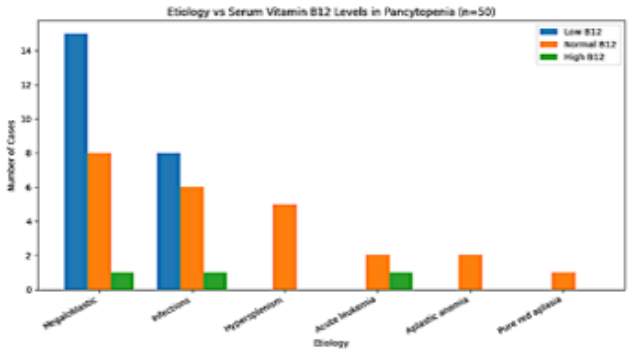

Fig 1. Aetiology and Serum Vitamin B12 Levels

Table 5. Bone marrow cellularity in patients with pancytopenia (n=39)

Bone marrow cellularity	Cases n	%
Hypercellular	35	89.8
Hypocellular	03	7.7
Normocellular	01	2.6

Among infectious causes, malaria was the most common infection (46.67%), followed by enteric fever (26.67%) and dengue (20%), while HIV accounted for 6.67% of cases. This highlights the significant role of tropical infections in the etiology of pancytopenia in endemic regions (Table 6).

Table 6. Infections in different cases of pancytopenia (n=15)

Infection Type	Cases n	%
Malaria	7	46.7
Enteric fever	4	26.7
Dengue	3	20
HIV	1	6.7

Discussion

Megaloblastic anemia was identified as the most common cause of pancytopenia in the present study, accounting for 48% of cases. This finding is comparable with the study conducted by Tilak V and Jain R, who reported megaloblastic anemia in 41% of cases [14]. Similarly, Gayathri BN and Rao KS observed a higher prevalence of 68% in their study [15]. The high rate of megaloblastic anemia observed in these studies highlights the substantial role of nutritional deficiencies especially deficiencies of vitamin B12 and folate, in the etiological spectrum of pancytopenia in developing countries 16.

Such deficiencies may be explained by factors including, inadequate dietary intake, malabsorption, and adverse socioeconomic factors. Similar findings have been reported in previous Indian studies, thus supporting nutritional deficiency as one of the key etiological causes of pancytopenia [17].

The findings of current study also indicate that infections and hypersplenism are also consequential aetiologies of pancytopenia, although their contribution was relatively lower compared to Megaloblastic anemia. Among the conspicuous hematologic abnormality was severe anemia emerged as the most prominent finding, with fatigue, dyspnea among the most common presenting symptoms among the affected patient [18].

The peripheral blood smear examination and bone marrow evaluation are the essential diagnostic tools for elucidating the underlying pathophysiological mechanism and determining the exact aetiology of pancytopenia [19]. Improved outcomes in the patients lead to early intervention in the reversible aetiologies such as nutritional deficiencies and infections through early diagnosis through careful clinical examination and detailed laboratory analysis [20].

Conclusion

The present study highlights that megaloblastic anemia is the most common aetiology of pancytopenia in adults, followed by infectious causes and hypersplenism. Nutritional deficiencies especially vitamin B12 deficiency constitute a major aetiological spectrum in developing countries and represents potentially reversible etiological cause.

The hematologic profile in affected patients is characterized by a severe anemia, fatigue, and dyspnoea being the common presenting complaints. Peripheral blood smears and bone-marrow analysis are remains valuable diagnostic tools for identifying the underlying pathology and guide proper therapeutic interventions. Early diagnosis through periodic clinical examination and comprehensive laboratory investigations enable prompt treatment of reversible diseases such as nutritional deficiencies and infections, thereby improving patient prognoses.

Limitations: However, the present study has certain limitations including single centre design, relatively small cohort, and lack of long-term longitudinal follow up. Therefore, larger, multicentre studies, which have a longer follow-up period, are warranted to better elucidate the epidemiology, etiological spectrum and longitudinal outcomes of pancytopenia.

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Conflict of interest: None declared.

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