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Etiological Profile of Pancytopenia in a Regional Cancer Centre: A Prospective Study

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Abstract: ***Introduction: Pancytopenia, the reduction of all peripheral blood lineages, arises from different etiologies, ranging from reversible nutritional deficiencies to life-threatening hematological malignancies. In a cancer care setting, its prompt evaluation is critical for diagnosis, prognostication, and treatment. The aim of this study was to elucidate the causes and clinical spectrum of pancytopenia in patients presenting to a regional cancer centre. Materials and Methods: A prospective study was conducted over six months (July 2023 to December 2023) at the Department of Medical Oncology, Kidwai Memorial Institute of Oncology. A total of 102 adult patients (>15 years) with pancytopenia (Hb <10g/dl, TLC <4000/µL, Platelets <100,000/µL) were enrolled. Patients with prior chemotherapy/radiotherapy or relapsed malignancies were excluded. All patients underwent detailed clinical evaluation, laboratory investigations, imaging, and bone marrow aspiration/biopsy. Results: The mean age was 41.75 ± 17.2 years with a male-to-female ratio of 1.12:1. The most common presenting symptoms were easy fatigability (61%) and fever (56%). Hematological malignancies constituted the majority of cases (90%). Acute leukemias were the leading cause (71%), with Acute Myeloid Leukemia (AML, 33%) being most prevalent, followed by Aplastic Anemia (7%), Myelodysplastic Syndrome (6%), and Lymphoma (6%). Solid malignancies with bone marrow infiltration (5%) and Megaloblastic Anemia (2%) were less common. Bone marrow examination was diagnostic in all cases of malignancy and aplastic anemia. Conclusion: In a tertiary cancer care setting, pancytopenia is most frequently a manifestation of an underlying hematological malignancy, predominantly acute leukemia. Bone marrow aspiration and biopsy, supplemented with immunohistochemistry and cytogenetics, are indispensable tools for accurate diagnosis, in cases of unexplained cytopenias, and are crucial for guiding appropriate management and prognostication.***

Keywords: Pancytopenia, Etiology, Bone Marrow Examination, Acute Leukemia, Hematological Malignancy, Cancer Centre

1. Introduction

Pancytopenia is a hematological condition characterized by a simultaneous reduction in all three cellular components of peripheral blood: erythrocytes, leukocytes, and platelets. It is a triad of findings indicative of an underlying pathology (1). The broad etiological spectrum encompassing conditions from benign and reversible causes like nutritional deficiencies (Vitamin B12, folate) to life-threatening disorders such as primary bone marrow failures (e.g., aplastic anemia) and hematological malignancies (e.g., acute leukemias, myelodysplastic syndromes) (2, 3).

The clinical presentation is variable and depends on the severity of the cytopenias and the nature of the underlying disease. Patients may present with symptoms of anemia (fatigue, weakness), neutropenia (fever, infections), or thrombocytopenia (bleeding diathesis) (4). Pancytopenia often results from Bone marrow infilteration, not only in primary hematological cancers but also in solid tumours, where it signifies stage IV disease and carries significant prognostic and therapeutic implications (5, 6).

While nutritional deficiencies remain as the leading cause of pancytopenia in several studies from general hospitals in India (7, 8), but it is expected to differ significantly in a specialized oncology setting. A systematic diagnostic workup is of prime importantce for implementing timely and appropriate therapy. The current study was undertaken to evaluate the various causes and clinical presentations of pancytopenia in patients presenting to a regional cancer centre over six months, to enhance accuracy of diagnosis and optimise the therapeutic approach in this specific patient population.

2. Materials and Methods

Study Design and Setting: This was a prospective, observational study conducted in the Department of Medical Oncology at Kidwai Memorial Institute of Oncology, a tertiary care cancer centre in South India, for a period of six months from July 2023 to December 2023.

Study Population and Inclusion/Exclusion Criteria: Adult patients of both sexes, aged above 15 years, presenting to the outpatient department or emergency with laboratory-confirmed pancytopenia were included. Pancytopenia was defined as: Hemoglobin (Hb) <10 g/dL, Total Leukocyte Count (TLC) <4000/µL, Absolute Neutrophil Count (ANC) <1500/µL, and Platelet count <100,000/µL. Patients who had recently received chemotherapy or radiotherapy, and those with relapsed hematological malignancies were excluded from the study to capture *de novo* presentations.

A total of 102 patients satisfying the criteria were included for the final analysis.

Evaluation Protocol: All enrolled patients underwent a systematic evaluation:

1) **Clinical Assessment:** Detailed history and physical examination, with documentation of age, sex, clinical presentation, and duration of symptoms.
2) **Laboratory Investigations:** Complete blood count with peripheral smear examination, renal and liver function tests, viral markers (HIV, HBsAg, HCV), Vitamin B12 and folate levels (where indicated). Red cell indices (MCV, MCH, MCHC) were recorded.
3) **Imaging and Other Tests:** Ultrasound of the abdomen and pelvis, chest X-ray, and 2D echocardiogram were performed as part of the initial workup.

4) **Bone Marrow Examination:** After obtaining written informed consent, all patients underwent bone marrow aspiration and biopsy under aseptic precautions. The samples were subjected to morphological assessment, flow cytometry, and cytogenetic analysis as clinically indicated to establish a definitive diagnosis.

Statistical Analysis: Descriptive statistics were used. Continuous variables were expressed as mean ± standard deviation, and categorical variables were expressed as percentages.

3. Results

A total of 102 patients were included in the final analysis. The demographic and clinical characteristics are summarized in Table 1.

Table 1: Demographic and Clinical Characteristics of the Study Population (n=102)

Characteristic	Value
Mean Age (years)	41.75 ± 17.2
Age Range (years)	16 - 80
Male:Female Ratio	1.12 : 1
Mean Duration of Symptoms (months)	2.78
Presenting Symptoms, n (%)	
Easy Fatigability	62 (61%)
Fever	57 (56%)
Bleeding Diathesis	30 (29%)
Weight Loss	10 (10%)
Cough	9 (9%)
Findings on Examination, n (%)	
Pallor	102 (100%)
Hepatosplenomegaly	20 (20%)
Splenomegaly	18 (18%)
Lymphadenopathy	8 (8%)

Hematological Parameters at Presentation:

- Mean Hemoglobin: 7.34 ± 1.2 g/dL
- Mean TLC: 2759.95 cells/µL
- Mean Platelet count: 32.05 x 10^3/µL
- Mean MCV: 91 fL
- Mean ANC: 737.87 cells/µL

Etiological Spectrum of Pancytopenia:

The final diagnoses are detailed in Table 2. Hematological malignancies were the predominant cause, accounting for 90% of cases.

Table 2: Final Diagnosis in 102 Patients with Pancytopenia

Diagnosis	Number of Patients	Percentage
I. Hematological Malignancies	**92**	**90%**
Acute Leukemias (Total)	**72**	**71%**
Acute Myeloid Leukemia (AML)	34	33%
B-cell Acute Lymphoblastic Leukemia (B-ALL)	9	9%
T-cell Acute Lymphoblastic Leukemia (T-ALL)	21	21%
Acute Promyelocytic Leukemia (APML)	5	5%
Hairy Cell Leukemia (HCL)	1	1%
Mixed Phenotypic Acute Leukemia (MPAL)	1	1%
Aplastic Anemia	**7**	**7%**
Myelodysplastic Syndrome (MDS)	**6**	**6%**
Lymphoma	**6**	**6%**
High-Grade B-cell Lymphoma	2	2%
Hepatosplenic T-cell Lymphoma	2	2%
Plasmablastic Lymphoma	1	1%
Classical Hodgkin Lymphoma (CHL)	1	1%
II. Solid Malignancies	**5**	**5%**
Carcinoma Breast	2	2%
Neuroendocrine Carcinoma	1	1%
Metastatic Colon Carcinoma	1	1%
Metastatic Prostate Carcinoma	1	1%
III. Nutritional Deficiencies	**2**	**2%**
Megaloblastic Anemia	2	2%
IV. Other Rare Hematological Malignancies	**3**	**3%**
Blastic Plasmacytoid Dendritic Cell Neoplasm (BPDCN)	1	1%
Waldenström Macroglobulinemia	1	1%
CML in Lymphoid Blast Crisis	1	1%

4. Discussion

This prospective study, conducted in a specialized oncology setting, reveals a distinct etiological profile of pancytopenia, in contrast with studies from general hospitals. Our findings underscore that in a regional cancer centre, pancytopenia is commonly presenting feature of an underlying malignancy, predominantly of hematological origin.

The mean age of our cohort was 41.75 years, with a slight male predominance, which is consistent with the demographic profile of several hematological cancers (9). The most common clinical manifestations—easy fatigability (61%) and fever (56%)—are direct consequences of anemia and neutropenia, respectively, and align with the findings of other studies (4, 10). The high prevalence of bleeding manifestations (29%) further highlights the severity of the cytopenias at presentation.

The most striking finding was that acute leukaemia constituted 71% of all cases, with AML (33%) being the single most common diagnosis. This is significantly higher than reported in general population studies. For instance, a study from Central India by Ojha et al. found megaloblastic anaemia (25.6%) as the leading cause, with acute leukaemia being second (16%) (7). Similarly, studies from Korea and other parts of the world have reported AML as a common cause, but with lower prevalence (25-26%) (2, 11). This discrepancy is expected and underscore the referral bias in a tertiary cancer centre, where malignant cases are concentrated. Our findings are consistent with other cancer centre-based studies, such as that of Devitt et al., which also identified AML as a leading cause (11).

Aplastic anemia was the next most common diagnosis (7%), followed by MDS and lymphoma (6% each). The prevalence of MDS and lymphoma in our study was comparable to that reported by Ojha et al. (7.1% and 5.7%, respectively) (7). The spectrum of lymphomas was diverse, including rare types like hepatosplenic T-cell lymphoma and plasmablastic lymphoma, diagnosed primarily through bone marrow biopsy and immunohistochemistry.

Notably, our study included five cases (5%) of advanced solid malignancies presenting with pancytopenia due to bone

marrow infiltration. This included one case of metastatic breast carcinoma and one case of neuroendocrine carcinoma, in addition to single cases of colon, rhabdomyosarcoma and prostate carcinoma. These cases highlight a critical, though less common, etiology. Bone marrow biopsy played a crucial role in detecting carcinomatous infiltration, which was subsequently confirmed with appropriate IHC markers. This finding is crucial as it upstages the disease to Stage IV and significantly alters management, underscoring the role of bone marrow evaluation in cases of unexplained pancytopenia, even in the absence of overt primary tumor symptoms (5, 6).

Nutritional deficiencies, particularly Megaloblastic Anemia, were rare (2%) in our cohort, contrasting sharply with their prominence as the leading cause in many Indian studies (7, 8). This again reflects the selected patient population referred to a cancer institute.

Illustrative Cases: The diagnostic challenge was exemplified by a case of a 44-year-old male with fever, pancytopenia, and hepatosplenomegaly. Initial inconclusive aspirate was resolved by cytogenetics and biopsy, leading to a diagnosis of high-grade B-cell lymphoma. Another case of a 52-year-old female with pancytopenia and back pain was diagnosed with metastatic breast cancer through bone marrow biopsy. These cases demonstrate that a comprehensive approach, integrating morphology, IHC, and cytogenetics, is essential for a definitive diagnosis.

5. Conclusion

This study concludes that in the context of a regional cancer centre, pancytopenia is predominantly caused by hematological malignancies, with acute leukemias being the most frequent. Bone marrow aspiration and biopsy with immunohistochemistry is vital not only for diagnosing primary hematological disorders but also for detecting unsuspected bone marrow involvement by solid tumours. While nutritional deficiencies are rare in this setting, they should still be considered in the differential diagnosis.

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