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TRILINEAGE HEMATOPOIESIS (PANCYTOPENIA) - A CLINICO-HAEMATOLOGICAL PROFILE AT A TERTIARY CARE HOSPITAL

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ABSTRACT:-
Introduction: Pancytopenia is an everyday finding in clinical practice, often associated with many critical illnesses. Suspicion arises when a patient presents with a triad of symptoms due to anemia, leukopenia, and thrombocytopenia. Primary causal condition coupled with the severity influences prognosis and treatment course. We aimed to analyze the clinical features in pancytopenic patients; and further to evaluate hematological distribution, inclusive of bone marrow aspiration. Methodology: Prospective cross-sectional study design was exercised in a 6 month span, from July to December 2023 at the Department of Hematology. In total, 106 patients with pancytopenia aged 15 to 65 years, were reviewed to scrutinize their demographic and clinical details with focus on their peripheral picture study and bone marrow analysis. Results: Of the 106 cases investigated, a hefty number were in the 15-25 years age group (40.57%), with a male predominance (57.55%). Most common symptoms were generalized weakness (87.74%) and fever (59.43%). Physical findings included pallor (83.02%), hepatomegaly (24.53%), and splenomegaly (16.98%). Dimorphic anemia (24.53%) was the predominant blood picture, followed by normocytic normochromic picture (12.26%) and normocytic hypochromic picture (5.66%). Megaloblastic erythropoiesis (72.64%) was the commonest bone marrow finding, seconded by iron deficiency anemia (12.26%). Conclusion: Comprehensive workup, consisting of clinical findings, hematological scrutiny, and bone marrow exploration, is imperative for dictating the cause in pancytopenic patients. These findings also help in further evaluation.

INTRODUCTION:-

Pancytopenia is a prevalent clinico-hematological condition experienced in daily habitude. It itself is not termed a disease, but a triumvirate of cytopenias caused by various underlying mechanisms(1).

Pancytopenia is characterized by reduction in all three blood cell types - red blood cells, white blood cells, and platelets - resulting from various cardinal causes, including infections, autoimmune conditions, bone marrow deterioration, nutritional insufficiency, and numerous medications. In adults, it is delineated by hemoglobin levels <13.5 g/dL in males and <11.5 g/dL in females, a leukocyte count <4,000/cumm, and a platelet count <1.5 lakhs/cumm(2). Diseases causing pancytopenia vary across populations due to differences in age, nutritional caliber, and infection prevalence(3).

Initial symptoms experienced by patients typically arise due to the effects of anemia or thrombocytopenia with the clinical effects of leukopenia being expressed in the late phase of anarchy(4). Pancytopenia, a clinical triumvirate of anemia (dyspnea, cardiac symptoms, and fatigability), leukopenia (severe infections receptivity), and thrombocytopenia (mucosal bleed with bruising). A study of general practitioners revealed that a hematologist is confabulated in approximately 90% of cases when pancytopenia is identified in laboratory workup(5).

A thorough assessment of blood elements is crucial as the initial phase in evaluating hematological function and diagnosing disease. Clinical manifestations and peripheral blood picture guide the further phases of pancytopenia

evaluation, aiding in the selection of further blood tests and studies on bone marrow. The prognosis and appropriate management of pancytopenic patients relies on the fundamental pathology and the associated co-morbidities.

We intended to survey the clinico-hematological profile and to make out the varying antecedents of pancytopenia in adults. Additionally, this study seeks to correspond the morphological characteristics of the peripheral blood picture with bone marrow aspirate findings, providing comprehensive understanding of the hematological alterations underlying pancytopenia.

METHODOLOGY:-

A prospective cross-sectional research was adopted in six months (July–December 2023), at our Hematology Unit, Department of Pathology, Saveetha Medical College and Hospital, Thandalam. Institutional Ethical Committee approval was accomplished. Adult patients of both genders with pancytopenia were included, regardless of the underlying cause, provided they met the inclusion criteria: hemoglobin <13.5 g/dL in males, <11.5 g/dL in females; leukocyte count <4000/cumm; platelet count <1.5 lakhs/cumm(2). Excluded patients were those who had undergone chemotherapy or radiotherapy. Demographic details with relevant clinical symptoms and physical findings were entered in a predetermined pro forma.

Routine blood investigations performed in EDTA anticoagulant samples comprised a complete blood count (CBC). Hematological analyses were performed using Fully Automatic SYSMEX XN-1000 6 part Hematology analyzer(6) based on the principle of aperture impedance counting, also called the Coulter principle(7). Blood films were stained with Leishman stain to evaluate morphological abnormalities. Wright's stain, commonly used for blood smear examination, often provides valuable insights for diagnosing anemias and various leukocyte and platelet malady(8).

All pancytopenic cases underwent bone marrow aspiration, together with bone marrow biopsy conducted selectively engaging standardised approach, following sterile measures, with patients given local anesthesia and taken from the posterior superior iliac spine. Leishman stain was employed, while Perl's Prussian blue stain was practiced to grade iron stores. Bouin’s fixative was utilized on Bone marrow biopsy specimens, and sections examined applying hematoxylin and eosin (H&E) stain.

The data were analyzed using SPSS 21.0 for Windows. Descriptive statistics summarized the demographic and clinical characteristics of the study population. Frequencies and percentages were also calculated.

RESULTS:-

In toto 106 cases were examined, containing 61 males [61/106, 57.55%] and 45 females [45/106, 42.45%]. The age of the patients encompassed between 15 and 65 years, with a mean age of 36.69 years (SD = 14.11). Preeminently, affected cases funneled in the 15–25 years age bracket [43/106, 40.57%], followed by 26–35 years [25/106, 23.58%], 56–65 years [15/106, 14.15%], 36–45 years [12/106, 11.32%], and 46–55 years [11/106, 10.38%]. Clinically, over 80% of study subjects manifested with generalized weakness, followed by fever (59.43%), breathlessness (46.23%) and weight loss (23.58%); and the least patients had some kind of bleeding (3.77%). The physical findings in descending order included pallor [88/106, 83.02%], hepatomegaly [26/106, 24.53%], splenomegaly [18/106, 16.98%], bone tenderness [6/106, 5.66%] and lymphadenopathy [5/106, 4.72%], as illustrated in table 1.

Table 1: Demographic attributes and clinical findings

Parameter	Category	No. (%)
Age (Years)	15 - 25	43 (40.57)
	26 - 35	25 (23.58)
	36 - 45	12 (11.32)

	46 - 55	11 (10.38)
	56 - 65	15 (14.15)
	Mean ± SD	34.69 ± 14.11
Presenting complaints	Generalized weakness	93 (87.74)
	Breathlessness	49 (46.23)
	Fever	63 (59.43)
	Weight loss	25 (23.58)
	Bleeding manifestation	4 (3.77)
Physical findings	Pallor	88 (83.02)
	Hepatomegaly	26 (24.53)
	Lymphadenopathy	5 (4.72)
	Splenomegaly	18 (16.98)
	Bone tenderness	6 (5.66)

The hematological parameters revealed hemoglobin levels between 1.8 and 9.2 g/dL, with the majority of study subjects having levels ranging 5.1 to 8 g/dL [59/106, 55.66%]. Leukocyte counts ranged from 500 to 3900 cells/cumm, with most patients falling in the range of 2501 - 3900 cells/cumm [77/106, 72.64%]. Reticulocyte counts fell in the range of 0.5% to 2%, with over half of the patients having counts between 0.6% and 1% [55/106, 51.89%]. Platelet counts were found in the range from 10,000 to 149,000 cells/cumm, with substantial patients having counts between 100,000 and 149,000 cells/cumm [45/106, 42.45%], as displayed in table 2.

Table 2: Distribution of hematological parameters among study population

Parameters	Range	No. (%)
Hemoglobin (g/dl)	1.8 - 5	32 (30.19)
	5.1 - 8	59 (55.66)
	8.1 - 9.2	15 (14.15)

Leucocyte count (cells/cumm)	500 - 1000	5 (4.72)
	1001 - 2500	24 (22.64)
	2501 - 3900	77 (72.64)
Platelet count (cells/cumm)	10000 - 50000	26 (24.53)
	50001 - 100000	35 (33.02)
	100001 - 149000	45 (42.45)
Reticulocyte count (%)	0 - 0.5	26 (24.53)
	0.6 - 1	55 (51.89)
	1.1 - 2	25 (23.58)

On peripheral smear study, a greater proportion of study subjects revealed macrocytic picture [61/106, 57.55%], with macro-ovalocytes and hypersegmented neutrophils, as portrayed in figure 1. This was followed by dimorphic picture [26/106, 24.53%], normocytic normochromic picture [13/106, 12.26%], with the least cases showing normocytic hypochromic picture [6/106, 5.66%].

Malarial infestation was found in 4 patients, with peripheral blood picture showing pancytopenia and Plasmodium falciparum gametocytes, as illustrated in figure 2.

In the present study, megaloblastic anemia [77/106, 72.64%] was the most common cause, trailed by iron deficiency anemia [13/106, 12.26%]. The meanest causes were myelofibrosis, multiple myeloma, myelodysplastic syndrome (MDS), and hypersplenism, each accounting for 1 case [1/106, 0.94%], as displayed in table 3.

More than half of the bone marrow (BM) aspirations revealed megaloblastic erythroid hyperplasia. Megaloblasts exhibited characteristic features, including asynchronous nuclear maturation, bluish cytoplasm with cytoplasmic blebs, and sieved nuclear chromatin, as displayed in figure 3. Multiple myeloma was diagnosed in one female subject, with bone marrow showing abnormal plasma cell proliferation, comprising more than 40% of marrow cells, containing numerous binucleate and trinucleate forms, as depicted in figure 4.

Table 3: Distribution of Pancytopenia causes

Causes	No. (%)
Megaloblastic anemia	77 (72.64)
Iron deficiency anemia	13 (12.26)
Malaria	4 (3.77)
Leukemia	3 (2.83)

Systemic Lupus Erythematosus (SLE)	3 (2.83)
Aplastic anemia	2 (1.87)
Multiple myeloma	1 (0.94)
Myelofibrosis	1 (0.94)
MDS	1 (0.94)
Hypersplenism	1 (0.94)
Total	106 (100)

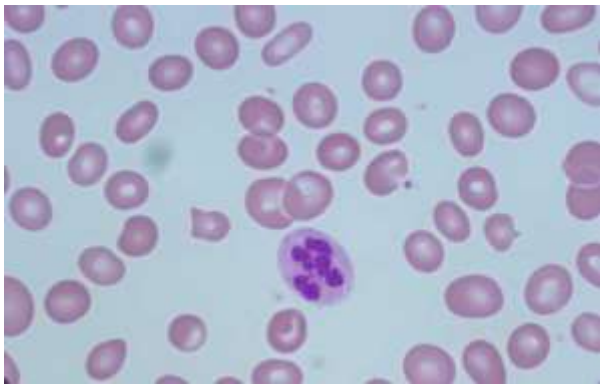

Figure 1: Peripheral blood film illustrating macro-ovalocytes with hypersegmented neutrophils (Leishman, ×1000)

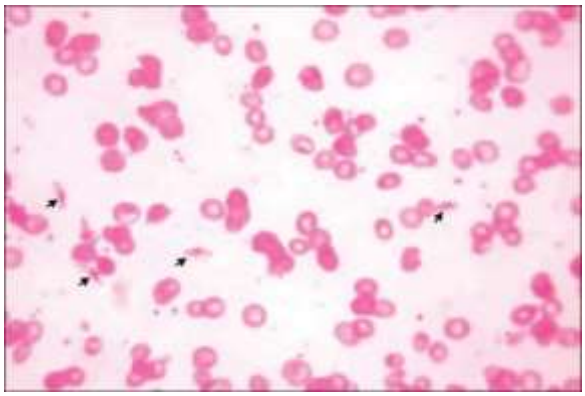

Figure 2: Peripheral blood picture featuring Pancytopenia and Plasmodium falciparum gametocytes (arrows) (Leishman, ×400)

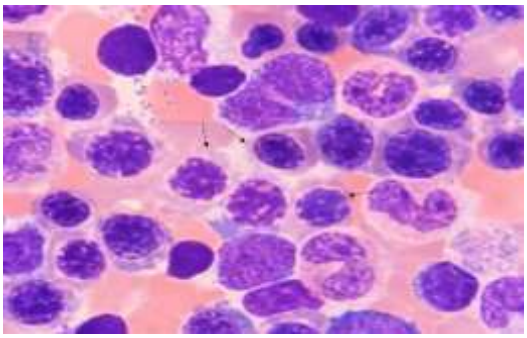

Figure 3: Bone marrow highlighting megaloblasts, containing sieve-like chromatin and royal blue cytoplasm (Leishman, ×1000)

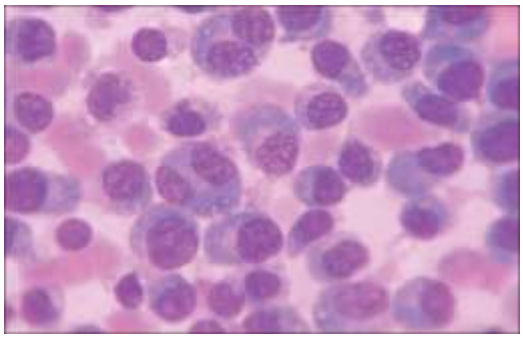

Figure 4: Bone marrow signifying abnormal plasma cells proliferation with binucleate forms (Leishman, ×1000)

DISCUSSION:-

Pancytopenia refers to the clinical triumvirate of anemia, leukopenia, and thrombocytopenia, and eventuality of a variety of underlying circumstances. Evaluating a case of pancytopenia comprises appropriate history taking and clinical findings with a constellation of hematological investigations, inclusive of bone marrow aspirates.

Cytopenias more commonly observed in males (57.5%) than females (42.5%), with gender distribution of 1.35:1, consistent with the impeachment by Ojha et al.(9), Gupta M et al.(10) and Anita et al.(3). We observed the peak incidence amongst the 10–30 years age bracket, in accordance with studies conducted by Khodke et al(11), Vaidya et al(12), Gupta M et al(10), Reddy GP et al(13) and Munde et al(14).

In our research, clinical manifestations pertinent to pancytopenia were primarily characterized by symptoms related to red blood cell and platelet defects, with infections being rare. A greater number of the patients conferred with generalized weakness (87.74%), seconded by fever (59.43%), which is aligned with the findings of Nanda et al(15) and Munde et al(14). Physical findings included pallor (83.02%), hepatomegaly (24.53%), Splenomegaly (16.98%), bone tenderness (5.66%), and lymphadenopathy (4.72%) which were in arraignment with the indictment by Santra et al(16), Patel et al(17) and Gupta M et al(10).

Megaloblastic anemia (72.64%) emerged as the governing determinant of pancytopenia. This finding is aligned with similar studies by Shyam Sundar et al.(18), Khunger JM et al.(19) and Tilak V et al.(20).

On peripheral blood film examination, dimorphic anemia, accounting for 24.53%, was second in order, in agreement with the arraignment of Munde et al.(14) and Prabhala et al.(21).

Malaria highlights its impact on pancytopenia, concurrent with the indictment by Osama Ishtiaq et al(22) and Aouba et al(23).

In systemic lupus erythematosus (SLE), pancytopenia is resultant of the concurrent suppression of red cell, platelet, and leukocyte production. Hypocellular marrows are the most commonly observed abnormal bone marrow findings in SLE(24,25). In our study, three cases of SLE with hypocellular marrow and pancytopenia were observed..

Pancytopenia associated with a diagnosis of myelodysplastic syndrome (MDS) was observed in a single case, confirmed by hypercellular marrow featuring dysplastic erythroblasts, myeloid cells, and megakaryocytes. This finding is analogous to other similar studies(3,10,20).

CONCLUSION:-

Severe pancytopenia is strongly associated with clinical outcomes and can serve as a prognostic indicator. We conclude that a thorough clinical evaluation is crucial when assessing pancytopenic patients, as it helps narrow down potential causes and guide further investigations. Bone marrow aspiration is a crucial part in this context. Bone marrow aspirates offer superior morphological details compared to biopsies, while biopsy specimens provide a more definite measure of cellularity.

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