

Clinicopathological Diversity of Pancytopenia: A Series of 400 Cases

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ABSTRACT

Introduction: Pancytopenia is characterised by decreased haemoglobin, Packed Cell Volume (PCV), Total Leukocyte Count (TLC) and Platelet Count (PC). Variety of haematological disorders can present with pancytopenia and hence, it has an extensive differential diagnosis. The clinical presentation is based on the severity of pancytopenia as well as its aetiology that warrants a systematic approach to identify the cause of pancytopenia.

Aim: To evaluate the clinicopathological characteristics of various causes of pancytopenia.

Materials and Methods: A total of 400 cases presenting with pancytopenia were clinically assessed, and the haematological investigations were collected from the haematology unit of Department of Pathology, from January 2010 to December 2016. The clinical data of the patients was obtained and the haematological findings were analysed. Bone marrow aspiration (200/400 cases) and biopsy (77/400 cases) were evaluated. Data was analysed using SPSS 22.0 version. The test of significance was performed by chi-square test. A p-value <0.05 was considered of statistical significant.

Results: Among the 400 cases, malaria was the most common cause for pancytopenia (n=108, 27%), followed by megaloblastic anaemia (n=93, 23.25%). Other causes included hypersplenism, liver disease, retroviral disease, acute leukaemia, hypoplastic marrow, sepsis, myelodysplastic syndrome, lymphoma, myelofibrosis, and certain infections. Rare causes such as fanconi anaemia, tuberculosis and mucopolipidosis were also encountered. The most common symptom with which the patients presented was weakness and easy fatigability (n=337, 84.3%) and pallor was the most common physical sign (n=400, 100%).

Conclusion: Pancytopenia is a commonly encountered entity in outpatient clinics which has got a wide variety of differential diagnosis. In certain diseases, pancytopenia is transient and uncomplicated; however, it can be a presenting feature of a life threatening disease as well. Therefore, a systematic approach in evaluating the underlying cause of pancytopenia is essential to plan and implement the timely intervention.

Keywords: Bone marrow, Cytopenia, Malaria, Megaloblastic anaemia

INTRODUCTION

Pancytopenia is a diagnostically challenging entity encountered commonly in routine clinical practice. It is not a disease entity by itself but an expression of an underlying disorder that can either be a haematopoietic or a non haematopoietic condition. It is characterised by the reduction of Red Blood Cells (RBCs), White Blood Cells (WBCs) and platelets below the normal reference range [1]. Initially, most of the clinical manifestations can be attributed to anaemia and thrombocytopenia, however, leukopenia is encountered late in the disease [2]. The underlying mechanisms maybe secondary to decreased marrow production, marrow infiltration, bone marrow suppression, ineffective haematopoiesis or increased peripheral destruction [2,3]. There are many studies in the literature stating the various causes of pancytopenia [1-3]. This study aimed to evaluating the clinicopathological profile of pancytopenia. The study also aimed to know whether there is a need for a bone marrow examination in every case of pancytopenia and also the importance of ancillary tests to identify the cause. To the best of our knowledge, this is the largest study from the Indian subcontinent.

MATERIALS AND METHODS

The present descriptive study was performed in the haematology laboratory of a Kasturba Medical College, Mangaluru, India (from January 2010 to December 2016). Cases with evidence of pancytopenia having Haemoglobin (Hb) less than 11 gm/dL, TLC less than 4000 cells/mm³, Absolute Neutrophil Count (ANC) of less than 1500 cells/mm³ and PC less than 150000/mm³ formed the core of the study [4]. Patients of all age groups were

included in the study while pancytopenia secondary to myelotoxic chemotherapy were excluded. A detailed relevant history with physical examination findings were evaluated. Samples collected in ethylenediaminetetraacetic acid anticoagulated vacutainer were processed through automated haematology analyser (SYSMEX XT-1800i). Laboratory parameters that were analysed included Hb, RBC count, TLC, Differential Leukocyte Count (DLC), ANC and PC. Red cell indices that included Mean Corpuscular Volume (MCV), Mean Corpuscular Haemoglobin (MCH), Mean Corpuscular Haemoglobin Concentration (MCHC), PCV and Red Cell Distribution Width (RDW) were also analysed along with reticulocyte count and Reticulocyte Production Index (RPI). Peripheral smear, stained using Leishman's stain, was evaluated. Bone marrow aspiration was performed only in those cases which had an absolute indication for pancytopenia and the slides were reviewed. Informed consent was taken from the patients due for bone marrow aspiration. Ethical clearance was obtained from the Institutional Ethics Committee.

STATISTICAL ANALYSIS

Data was analysed using SPSS 22.0 version software and the test of significance was performed by chi-square test. A p-value <0.05 was considered of statistical significant.

RESULTS

A total of 400 patients with pancytopenia were included in the study, and bone marrow aspiration was performed in 200 cases, out of which biopsy correlation was available in 77 cases. The age ranged from two days to 90 years (mean±SD age: 34±19.6 years). The

maximum number of cases was noted in fourth decade. There were 245 males and 155 females with male to female ratio of 1.6:1. In the present study, 82 cases were seen in paediatric age group (2 days-18 years, mean age=8 years).

The most common presenting complaint was weakness and easy fatigability (n=337, 84.3%) and pallor was the most common physical sign (n=400, 100%). The clinical features and findings of physical examination are tabulated and distribution of various causes of pancytopenia [Table/Fig-1,2].

Presenting symptoms and signs	Number of cases	Percentage of cases (%)
Presenting symptoms		
Weakness and easy fatigability	337	84.3%
Fever	251	62.8%
Chills and rigors	147	36.75%
Nausea and vomiting	125	31.25%
Loss of weight	120	30%
Exertional breathlessness	89	22.25%
Cough and expectoration	25	6.25%
Bleeding manifestations	72	18%
Sternal tenderness	19	4.75%
Myalgia	12	3%
Physical signs		
Pallor	400	100%
Splenomegaly	267	66.75%
Haepatomegaly	200	50%
Bald tongue	73	18.25%
Bleeding signs	72	18%
Icterus	53	13.25%
Angular stomatitis	53	13.25%
Oedema	48	12%
Lymphadenopathy	48	12%
Gum hypertrophy	7	1.7%

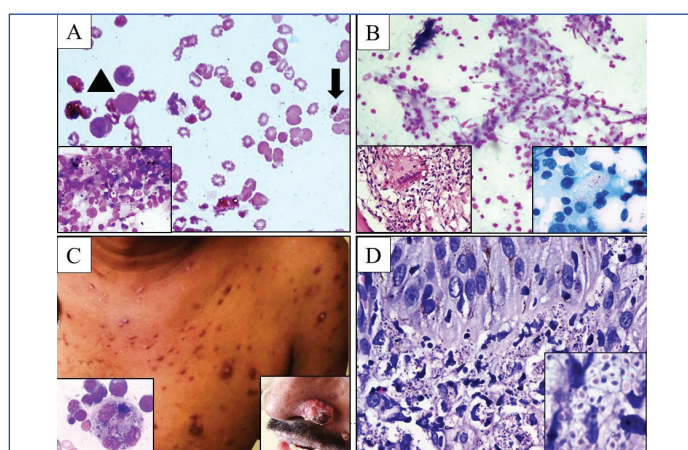
[Table/Fig-1]: Clinical findings in pancytopenia.

Diseases	Number of cases	Percentage of cases (%)	M:F Ratio	Age range
Infections				
Malaria	108	27%	1.7:1	7-47 years
<i>Plasmodium vivax</i>	52	13%	1.3:1	7-66 years
Mixed vivax and falciparum	41	10.25%	1.2:1	15-68 years
<i>Plasmodium falciparum</i>	15	3.75%	1.3:1	10-52 years
HIV	33	8.25%	2.3:1	8-61 years
Sepsis	19	4.75%	0.6:1	1 day-44 years
Dengue fever	08	2%	1.7:1	8-50 years
Tuberculosis	05	1.25%	4:1	39-68 years
Viral fever	02	0.5%	1:1	29-33 years
Nutritional				
Megaloblastic anaemia	93	23.25%	1.8:1	17-87 years
Neoplastic conditions				
Acute myeloid leukaemia	13	3.25%	0.7:1	2-81 years
AML-M2	06	1.5%	2.5:1	4-81 years
AML-M4	04	1%	0.6:1	16-30 years
APL	03	0.75%	1:2	2-24 years

Acute lymphoid leukaemia	12	3%	0.8:1	2-77 years
Hodgkin's lymphoma	01	0.25%	Male	65 years
Non-Hodgkin's lymphoma	07	1.75%	2.5:1	34-69 years
DLBCL	04	1%	3:1	34-64 years
Follicular lymphoma	01	0.25%	Female	55 years
Peripheral T-cell lymphoma	01	0.25%	Male	69 years
Atypical burkitt lymphoma	01	0.25%	Male	52 years
MDS	08	2%	1:1	45-80 years
Myelofibrosis	07	1.75%	1.7:1	29-68 years
Multiple myeloma	02	0.5%	Male	72 years
Hypoplastic marrow				
Idiopathic aplastic anaemia	11	2.75%	2:1	22-80 years
Fanconi anaemia	08	2%	1.3:1	2-14 years
Drug induced aplastic anaemia	03	0.75%	2:1	18-35 years
Hepatitis B infection induced	01	0.25%	Female	22 years
Chronic Liver Disease (CLD)				
Alcoholic liver disease	36	9%	17:1	24-76 years
Viral haepatitis	13	3.25%	1.6:1	13-90 years
Autoimmune hepatitis	04	1%	1:3	25-42 years
Nonalcoholic liver disease	03	0.75%	2:1	16-76 years
Mucopolipidosis	01	0.25%	Male	4 months
Primary hypersplenism				
	02	0.5%	1:1	45-55 years

[Table/Fig-2]: Distribution of various causes of pancytopenia.

M- Male, F-Female, AML-M2- Acute myeloblastic leukaemia with maturation, AML-M4- Acute myelomonocytic leukaemia, APL- Acute promyelocytic leukaemia, DLBCL- Diffuse large B-cell lymphoma, MDS- Myelodysplastic syndrome, HIV- Human immunodeficiency virus



[Table/Fig-3]: a) Pancytopenia in malaria: a case of pyrexia of unknown origin with gametocyte of *Plasmodium falciparum* (arrow) detected in the marrow along with few myeloid precursors (arrow head) (Leishman; 200X). Inset: Bone marrow showing numerous malaria pigment laden macrophages (Leishman; 400X); b) Pancytopenia in tuberculosis: a case of persistent pancytopenia evaluated with bone marrow showing epithelioid granulomas (Leishman; 100X). Inset-left: Epithelioid granuloma with Langhan's giant cell (H&E, 200X). Inset-right: Positive acid fast bacilli in marrow aspirate (Ziehl Neelson; 1000X); c,d) Pancytopenia in disseminated histoplasmosis in a HIV case; c) Disseminated cutaneous nodules with conjunctival involvement. Inset-left: Bone marrow aspirate showed macrophages with engulfed histoplasmosis (Leishman; 1000X). Inset-right: Largest cutaneous nodule on the left nasal ala; d) The conjunctival biopsy showed granulomatous infiltrate and histiocytes with intracellular histoplasma spores (H&E, 1000X). Inset: Intracellular histoplasma capsulatum (H&E, 1000X).

Pancytopenia in Infections

Infections was the most common disease category in the present study which presented with pancytopenia and malaria was the most common infection (n=108, 27%) cases. *Plasmodium vivax* was observed in 52 cases, mixed infection of *Plasmodium vivax* and *Plasmodium falciparum* in 41 cases and remaining 15 cases were of *Plasmodium falciparum* infection [Table/Fig-3a]. The diagnosis of malaria was established by peripheral smear examination and only one case required bone marrow evaluation as it was referred as pancytopenia in a case of pyrexia of unknown origin. On follow up, all patients had haematological recovery with normalisation of blood counts after anti-malarial treatment. Pancytopenia was a common presentation in retroviral disease patients with 23 males and 10 females. Seventeen patients of neonatal sepsis presented as pancytopenia, similarly 30-year-old postpartum patient and a 44-year-old male with multi organ dysfunction syndrome also presented with pancytopenia secondary to sepsis.

We encountered five cases of tuberculosis which showed the presence of epithelioid granulomas and Acid-Fast Bacilli (AFB) positivity in bone marrow [Table/Fig-3b]. The blood counts improved after Anti-Tubercular Therapy (ATT) treatment in these patients. Transient pancytopenia was evidenced in patient with dengue fever (n=8, 2%) and viral fever (n=2, 0.5%).

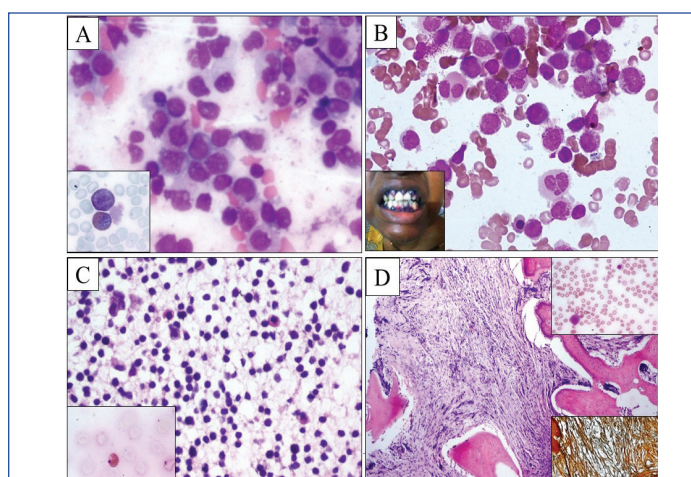
One case of retroviral disease with disseminated histoplasmosis was encountered. The bone marrow showed numerous macrophages with intracytoplasmic histoplasma capsulatum organisms. The Periodic Acid-Schiff (PAS) stain demonstrated the capsule of the organism [Table/Fig-3c,d].

Pancytopenia in Anaemia

Megaloblastic anaemia (n=93, 23.25%) was the second most common disease category in the present study. Morphological evidence of associated microcytic hypochromic anaemia was observed in (n=65, 69.9%). These cases were evaluated for serum vitamin B12 and folic acid assays. The aetiology observed in the study group were vitamin B12 deficiency (n=27, 29%), folic acid deficiency (n=12, 12.9%), combined vitamin B12 and folic acid deficiency (n=6, 6.5%), chronic liver disease (n=4, 4.5%) and malabsorption syndrome (n=1, 0.25%).

Pancytopenia with Malignancy

In the present study, a wide range of neoplastic conditions presented with pancytopenia as depicted and [Table/Fig-2,4a-d]. Four cases of Acute Myelomonocytic Leukaemia (AML-M4) had developed

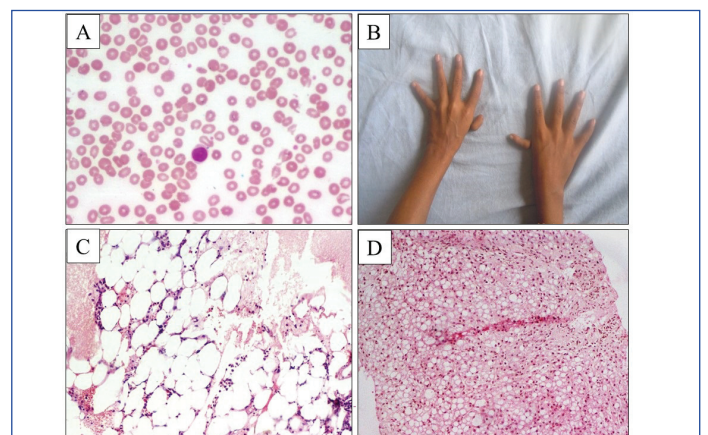


[Table/Fig-4]: a) Pancytopenia in AML: bone marrow aspirate showing myeloblasts (400X; Leishman). Inset: MPO positivity in blasts (1000X; Leishman); b) Pancytopenia in AML: bone marrow aspirate with abnormal hypergranular promyelocytes in a case of APL (400X; Leishman). Inset: a case of AML-M4 with gum hypertrophy; c) Pancytopenia in all: bone marrow biopsy with diffuse infiltration by lymphoblasts. (200X; H&E). Inset: PAS positivity in lymphoblasts (1000X; Leishman); d) Pancytopenia in myelofibrosis: bone marrow biopsy showing extensive fibrosis (40X; H&E). Inset-top right: Leucoerythroblastic blood picture in myelofibrosis (400X; Reticulin stain). Inset-bottom right: Grade 3 reticulin fibres in marrow (40X; Reticulin stain).

in a background of myelodysplastic syndrome. Atypical Burkitt's lymphoma patient was a 52-year-old man with fever, cough, expectoration and unexplained bleeding tendency. A terminal ileal ulcer biopsy revealed extranodal atypical Burkitt's lymphoma. The neoplastic cells were CD45, CD20, Ki-67 and CD10 positive with focal positivity to BCL2 and were MUM1 negative. Bone marrow involvement was seen. Hodgkin's lymphoma case showed involvement of bone marrow with lymph node biopsy revealing classical Hodgkin's lymphoma (lymphocyte depletion type; diffuse fibrosis subtype). On immunohistochemistry, the Reed-sternberg cells were CD15 and CD30 positive, and CD20 negative.

Pancytopenia with Hypoplastic Marrow

Pancytopenia secondary to hypoplastic marrow was seen in 23 (5.75%) patients in present study. On evaluation, these cases were categorised as idiopathic aplastic anaemia (n=11, 2.75%), Fanconi anaemia (n=8, 2%), drug induced hypoplastic marrow (n=3, 0.75%)



[Table/Fig-5]: Pancytopenia in fanconi anaemia: a) Peripheral smear showing severe neutropenia (Leishman; 400X); b) Deformity of the hands in fanconi anaemia; c) Bone marrow biopsy with hypoplastic marrow (H&E, 40X); d) Pancytopenia in mucopolipidosis: Liver biopsy of four month old child with extensive infiltration by storage cells (H&E, 400X).

and hepatitis B (n=1, 0.25%) [Table/Fig-5a-c]. Patient with hepatitis B infection case was referred for evaluation of severe pancytopenia where marrow showed marked hypoplasia at presentation. The three cases of drug induced hypoplastic marrow were secondary to phenytoin and carbamazepine for epilepsy, methotrexate therapy for rheumatoid arthritis and prolonged antithyroid medication for hyperthyroidism.

Pancytopenia with Chronic Disorders

In the present study, CLD was an aetiological cause of pancytopenia in (n=57, 14.25%) of cases. An associated megaloblastic anaemia was seen in (n=14, 24.6%) of CLD patients, and, functional hypersplenism was noted in (n=8, 14%) cases of pancytopenia. The causes of CLD was found to be alcoholic liver disease (n=36, 9%), viral hepatitis (n=13, 3.25%), autoimmune hepatitis (n=13, 1%), non alcoholic steatohepatitis (n=3, 0.75%) and mucopolipidosis (n=1, 0.25%). The liver biopsy in mucopolipidosis revealed storage cell infiltration [Table/Fig-5d]. Primary idiopathic hypersplenism was diagnosed in two cases.

The haematological parameters of patients with pancytopenia revealed that the Hb was lowest in megaloblastic anaemia (4.62 gm/dL), lowest TLC in acute leukaemia (2077.93 cells) and lowest PC in retroviral disease (38,000 cells) and dengue fever (38,000 cells) compared to other causes and were also found statistically significant (p-value: 0.02, 0.045 and 0.001 respectively). High MCV of more than 100 was seen in megaloblastic anaemia (n=74, 79.22%), retroviral disease (n=9, 27.27%), myelodysplastic syndrome (n=2, 25%), aplastic anaemia (n=4, 17.39%), CLD (n=9, 15.78%) and acute leukaemia (n=2, 8%). An MCV of more than 99.6 fL was seen in (n=93, 100%) cases of megaloblastic anaemia. Various haematological parameters between megaloblastic and non

megaloblastic causes of macrocytosis were statistically insignificant with a p-value of >0.05. Reticulocyte count and RPI were found statistically significant with a p-value of <0.05 and hypoplastic marrow presented with lowest reticulocyte count and RPI compared to other causes of pancytopenia.

The bone marrow aspiration was hypocellular in (n=34, 17%) cases, hyper cellular (n=124, 62%) and normocellular (n=8, 4%) and yielded only sinusoidal blood in (n=34, 17%) cases. In the present study, the common causes of hypocellular marrow were hypoplastic marrow (n=23, 11.5%) and myelofibrosis (n=8, 4%). Bone marrow biopsy evaluation was an important diagnostic tool to evaluate certain causes of pancytopenia such as aplastic anaemia, myelofibrosis and abnormal localisation of immature precursors in myelodysplastic syndrome.

DISCUSSION

Pancytopenia can be detected when an abnormal clinical finding such as easy fatigability, infection or bleeding is subjected for further evaluation or sometimes, can even be spotted incidentally during routine checkups. It is a presenting feature in many diseases, and the severity and prognosis depends on the aetiological cause of pancytopenia. Differences in various methodology, stringency of criteria, topographical variations, and duration of observation and follow up, genetic variability and cytotoxic exposure directly influence the incidence of disorders leading to pancytopenia [3].

The common aetiologies for pancytopenia in the present study were malaria, megaloblastic anaemia, CLD, retroviral disease and acute leukaemia together accounting for (n=320, 80%) cases of pancytopenia with malaria and megaloblastic anaemia exclusively accounting for (n=201, 50.25%) of cases. In contrast, aplastic anaemia has been reported as the most common cause of pancytopenia throughout the world and this difference can be attributed to improved nutritional conditions and lower prevalence of infectious diseases in the west [5]. Malaria and megaloblastic anaemia can be easily detected and are the treatable causes and hence, should be reported promptly [6]. A diagnosis of megaloblastic anaemia does not warrant a bone marrow examination routinely, however, it may be performed to rule out other haematological causes if the diagnosis is not straightforward and in peripheral centers where folic acid and Vitamin B12 levels estimation are not available routinely [7]. In the literature, megaloblastic anaemia is the commonest cause of pancytopenia in India unlike the present study, where malaria constituted for (n=108, 27%) of cases which explains the endemicities of malaria in our region [3,6,7]. Bhatnagar SK et al., and Jain A and Naniwadekar M, have reported malaria as a

cause of pancytopenia [8,9]. In a study by Hamid GA and Shukry SA, conducted in Yemen, the most common cause of pancytopenia was malaria (n=23, 30.6%) [4].

Similar to the present study, wide distribution of causes of pancytopenia were also encountered in various studies conducted in the past and results of age and sex distribution, and presenting complaints were similar [Table/Fig-6] [1,3-8,10,11]. In the present study, the age ranged widely (two days-90 years) and pancytopenia was seen even during neonatal period.

Aplastic anaemia has been reported as one of the common aetiological cause of pancytopenia with a wide incident range of 10-52% [3,10,12,13]. Kumar R et al., has reported the highest incidence with (n=49, 29.5%) cases of hypoplastic marrow [12]. In a retrospective analysis of 118 patients with hypocellular marrow, Pol S et al., reported 61 patients with aplastic anaemia of undetermined cause, 19 patients with hepatitis induced aplasia and 38 patients with an inherited form [14]. In the present study, the common cause of hypoplastic marrow was idiopathic aplastic anaemia 13 (3.25%) cases.

Paediatric pancytopenia was seen in 68 (17%) cases in present study and malaria (n=23, 5.75%) was found to be the commonest cause of pancytopenia in paediatric age group as well. The other causes of paediatric pancytopenia were sepsis (n=17, 4.25%), acute leukaemia (n=12, 3%), hypoplastic marrow (n=7, 1.75%), CLD (n=3, 0.75%), megaloblastic anaemia (n=3, 0.75%), dengue fever (n=2, 0.5%), and a case of glycogen storage disorder (n=1, 0.25%). In a study conducted by Gayathri BN and Rao KS, paediatric pancytopenia accounted for (n=31, 29.8%) of cases with megaloblastic anaemia being the commonest cause followed by aplastic anaemia and similar outcomes were also reported by Bhatnagar SK et al., [1,8]. Gupta V et al., studied 105 patients aged 1.5 to 18 years presenting with pancytopenia and reported a mean age of 8.6 years [15]. In the same study, commoner causes of pancytopenia reported were aplastic anaemia (n=45, 43%) and acute leukaemia (n=26, 25%), and megaloblastic anaemia (n=7, 6.7%) [15].

An MCV of more than 99.6 fL was observed in 100% of megaloblastic anaemia cases thus, proving the sensitivity of the parameter in the diagnosis of megaloblastic anaemia. Hamid GA and Shukry SA, analysed MCV in various diseases causing pancytopenia and the results were comparable with the present study [Table/Fig-7] [4]. Macrocytosis in aplastic anaemia is a known fact [16]. A study conducted by Gupta PK et al., to differentiate aplastic anaemia and megaloblastic anaemia using red cell indices states that MCV in megaloblastic anaemia was higher in contrast to aplastic

Study	Country	No of cases	MC* cause	Second MC* cause
Kumar R et al., [12]	India	166	Aplastic anaemia (30%)	Megaloblastic anaemia (22%)
Khodke K et al., [3]	India	50	Megaloblastic anaemia (44%)	Aplastic anaemia (14%)
Khunger JM et al., [6]	India	144	Megaloblastic anaemia (72%)	Aplastic anaemia (14%)
Jha A et al., [13]	Nepal	148	Aplastic anaemia (29.05%)	Megaloblastic anaemia (23.64%)
Gupta V et al., [15]	India	155	Aplastic anaemia (43%)	Acute leukaemia (25%)
Hamid GA and Shukry SA [4]	Yemen	75	Hypersplenism (28%)	Malaria (17.3%)
Santra G and Das BK [10]	India	111	Aplastic anaemia (22.72%)	Hypersplenism (13.51%)
Gayathri BN and Rao KS [1]	India	104	Megaloblastic anaemia (74.04%)	Aplastic anaemia (19%)
Makheja KD et al., [5]	Pakistan	62	Megaloblastic anaemia (41.9%)	Acute myeloid leukaemia (27.4%)
Jain A and Naniwadekar M [9]	India	250	Hypersplenism (29.2%)	Infections (25.6%)
Yokus O and Gedik H [7]	Istanbul	137	Vitamin B12 deficiency (17%)	Chronic liver disease (15%)
Present study	India	400	Malaria (27%)	Megaloblastic anaemia (23.25%)

[Table/Fig-6]: Comparison of common causes of pancytopenia among various studies.

MC- Most common

Diseases	MCV	
	Hamid GA and Shukry SA, [4]	Present study
Malaria	80.8	81.5
Aplastic anaemia	88.4	91.4
Megaloblastic anaemia	101.2	100.5
Myelofibrosis	82.2	91.2
Acute leukaemia	86.1	89.7
Myelodysplastic syndrome	94	96.8

[Table/Fig-7]: Comparison of MCV of present study with Hamid GA and Shukry SA, [4].

MCV- Mean corpuscular volume

anaemia, where it was not statistically significant [16]. In addition, the presence of macroovalocytes and hypersegmented neutrophils in the former and the bone marrow biopsy findings in the latter will definitely help in differentiating the two entities [16]. The MCV will be increased secondary to CLD due to toxic effect of excess alcohol intake. Macrocytic anaemia is relatively common in patients with a myelodysplastic syndrome [17,18]. Macrocytosis, hypogranular neutrophils along with other features of dyshaematopoiesis and a normal serum levels of vitamin B12 and folic acid levels are found in peripheral blood and bone marrow of MDS [18].

The significance of bone marrow examination in evaluating the aetiology of pancytopenia has been well emphasised in earlier studies [19]. However, bone marrow examination is not a requirement in every pancytopenic patient, especially when a diagnosis can be made on a peripheral smear or the ancillary tests. However, in patients with sepsis, or bleeding when associated with significant neutropenia or thrombocytopenia, bone marrow evaluation is mandatory to rule out marrow suppression. Presence of blasts in peripheral smear, hypogranular or hyposegmented neutrophils, refractory cytopenias, unexplained splenomegaly, monoclonal gammopathy, or evaluation of metastatic tumours also requires bone marrow examination [12,19]. However, in megaloblastic anaemia and reactive marrow with obvious causes such as CLD, HIV and malaria bone marrow aspiration and biopsy may not provide any additional information and can be avoided. Simultaneous, bone marrow aspiration and biopsy should be performed where diagnosis is not straightforward that cannot be established using the other blood tests. While aspiration yields greater morphological details over biopsy, biopsy is superior to evaluate an accurate and more reliable cellularity index. It is noted that marrow infiltration, fibrosis and granulomas that are generally missed on aspiration can be easily detected on biopsy. Hence, aspiration and biopsy complement each other in providing a rapid yet precise diagnosis in the background of pancytopenia [12,19].

LIMITATION

The study is limited by lack of follow up in a small proportion of cases. A larger multicentric prospective study with emphasis on follow up for haematological recovery of blood counts may guide in understanding the clinical outcomes in various causes of

pancytopenia.

CONCLUSION

This study highlights that in a developing country like India, where nutritional anaemia and aplastic anaemia are found to be the common causes for pancytopenia, malaria can be an important cause in the endemic regions, like ours. However, the management of pancytopenia is based on identifying and treating the underlying cause and also providing an adequate supportive therapy to deal with consequences of cytopenias. This necessitates a systematic approach in determining the cause since pancytopenia has a wide range of differential diagnosis. Awareness about the various causes, which is generally region specific and about the specific laboratory findings associated with each one, one can narrow down the differential diagnosis, guiding the clinician to initiate appropriate treatment modality and also to avoid unnecessary invasive procedures when not indicated.

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FINANCIAL OR OTHER COMPETING INTERESTS: None.

Date of Submission: **Sep 01, 2017**

Date of Peer Review: **Sep 14, 2017**

Date of Acceptance: **Jan 04, 2018**

Date of Publishing: **Mar 01, 2018**