A cross-sectional study of the clinical profile and aetiological spectrum of pancytopenia in a tertiary care centre

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ABSTRACT

Introduction: Pancytopenia is a common haematological problem. It is suspected when a patient presents with anaemia, prolonged fever and a bleeding tendency. Pancytopenia has multiple causes, but the frequency of these causes has been reported in a limited number of studies. The present study was conducted to assess the aetiological pattern, clinical profile and bone marrow morphology of pancytopenia patients.

Methods: A total of 111 adult pancytopenia patients aged 13 to 65 years were studied during a one-year period to determine their clinical features, peripheral blood pictures and bone marrow morphologies. The aetiological pattern was assessed through the relevant investigations in the respective patients.

Results: 45.95 percent of the pancytopenic patients had a hypocellular marrow, while 54.05 percent had normocellular or hypercellular marrow. Idiopathic aplastic anaemia (20.72 percent) was the commonest cause of pancytopenia, followed by hypersplenism due to chronic liver disease (11.71 percent). Other important causes were kala-azar (nine percent), megaloblastic anaemia, systemic lupus erythematosus (SLE), infections and drug inducement. Infections such as kala-azar, falciparum malaria and enteric fever, megaloblastic anaemia as well as SLE were found to be treatable and reversible causes of pancytopenia.

Conclusion: As a large number of pancytopenic patients have a reversible aetiology, early and proper diagnosis may be life-saving.

Keywords: aplastic anaemia, bone marrow, hypersplenism, kala-azar, pancytopenia

Singapore Med J 2010; 51(10): 806-812

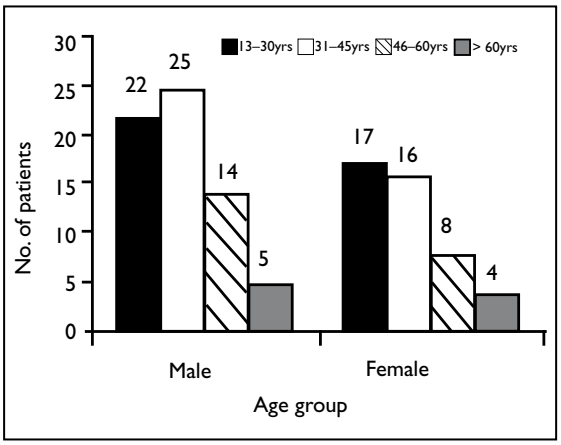

Fig. 1 Age and gender distribution of patients with pancytopenia.

INTRODUCTION

Pancytopenia refers to a reduction in all the three formed elements of blood: red blood cells, white blood cells and platelets. It should be suspected on clinical grounds when a patient presents with pallor, prolonged fever and a tendency to bleed. The aetiology of pancytopenia varies in different populations depending on the differences in age patterns, nutritional status, climate and the prevalence of infections. The aim of this study was to identify the clinical profile, aetiological spectrum and bone marrow morphology of pancytopenia patients. The study focused on identifying easily treatable and reversible causes of pancytopenia.

METHODS

This observational study was conducted for a period of one year. Patients of both genders who presented to the outpatient department (OPD) and inpatients of the Department of Medicine, Medical College and Hospital Kolkata, who had peripheral blood pancytopenia were recruited into the study. The inclusion criteria included patients with pancytopenia as detected on peripheral blood smear, who consented to bone marrow examination, and patients aged 13–65 years. The exclusion criteria were patients aged < 13 years who

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Table I. Age and gender distribution of the patients and causes of pancytopenia.

Cause	No. of patients (%)						
	Age (yrs)				Total	Male (n= 66)	Female (n = 45)
	13–30	31–45	46–60	> 60			
Cellular marrow*	16 (14.41)	26 (23.42)	13 (11.71)	5 (4.50)	60 (54.05)	36 (32.43)	24 (21.62)
Hypersplenism	2 (1.80)	8 (7.21)	5 (4.50)	-	15 (13.51)	11 (9.91)	4 (3.60)
Megaloblastic anaemia	2 (1.80)	1 (0.90)	-	1 (0.90)	4 (3.60)	1 (0.90)	3 (2.70)
Mixed nutritional deficiency anaemias	4 (3.60)	3 (2.70)	-	-	7 (6.31)	2 (1.80)	5 (4.50)
Kala-azar	2 (1.80)	5 (4.50)	3 (2.70)	-	10 (9.01)	7 (6.31)	3 (2.70)
Falciparum malaria	1 (0.90)	1 (0.90)	-	-	2 (1.80)	2 (1.80)	0
Histoplasma	-	1 (0.90)	-	-	1 (0.90)	1 (0.90)	0
Disseminated tuberculosis	-	1 (0.90)	-	-	1 (0.90)	1 (0.90)	0
SLE	2 (1.80)	3 (2.70)	-	-	5 (4.50)	0	5 (4.50)
Felty's syndrome	-	1 (0.90)	-	-	1 (0.90)	1 (0.90)	0
CLL	-	-	-	1 (0.90)	1 (0.90)	1 (0.90)	0
Bonemarrow NHL	-	-	1 (0.90)	-	1 (0.90)	1 (0.90)	0
Subleukaemic leukaemia/AML	2 (1.80)	-	-	-	2 (1.80)	1 (0.90)	1 (0.90)
Myelodysplastic syndrome	-	-	2 (1.80)	1 (0.90)	3 (2.70)	2 (1.80)	1 (0.90)
Multiple myeloma	-	-	-	1 (0.90)	1 (0.90)	1 (0.90)	-
No cause identified	1 (0.90)	2 (1.80)	2 (1.80)	1 (0.90)	6 (5.41)	4 (3.60)	2 (1.80)
Hypocellular†	23 (20.72)	15 (13.51)	9 (8.12)	4 (3.60)	51 (45.95)	30 (27.03)	21 (18.92)
Idiopathic	13 (11.71)	7 (6.31)	2 (1.80)	1 (0.90)	23 (20.72)	14 (12.61)	9 (8.12)
Secondary	10 (9.01)	8 (7.21)	7 (6.31)	3 (2.70)	28 (25.23)	16 (14.41)	12 (10.81)
NSAIDs (ibuprofen/ diclofenac)	1 (0.90)	1 (0.90)	-	-	2 (1.80)	1 (0.90)	1 (0.90)
Linezolid	-	-	1 (0.90)	-	1 (0.90)	1 (0.90)	-
Chloramphenicol	-	-	1 (0.90)	-	1 (0.90)	1 (0.90)	-
Chemotherapy	2 (1.80)	1 (0.90)	3 (2.70)	2 (1.80)	8 (7.21)	5 (4.50)	3 (2.70)
MTX in RA	2 (1.80)	1 (0.90)	-	-	3 (2.70)	-	3 (2.70)
Dengue	1 (0.90)	-	-	-	1 (0.90)	1 (0.90)	-
Enteric fever	-	1 (0.90)	-	1 (0.90)	2 (1.80)	2 (1.80)	-
Hepatitis B	-	1 (0.90)	1 (0.90)	-	2 (1.80)	2 (1.80)	-
HIV	1 (0.90)	1 (0.90)	-	-	2 (1.80)	1 (0.90)	1 (0.90)
Other virus	1 (0.90)	1 (0.90)	-	-	2 (1.80)	1 (0.90)	1 (0.90)
SLE	2 (1.80)	1 (0.90)	-	-	3 (2.70)	-	3 (2.70)
Hypoplastic PNH	-	-	1 (0.90)	-	1 (0.90)	1 (0.90)	-

* Mean age ± 2SD of patients was 38 ± 24 years and the male-female ratio was 3:2.
† Mean age ± 2SD of patients was 34 ± 26 years and the male-female ratio was 10:7.
CLD: chronic liver disease; NHL: non-Hodgkin's lymphoma; AML: acute myeloid leukaemia; NSAIDs: nonsteroidal anti-inflammatory drugs; MTX: methotrexate; RA: rheumatoid arthritis; SLE: systemic lupus erythematosus; CLL: chronic lymphocytic leukaemia; HIV: human immunodeficiency virus; PNH: paroxysmal nocturnal haemoglobinuria; SD: standard deviation

attended the paediatric OPD, patients aged > 65 years (bone marrow cellularity declines physiologically with age), and those with a history of recent blood transfusion.

A detailed relevant history, including drug intake, was obtained and a meticulous physical examination was conducted for all patients. Complete blood counts (haemoglobin [Hb], total leucocyte count, differential leucocyte count, platelet, reticulocyte and absolute neutrophil count [ANC]) as well as bone marrow aspirations were performed in all patients. Complete blood count was performed using an automated blood counter. In cases of very low counts and abnormal cells, a manual review of the instrument's results was performed using the improved Neubauer counting chamber (Hausser Scientific, Blue Bell, PA, USA). Bone marrow trephine biopsy was conducted in dry tap, insufficient cells or hypoplastic marrow. The peripheral blood and bone marrow pictures were

Table II. Clinical manifestations of pancytopenia patients with hypocellular and cellular marrow.

Clinical manifestation	No. of patients													p-value
	Total (%)	Hypocellular marrow					Cellular marrow							
		All	AA (n = 23)	DR (n = 15)	INF (n = 9)	SLE (n = 3)	All	HS (n = 15)	MA (n = 4)	MDS (n = 3)	FM (n = 2)	KZ (n = 10)	SLE (n = 5)	
Weakness	50 (45.04)	23	11	5	6	1	27	8	2	1	2	8	2	> 0.05
Fatigability	83 (74.77)	45	21	11	9	3	38	9	3	2	2	6	2	> 0.05
Anorexia	78 (70.27)	30	13	7	7	2	48	12	2	1	2	7	3	> 0.05
Weight loss	24 (21.62)	6	3	0	2	1	18	4	2	1	0	5	0	> 0.05
Dizziness	37 (33.33)	21	15	3	2	1	16	5	1	0	2	3	0	> 0.05
Pallor	94 (84.68)	46	22	13	8	2	48	12	3	2	2	9	2	> 0.05
Respiratory distress	36 (32.43)	20	11	5	4	0	16	5	0	0	2	2	1	> 0.05
Bleeding manifestation	46 (41.44)	31	15	9	5	2	15	8	0	1	1	0	1	> 0.05
Joint/leg pain	14 (12.61)	6	0	3	0	3	8	0	0	0	0	0	5	> 0.05
Fever	56 (50.45)	23	5	8	9	1	33	5	0	1	2	10	3	> 0.05
Splenomegaly	49 (44.14)	5	0	1	3	0	44	15	0	3	2	10	5	0.0001
Hepatomegaly	27 (24.32)	2	0	0	2	0	25	3	0	2	2	10	4	0.0001
Lymphadenopathy	7 (6.31)	2	0	0	2	0	4	0	0	0	0	0	1	> 0.05

AA: idiopathic aplastic anaemia; DR: drugs; INF: infections; SLE: systmic lupus erythematosus HS: hypersplenism; MA: megaloblastic anaemia; MDS: myelodysplastic syndrome; FM: falciparum malaria; KZ: kala-azar

reviewed by an investigator who had no knowledge of the patient's clinical presentation. Pancytopenia was defined as Hb < 12 gm%, leucocyte count < 4×10^9/L and platelet count < 100×10^9/L. Anaemia was defined as mild (Hb 9–12 gm%), moderate (Hb 5–9 gm%) and severe (Hb < 5 gm%). Leucopenia was defined as mild (leucocyte count > 3,000/mm^3), moderate (leucocyte count 1,000–3,000/mm^3) and severe (leucocyte count < 1,000/mm^3). Thrombocytopenia was defined as mild (platelet count > 50,000/mm^3), moderate (platelet count 20,000–50,000/mm^3) and severe (platelet count < 20,000/mm^3). Other investigations were performed in selected cases according to their provisional diagnosis, including malarial parasite and antigen, serological tests for enteric fever, blood culture, anti-nuclear factor (immunofluorescent method), rheumatoid factor, liver function test, assay of vitamin B_{12} and folic acid, enzyme-linked immunosorbent assay for the human immunodeficiency virus (HIV) I and II, and the hepatitis B surface antigen (HBsAg).

The patients' history, physical examination results and haematological parameters were recorded on the study proforma and the data was tabulated. The statistical methods used included descriptive statistics (mean, median and standard deviation [SD]). The data was expressed as number and percentage, and analysed using GraphPad QuickCalcs online statistical calculators (GraphPad Software Inc, La Jolla, CA, USA). Fisher's exact test was used for the assessment of statistical significance.

RESULTS

Out of a total of 215 patients who were recruited in the study, 111 adult patients were selected for inclusion, of which 66 were male and 45 were female (male-to-female ratio 1.47:1) (Fig. 1). The mean age of the patients was 36.9 (range 13–65) years. 70% of the patients were from the rural areas. In terms of the socioeconomic status, 57% of the patients were from the middle income group, 30% were from the lower income group and 13% were from the higher income group. The most common clinical feature in our study was pallor (84.68%), followed by fatigability (74.77%). Bleeding from various sites was

Table III. The severity of pancytopenia in relation to bone marrow cellularity.

Bone marrow cellularity and parameter	No. (%)		
	Mild	Moderate	Severe
Hypocellular (n = 51)			
Hb%	-	5 (9.80)	46 (90.20)
TLC	6 (11.76)	40 (78.43)	5 (9.80)
Platelet count	17 (33.33)	19 (37.25)	15 (29.41)
Cellular* (n = 60)			
Hb%	3 (5.00)	39 (65.00)	18 (30.00)
TLC	39 (65.00)	21 (35.00)	-
Platelet count	50 (83.33)	9 (15.00)	1 (1.67)

* Includes normocellular and hypercellular.
Hb: haemoglobin; TLC: total leucocyte count

encountered by 41.44% of the patients, and this included skin (25.23%) and gum (32.43%) bleeding, epistaxis (14.41%), haematemesis (14.41%), melaena (10.81%), menorrhagia (10.81%) and retinal haemorrhage (18.92%). Other common features were fever (50.45%), weakness (45.04%) and respiratory distress (32.43%). Splenomegaly (44.14%), hepatomegaly (24.32%) and lymphadenopathy (6.31%) were also noted.

The haematological parameters revealed a mean haemoglobin concentration of 5.90 ± 1.90 g/dl. Anaemia was severe in 57.66%, moderate in 39.64% and mild in 2.70% of the cases. The leucocyte count was 850–3,800/mm^3 of blood (mean 2,633/mm^3). 54.95% of the patients had moderate leucopenia, while 40.55% and 4.50% had mild and severe leucopenia, respectively. The mean ANC was 705.40 ± 530.10/mm^3. ANC < 200/ul was observed in three patients, including one with paroxysmal nocturnal haemoglobinuria (PNH) and two with aplastic anaemia. The platelet count was 4,500–100,000 (mean 45.20 ± 38.60 × 10^3)/mm^3 of blood. 60.36% of the patients had a mild degree of thrombocytopenia, 25.23% had moderate and 14.41% had severe thrombocytopenia. Four patients had platelet counts < 5,000/mm^3, including two with aplastic anaemia, one with acute myeloid leukaemia and one with PNH.

The bone marrow study showed that 45.95% of the patients had hypocellular bone marrow and 54.05% had cellular marrow (including hypercellular [37.83%] and normocellular [16.22%]). Various aetiological factors were identified for both cellular and hypocellular marrow patients (Table I). The clinical manifestations based on the aetiology of pancytopenia are presented in Table II. The majority of the hypocellular bone marrow patients had severe anaemia (90.20%), moderate leucopenia (78.43%) and moderate thrombocytopenia (37.25%). On the other hand, the majority of the cellular bone marrow patients had a moderate degree of anaemia (65%), mild leucopenia (65%) and mild thrombocytopenia (83.33%) (Table III). Anaemia was most marked in patients with idiopathic aplastic anaemia (AA). The mean haemoglobin concentration in AA was 4.70 ± 2.40 g/dl. Severe anaemia was more common in patients with a hypocellular marrow (90.20%) than in those with a cellular marrow (30%) ($p < 0.001$).

DISCUSSION

Pancytopenia has either cellular or hypocellular bone marrow morphology. There are very few studies in the literature that explore the various aetiological factors of pancytopenia with hypocellular and cellular marrows.[1-9] The common causes of pancytopenia vary in different studies.[1-9] In the present study, 45.95% of the pancytopenic patients were found to have hypocellular bone marrow, and AA accounted for the majority (23 out of 51 patients) of them. AA (22.72%) was also the commonest cause of pancytopenia as a whole. In a retrospective analysis of 118 patients with hypocellular marrow, Pol et al reported 61 patients with AA of an undetermined cause, 19 patients with hepatitis-associated aplasia and 38 patients with an inherited form.[10] Secondary causes of hypocellular marrow in our study included drugs (e.g. nonsteroidal anti-inflammatory drugs), linezolid, chloramphenicol, chemotherapy, methotrexate in rheumatoid arthritis, infections (dengue, enteric fever, hepatitis B, HIV and other viral infections), systemic lupus erythematosus (SLE) and hypoplastic PNH. The only case of PNH in our study had pancytopenia with hypoplastic marrow and splenomegaly diagnosed by the Ham test, and a deficiency of CD55 and CD59. A literature search revealed that bone marrow is usually cellular in PNH, with marked to massive erythroid hyperplasia, but sometimes, a patient with PNH becomes less haemolytic and more pancytopenic with a bone marrow picture of AA.[11]

In our study, out of the eight SLE patients, three had hypocellular marrow, among whom one was on pulse cyclophosphamide therapy (third cycle). Bone marrow hypoplasia in SLE may be a result of disease activity. Bone marrow involvement is also common with cytotoxic drugs in SLE. In a study of peripheral cytopenias in 21 SLE patients without any cytotoxic therapy, global hypocellularity was found in 47.6% of the patients, increased reticulin proliferation in 76.2% (with myelofibrosis in one patient) and necrosis in 19% of the patients.[12] In our study, enteric fever was responsible for two cases of hypocellular marrow due to haemophagocytosis. Varying degrees of cytopenias have been reported in enteric fever.[13,14] Pancytopenia in enteric fever is caused by various mechanisms. Bone marrow may undergo histiocytic hyperplasia along with haemophagocytosis or complete necrosis. Immune mediated cellular destruction,

Table IV. Aetiological spectrum of pancytopenia derived from various Indian studies.

Study; location	Age group (yrs)	No. of patients	Commonest cause	Other common causes	Rare causes
Kumar et al;[1] Delhi	All ages	166	AA (29.51%)	MA (22.28 %), aleukaemic leukaemia or lymphoma, hypersplenism	-
Khunger et al;[2] Delhi	2–70	250	MA (72%)	AA (14%)	Subleukaemic leukaemia, MDS, KZ, malaria, NHL, WM, dTB, myelofibrosis, MM
Tilak et al;[3] Chandigarh	5–70	77	MA (68%)	AA (7.7%)	Malaria, KZ, NHL, AML, haemophagocytic syndrome, drug-induced, dTB, MM, WM, myelofibrosis
Varma et al;[4] Chandigarh	Adults	202	AA (40.6%)	MA (23.26%), AML (12.8%)	-
Gupta et al;[5] Varanasi	1.5–18	105	AA (43%)	Acute leukaemia (25%), infection (KZ commonest), MA (6.7%)	MDS, enteric fever, malaria, sepsis, dTB, NHL, TSS, neuroblastoma
Khodke et al;[6] Delhi	3–69	50	MA (44%)	AA (14%), KZ (14%)	MM, HIV infection, MDS, dTB drug-induced, erythroleukaemia
Present study;	13–65	111	AA (22.72%)	Hypersplenism (CLD), KZ (9%), mixed deficiency anaemia, MA, SLE, drugs	Falciparum malaria, dTB, NHL, histoplasma, CLL, subleukaemic leukaemia, AML, MM, MDS, Felty's syndrome, enteric fever, dengue, hepatitis B, HIV, other viral infections, hypoplastic PNH

AA: aplastic anaemia; MA: megaloblastic anaemia; WM: Waldenstrom's macroglobulinaemia; dTB: disseminated tuberculosis; KZ: kala-azar; MM: multiple myeloma; AML: acute myeloid leukaemia; CLD: chronic liver disease; SLE: systemic lupus erythematosus; MDS: myelodysplastic syndrome; NHL: non-Hodgkin's lymphoma; CLL: chronic lymphocytic leukaemia; HIV: human immunodeficiency virus; PNH: paroxysmal nocturnal haemoglobinuria; TSS: tropical splenomegaly syndrome

hypersplenism and transient disseminated intravascular coagulation are other contributing mechanisms.[15] Garewal et al reported gram-negative septicaemia leading to bone marrow necrosis in two patients.[16] One case of dengue in our study had hypoplasia of the bone marrow due to haemophagocytosis.

In the present study, 54.05% of the patients had cellular marrow (normocellular or hypercellular). Hypersplenism was the most common cause of pancytopenia with cellular marrow. Out of the 15 cases of hypersplenism, 13 were secondary to portal hypertension (cirrhosis) and two had tropical splenomegaly syndrome. Megaloblastic anaemia was relatively uncommon compared to other series.[2,3,6,9] However, kala-azar was an important cause of pancytopenia (ten cases), along with SLE and myelodysplastic syndrome (MDS). Rare causes included falciparum malaria, histoplasma, disseminated tuberculosis, Felty's syndrome, bone marrow non-Hodgkin's lymphoma, subleukaemic leukaemia and multiple myeloma. The cause was not identified in six patients. A patient with chronic lymphocytic leukaemia (CLL) had pancytopenia with cellular marrow due to bone marrow infiltration. Pancytopenia in CLL can be explained by the immunologic mechanism, bone marrow infiltration or hypersplenism. In addition, five of the SLE patients had hypercellular marrow. Peripheral destruction of blood cells by autoantibodies causes cytopenias with hypercellular marrow in SLE. Two falciparum malaria cases were the results of secondary haemophagocytosis. Malaria (especially falciparum malaria) may cause pancytopenia as a result of direct bone marrow invasion by a parasite, immune haemolysis, disseminated intravascular coagulation, hypersplenism, bone marrow necrosis or haemophagocytosis.[17-20] Secondary haemophagocytosis may be associated with both cellular and hypocellular marrow depending on the stage of haemophagocytosis. In our study, secondary haemophagocytosis was associated with bone marrow hyperplasia in falciparum malaria, and hypoplasia in dengue and enteric fever.

Very few studies regarding the aetiological spectrum of pancytopenia (Table IV) have been reported from India. AA and megaloblastic anaemia were the commonest causes of pancytopenia. Other common causes included haematological malignancies, hypersplenism, kala-azar, malaria, drug inducement and other infections.[1-6] AA was also the

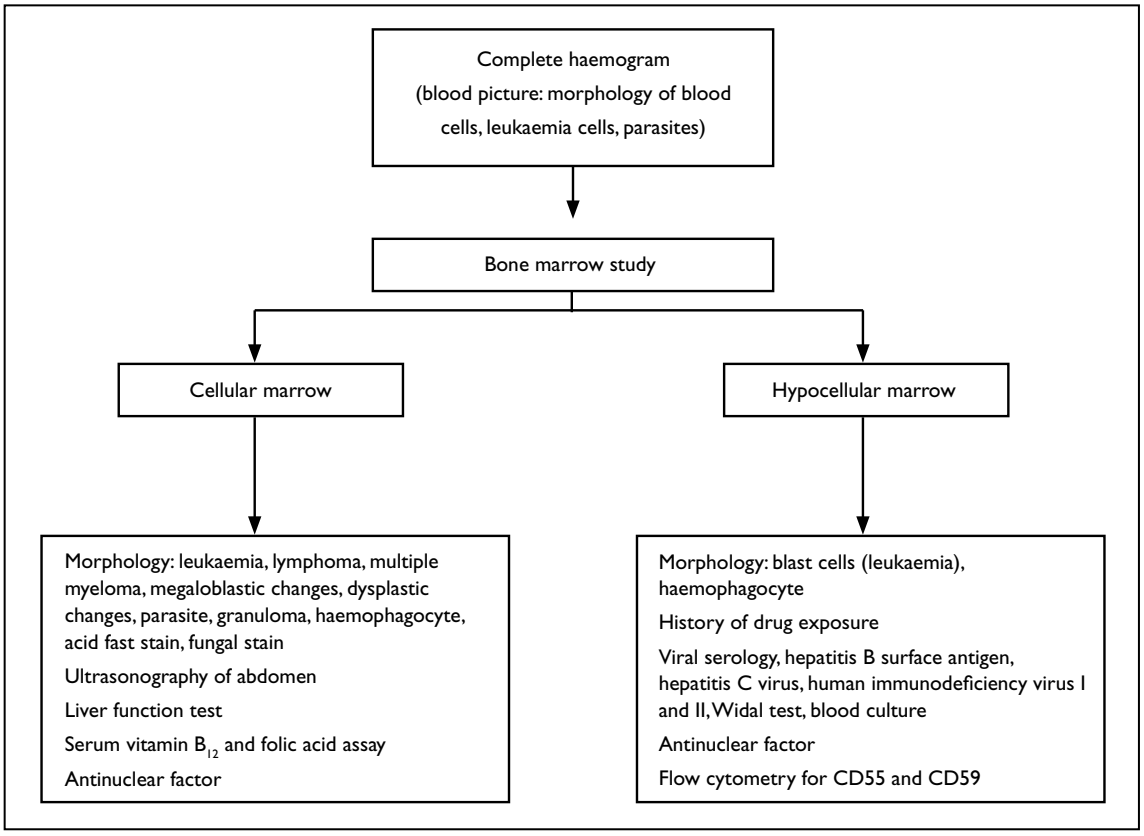

Fig. 2 Proposed algorithm for investigation of pancytopenia.

commonest cause of pancytopenia in our study (22.72%). However, hypersplenism, especially from chronic liver disease (CLD) was more prevalent in our study than in other studies. Kala-azar was the third most common cause of pancytopenia in our study, while mixed deficiency nutritional anaemia and megaloblastic anaemia were important but relatively less prevalent causes of pancytopenia. SLE was also an important cause of pancytopenia. Previous studies have rarely reported haemophagocytosis as a cause of pancytopenia, but our study found haemophagocytic syndrome to be an important cause of pancytopenia, especially in relation to infections such as falciparum malaria, enteric fever and dengue. Based on the aetiological spectrum of pancytopenia, we propose an algorithm for investigation that is relevant to clinical practice in our set-up (Fig. 2). Clinical presentations of pancytopenia depend on the primary cause and the degree of pancytopenia. In our study, fever was frequently observed in pancytopenia as a result of infective disorders. Hepatomegaly and splenomegaly were significantly more common in patients with cellular marrow ($p < 0.001$). In AA patients, pallor was the most common early symptom, followed by bleeding. Infection was relatively uncommon in AA.

In conclusion, AA was the most common cause of pancytopenia in our study, followed by hypersplenism (due to CLD), and then kala-azar (9%). Other causes included megaloblastic anaemia, enteric fever, falciparum malaria and SLE. A high level of suspicion and attention is required for the diagnosis of uncommon causes of pancytopenia, including the newer antibiotic linezolid, PNH, CLL, HIV and secondary haemophagocytic syndrome. Causes such as megaloblastic anaemia, and infections such as kala-azar, falciparum malaria and enteric fever are reversible. SLE patients can be managed effectively with immunosuppressive therapy. As a large proportion of pancytopenia is of reversible aetiology, early and accurate diagnosis may be life-saving.

REFERENCES

1. Kumar R, Kalra SP, Kumar H, Anand AC, Madan H. Pancytopenia--a six year study. J Assoc Physicians India 2001; 49:1078-81.
2. Khunger JM, Arulselvi S, Sharma U, Ranga S, Talib VH. Pancytopenia--a clinico haematological study of 200 cases. Indian J Pathol Microbiol 2002; 45:375-9.
3. Tilak V, Jain R. Pancytopenia--a clinico-hematologic analysis of 77 cases. Indian J Pathol Microbiol 1999; 42:399-404.
4. Varma N, Dash S. A reappraisal of underlying pathology in adult patients presenting with pancytopenia. Trop Geogr Med 1992; 44:322-7.
5. Gupta V, Tripathi S, Tilak V, Bhatia BD. A study of clinico-haematological profiles of pancytopenia in children. Trop Doct 2008; 38:241-3.
6. Khodke K, Marwah S, Bux G, Yadav RB, Chaturvedi NK. Bone marrow examination in cases of pancytopenia. J Indian Acad Clin

Med 2001; 2:55-9.
7. Jha A, Sayami G, Adhikari RC, Panta AD, Jha R. Bone marrow examination in cases of pancytopenia. J Nepal Med Assoc 2008; 47:12-7.
8. Hamid GA, Shukry SAR. Patterns of pancytopenia in Yemen. Turk J Hematol 2008; 25:71-4.
9. Savage DG, Allen RH, Gangaidzo IT, et al. Pancytopenia in Zimbabwe. Am J Med Sci 1999; 317:22-32.
10. Pol S, Driss F, Devergie A, et al. Is hepatitis C virus involved in hepatitis-associated aplastic anemia? Ann Intern Med 1990; 113:435-7.
11. Luzzatto L. Hemolytic anaemias and anaemia due to acute blood loss. In Fauci AS, Braunwald E, Kasper DL, et al, eds. Harrison's Principles of Internal Medicine. 17th ed. New York: McGraw-Hill, 2008: 660-2.
12. Pereira RM, Velloso ER, Menezes Y, et al. Bone marrow findings in systemic lupus erythematosus patients with peripheral cytopenias. Clin Rheumatol 1998; 17:219-22.
13. James J, Dutta TK, Jayanthi S. Correlation of clinical and haematologic profiles with bone marrow responses in typhoid fever. Am J Trop Med Hyg 1997; 57:313-6.
14. Paydas S, Ergin M, Baslamisli F, et al. Bone marrow necrosis: clinicopathologic analysis of 20 cases and review of the literature. Am J Hematol 2002; 70:300-5.
15. Malik AS. Complications of bacteriologically confirmed typhoid fever in children. J Trop Pediatr 2002; 48:102-8.
16 Garewal G, Marwaha N, Marwaha RK, Das KC. Bone marrow necrosis and pancytopenia associated with gram negative septicemia. Indian Pediatr 1991; 28:79-81.
17. Arya TV, Prasad RN. Fatal pancytopenia in falciparum malaria. J Assoc Physicians India 1989; 37:469-70.
18. Aouba A, Noguera ME, Clauvel JP, Quint L. Haemophagocytic syndrome associated with plasmodium vivax infection. Br J Haematol 2000; 108:832-3.
19. Zvulunov A, Tamary H, Gal N. Pancytopenia resulting from hemophagocytosis in malaria. Pediatr Infect Dis J 2002; 21:1086-7.
20. Ohno T, Shirasaka A, Sugiyama T, Furukawa H. Hemophagocytic syndrome induced by Plasmodium falciparum malaria infection. Int J Hematol 1996; 64:263-6.