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Profile of Pancytopenia Patients Presenting to a Tertiary Care Hospital in North India

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Abstract

***Introduction:** Pancytopenia is a common haematological entity encountered in clinical practise with various underlying causes, most of which are treatable. Therefore, there is a need to diagnose them early with non-invasive and invasive investigations. This study was aimed to study the common causes of pancytopenia in North India with special emphasis on the clinical, haematological, biochemical profile in the various aetiologies of pancytopenia.*

***Methods:** Cases of pancytopenia presenting in the department of Medicine of University College of Medical Sciences and GTBH, Delhi, India from November 2016 to April 2018, fulfilling the inclusion criteria were included in the study. The clinical features, biochemical, haematological parameters along with bone marrow aspiration and biopsy were recorded in all patients.*

***Observations:** Out of the 90 cases of pancytopenia, 53 had megaloblastic anaemia (58.8%), which was the most common aetiology. This study also revealed few interesting and uncommon causes like paroxysmal nocturnal haemoglobinuria, iron deficiency anaemia and haemophagocytic lymphohistiocytosis presenting as pancytopenia. On further correlating the haematological and biochemical parameters (including MCV, LDH, vitamin B12) with bone marrow studies to predict the common aetiology of pancytopenia in our study, MCV > 100 fl, LDH > 350 IU/L and vitamin B12 < 200 pg/ml taken together, had 87.8% chances (predicted value) of the patient having megaloblastic anaemia as the cause of pancytopenia.*

***Conclusion:** Early identification of the underlying pathology of pancytopenia with less invasive investigations can help in implementing appropriate therapy and management. We propose a composite value including MCV > 100 fl, LDH > 350 U/l, and vitamin B12 < 200 pg/ml taken together as a predictor of megaloblastic anaemia, which was the most common aetiology of pancytopenia in our study, avoiding the need of bone marrow examination, though extensive research in larger groups is required to further validate the above.*

Introduction

Pancytopenia is an important clinico-haematological entity in which all the three major formed elements of the blood (red blood cells, white blood cells, and platelets) are decreased in number. Pancytopenia exists in an adult when the haemoglobin (Hb) level is less than 13.3 g/dl in males or 11.5 g/dl in females, the total leukocyte count (TLC) is less than 4×10^9/l, and the platelet count is less than 150×10^9/l[1]. Patients of pancytopenia usually present with symptoms and signs of anaemia and thrombocytopenia, and less commonly with leukopenia. The essential investigations required to make a diagnosis of pancytopenia are routine haematological and biochemical tests and bone marrow examination.

Material and methods

This was a cross-sectional study conducted in the department of Medicine at Guru Teg Bahadur Hospital and University College of Medical Sciences, Delhi, India, from November 2016 to April 2018. It was approved by Ethics Committee of the institute. During this period, 90 cases of pancytopenia, who attended our outpatient and emergency department, were recruited. All the cases between 18 - 75 years were subjected to a set of haematological and biochemical investigations. Bone marrow aspiration/biopsy were done in all the patients after taking written informed consent.

Inclusion criteria for this study were: Patients with haemoglobin (Hb) level less than 13.3 g/dl in males or 11.5 g/dl in females, total leukocyte count (TLC) less than 4×10^9/l, and platelet count less than 150×10^9/l.

Exclusion criteria for this study were: Patients who received blood and blood products in the past 10 days, patients on radiotherapy and chemotherapy, patients on any haematinics, and patients refusing to give consent.

Results

The age of the patients included in the study ranged from

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18 - 75 years.The median age of the study population was 27.5 years.The maximum number of cases lay in the age group of 18 - 29 years (46%) with a female: male ratio of 1.5: 1. 79% of the study population was vegetarian by diet.

The aetiological profile of the total 90 cases recruited has been shown in Fig. 1.

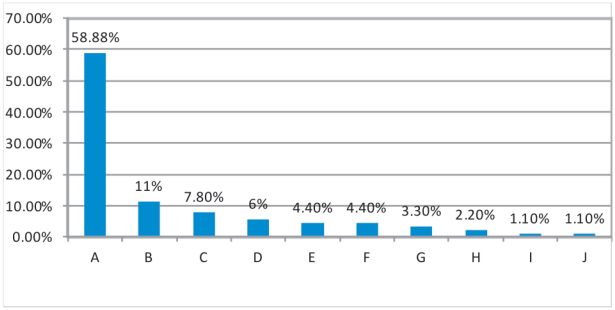

Fig. 1: *Frequency of various aetiologies of pancytopenia in the study population.*

A – Megaloblastic anaemia
B – Combined deficiency anaemia
C – Infections
D – Aplastic anaemia
E – Leukaemia
F – Hypersplenism
G – Paroxysmal nocturnal haemoglobinuria
H – Iron deficiency anaemia
I – Myelodysplasia
J – Hypoplastic marrow

The most common presenting symptom in patients of pancytopenia was weakness and fatigue seen in 50% of the total 90 cases. It was followed by fever (40%), dyspnoea (12.2%), swelling and abdominal pain (10% each), jaundice (4.4%), bleeding manifestation (3.3%) in the form of gum bleeding.

The most common sign in the study was pallor which was seen in all the 90 cases of pancytopenia (100%). It was followed by hyperpigmented knuckles (13.3%), pedal oedema (12.2%), icterus (8.9%), lymphadenopathy (2.2%), and gum hypertrophy (1.1%). Splenomegaly was present in 31.1% of the cases and 4.4% of patients had hepatosplenomegaly.

The mean haemoglobin of the patients (N = 90) presenting with pancytopenia was 5.09 ± 1.87 g/dl with the least value seen in patients of aplastic anaemia (4.04 ± 1.6 g/dl). Majority of patients had severe anaemia (84.4%) with Hb value of less than 7 g/dl. The mean platelet count was 62668.89 ± 34650.84/mm^3 (N = 90) and the least value was seen in patients of aplastic anaemia (38900 ± 21326/mm^3. Majority of the patients had moderate thrombocytopenia (48.9%) with platelet count in the range of 50,000-1,00,000/mm^3. The mean total leucocyte count was 2697.78 ± 807.12/mm^3 (N = 90) (Table I).

Table I: Mean and standard deviation of the three blood cell lineages in common aetiologies of pancytopenia.

S. No.	Aetiology	Mean ± SD		
		Haemoglobin g/dl	TLC/mm^3	Platelet/mm^3
1.	Megaloblastic anaemia	4.92 ± 1.96	2,795.7 ± 835.3	62,319 ± 33,400
2.	Combined deficiency anaemia	4.76 ± 0.87	2,560 ± 830	64090 ± 33682.7
3.	Infections	6.35 ± 1.4	2100 ± 637	49685.7 ± 34216.3
4.	Aplastic anaemia	4.04 ± 1.6	2480 ± 878.6	38900 ± 21326

The most common peripheral smear finding seen in our study was anisocytosis (91.1%) followed by macro/macro-ovalocytes (81.1%), microcytes (38.8%), poikilocytosis (35.5%), hypochromia (34.4%), polychromatophils (27.7%), hypersegmented neutrophils (21.1%), tear drop cells (13.3%), normocytic normochromic RBCs (12.2%), and blast cells (11.1%). None of the peripheral smear finding was suggestive of any type of anaemia except for hypersegmented neutrophils, which were seen in patients with megaloblastic anaemia (Table II).

Table II: The frequency of various peripheral smear findings in different aetiologies of pancytopenia.

S. N.	Aetiology	P1	P2	P3	P4	P5	P6	P7	P8	P9	P10
1.	MA	48	22	51	17	3	19	14	17	9	5
2.	CDA	10	5	8	7	0	4	5	2	1	1
3.	AA	4	0	3	1	1	0	2	0	0	0
4.	Leukaemia	4	0	1	1	1	0	2	0	0	4
5.	Infection	6	1	4	2	2	0	3	0	0	0
6.	Myelodysplasia	1	0	1	1	0	0	1	0	0	0
7.	Hypersplenism	4	2	1	0	2	0	2	0	1	0
8.	PNH	3	0	3	3	1	1	0	0	0	0
9.	IDA	1	2	0	2	1	1	1	0	1	0
10.	Hypoplastic	1	0	1	1	0	0	1	0	0	0
	Total	82	32	73	35	11	25	31	19	12	10

MA: Megaloblastic anaemia, CDA: Combined deficiency anaemia, AA: aplastic anaemia, PNH: Paroxysmal nocturnal haemoglobinuria, DA: Iron deficiency anaemia.

P1 – anisocytosis
P2 – poikilocytosis
P3 – macro and macro-ovalocytes
P – microcytes
P5 – normocytic normochromic RBCs
P6 – polychromatophils
P7 – hypochromia
P8 – hypersegmented neutrophils
P9 – tear drop cells
P10 – blast cells

The mean MCV was highest in patients with megaloblastic anaemia (105.96 ± 15.3 fl).The mean MCV was in the lower normal range in patients of combined deficiency anaemia (83.75 ± 1.90 fl) and infections (80.14 ± 7.71 fl) while it was in the upper normal range in patients of aplastic anaemia (97.14 ± 12.42 fl).

The mean reticulocyte was lowest in aplastic anaemia (0.50 ± 0.27%) and patients with infections had reticulocyte count in the lower normal range (1.11± 0.61%).

The mean LDH was 1844.5 ± 1080 IU/L and serum LDH was significantly raised in patients with megaloblastic anaemia with a mean of 2822.98 ± 2100.98 IU/L while it was in the normal range in patients of combined deficiency anaemia (333 ± 136 IU/L) and aplastic anaemia (265.4 ± 115.6 IU/L). The mean vitamin B12 was 261.3 ± 92.4 pg/ml and vitamin B12 levels were found to be significantly low in megaloblastic anaemia with a mean of 157.83 ± 113.2 pg/ml, while they were normal in rest of the cases (Table III).

Table III: The mean and standard deviation of the various haematological and biochemical parameters in common aetiologies of pancytopenia in North India.

Aetiology	MCV (fl)	Reticulocyte count (%)	S. LDH (IU/L)	Vitamin B12 (pg/ml)
Megaloblastic anaemia	105.96 ± 15.3	1.45 ± 0.75	2822.98 ± 2100.98	157.83 ± 113.2
Combined Deficiency anaemia	83.75 ± 19.0	1.40±0.59	333.00 ± 136.32	237.30 ± 84.82
Aplastic anaemia	97.14 ± 12.42	0.50 ± 0.27	265.4 ± 115.65	739.98 ± 330.93
Infections	80.14 ± 7.71	1.11 ± 0.61	461.71 ± 550.89	482.86 ± 470.49

Discussion

In studies from literature, there is variable data regarding socio-demographic profile, common aetiologies, and presenting clinical features in patients of pancytopenia. No comprehensive studies could be found that correlate the aetiology of pancytopenia with clinical profile, haematologic profile, biochemical profile and socio- demographic profile. So, our study was planned to evaluate the proportion of various underlying aetiologies of pancytopenia and to find the correlation of the aetiology with clinical profile, haematologic profile, biochemical profile and socio-demographic profile in a tertiary care centre in North India.

The most common aetiology of pancytopenia in our study was megaloblastic anaemia (58.88%) which was similar to many studies reported previously by Mallik *et al*[2], Sweta *et al*[3], Gayathri and Rao[4], and Khunger[5] *et al*. This can be explained by the dietary pattern followed in India due to social and religious practices, where most of the population followed vegetarian diet. Among vegetarians, milk and dairy products are the major source of vitamin B12, which due to regional and social practices and prevalent lactase deficiency is being consumed in less quantity among Indians[6].

The most common symptom present in patients of pancytopenia in our study was weakness and fatigue (50%) which can be attributed to anaemia causing decreased oxygen supply to various organs and consequent manifestation of weakness and fatigue. Our findings were in corroboration with studies done by Sweta *et al*[3], Gayathri and Rao[4], Santra *et al*[7], Niazi *et al*[8].

The most common sign at the time of presentation in our study was pallor (100%) which was consistent with all other studies and can be attributed to the presence of anaemia seen in all the cases of pancytopenia.

The frequency of splenomegaly reported in different studies is similar to that obtained in our study, i.e., in the range of 33-44%[2,3,7,9]. While hepatosplenomegaly was found in a slightly higher range (14% - 60%) in other studies, as reported by Mallik *et al*[2], Sweta *et al*[3], and Santra *et al*[7]. It was due to the presence of more number of kala azar and malaria cases in these studies, which contributed to the presence of hepatosplenomegaly in the above studies.

The following parameters namely: MCV, reticulocyte count, LDH, and vitamin B12 have not been correlated with the aetiology in patients of pancytopenia in the published literature. So, we studied the correlation of these four parameters to find the aetiology of pancytopenia by non invasive method. We correlated the MCV, reticulocyte count, LDH, vitamin B12 levels with the bone marrow aspiration/biopsy findings in our study by multiple logistic regression analysis. To find the best correlating factor for the aetiology of pancytopenia, we found that MCV > 100 fl, LDH > 350 IU/L, and vitamin B12 > 200 pg/ml taken together significantly predict megaloblastic anaemia in patients of pancytopenia while reticulocyte count was not a significant predictor.

If the MCV increases to more than 100 fl, the risk of megaloblastic anaemia being the aetiology increases by 1.049 (odds ratio). If the LDH increases more than 350 IU/L, then the probability of the aetiology being megaloblastic anaemia increases by 1.002 (odds ratio). If vitamin B12 decrease by less than 200 pg/ml, then the probability of the aetiology being megaloblastic anaemia increases by 0.995 (odds ratio). Taken together the above three parameters; MCV > 100 fl, LDH > 350 IU/L and vitamin B12 < 200 pg/ml, had 87.8% positive predictive

value to correctly identify the aetiology of pancytopenia as megaloblastic anaemia.

Conclusion

Pancytopenia is a common disease entity suspected by clinical examination and diagnosed by basic haematological and biochemical investigations. The commonest aetiologies of pancytopenia can be avoided by simple health education measures focussing on the need of balanced diet, avoidance of alcohol and improved personal and environmental hygiene. We propose a composite value including MCV > 100 fl, LDH > 350 U/l, and vitamin B12 < 200 pg/ml taken together as a predictor of megaloblastic anaemia, which was the most common aetiology of pancytopenia in our study, avoiding the need of bone marrow examination, though more studies in larger groups are required to further validate the above.

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