ORIGINAL ARTICLE

A Diagnostic Evaluation of Etiology of Pancytopenia at a Tertiary Care Hospital

NIGHAT NASEEM, KALIM UD DIN MALIK, NAUMAN ASLAM MALIK, ROZINA JAFFAR
Department of Pathology, Post Graduate Medical Institute, Lahore, Pakistan
Correspondance to: Dr. Nighat Naseem, Contact number: 0322-4049967, E-mail: nighat.pgmi@hotmail.com

ABSTRACT

Objective: The objective of the study is to evaluate the etiology of pancytopenia in indoor and outdoor patients at LGH/PGMI Lahore.
Study Design: A cross-sectional prospective observational study.
Setting: Bone marrow clinic at LGH and PGMI Lahore.
Duration: Jan 2008 – Dec 2011. A 4-year study conducted from Jan 2008 – Dec 2011.404 patients with pancytopenia were observed.
Methodology: Complete blood counts, bone marrow aspiration and trephine biopsy were performed according to standard methods. Patients on cancer chemotherapy and radiotherapy were excluded.
Results: Diseases leading to pancytopenia in the study in descending order of frequency were double deficiency anemia(iron deficiency anemia and megaloblastic anemia) 88 (25.6%), megaloblastic anemia 74 (21.5%), leukemia/lymphoma 66 (19.2%) and aplastic anemia 52 (15.1%). The less common causes include hypersplenism, 24 (7.0%), immune thrombocytopenic purpura 20 (5.8%), myclodysplastic/mycloproliferative disorders 10 (2.9%), storage disorders 6 (1.7%) and metastatic tumors 4 (1.2%).
Conclusion: Double deficiency anemia (iron deficiency anemia and megaloblastic anemia), megaloblastic anemia, leukemia/lymphoma and aplastic anemia were the common causes of aplastic anemia.

Key Words: Pancytopenia, aplastic anemia, megaloblastic anemia.

INTRODUCTION

Pancytopenia is the simultaneous presence of anemia, leucopenia and thrombocytopenia[1]. It may result from a spectrum of disorders which affect the bone marrow primarily or secondarily[2]. Patients usually present with complaints attributable to anemia, thrombocytopenia and less commonly leucopenia which in later stages can become life threatening. Certain factors are responsible for the variation in the incidence of disorders causing pancytopenia. Geographical distribution, genetic disturbances,[3,4,5] nutritional factors and infection[6,7] are the most important among them. Underlying pathology determines the management and prognosis of patients[8.]

Pancytopenia is a common problem with an extensive differential diagnosis. Still there is a relatively less description of the disorder in the texts books of internal medicine and hematology[9,10.] Pancytopenia can be due to a decrease in the bone marrow of haempoietic cell production by infections, toxins and malignant cell infiltration. The marrow can be normo-cellular or hyper-cellular without any abnormal cells e.g. ineffective hematopoiesis, dysplasia, maturation arrest of all cell lines and peripheral sequestration of blood cells[11]. Patients who present with pancytopenia have to be investigated clinically for possibility of bone marrow failure syndrome or acute malignancy especially if it is associated with hepatosplenomegaly or lymphadenopathy. Bone marrow aspiration and trephine biopsy are the most frequent investigative procedures to find out the cause[12,13.] They are invasive but relatively safe procedures which can be carried out easily even in the presence of severe thrombocytopenia with little or risk of bleeding.

The most common causes of performing bone marrow examination are the presence of unexplained cytopenias and malignant conditions like leukemias. The less common causes are staging of a lymphoma or presence of storage disorders. A trephine biopsy should always be performed if there is hypoplasia or aplasia. Bone marrow examination provides diagnostically

important information in a wide variety of disorders in children[14,15.]

MATERIALS AND METHODS

The present study was carried out in the pathology department of Post Graduate Medical Institute/ Lahore General Hospital over a period of 4 years from January 2008 to December 2011. A total of 404 patients were included in the study. All indoor patients with pancytopenia and few outdoor patients from LGH or INMOL Hospital were included in the study. Patients on cancer chemotherapy or radiotherapy were excluded.

Detailed relevant history, clinical examination and hematological parameters at presentation were obtained. Detailed relevant history included occupation, drug intake or treatment history, chemical exposure or a recent history of virus infection. Clinical examination included signs of pallor, jaundice, hepatomegaly, splenomegaly and lymphadenopathy.

The hematological parameters were hemoglobin level, red cell indices, total and differential leucocyte count and peripheral blood smear examination or blood samples. Bone marrow examination included bone marrow aspiration and trephine biopsy. Blood counts were done on automated hematology analyzer. Platelet counts obtained from counter were confirmed by peripheral blood smear examination. Bone marrow aspiration and trephine biopsy were carried out in all patients of pancytopenia except children under one year age group in whom aspiration from tibia was done.

The bone marrow procedure and further staining were carried out by standard method. All the peripheral blood smears, bone marrow aspirates and trephine biopsies were obtained with May-Grunwald Geimsa and Hematoxylin and Eosin stains respectively. Special stains like Sudan Black B (on peripheral blood and bone marrow aspirates) and Perl's stain for iron (on bone marrow aspirate smears) were done when indicated[17]. Findings of bone marrow aspiration and trephine biopsies were interpreted in the light of history, clinical examination and peripheral blood findings. A standard morphologic criterion was used in diagnosis.

RESULTS

Out of the total 404 patients 232 (57.5%) were males and 172 (42.5%) were females. The male to female ratio was 1.35:1 (Figure 1).

The age range of patients was from 1 month to 78 years with a mean of 39.1 years. Maximum number of cases were observed in the age group under 1 year to 15 years i.e. 175 (43.3%) while minimum number of cases were observed in the age group 76-90 years i.e. 11 patients (2.7%) (Table 1 and Figure 2).

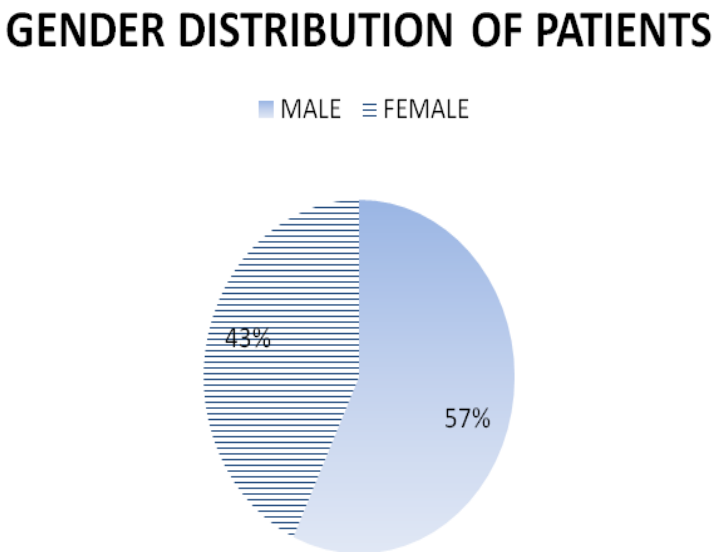

Figure 1:

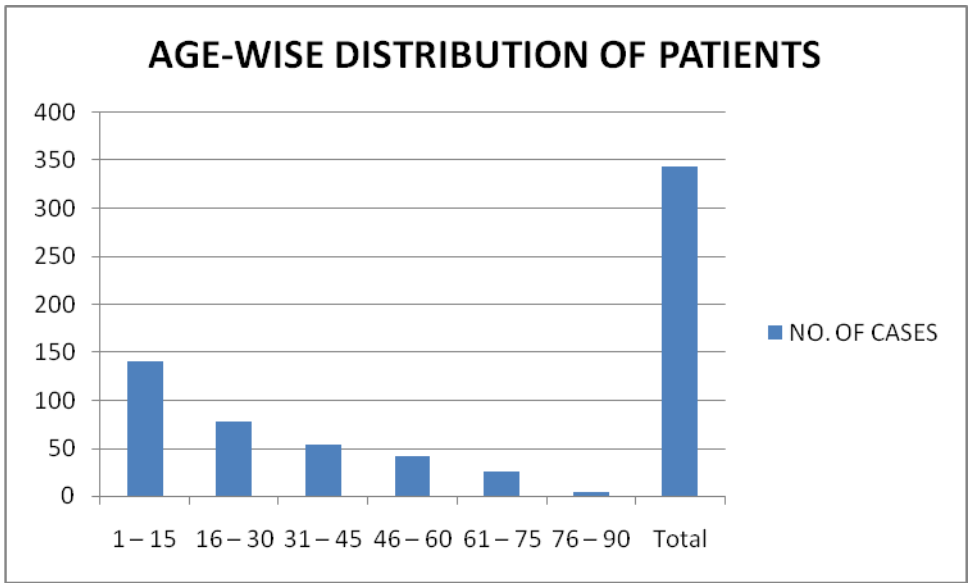

Figure 2:

Table 1: Age-Wise Distribution of Patients

	Age groups (years)	No. of cases	Percentage
1	1m – 15	140	40.7
2	16 – 30	78	22.7
3	31 – 45	54	15.7
4	46 – 60	42	12.2
5	61 – 75	26	7.5
6	76 – 90	04	1.2
	Total	344	100

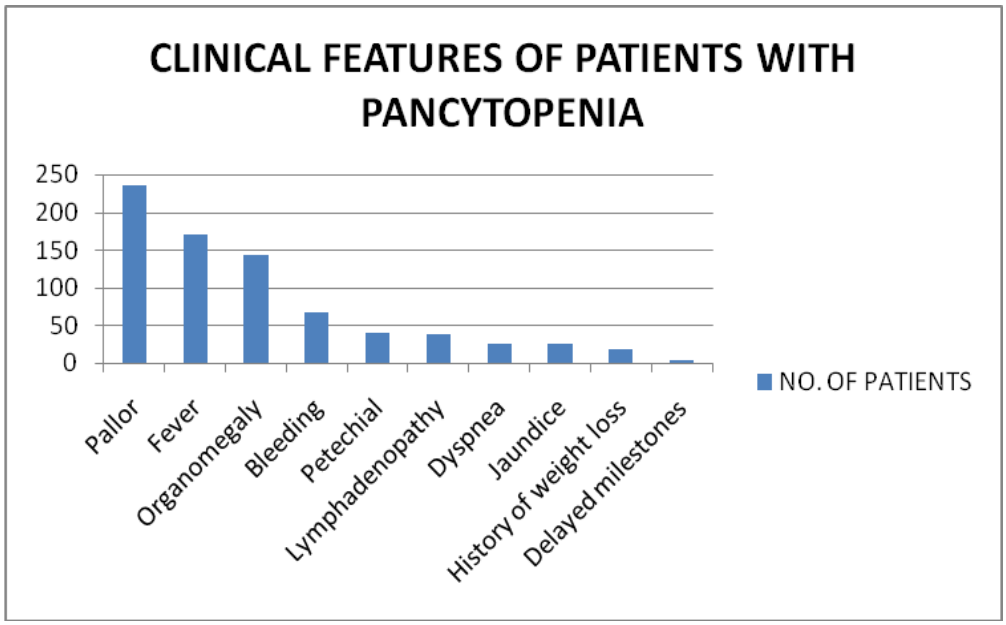

Figure 3:

Table 2: Clinical Features Of Patients With Pancytopenia

	Clinical features	No. of patients	Percentage
1	Pallor	235	68
2	Fever	170	49
3	Organomegaly	144	42
4	Bleeding	67	19
5	Petechiae	40	12
6	Lymphadenopathy	38	11
7	Dyspnea	26	8
8	Jaundice	25	7
9	History of weight loss	18	5
10	Delayed milestones	03	0.9

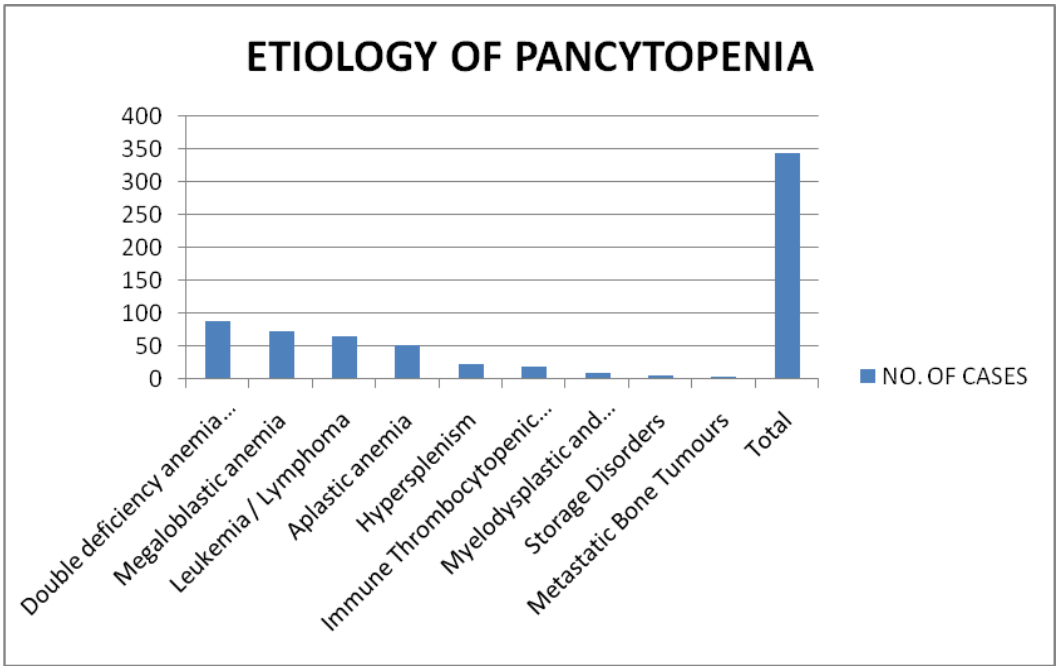

Figure 4:

Table 3: Etiology of Pancytopenia

	Disease	No. of cases	Percentage
1	Double deficiency anemia (Megaloblastic & iron deficiency anemia)	88	25.6
2	Megaloblastic anemia	74	21.5
3	Leukemia / Lymphoma	66	19.2
4	Aplastic anemia	52	15.1
5	Hypersplenism	24	7.0
6	Immune Thrombocytopenic Purpura	20	5.8
7	Myelodysplastic and Myeloprolifelative Disorders	10	2.9
8	Storage Disorders	06	1.7
9	Metastatic Bone Tumours	04	1.2
	Total	344	100

Constitutional signs and symptoms of patients in the study are in order of pallor (235: 68%), fever 170 (49%), organomegaly 144 (42%), bleeding 67 (19%), petechiae 40 (12%), lymphadenopathy 38 (11%), dyspnea 26 (8%), jaundice 25 (7%), weight loss 4 (5%) and delayed milestones 3 (0.9%) (Table 2 and Figure 3).

During this 4 year study period, a total of 404 patients were referred for bone marrow examination including aspiration and trephine biopsy owing to the presence of pancytopenia in the peripheral blood.

Out of these 404 patients with pancytopenia, bone marrow examination revealed a normocellular bone marrow in 60 patients. In remaining 344 patients, the etiological break-up of the cases revealed as follows. Double deficiency anemia (88 cases:25.6%) was the most common cause of pancytopenia followed by megaloblastic anemia (74 cases: 21.5%) as the second common cause and leukemia/lymphoma (66cases : 19.2%) as the third common cause of pancytopenia. Aplastic anemia (52cases: 15.1%) was the fourth common cause and the less common causes include hypersplenism(24cases:7.0%), immune thrombocytopenic purpura (20:5.8%) myclodysplastic/mydoproliferative disorders (10 cases: 2.9%), storage disorders (6 cases: 1.7%) and metastatic tumors (4 cases: 1.2%) (Table 3 and Figure 4).

DISCUSSION

Pancytopenia is not an uncommon hematological finding in our clinical practice. It should be expected on clinical grounds if a patient presents with unexplained anemia, prolonged fever and a tendency to bleed. Till date there are a limited number of studies on the frequency of various causes of pancytopenia.

In the present study, the most common diagnosis in patients presenting with pancytopenia was double deficiency anemia (iron deficiency anemia and megaloblastic anemia). This increased frequency of double deficiency anemia correlates with the high prevalence of nutritional anemia in our country. Megaloblastic anemia was the second most common diagnosis. Usually the patients of nutritional deficiency anemias respond very well to the appropriate therapy and improve soon. Leukemia/lymphoma, aplastic anemia and hypersplenism were the other common causes of pancytopenia. The studies by Ishtiaq O et al[16], Savage et al[9], Iqbal et al[18] and Qazi et al[19] show megaloblastic anemia as the most common cause of pancytopenia. However, in the present study, double deficiency anemia is the most common cause and megaloblastic anemia constitutes the second common cause.

There are varying reports on underlying etiology of pancytopenia from various parts of the world. In France, a study by Imbert et al[20] (1989) revealed myeloid leukemia the most frequent cause, followed in order by lymphoma and aplastic anemia. In a study from Zimbabwe by Savage et al, megaloblastic anemia followed by aplastic anemia and acute leukemia were the most common causes. Jha et al[21] from Nepal concluded aplastic anemia (29%) followed by megloblastic anemia (23%) and hematological malignancies (21%).

A study in India by Verma et al and Kumar et al[22] show aplastic anemia as the most frequent cause of pancytopenia.

Therefore, the most frequent causes of pancytopenia reported by different studies throughout the world are aplastic anemia, megaloblastic anemia and leukemia.

CONCLUSION

The study evaluated the etiology and clinic-hematological profile of patients of pancytopenia at Post Graduate Medical Institute/Lahore General Hospital.

Double deficiency anemia (iron deficiency and megaloblastic anemia), megaloblastic anemia, leukemia/lymphoma and aplastic anemia were the most frequent causes of pancytopenia.

Physical examination and peripheral blood counts provide valuable information in the work up of patients with pancytopenia and help in the diagnosis. They aid in panning investigations from bone marrow samples such as immunophenotyping and cytogenetic studies. In addition, an early diagnosis of the underlying disease will have an impact on the mortality and morbidity in vulnerable patients, especially in children[19.]

REFERENCES

1. Firkin F, Chesterman C, Pennington D, Rush B. De Gruchy's Clinical Hematology in Medical Practice 5th Ed. Oxford Blackwell; 1989.
2. Williams WJ, Bentkr E, Erskv AJ. Haematology-third edition, Singapore, McGraw Hill Book Company 1986; 181-84.

3. International agranulocytosis and aplastic anaemia study. Incidence of aplastic anaemia, the relevance of diagonostic criteria. Blood 1987; 70:1718-21.
4. Wintrobe MM (ed). Clinical Haematology. Eighth edition, Philadelphia. Lea and Febiger 1981;pp 699-915.
5. Keisu M, Ost A. Diagnosis in patients with severe pancytopenis suspected of having aplastic anaemia. Eur J Haematol 1990; 45:11-4.
6. Katar S, Nuri O M, Yaramis A, Ecer S. Nutritional megaloblastic anemia in young Turkish children is associated with vitamin B12 deficiency and psychomotor retardation.
7. Fazal R, Ahmed l, Saif ul Islam, Hussain M, Khattak TAK, Bano Q. Spectrum of hematological disorders in children observed in 424 consecutive bone marrow aspirations/ biopsies. Pak J Med Sci 2005; 21: 433-6.
8. Verma N, Dash S. Reappraisal of underlying pathology in adult patients presenting with panytopenia. Trop Geog Med 1992; 44:322-7.
9. Savage DG, Allen RH, Gangaidzo IT, Levy LM, Gwanzura C, et al. Pancytopenia in Zimbabwe. Am J Med Sci 1999 Jan; 317(1):22-32.
10. Rappeport JM, Bunn HF. Bone marrow failure: aplastic anemia and other primary bone marrow disorders. In: Isselbacher KJ, Braunwald E, Wilson JD, Martin JB, Fauci AS, Kasper KL, eds. Harrison's Priniciples of Internal Medicine. 13th ed. New York: McGraw-Hill; 1994:1754-7.
11. Pizzo PA, D' Andera AD. The pancytopenias. In: Behrman RE, Kleigman RM, Jenson HB. Nelson textbook of pediatrics. 17th ed. Philadelphia: Saunders: 2003: 1642-6.
12. Chandra J, Jain V, Narayan S, Sharma S, Singh V, Kapoor AK, et al. Folate and cobalamin deficiency in megaloblastic anemia in children. Indian pediatr 2002; 39:453-7.
13. Gutiernez-Unena S, Molina JF, Garcia CD. Espinoza LR. Pancytoepenia secondary to methotrexate therapy in rheumatoid arthritis. Arthritis rheum 1996; 39 (2): 272-6.
14. Bhatnagar SK, Chandra J, Narayan S, Sharma S, Singh V, Dutta AK. Pancytopenia in children: etiological profile. J Trop Pediatr. 2005 Aug; 51(4):236-9.
15. Gupta V, Tripathi S, Singh TB, Tilak V, Bhatia BD. A study of bone marrow failure syndrome in children. Indian J Med Sci. 2008 Jan; 62(1):13-8.
16. Ishtiaq O, Baqai HZ, Anwar F, et al. Patterns of pancytopenia patients in a general medial ward and a proposed diagnostic approach. J Ayub Med Col Abbotabad. 2004; 16:8-13.
17. Bain BJ, Lewis SM. Preparation and staining methods for blood and bone marrow films. In: Lewis SM, Bain BJ, Bates I, editors. Dacie and Lewis Practical Haematology. 10 th ed. Philadelphia: Churchill Livingstone; 2006. p. 59-78.
18. Iqbal W, Hassan K, Ikram N, Nur S, Aetiological breakup of 208 cases with pancytopenia. J Rawal Med Coll 2001: 5(1) 7-9.
19. Qazi RA, Masood A. Diagnostic evaluation of pancytopenia. J Rawal Med 2002, 6 (1): 30-3.
20. Imbert M, Scoazee JY, Mary JY, Jouzult H, Rochant H, Sultan C. adult patients presenting with pancytopenia. A reappraisal of underlying pathology and diagnostic procedures in 213 cases. Hematol Pathol 2989; 3: 159-67.
21. Tha A, Sayarni G, Adhikari RC, Panta AD, Tha R. Bone marrow examination in cases of pancytopenia. J Nepal Med Assoc 2008; 47: 12-17.
22. Kumar R, Kabra SP, Kumar H, Anand AC, Madan H. Pancytopenia – a six year study. J Assoc Phys India 2001; 49: 1078-81.