ORIGINAL ARTICLE

Common Hematological Disorders Causing Pancytopenia and Importance of Bone Marrow Examination

Riaz Ahmed Qazi[*], *Aijaz Ahmed Memon*[*], *Bharat Lal*[**], *Ameer Abbas Ali*[*], *Javed Husain Memon*[*]

ABSTRACT

Objective: To evaluate the frequencies of common hematological disorders leading to Pancytopenia. We highlight the importance of bone marrow examination among the pancytopenic patients to rule out causes or diagnosis of common hematological disorders.

Study Design: Observational study.

Place & Duration: Diagnostic and Research Laboratory, Pathology Department, Peoples University of Medical & Health Sciences, Shaheed BanazeedAbad from June 2013 to June 2014.

Material and Methods: Total 91 patients, 67 males and 24 females with their ages ranging from 5-59 years were included in this study. These patients were coming from rural and urban areas of district: (SBA), Sanghar and Naushahroferoze referred by different physicians for the laboratory diagnosis of pancytopenia. The diagnosis of pancytopenia was made by detailed history, clinicohematological findings and blood examination, bone marrow biopsy samples of these patients were taken and sent to the D&R lab in pathology department for the diagnosis of pancytopenia.

Results: The mean age was 37±32 years and male to female ratio 1.6:1 were detected in our study. The frequency of megaloblastic anemia was 46.16% followed by aplastic anemia 30.76%, acute myeloid leukemia 17.58% and acute lymphoblastic leukemia 5.5% among the total 91 pancytopenic patients.

Conclusion: The frequency of megaloblastic anemia was higher among the patients with pancytopenia followed by aplastic anemia, acute myeloid leukemia, and acute lymphoblast leukemia required prevention and treatment of these disorders that causes pancytopenia by the reliable diagnostic method such as bone marrow examination.

Key Words: Frequency, Hematological Disorders, Pancytopenia, Bone marrow.

INTRODUCTION:

Pancytopenia is defined as a decrease in all the three cell lines of blood; it is not a disease but clinical hematological entity encountered in megaloblastic anemia, aplastic anemia and leukemias[1].

The Pancytopenia varies according to population, age, nutritional status, infections and megaloblastic anemia is common in adults due to the nutritional deficiency of vitamin B12 and Folic acid while acute leukemia and aplastic anemia are most common causes of pancytopenia in children[2].

The etiological factors for pancytopenia are idiopathic aplastic anemia in 70% of cases and other risk factors include exposure to ionizing radiation, chemicals like benzene, viral infection such as parvovirus B19, HBV and HCV, parasitic infections including malaria and kalazar, exposure to the drugs such as interferon, chloramphenicol, gold, sulphonamides, anti epileptic, cytotoxic and anti-malarial, aplastic anemia is also common in heroin addict, peoples receiving Kushtas from Hakim's while pancytopenia also associated with systemic lupus erythromatosis and paroxysmal nocturnal hemoglobinuria[3].

The underlying pathological mechanisms

* *Assistant Professor, Pathology Deptt: PUMHSW Nawabshah.*

** *Senior Registrar, Deptt. of Medicine, PUMHSW Nawabshah.*

Correspondence to:
Dr. Riaz Ahmed Qazi
Assistant Professor
Pathology Department
PUMHSW, Nawabshah.
Email: dr_ameer75@yahoo.com

that cause pancytopenia are impaired production of blood cells and ineffective hematopoiesis within the bone marrow seen in the aplastic anemia and megaloblastic anemia while increased destruction of blood cells in the spleen and replacement of the normal haemopoeitic tissue by leukemic cells and metastatic malignant cells in the bone marrow also causes pancytopenia[4].

The Patient with pancytopenia presents with anemia, fever, bleeding tendency, hepato-splenomegaly in leukemia's and laboratory diagnosis is made by analysis of complete blood count, examination of peripheral blood and bone marrow smears[5]. The trephine biopsy is performed in special cases of pancytopenia to access the cellularity of bone marrow and detection of myelofibrosis, milliary tuberculosis, lymphoma, myeloma and infiltration of metastatic malignant cells within bone marrow[6] .This study was carried out to evaluate the frequencies of common hematological disorders producing pancytopenia in patients. The bone marrow examination is important and most reliable method to sort out the causes and diagnosis of hematological disorder that causes pancytopenia and treatment planning of pancytopenia would be made by this potent laboratory investigation along with history, clinical findings, complete blood count analysis and examination of peripheral blood smears.

MATERIALAND METHODS:

This study was conducted in the Diagnostic and Research (D&R) Laboratory, Pathology Department, Peoples University of Medical & Health sciences (PUMHS), Nawabshah, from June 2013 to June 2014. A total number of 91 patients were selected fulfilling the selection criteria, including 57 male and 34 female at the age of 5-59 years, majority of these patients were poor with occupation of farmer, government employee, school children, house hold ladies, carpenter, painter and industrial worker. These patients were uneducated and lived in rural areas in majority. All the patients were subjected to examination of their complete blood count and examination of peripheral blood as well as bone marrow smears. The bone marrow biopsies were done in cases when ever required. Bone marrow was examined for cellularity, myeloid erythroid ratio, erythropoiesis, myelopoiesis, megakaryo-poiesis, other cells such as plasma cells, L.D bodies, malarial parasite and lymphoblast or myeloblasts in cases of acute leukaemias. Special investigations were done in cases where indicated.

Inclusion Criteria : Patient of any age having history of weakness, loss of weight, frequent dyspnea on exertion, fever, cough, bleeding tendency in the form of nose bleeding or bleeding spots over the skin. On examination having pallorness, temperature, with hepatosplenome-galy.

Exclusion Criteria: Diagnosed cases of malignancies including leukemia, received chemotherapy or radiotherapy and pregnant women were excluded from this study.

RESULTS:

Total 91 patients including 57 (62.7%) male and 34 (37.3%) female at their mean age 37±32 years with male to female ratio of 1.6:1 were selected for this study. Majority of these patients were poor 58.2%, belonging to lower middle class 29.6% with the occupation of farmers 43.1%, residing in the rural 79.5% areas (Table-1). The clinocohematological findings in these patient were; moderate to severe anemia 61%, infections in the form of fever and cough 21.97%, bleeding tendency 16.48% mean values of hemoglobin, mean corpuscular volume femtolitter, packed cell volume, mean corpuscular hemoglobin, mean corpuscular hemoglobin concentration, RBC count, total leukocyte counts, differential leukocyte count such as neutrophils, lymphocytes, monocytes, eosinophils and platelet count were 8.6 ± 2.3 g/dl, 90.2 ± 25.5, 37.0±12.0%,19.5±9.9%, 29.2±7.8%, 3.1±1.9 ML/CUMM, 2850 ± 1050 /cumm, 5.0±2.0% , 35.0± 10.0%, 45.0±12.0%, 7.0±3.0% 62500 ± 23500 /cumm detected by clinical examinations and hematology analyzer. The examinations of stained peripheral blood smears with field's stains were showing normocytic normochromic picture in aplastic anemias and acute leukemia's while

macrocytic hypochromic picture with Hyper segmented neutrophils and Giant platelets in magaloblastic anemia. The examination of bone marrow smears showing hyper cellular, hypocellular and normocellular bone marrow with increased erythropoiesis of megaloblastic type along with giant myelocytes, meta-myelocytes as well as giant megacrocytes seen in cases of megaloblastic anemia. Cellularity was decreased in cases of aplastic anemia.

The bone marrow is hypercellular with presence of myeloblasts and lymphoblast found in acute leukemia of myeloblastic or lymphoblastic types (Table-2). In our study, the frequency of megaloblast amemia was 46.16% followed by aplastic anaemia 30.76%, acute myeloblastic leukemia 17.58%and acute lymphoblastic leukemia 5.5% among the total 91 patients (Table-3).

DISCUSSION:

The evaluation of frequencies of common hematological causes of pancytopenia were observed by different international and local

TABLE - I: The Distribution of Pancytopenia on the basis of age, sex,socio-economic status, occupation, education and area of residence
N=91

PANCYTOPENIA	NUMBER OF PATIENTS	PERCENTAGE
MEAN AGE		
37±32 YEARS	91	
SEX		
Male	57	62.7%
Female	34	37.3%
Male Female Ratio		1.6:1
SOCIO-ECONOMIC STATUS		
Poor	53	58.2%
Lower Middle class	27	29.6%
Upper Middle class	11	13.2%
OCCUPATION		
Farmers	31	43.1%
Government employees	15	16.6.8%
School children	13	14.2%
House holders	11	12.1%
Carpenters	9	9.7%
Painters	7	7.8%
Industrial workers	5	5.5%
EDUCATION		
Un-educated	71	78.2%
Educated	20	21.8%
AREA OF RESIDENCE		
Rural	72	79.5%
Urban	19	20.5%

TABLE - 2: Clinical Findings of Pancytopenic Patients (N=91)

Clinical Finding	Hematology Findings
Anemia Mild 39 (42.85) Moderate 30 (32.96) Severe 22 (24.17)	Hemoglobin 8.6+2.3 g/dl Packed cell volume 37.0+12.0% Absolute Values: Mean corpuscular volume 90.2+25.5 femtolitter Mean corpuscular hemoglobin 19.5+9.9% pg/dl Mean corpuscular hemoglobin concentration 29.2+7.8% RBC count 3.1+1ML/CUMM Total leukocyte count 2850+1050 / cumm Differential leukocyte count Neutrophil 35.0+10.0% Lymphocyte 45.0+12.0% Monocyte 5.0+2.0% Eosinophil's 7.0+3.0% Platelet Count 62500+23500 /cumm
Signs and symptoms of Infections due to leucopenia in the form of fever, cough, anorexia and loss of weight. 20 (21.97)	
Bleeding tendency in form of nose bleeding and purpura due to thrombocytopenia 15 (16.48)	
Splenohepatomegaly in acute leukemia 21 (23.07)	
Examination of Peripheral Blood Smears	**Examination of Bone Marrow Smears**
Normocytic normochromic picture in the leukemia and aplastic anemia's while macrocytic hyperchromic picture seen in Megaloblastic along with giant platelet and hypersegmented neutrophils the myoblasts in acute myeloblastic leukemia and lymphoblasts in acute lymphoblastic leukemia. Both blast cells were differentiated from each other on the basis of morphology and special stain P.A.S and S.B.B	Hypercellular or hypo-cellular or normo-cellular with Megaloblastic erythropoisis and the giant megakaryocytes and myelocytes as well as metamylocytes are seen in Megaloblastic anemia while it was hypo-cellular in aplastic anemia and hypercellular bone marrow with presence of myeloblasts or lymphoblasts in respective type of acute leukemia

TABLE -3: The Frequencies of Hematological Disorders Causes Pancytopenia (N=91)

COMMON DISORDERS	NO.OF PATIENTS	PERCENTAGE
Megaloblastic anemia	42	46.16
Aplastic anemia	28	30.77%
Acute myeloid leukemia	16	17.58%
Acute lymphoid leukemia	5	5.50%
TOTAL	**91**	**100%**

studies. Hence Katherine A. D et al[7] reported that frequency of leukemia due to genetic abnormalities among the pancytopenic patients was higher in the population of United States and western countries as compared to the eastern population where incidence of megaloblastic anemis due to malnutrition with vitamin B12, folic acid or both and aplastic anemia caused by exposure of insecticide and chemicals like benzene were higher. The hypersplenism, infections, leukemia's, lymphomas, megaloblastic anemia and aplastic anemia were common causes of pancytopenia in

India as observed by Jain A, Naniwadekar M.[8] The high frequency of megaloblastic anemia's such as 74%, followed by aplastic anemia 18.2%,among the 104 patients with male predominance were reported by Gaythri BN & Kadam SR[9] while frequency of megalo-blastic anemia such as 56%, 66% followed by 14% and 18% among the, 50, 100 patients including 74% vegetarian and 24% non-vegetarian with male to female ratios of 1.6:1 & 1.5:1 were reported by Fahim M et al[10] and Sweta S.B et al.[11] The mean ages of these patients such as 42±38, 32±27 and 42.5±37.5 respectively were detected by above three studies. The clinico-hematological findings in all these patients were weakness, pallorness fever, Splenomegaly and hepatomegaly, low hemoglobin, erythrocytes, leukocytes and platelet counts, macrocytic hyperchromic or normocytic normochromic anemia seen in peripheral blood smear and on bone marrow examinations of these patients, they founded normocellular, hyper-cellular and hypocellular bone marrow with megaloblastic erythropoiesis seen in megaloblastic anemia while hypo cellularity seen in aplastic anemia and hyper cellularity with presence of myeloblasts in acute myeloblastic leukemia and lymphoblasts in acute lymphoblastic leukemia and laboratories workers in the above studies described that bone marrow examination is accurate diagnostic as well as treatment modalities of pancytopenia. Lakhey A et al[12] detected 28.5% of the patients with aplastic anemia followed by 23.9% cases of hematological malignancy such as acute myeloid leukemia and 19.5% patients with megaloblastic anemia out of total 54 cases on their bone marrow examination. The study conducted by Kirpal DM et al.[13] in Pakistan reported that among the 62 patients of pancytopenia with mean age of 37.7±16.38 years with similar clinico hematological findings described in the above studies founded 41.2% of megaloblastic anemia followed by 37.4% of AML and 19.4% of aplastic anemia among all the patients with pancytopenia. The megaloblastic anemia is still common cause of pancytopenia in our country and high frequency of Megaloblastic anemia 41.2% followed by aplastic anemia 31.8% with male to female ratio of 1:1.4 among the pancytopenic patients were reported by Aziz T et al.[14] They stated that in northern areas, males are the main source of earning for their family and they usually remain outdoor for long period for working in their fields and industries, hence farmers, painter and industrial workers are suffering from aplastic anemia more as a result of high exposure to insecticides and pesticides, or industrials toxins. On the other hand, females usually remain indoor in household activities and less exposed to these hazards, they are devoid of early medical advice due to illiteracy and malnutrition, so they are suffering form megalo-blastic anemia. They observed that male and females both are affected equally because of urban lifestyle in Karachi and remaining area of Pakistan rather than the northern area, where females also perform jobs almost in every sector along with males and equally exposed to chemicals and environmental toxins hence aplastic anemia is common in both sexes. In contrast to above studies Santra G[15] reported that males were affected with aplastic anemia than the females due to higher occupational exposure of chemicals and pesticides in industries of Philippines. Jalbani A et al[16] concluded aplastic anemia 32.5% followed by hypersplenism 22.5%, megaloblastic anemia 17.9% and acute myeloblastic leukemia's 12.9%, among the 40 pancytopenic patients of 30-40 years of ages with male to female ratio of 2.6:1. They also stated that aplastic anemia were mostly caused by uses of toxic and banned drugs by quacks and journal practitioners at their clinics, and use of insecticides and pesticides by farmers in their fields, exposure to viral infections, chemicals as well as radiation in industries and exposure to hydrocarbons expelled from motor vehicles. The study carried out by Tariq M[17] who showed frequency of aplastic anemia 36% followed by megaloblastic anemia 17.6% and acute lymphoblastic anemia 14% among the pancytopenic patient. Current study is in contrast with above study in which acute myelogenous leukemia was dominant malignant disorders in our country as compared to the acute

lymphoblastic leukemia that is common in western countries. In contrast to this study, Zeb jan A et al[18] concluded 28.5% of aplastic anemia, 23.9% hematological malignancies and 19.5% megaloblastic anemia cases among 205 pancy-topenic children with their age ranged between 6 month and 14 years, male to female ratio of 1.8:1 and clinicohematological findings were similar to the above study. Khan FS[19] stated that acute leukemia (32.2%) was the commonest cause of pancytopenia fallowed by aplastic anemia (30.8%) among the pancytopenic children on bone marrow examination. In our study total 91 patients with mean age of 37±32 years and male to female ratio of 1.6:1 were observed, the frequency of megaloblastic anemia was 46.16% followed by aplastic anemia 30.76% and acute leukemia's including myeloblastic 17.58% and lymphoblastic 5.5% types were detected on the basis of age, sex and clinico hematological findings.

CONCLUSION:

In our study, the frequency of megaloblastic anemia was higher among the patients with pancytopenia followed by aplastic anemia, acute myeloid leukemia, and acute lymphoblast leukemia required prevention and treatment of these disorders that causes pancytopenia by the reliable diagnostic method such as bone marrow examination. However poverty, poor eating habits, poor quality of food and self avoidance of necessary food may be the cause of nutritional deficiency leading to megaloblastic anemia would be controlled. Pakistan as agriculture country exposure to pesticides among the farmers, chemicals among the industrial workers and uses of toxic ban drugs by quacks and general practitioner at their clinics would be the major causes of aplastic anemia.

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