International Journal Dental and Medical Sciences Research
Volume 4, Issue 6, Nov-Dec 2022 pp 886-892 www.ijdmsrjournal.com ISSN: 2582-6018

Analysis of Peripheral Smear and Bone Marrow Morphology in Evaluation of Pancytopenia /Bicytopenia – A Prospective Study

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Submitted: 18-12-2022 Accepted: 31-12-2022

ABSTRACT
Introduction:pancytopenia is reduction of three cellular elements of blood (rbc, wbc. Platelet).this triad results in various diseases primarily/secondarily involving bone marrow varying range: normal to malignant, iatrogenic to chemo/radiotherapy. This study is carried to identify causes of pancytopenia and to find out bone marrow morphology in cases of pancytopenia. Bone marrow aspiration smears of patients fulfilling criteria of pancytopenia are examined. The data obtained were analyzed using measures of central tendency.
Methods and materials:130 cases underwent bone marrow aspiration and it constituted 15.74% of total cases.Mean age is 42 years (range, 1-79 years). 36 cases are children (28.37%). Male: female ratio is 1.5:1.Commonest cause is hypoplastic bone marrow seen in 40 cases (30.76%) followed by megaloblastic anemia in 35 cases (26.92%), and hematological malignancy in 30 cases (23.07%).Erythroid hyperplasia in 23 cases (17.69%) and normal in 2 cases (1.53%).
Results:Out of 130 cases, Acute leukemia is commonest hematological malignancy. In children, commonest finding is hypoplastic bone marrow (30.76%) while in adults' megaloblastic anemia (26.92%) is commonest finding followed by hypoplasticanemia (25.47%).
Conclusion:In present study bone marrow examination is able to establish diagnosis in 83% of cases. Hypoplastic marrow is the commonest diagnosis, followed by megaloblasticanemia, and hematological malignancies.
Key Words: Bone marrow aspiration, leukemia, megaloblasticanemia, pancytopenia

I. INTRODUCTION

In our day to day practice, Pancytopenia and bicytopenia is an important clinico-hematological disorder. Pancytopenia is defined as reduction in all the three cellular elements of blood, that is, red cells, white cells and platelets. Bicytopenia is reduction in any of the two cell lines[2].

It is not a disease entity, but a triad of findings that may result from various disease processes primarily or secondarily involving the bone marrow. The etiology of pancytopenia and bicytopenia ranges from transient marrow viral suppression to marrow infiltration by malignant process. Also caused iatrogenically secondary to radiotherapy, chemotherapy and drugs[3].

A careful examination of the blood film is often helpful in giving a lead to diagnosis and bone marrow examination usually establishes the diagnosis. In cytopenias, the cellularity of bone marrow and its composition varies with the causes. The bone marrow is normocellular or hypercellular in case of cytopenias resulting from ineffective hematopoiesis, bone marrow infiltration and increased peripheral utilization or destruction of cells. The marrow is hypocellular in cases of primary defect.

The presenting symptoms are usually related to anemia, thrombocytopenia and rarely leucopenia. The common clinical manifestations are pallor, fatigue, splenomegaly, lymphadenopathy, fever, bleeding, weight loss, hepatomegaly and jaundice[5].

The essential investigations required for a diagnosis of pancytopenia and bicytopenia are hematology and bone marrow examination. Other tests include radiological, microbiological and biochemical investigations in selected case[6].

The management and prognosis of the patients depends on the severity of cytopenias and the underlying pathology. The present study has beenundertaken to evaluate the various causes and to correlate the peripheral blood findings with bone marrow aspirates. The data would help in planning the diagnostic and therapeutic approach in patients with pancytopenia and bicytopenia

II. AIMS AND OBJECTIVES

- To study the various causes of pancytopenia/ bicytopenia at Hi-tech medical college and hospitals, Bhubaneswar.

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- To correlate anDAnalyse the haematological indices, peripheral smear and bone marrow morphology in etiological diagnosis of pancytopenia / bicytopenia patients.

III. REVIEW OF LITERATURE

Pancytopenia with hypo cellular bone marrow	Pancytopenia with hyper cellular bone marrow
1. Acquired aplastic anemia 2. Inherited aplastic anemia –Fanconi anemia -Dyskeratosis congenita - Shwachman-Diamond syndrome - Amegakaryocytic thrombocytopenia -Reticular dysgenesis 3. Hypoplastic myelodysplastic syndrome 4. Large granular lymphocytic leukemia 5. Hypoplastic PNH	A.Primarymarrow disorders 1. Acuteleukemia 2. Lymphomas 3. Hairy cell leukemia 4. Myelofibrosis 5. Myelodysplastic syndrome 6. Paroxysmal nocturnal hemoglobinuria 7. multiple myeloma 8. bone marrow metastasis B.systemic disorders: 1hypersplenism 2. deficiency of vit B 12 and folic acid 3. alcohol4. SLE

IV. MATERIALS AND METHODS

STUDYDESIGN

The present study is a Prospective study conducted in the Department of Pathology during the period from November 2020 to October 2022. Ethical clearance was obtained from the Ethics Committee of Hi-tech Medical College, Bhubaneswar for the study.
Thestudysampleincluded150casesofPancytopenia/ bicytopenia. For all

150 cases, complete blood count, peripheral smear and bone marrow examination were analyzed for etiological diagnosis. Special stains like Sudan Black B, Periodic Acid Schiff stain and Perl's stain were done if needed.

PLACEOFSTUDY:

Department of Pathology, Hitech Medical College, Bhubaneswar.

STUDY PERIOD:

November 2020–October 2022

INCLUSION CRITERIA

1. Age-All ages
2. Gender-both male and female
3. Haemoglobin -lessthan10 g/dl
4. Total leucocyte countless than 4000 cells/mm3
5. Platelet countless than 1,00,000/mm3.

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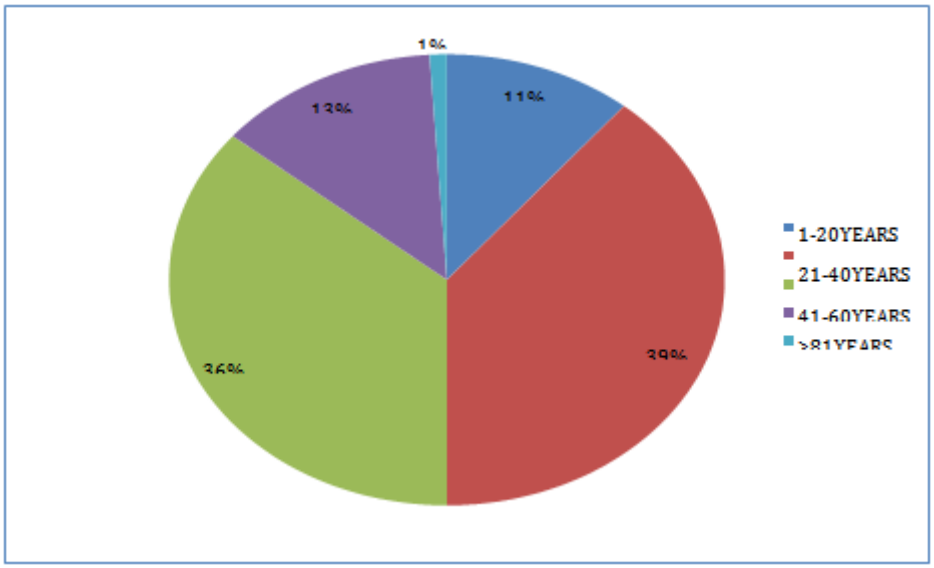
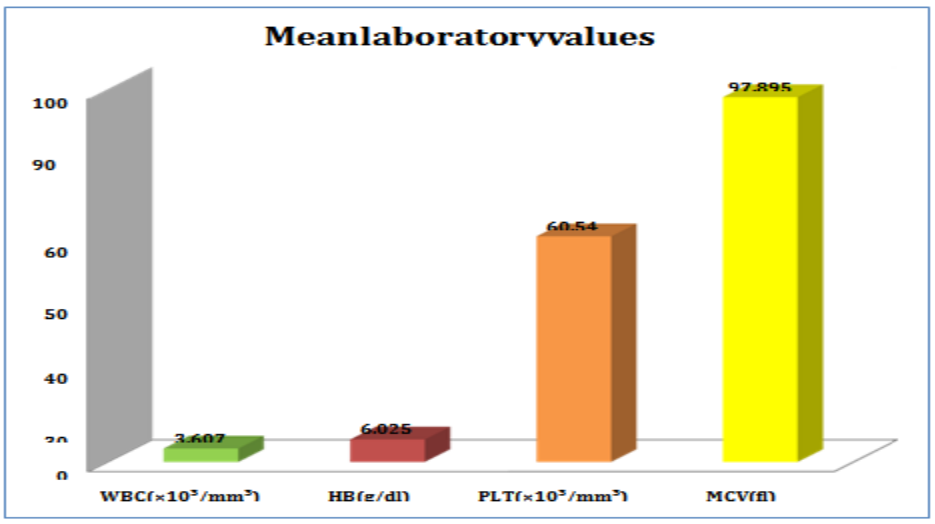
	Total Noofpatients(n)	lowest	highest	Mean+/-SD
WBC(x1000percumm)	130	0.6	11.0	3.60+/-2.0
Hb(g/dl)	130	1.9	10.0	6.02+/-1.7
Platelet(x1000percumm)	130	3.0	282.0	11.02+/-2.3
Mcv(fl)	130	68.9	128.9	97.89+/-13.97

V. OBSERVATION AND RESULTS





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TYPE OF ANEMIA	PERIPHERAL SMEAR	
	PANCYTOPENIA	BICYTOPENIA
ACUTE LEUKEMIA	1(1.0%)	1(2.0%)
DIMORPHIC ANEMIA	43(42.6%)	32(65.3%)
MACROCYTIC ANEMIA	46(45.5%)	11(22.4%)
MICROCYTIC HYPOCHROMIC ANEMIA	6(5.9%)	4(8.2%)
NORMOCYTIC NORMOCHROMIC ANEMIA	3(3.0%)	1(2.0%)
SUBLEUKEMIC LEUKEMIA	2(2.0%)	0(0.0%)
BONE MARROW DIAGNOSIS	**PANCYTOPENIA**	**BICYTOPENIA**
ACUTE LEUKEMIA	3 (3.0%)	3 (6.1%)
IMMUNE THROMBOCYTOPENIA	0 (0.0%)	4 (8.2%)
COMBINED DEFICIENCY	42 (41.6%)	21 (42.9%)
MEGALOBLASTIC ANEMIA	46 (45.5%)	11 (22.4%)
METASTASIS	1 (1.0%)	2 (4.1%)
MICRONORMOBLASTIC ERYTHROID HYPERPLASIA	5 (5.0%)	3 (6.1%)
MYELOFIBROSIS	2 (2.0%)	0 (0%)
MYELODYS PLASTIC SYNDROME	2 (2.0%)	4 (8.2%)
PLASMACYTOMA	0 (0.0%)	1 (2.0%)

VI. DISCUSSION

The incidence of pancytopenia / bicytopenia is increasing in frequency due to multifactorial causation. Pancytopenia/ bicytopenia are becoming the common hematological findingswithvariableclinical manifestations.Itbecame a challenging one for the clinicians to diagnose the correct etiology for the management of the patients. The causes of pancytopenia/ bicytopenia are many diseases which are diagnosed by doing complete hematological profile, peripheral smear and bone marrow study. The current study was done to evaluatetheetiologicaldiagnosisbyanalyzinghematologicalindices,peripheral smear and bone marrow aspiration study for 150 cases of pancytopenia/ bicytopenia.

AGEANDSEX

The age of presentation ranged from 1 year to 85 years. The maximum number of cases was seen in the age group of 21 - 40 years. Males (54.7%) are more commonly involved than females(45.3%)with a male to female ratio of 1.2:1. The results are similar to the study done by Gayathri et al[83]and Neelimabahal et al[92] but in

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contrast to Kirti S Dagdia et al[3] which showed slight female predominance.

HEMOGRAMS

In the present study, the hematological criteria for pancytopenia were hemoglobinlessthan10gm/dl,total white blood cell countless than 4000 cells/mm³ and platelet count less than 1,00,000/mm³. In cases ofbicytopenia any two of the above criteria with other value being normal. So the range of each parameter ranged from low to normal values. In 150 cases, there were 101 cases of pancytopenia and 49 cases of bicytopenia. The hemoglobin value ranged from 1.9 to 10 gm/dl, the total count ranged from 600 to 11,000 cells/mm³ and the platelet count ranged from 3000 to 2,82,000/mm³.

The mean value of hemoglobin, white blood cell count and platelet count are low in cases of pancytopenia than bicytopenia. So the severity of anemia, leucopenia and thrombocytopeniaare high in case ofpancytopeniathan bicytopenia which are statistically significant. The mean corpuscular volume ranged from 68.9 to 128.9 fl. The mean value of MCV is 93.8 in cases of bicytopenia and 99.8 in cases of pancytopenia which shows MCV is increasedin pancytopenia. The increase in MCV indicates macrocytic anemia is high in pancytopenia cases. The normal MCV indicates normocytic normochromic anemia and dimorphic anemia are high in cases of bicytopenia.

PERIPHERAL SMEAR DIAGNOSIS

In total of 150 cases, the most common anemia in peripheral smear is dimorphic anemia in 75 cases (50%), followed by macrocytic anemia in 57 cases (38%). But in pancytopenia cases (101 cases) the most common anemia is macrocytic anemia in 46 cases (45.5%) followed by dimorphic anemia in 43 cases (42.6%). In bicytopenia (49 cases), the most common anemia is dimorphic anemia in 32 cases (65.3%) followed by macrocytic anemia in 11 cases (22.4%). Acute leukemia and subleukemic leukemia constitute 2 cases each (2.6%). Bone marrow aspiration study yielded the final etiological diagnosis as follows.

CAUSES OF PANCYTOPENIA

The most common etiology of pancytopenia is megaloblastic anemia in 46 cases (45.5%). The second common is combined deficiency with megaloblastic and micronormoblastic maturation in 42 cases (41.5%) followed by micronormoblastic erythroid hyperplasia (5%), leukemia (3%), myelodysplastic syndrome (2%), myelofibrosis (2%) and metastatic deposits (1%).

CAUSES OF BICYTOPENIA

The most common etiology of bicytopenia is combined deficiency with megaloblastic and micronormoblastic maturation in 21 cases (42.8%). The second common is megaloblastic anemia in 11 cases (22.4%) followed by myelodysplastic syndrome (8.2%), immune thrombocytopenia (8.2%), leukemia (6.1%), micronormoblastic erythroid hyperplasia (6.1%), metastasis (4.1%) and plasmacytoma (2%).

COMPARISON OF VARIOUS ETIOLOGY OF PANCYTOPENIA/BICYTOPENIA IN DIFFERENT STUDIES

STUDIES	PANCYTOPENIA		BICYTOPENIA	
	FIRST CAUSE	SECOND CAUSE	FIRST CAUSE	SECOND CAUSE
Mousa SM[87]; Egypt2014	Clonal hematopoietic disorders (34%)	Hypersplenism (27.4%)	Clonal hematopoietic disorders(34%)	Immune thrombocytopenia (24%)
Akhtar Muniret al[86]; Pakistan 2014	Malignant hematological disorders (33.1%)	Megaloblastic anemia (18.2%)	Malignant hematological disorders (33.1%)	Megaloblastic anemia(18.2%)
Neelima Bahalet al[92];India 2016	Megaloblastic anemia (46.6%)	Leukemia (20%)	Megaloblastic anemia (28.98%)	Leukemia (23.18%)

KirtiS Dagdiaet al[3]; India 2016	Megaloblastic anemia (29.3%)	Aplastic anemia (18.6%)	Megaloblastic anemia(29.3%)	Aplasticanemia (18.6%)
Present study	Megaloblastic anemia (45.5%)	Combined deficiency (41.5%)	Combined deficiency (42.8%)	Megaloblastic anemia(22.4%)

VII. CONCLUSION

As pancytopenia and bicytopenia is increasing in frequency, it is important to evaluate the various etiologies for the management of patients. Many studies were done on pancytopenia but for bicytopenia very limited number of studies available. In this study, causes for bicytopenia also evaluated as it is equally important as pancytopenia in the management of patients. In this study, 150 cases were studied with maximum number of patients were in theage group of 21-40 years with slight male predominance.

The most common cause of pancytopenia was megaloblastic anemia followed by combined deficiency whereas for bicytopenia it was combined deficiency followed by megaloblastic anemia. The causes of cytopenias differ between countries according to health problems which is prevalent there. In other countries hematological malignancies are the most common cause of pancytopenia / bicytopenia. The higher incidence of combined deficiency in our country can be attributed to low socioeconomic status, inadequate nutrition,poor hygiene and lifestyle modification. So analysis of hematological indices, peripheral smear and bone marrow study are very important for an early intervention for to enhance the survival rate for the patients.

BIBLIOGRAPHY

[1]. Smock KJ, Perkins SL. Examination of blood and bone marrow. In: Lee GR, Lukons FJ, Paraskevar F, Greer JP, Rodgers GM, eds. Wintrobe's clinical hematology. 10th ed. Baltimore, MD: Lippincott Williams and Wilkins; 1999:23-32.

[2]. BatesI.Bonemarrowbiopsy.In:LewisSM,BainBJ,BatesI,eds. Dacie and Lewis practical haematology. 10th ed. Philadelphia, PA: Churchill Livingstone: 2006:115 - 130.

[3]. Dagdia KS, Deshmukh AT, Soni RR, Jane DS. Haematologicalindices and bone marrow morphology in pancytopenia/bicytopenia. Egyptian J Haematol 2016;41:23-26.

[4]. De Gruchy G C. Pancytopenia , aplastic anemia.In: De Gruchy's clinical hematology in medical practice , 5th edition. Edited by Firkin F, ChestermanC, Penington D, Rush B.Berlin, Germany: Blackwell Science;1989:119-136.

[5]. Pathak R, Jha A, Sayami G. Evaluation of bone marrow in patients with pancytopenia. J Path Nepal 2012;2:265-271.

[6]. Graham S, Marla NJ, FernandesH,Jayaprakash CS. A clinicohematological evaluation of pancytopenia in a tertiary care hospital in south india. Muller J Med Sci Res 2015; 6:5-9.

[7]. Dzierzak E, Speck NA of lineage and legacy: the development of Mammalian haemopoietic stem cells. Nature Immunology 2008; 9:129-36.

[8]. North TE, Goessling W, Peeters M et al. Haemopoietic stem cell development on blood flow. Cell 2009;137:736-48.

[9]. Kumaravelu P, Hook L, Morrison AM et al. Quantitative developmental anatomy of definitive haematopoietic stem cells/long-term repopulating units(HSC/RUs): role of the aorta-gonad- mesonephros(AGM) region and the yolk sac in colonisation of the mouse embryonic liver. Development 2002; 129:4891-9.

[10]. Murre C. Defining the pathway of early adult hematopoiesis. Cellstem cell 2007; 1:357-8.

[11]. Orkin SH, Zon LI. Hematopoiesis: an evolving paradigmfor stem cell biology. Cell 2008; 132:631-4.

[12]. Beguin Y. Soluble transferrin receptor for the evaluation of erythropoiesis and iron status. ClinicaChimicaActa 2003; 329:9-22.

[13]. De Maria R, Zeuner A, Eramo A et al. Negative regulation of erythropoiesis by

caspase-mediated cleavage of GATA-1. Nature 1999;401:489-93.
[14]. Bunn HF. New agents that stimulate erythropoiesis. Blood 2007; 09:868-73.
[15]. Panzenbock B, Bartunek P, Mapara MY et al. Growth and differentiation of human stem cell factor/erythropoietin - dependent erythroid progenitors cells in vitro. Blood 1998; 92:3658-68.
[16]. McGrath K, Palis J. Ontogeny of erythropoiesis in the mammalian embryo. Curr Top Dev Biol 2008; 82:1.
[17]. Pereda J, Niimi G. Embryonic erythropoiesis in human yolk sac: Two differentcompartments for two different processes. Microsc Res Tech 2008;71:856.
[18]. Bessis M. Living blood cells and their ultrastructure. Springer Verlag, Berlin, 1973.
[19]. Dao C, et al. Eosinophil and neutrophil colony-forming cells in culture. Blood 1977;50:833.
[20]. Ogawa M, et al. Renewal and commitment to differentiation of hemopoietic stem cells(an interpretive review). Blood 1983;61:823.
[21]. Quesenberry P, Levitt L. Hematopoietic stem cells. N Engl J Med 1979; 301:755,819,868.
[22]. Boll I, Kuhn A. Granulocytopoiesis in human bone marrow cultures studiedby means of kinematography. Blood 1965; 26: 449.
[23]. Bainton DF, Ullyot JL, Farquhar MG. The development of neutrophilicpolymorphonuclear leukocytes in human bone marrow. J Exp Med 1971 ;134 : 907.