Clinico - Pathological profiles of pancytopenia in University of Gondar Comprehensive Specialized Hospital, Gondar, Northwest Ethiopia : a retrospective cross-sectional, 2018-2021

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Abstract

Introduction: Pancytopenia can be caused by a wide variety of etiologies, leading to a diagnostic dilemma. These etiologies range from congenital bone marrow failure to marrow space-occupying lesions, infection, and peripheral destruction, to name a few. Bone marrow examination, in addition to a detailed clinical history, is often required for an accurate diagnosis. This study aimed to provide a brief overview of causes of pancytopenia in adults and children by age and sex with emphasis on bone marrow findings.

Methods: A retrospective descriptive cross-sectional study was conducted from January 2018 to January 2021 in the Department of Pathology, College of Medicine and Health Sciences, University of Gondar Comprehensive Specialized Hospital, Gondar, Northwest Ethiopia based on bone marrow aspiration finding results.

Results: There were 720 patients who had pancytopenia, 548(76%) were males and 172(24%) were females. The most common cause of pancytopenia in our study was megaloblastic anemia 385(53.5%) followed by Hyperreactive Malarial Splenomegaly 170(23.6%), leukemia 70(9.7%), VL 40(5.6%), aplastic anemia and stage IV RVI per se each 20(2.8%) and others 15(2.1%). Most age group affected by pancytopenia were 11–30 yrs and the most common presenting symptom and sign was fatigue and splenomegaly respectively.

Conclusions: This study showed that the most common cause of pancytopenia was megaloblastic anemia and that is reversible by therapy. Thus in pancytopenia, thorough evaluation has to be done to identify the cause at the earliest, so the treatable causes are identified without delay and the patient is benefited.

Highlights

What is already know on this topic

There is few data on epidemiology or clinico-pathology of pancytopenia in Ethiopia.

Geographic location appear to represent a risk factor for any particular cause of pancytopenia.

What this study adds

Figures are now available and will serve as a template upon which future studies in this field can be built.

This study also provides the causes of pancytopenia which is not widely studied.

Introduction

Pancytopenia is a reduction in the number of white blood cells, red blood cells and platelets in the peripheral blood below the lower limits of the age adjusted normal range for healthy people. It is therefore the combination of anemia, leucopenia and thrombocytopenia [1].

Pancytopenia is a common indication for bone marrow examination and can have numerous causes. Cytotoxic therapies, including myeloablative radiation therapy and chemotherapy, are common, but predictable, causes of pancytopenia in patients being treated systemically for neoplasia. New-onset pancytopenia outside this setting, in both children and adults, can prove to be a diagnostic dilemma, and causes include congenital and acquired bone marrow failure syndromes, marrow space-occupying lesions, peripheral destruction of hematopoietic cells, autoimmune disorders, infection, and ineffective marrow production. Often, the workup of new-onset pancytopenia is extensive and should include a detailed clinical, medication, recreational drug, and environmental exposure history. Although bone marrow examination often reveals an underlying condition causing pancytopenia, it is not always conclusive. Understanding the various disorders that may cause pancytopenia can aid in the recommendation of additional testing and clinical evaluation when the marrow studies are not specific for a single etiology. The severity of pancytopenia and the underlying pathology determine the management and prognosis of the patients, there by identifying the correct etiopathology, helps in planning the diagnostic and therapeutic approach in patients with pancytopenia [2].

In Ethiopia, the causes of pancytopenia are not well defined, so the present study has been undertaken to provide a brief overview of causes of pancytopenia in adults and children by age and sex with emphasis on bone marrow findings.

Methods

Study design and setting

This is a retrospective descriptive cross-sectional study which was based on bone marrow aspiration specimens submitted to the Pathology Department, University of Gondar Comprehensive Specialized Hospital for cytopathologic examination.

Study population

All Pancytopenic patients who presented to the department of Pathology at University of Gondar Comprehensive Specialized Hospital between the study periods of January 1st 2018 and January 1st 2021 were recruited. There were seven hundred twenty cases which met the criteria of pancytopenia that is hemoglobin < 10 g/dL, total leukocyte count < /L and platelet count < 100x /L. Cases with inadequate data entries , duplicate registrations, cases that were not straightforward morphologically and on chemotherapy were excluded from the study.

Data collection

All bone marrow aspiration results in the files of the Department of Pathology were reviewed by the author in order to identify all patients with pancytopenia. The clinical data and /or hematological profile (hemoglobin, red cell indices, total and differential leukocyte counts, platelet count) were utilized for accurate interpretation of peripheral blood smear and bone marrow aspiration finding. Bone marrow aspiration and peripheral morphology slides were stained with wright stain in all cases and examined microscopically. Bone marrow biopsy was done when necessary. All pancytopenias were analyzed according to age, sex, and clinical presentation.

Definitions

Pancytopenia was dependent variable while age, sex and clinical presentation were independent variables in this study.

Statistical analysis

The data were entered and analysed based on the causes of pancytopenia and their distribution according to age, sex and clinical presentation using statistical software,SPSS version 23. The mean age of presentation for the most common causes of pancytopenia were calculated. This is purely a descriptive study and no statistical association test performed (Analytical component was not done).

Results

General characteristics

Of the 720 patients who had pancytopenia , 548(76%) were males and 172(24%) were females. The minimum age was of 3 yrs and maximum age 78 yrs was seen. Pancytopenia involved all age groups but the majority of pancytopenia occurred in patients between 11 and 30 years of age.

Clinical presentations

The most common presenting symptom was fatigue in 100% followed by weight loss 62.5%, fever 58%, pallor 27.8%, chills and rigor 9.7%, bleeding 8.3%. The most common presenting sign was splenomegaly 75% followed by hepatosplenomegaly 16.7%, hepatomegaly 11%. Duration of symptoms before presentation ranged from 1 month to 8 years. Table 1 shows the various presenting complaints and physical findings in our study.

Clinico-Pathological profiles of pancytopenia

The most common cause of pancytopenia in our study was megaloblastic anemia 385(53.5%) followed by Hyperreactive Malarial Splenomegaly 170(23.6%). Leukemia were the 3rd most common cause of pancytopenia encountered in this study accounting for 9.7%. There were 50 cases of ALL and 20 cases of

AML . VL were the 4th most common cause of pancytopenia encountered in this study accounting for 5.6 %. Aplastic anemia and stage IV RVI per se each accounted for 2.8% of pancytopenia in this study. The other rare causes of pancytopenia encountered in this series were MDS, myelofibrosis and Hairy cell leukemia which were confirmed by bone marrow biopsy. Table 2 shows distribution of various causes of pancytopenia.

Association of age and sex with causes of pancytopenia

As shown in Table 3, most age group affected by pancytopenia were 11-30 years, 396(55%). There were 314(79%) male and 82(21%) female patients with pancytopenia. The distribution of causes of pancytopenia by sex of patient is listed in table 4.

Discussion

Pancytopenia is defined as reduction in all the 3 formed elements of blood: Red blood cells, white blood cells, and platelets below the normal reference range [3]. There is a variety in etiologies of pancytopenia in different studies [4-7]. In European populations, pancytopenia is mostly observed in hematological malignancies and rarely caused by infection [8]. In a study by Keisu M. et al., on Swedish population, results revealed that patients with pancytopenia should be carefully followed up for aplastic anemia and MDS [9]. A comparison of cause of pancytopenia in different studies is presented in table 5. In a series of a clinco-hematologic analysis of 77 cases of pancytopenia conducted in the department of Hematology and Transfusion Medicine, Government Medical College & Hospital, Chandigarh over a period of 32 months; megaloblastic anemia was the most common cause of pancytopenia accounting for 68% followed by aplastic anemia - 7.70% [10]. In the current study, megaloblastic anemia was the first most common etiology in 385(53.5%) patients, followed by HMS 170(23.6%) followed by leukemia 70(9.7%) and VL 40(5.6%). In patients below 31 years old, megaloblastic anemia was the commonest etiology detected in 190(64.2%) cases, followed by HMS in 70(23.6%) and VL 16(5.4%). Similar to young patients, in cases over 40 years old, megaloblastic anemia was the most prevalent cause detected in 55(56.1%) cases, followed by HMS and leukemia each 10(10.2%) and VL 8(8.2%). The majority of patients in the study were below 31 years old, 466(64.7%) cases. There were 280(38.9%) male and 105(14.6%)female megaloblastic anemia cases with incidence peak in the 3rd decade. There were 150(20.8%) male and 20(2.8%) female HMS cases with incidence peak in the 3rd decade.

Out of 75 cases of pancytopenia in South Indian tertiary hospital, megaloblastic anemia was the most common cause of pancytopenia accounting for 68% followed by hypoplastic/ aplastic marrow 13.3% and leukemia/lymphoma 5.33% [11]. Out of 25 cases admitted as pancytopenia at Affiliated Hospital of Dali University between the calendar year 2013 and 2014; 28% were diagnosed as megaloblastic anemia, 20% were diagnosed as aplastic anemia, 16% were diagnosed as MDS, 12% were diagnosed as AML, remaining 24% consists of SLE, Non Hodgkin's lymphoma, hypersplenism, HIV infection and hemophagocytic syndrome. 52% of diagnosed cases were male and rest 48% were female[12]. In the present series there were 20 cases of stage IV RVI with male predominance.

In the present series there were 50(71.4%) cases of ALL and 20(28.6%) cases of AML occurred mainly in adults; their age ranged from 1 ½ to 65 years, with a mean age of 26 years. Males 45(6.3%) affected predominantly than females 25(3.5%). The commonest presentation was fatigue followed by fever, bleeding , weight loss and bone pain. Out of 665 cases of pancytopenia in Iranian population, acute leukemia was the first most common etiology detected in 235(35.4%) patients in which acute myeloid leukemia comprised the majority of cases 142(21.4%), followed by myelodysplastic syndrome 100(15%). In patients less than 20 years old, acute leukemia was also the commonest cause identified in 56(57.7%) cases in which acute lymphoblastic leukemia with 38.7% was the most common etiology; however in adults (>45 year old), AML accounted for the majority of cases 76(53.5%).The commonest presentation was fatigue in 30% followed by fever 21.8%, bleeding 15.3%, weight loss 10.8%, bone pain 7.1%, headache dizziness 5.4%, abdominal pain 4.3%, jaundice 2.1%, and short of breath 1.6% [13].

In the present series there were 40(5.6%) VL cases; age of patient ranged from 22 to 45 yrs with a mean age of 36 yrs and male predominance. The commonest presenting sign 100% was fever and splenomegally followed by hepatosplenomegaly 75% and pallor 70%. Hematological profiles of all visceral leishmaniasis patients was pancytopenia. Hematological profile in visceral leishmaniasis; a hospital based cross sectional study conducted on 40 LD bodies positive cases in the department of pathology, BPKIHS, Dharan, for the period of one year reveals pyerxia was the most common sign 100% followed by splenomegaly 82.5%, hepatomegaly 65%, and pallor 75%. Anemia was present in 90%, leucopenia in 67.5% and thrombocytopenia in 72.5% cases. Bicytopenia and pancytopenia were observed in 40% and 25% cases, respectively. The age ranged from 2-60 years with mean age 16.5 years. Male 55% affected predominantly than females 45% [14].

In the present study there were 20(2.8%) cases of aplastic anemia; age of patient ranged from 8 to 28 years with a mean age of 22 yrs and male predominance. In a series of etiology of pancytopenia: an observation from a referral medical institution of eastern region of India; conducted for a period of 2 years in which 248 patients were included,156(62.9%) were males and 92(37.09%) were females.

The mean age of the patients was 33 years. Aplastic anemia was the most common cause of pancytopenia that was observed in 83(33.47%) cases followed by megaloblastic anemia in 52(20.97%) cases, leishmaniasis in 34(13.71%) patients, hypersplenism also in 34(13.71%) patients, and tuberculosis and other connective tissue disorders in 18(7.26%) cases [15].

In a series of pediatric patients with bicytopenia/pancytopenia: Review of etiologies and clinico-hematological profile at a tertiary center in India; there were 175 children with pancytopenia. Most common non-malignant condition associated with pancytopenia was aplastic anemia 33.8%, followed by megaloblastic anemia 13.7%. Malignancy leading to pancytopenia was acute leukemia 26.6% in all the cases [16]. In the present study there were 50 cases of ALL. It is interesting that in young patients below 20 year old with acute leukemia, ALL accounted for the highest frequency 50(71.4%). Other rare causes of

pancytopenia were Hairy cell leukaemia ,myelofibrosis and myelodysplastic syndromes each accounted for 0.7 % of all causes of pancytopenia.

This study further contributes to what is already known regarding the causes of pancytopenia and creates a paradigm for future studies of pancytopenia in our environment. Limitations encountered include sociodemographic factors were not fully documented on patients' files of department of pathology as well as our inability to carry out further high end cytopathological analysis due to dearth of requisite technology.

Conclusion

Megaloblastic anemia was the most common cause of pancytopenia. Most age group affected by pancytopenia were 11–30 years and the commonest presentation was fatigue. Thus this study concludes that detailed primary hematological investigations along with bone marrow aspiration in pancytopenic patients is helpful in understanding the disease process; to diagnose, or to rule out the less treatable causes of pancytopenia; and to plan for further investigations and management of pancytopenic patients.

Acronyms

HMS-Hyperreactive Malarial Splenomegaly

VL- Visceral leishmaniasis

AML- Acute myeloid leukemia

ALL-Acute lymphoblastic leukemia

RVI-Retroviral infection

MDS-Myelodysplastic syndrome

LD bodies-Leishmania donovani bodies

HIV-Human immunodeficiency viruse

SLE- Systemic lupus erythematosus

Declarations

Ethics Approval

Ethical clearance was obtained from research and ethics committee of the department of pathology, College of Medicine and Health Sciences, University of Gondar Comprehensive Specialized Hospital with a reference number of 06/01/ Patho / 781 /2021.

Consent to participate

Not applicable

Consent for publication

Not applicable

Availability of data and materials

Data is available from the corresponding author upon reasonable request.

Competing interests

Authors' have declared no conflicts of interest.

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Authors' contributions

Conception and study design: EAK

Data collection: EAK

Data analysis and interpretation: EAK

Manuscript drafting: EAK

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Tables

Table 1 : Presenting complaints and physical findings in Pancytopenia, Department of Pathology, Faculty of Medicine, University of Gondar College of Medicine and Health Sciences, 2018-2021

Symptoms / Signs	Number of cases	Percentage (%)
Fatigue	720	100 %
Fever	420	58%
Splenomegaly	540	75 %
Pallor	200	27.8%
Hepatomegaly	80	11%
Hepatosplenomegaly	120	16.7%
Dyspnea	45	6.3%
Bleeding manifestation	60	8.3%
Weight loss	450	62.5%
Chills and rigor	70	9.7%
Jaundice	45	6.25%
Abdominal pain	25	3.5%
Portal hypertension	35	4.86%
Lymphadenopathy	15	2.1%

Table 2 : Distribution of various causes of pancytopenia, Department of Pathology, Faculty of Medicine, University of Gondar College of Medicine and Health Sciences, 2018-2021

Causes of Pancytopenia	Number of cases	Percentage (%)
Megaloblastic anemia	385	53.5 %
HMS	170	23.6 %
Leukemia	70	9.7 %
VL	40	5.6%
Aplastic anemia	20	2.8%
Stage IV RVI	20	2.8%
Myelofibrosis	5	0.7 %
Hairy cell leukemia	5	0.7 %
MDS	5	0.7 %
Total	720	100 %

Table 3 : Distribution of various causes of pancytopenia with age of patient, Department of Pathology, Faculty of Medicine, University of Gondar College of Medicine and Health Sciences, 2018-2021

Causes of Pancytopenia	Age groups in years								Total	Percentage
	0-10	11-20	21-30	31-40	41-50	51-60	61-70	71-80		
Megaloblastic anemia	15	30	190	95	15	15	20	5	385	53.5%
HMS	20	40	70	30	5	5	0	0	170	23.6%
Leukemia	30	25	0	5	0	5	5	0	70	9.8%
VL	0	0	16	16	8	0	0	0	40	5.5%
Aplastic anemia	5	5	10	0	0	0	0	0	20	2.8%
Stage IV RVI	0	0	10	10	0	0	0	0	20	2.8%
Myelofibrosis	0	0	0	0	0	5	0	0	5	0.7%
Hairy cell leukemia	0	0	0	0	0	5	0	0	5	0.7%
MDS	0	0	0	0	0	0	0	5	5	0.7%
Total	70	100	296	156	28	35	25	10	720	100%

Table 4 : Distribution of various causes of pancytopenia with sex of patient, Department of Pathology, Faculty of Medicine, University of Gondar College of Medicine and Health Sciences, 2018-2021

Causes of pancytopenia	Number of males	Percent(%)	Number of females	Percent(%)	Total number of cases	Percent(%)
Megaloblastic anemia	280	38.9%	105	14.6%	385	53.5%
HMS	150	20.8%	20	2.8%	170	23.6%
Leukemia	45	6.3%	25	3.5%	70	9.8%
VL	32	4.4%	8	1.1%	40	5.5%
Aplastic anemia	15	2.1%	5	0.7%	20	2.8%
Stage IV RVI	13	1.8%	7	0.97%	20	2.8%
Myelofibrosis	5	0.7%	0	0%	5	0.7%
Hairy cell leukemia	5	0.7%	0	0%	5	0.7%
MDS	3	0.42%	2	0.28%	5	0.7%
Total	548	76.1%	172	23.9%	720	100%

Table 5 : Comparison of cause of pancytopenia in different studies

ond Common ıse	Commonest Cause	No.of cases	Year	Country	Study
galoblastic mia 23%	Myelodysplastic syndrome 33%	100	2014	Iran	Safaei A. et al [4]
astic anemia 26%	Megaloblastic anemia 74.04%	104	2011	India	Gayathri et al [5]
galoblastic mia 22.3%	Hypoplastic anemia 29.51%	166	1999	India	Hayat A. et al [6]
ɔersplenism 71%	Aplastic anemia 22.72%	111	2010	India	Santra G et al [7]
S 4.5%	Hypoplastic anemia 52.7%	100	1990	Sweden & Europe	Keisu M et al [9]
elodysplastic drome 15%	Acute leukemia 35.4%	665	2017	Iran	Iran J pathol[13]
galoblastic mia 20.97%	Aplastic anemia 33.47%	248	2015	India	Dasgupta, et al[15]
te leukemia 6%	Aplastic anemia 33.8%	175	2011	India	Indian J Pathol Microbiol[16]
S 23.6%	Megaloblastic anemia 53.5%	720	2018-2021	Ethiopia	Present study