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Original Article

Clinicohematological Profile of Patients with Bicytopenia

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Abstract

Background Bicytopenia (BC) is a reduction in counts in any of two cell lineages of blood, which can be a combination of anemia with thrombocytopenia, anemia with leukopenia, or leukopenia with thrombocytopenia. The etiology of BC can be a malignancy, nonmalignant disease, infectious cause, or drug-induced.

Aim To assess the clinicohematological profile in patients with BC.

Materials and Methods This prospective study was conducted in the hematology laboratory at the Justice K.S. Hegde Charitable Hospital. Patients with BC detected during the analysis of blood for any clinical condition were included in the study. Blood parameters assessed were hemoglobin, red blood cell count, total leukocyte count, and platelet count.

Results In this study, 86 patients' samples with BC were collected, out of which 55.8% were male, and 44.2% were female. The most common BC was anemia with thrombocytopenia (69.8%). The most common etiology of BC was found to be nonmalignant (37.2%), followed by malignant (37.2%), infectious (25.6%), and drug-induced (4.7%) cases. Most of the patients with BC presented with fever, pallor, and generalized weakness.

Conclusion Anemia with thrombocytopenia emerged as the predominant form of BC in the nonmalignant group, while the malignant etiology group presented with anemia with leukopenia. The infectious etiology group presented with leukopenia with thrombocytopenia. Neonatal sepsis emerged as the most prevalent cause of BC in the age group younger than 10 years, viral fever in the age group of 10 to 39 years, acute lymphoblastic leukemia in the age group of older than 70 years, and chronic liver disease in patients aged between 40 and 69 years.

Keywords
- bicytopenia
- malignant
- nonmalignant
- infectious
- drug-induced

Introduction

Peripheral blood cytopenia is defined as a decrease in either of the cellular elements of blood: red blood cells, white blood cells, or platelets. It can be of three types: isolated cytopenia, bicytopenia (BC), and pancytopenia. Pancytopenia is the reduction in all the three cellular elements of peripheral blood, leading to anemia, leukopenia, and thrombocytopenia.[1] BC is defined as a reduction in counts in any of the two cell lineages of blood that are less than normal for that sex and age. It can be a combination of anemia with thrombocytopenia, anemia with leukopenia, and leukopenia with thrombocytopenia.[2] According to studies done by Singh et al and Thakur et al,[3,4] the prevalence of BC in adults was 55.5 and 66.17%, respectively, whereas the prevalence of BC in children was 40 and 65.3%, respectively.[5,6] Alterations in blood counts have the potential

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to serve as indicators for specific diseases.[7] Peripheral smear examination helps assess the cell morphology of blood cells and confirm the decreased blood cell count. It also helps identify blood parasites and abnormal cells.[8] Examination of bone marrow aspiration smears will aid in diagnosing malignant hematological conditions. Although pancytopenia and isolated cytopenia are extensively researched, the literature has limited information on BC. There are only a few articles which study on the etiology, clinical characteristics, and hematological profile of bicytopenic patients in various age groups.[5]

This study aimed to evaluate the demographic profile of patients with BC in terms of age, sex, and clinical presentation, to identify the causes of BC in various age groups, and to describe the pattern of BC in various etiological groups. The findings from this study will provide valuable insights into the underlying causes of BC in our population.

Materials and Methodology

This is a prospective study conducted at the Justice K.S. Hegde Charitable Hospital during the 2 years between September 2021 and August 2023. The institutional ethics committee clearance was obtained before the commencement of the study. Patients with BC detected during the analysis of blood for any clinical condition were included in the study. The analysis of the EDTA anticoagulated venous blood was processed in an autoanalyzer *SYSMEX XN 1000*. Parameters assessed were hemoglobin, red blood cell count, total leukocyte count, and platelet count, which were standardized by routine external and internal quality control checks. The peripheral smear was stained with Leishman's stain and was examined for blood cellular morphology, count, abnormal cells, and inclusion bodies. Bone marrow examination was performed in cases clinically indicated, and bone marrow smears were stained with Leishman's stain. Special stains such as myeloperoxidase, periodic acid–Schiff, and Perl's stain were done whenever necessary. Other relevant clinical data, demographic details, working diagnosis, supportive investigations, and serological test results of the cases were collected from the laboratory information system.

The study subjects were divided into four age groups: < 10, 10 to 39 years, 40 to 69 years, and ≥ 70 years. The causes of BC were classified into four main groups: malignant, nonmalignant, infectious, and drug-induced. The malignant category included all cases where BC was attributed to hematological and nonhematological malignancies. Nonmalignant cases encompass all nonmalignant conditions that do not result from active infections or drug-induced effects. The infectious category consisted of cases where BC is associated with confirmed active infections based on serological tests. The drug-induced category included cases in which BC occurred as a result of certain medications or posttherapy.

Clinicohematological profiles of bicytopenic patients were described using descriptive statistics (mean, standard deviation, and percentage). Categorical variables were compared using a chi-square test, and a significance level of $p < 0.05$ was used to determine the association between different variables and BC. Data were entered in an Excel sheet and analyzed using SPSS software.

Results

This study involved 86 patients with BC. Among these, 48 (55.8%) were male and 38 (44.2%) were female. The male-to-female ratio was 1.3:1. Maximum number of patients was in the age group of 40 to 69 years (55.8%), followed by 10 to 39 years and >70 years (19.8% each). The mean age of the participants was 52.2 years, with the age ranging from 1 day to 99 years. The standard deviation of age was 31.8 years. Across all ages in patients with BC, males outnumbered females.

Anemia with thrombocytopenia was the most common morphological type noted in 60 (69.8%) patients, followed by anemia with leukopenia in 24 (27.9%). The least common was leukopenia, with thrombocytopenia seen in only two (2.3%) patients.

The most common etiology of BC was found to be nonmalignant (32 cases, 37.2%), followed by malignant (28 cases, 37.2%), infectious (22 cases, 25.6%), and drug-induced (4 cases, 4.7%).

The most common etiology of BC observed in the age group younger than 10 years was infectious cases (50%), followed by malignant and drug-induced cases (25%). In the age group 10 to 39 years, the most common etiology observed was malignancy (41.2%), followed by infectious (29.4%). No drug-induced BC was seen in this age group. Between 40 and 69 years, the most common etiology was nonmalignant (43.7%), followed by malignant (13%), infectious (12%), and drug-induced (4.2%). In the elderly age group, the most common etiology was malignant (41.2%), followed by nonmalignant (35.3%), infectious (17.6%), and drug-induced (5.9%) (►**Table 1**).

Anemia with thrombocytopenia was the most frequently observed morphological type of BC in the nonmalignant etiology group, accounting for 43.3% of cases. Anemia with leucopenia was most significant in malignant etiology, comprising 58.3% of cases. Leukopenia with thrombocytopenia was significant equally (50%) in the infectious and nonmalignant etiology groups (►**Table 2**).

The most common symptom at the time of presentation was fever (41.95%), followed by generalized weakness (30.2%), abdominal pain (25.6%), vomiting (17.4%), bleeding (14.0%), and cough (10.5%).

Pallor and fever were the most common clinical findings (21.5% each) in malignant etiology. Pallor (16.7%), abdominal pain (14.8%), and icterus (13%) were the most prevalent sign in nonmalignant etiology. Fever (32.1%) and generalized weakness (15.1%) were the most frequent clinical finding in the infectious category. The drug-induced etiology group had pallor (40%), fever, abdominal pain, and vomiting (20% each) as the most common sign (►**Table 3**).

Discussion

There is a broad spectrum of etiology of BC ranging from malignancies to nonmalignant conditions, infections, and following exposure to certain drugs. Only a few studies in

Table 1 Agewise etiology distribution

Age	Malignant	Nonmalignant	Infectious	Drug-induced
<10 y	ALL B-cell (1)	Nil	Neonatal sepsis (2)	Burkitt's lymphoma (on chemotherapy) (1)
10–39 y	AML and AML (M3) (2) Hodgkin lymphoma (2) Adenocarcinoma of rectum (1) CML-blast phase (1) Olfactory neuroblastoma (1)	Severe aortic regurgitation (1) Megaloblastic anemia (1) Right parieto-occipital glioma (1) H/o fall from height SDH falx cerebri (1) Alcohol hepatitis (1)	Viral fever (2) Leptospirosis (1) Viral fever (suspected infectious mononucleosis) (1) Pulmonary embolism (1)	Nil
40–69 y	Carcinoma of left breast (2) Carcinoma of cervix stage 2b (1) MM (3) AML (M5) (1) Ovary cancer stage 3c (2) Neuroblastoma stage 4 (1) NHL (1) Cutaneous T-cell lymphoma (1) GI cancer (1)	Myocarditis in cardiac failure (1) Chronic pancreatitis (1) Chronic kidney disease (1) Hemophilia A (1) Vasculitis (1) Chronic liver disease (10) Coronary artery disease (1) Ischemic heart disease (1) Left femur trochanter lesion (1) ITP (2) TTP (1)	Bronchopneumonia (1) Acute febrile illness (1) Lower respiratory tract infection (1) Appendicitis (1) Sepsis with septic shock (1) Leptospirosis (1) Acute gastroenteritis with sepsis (1) Viral encephalitis (1) COVID-19 positive status (1) Sepsis with MRSA (1) Dengue fever (1) Vestibular neuritis (1)	AML (under chemotherapy) (2)
>70 y	Papillary adenocarcinoma (right parietal pleura) (1) Carcinoma of rectum (1) Retroperitoneal abdominal mass—liposarcoma (1) ALL (1) ALL T-cell (1) MM (1) MDS (RAEB-2) monosomy 7 (1)	Chronic liver disease (1) Hepatic encephalopathy (1) Mitral valve prolapses (1) Coronary artery disease (1) Common bile duct calculus (1) Splenomegaly with splenic abscess (1)	COVID-19 positive status (1) Leptospirosis (1) Right-sided pleural effusion (1)	Squamous cell carcinoma of the left cervical (under chemotherapy) (1)

Abbreviations: AML, acute myeloid leukemia; ALL, acute lymphoblastic leukemia; CML, chronic myeloid leukemia; GI, gastrointestinal; H/o, history of; ITP, immune thrombocytopenic purpura; MDS, myelodysplastic syndrome; MM, multiple myeloma; MRSA, methicillin-resistant *Staphylococcus aureus*; NHL, non-Hodgkin lymphoma; RAEB-2, refractory anemia with excess blasts type 2; SDH, subdural hematoma; TTP, thrombotic thrombocytopenic purpura.

Table 2 Distribution of bicytopenia in different etiology groups

Bicytopenia	Etiology							
	Malignant		Nonmalignant		Infectious		Drug-induced	
	N	%	*N*	%	*N*	%	*N*	%
Anemia with thrombocytopenia	17	28.3%	26	43.3%	15	25.0%	2	3.3%
Anemia with leukopenia	14	58.3%	2	8.3%	6	25.0%	2	8.3%
Leukopenia with thrombocytopenia	0	0.0%	1	50.0%	1	50.0%	0	0.0%

Notes: Chi-square test = 14.381; *p*-value = 0.026. There is statistical significance between bicytopenia and different etiology groups with chi-square test = 14.38; *p*-value < 0.05.

Table 3 Distribution of clinical features in different etiology groups

Clinical feature	Etiology							
	Malignant		Nonmalignant		Infectious		Drug-induced	
	N	%	*N*	%	*N*	%	*N*	%
Fever	14	21.5	4	7.4	17	32.1	1	20.0
Pallor	14	21.5	9	16.7	6	11.3	2	40.0
Icterus	2	3.1	7	13.0	2	3.8	0	0.0
Bleeding	7	10.8	3	5.6	1	1.9	0	0.0
Lymphadenopathy	4	6.2	1	1.9	1	1.9	0	0.0
Hepatomegaly	2	3.1	5	9.3	0	0.0	0	0.0
Splenomegaly	1	1.5	3	5.6	0	0.0	0	0.0
Abdominal pain	6	9.2	8	14.8	7	13.2	1	20.0
Vomiting	4	6.2	6	11.1	4	7.5	1	20.0
Cough	0	0.0	1	1.9	7	13.2	0	0.0
General weakness	11	16.9	7	13.0	8	15.1	0	0.0
Total	65	100.0%	54	100.0%	53	100.0%	5	100.0%

the literature have evaluated the clinical variables and etiological factors of BC in different age groups. Considering these facts, data from bicytopenic patients were collected for the first time in southern region of India.

In India, BC is most prevalent in adults, whereas the prevalence of BC in children is slightly lower than in adults.[9] In our study, BC was seen most frequently in adults between 40 and 69 years of age (55.8%), followed by elderly >70 years (19.8%) and 10 to 39 years (19.8%), while children <10 years of age (4.7%) were the least affected.[4] The findings are comparable to the study conducted by Singh et al, where BC was most frequently observed in adults (55.5%), followed by children (17.25%), elderly individuals (11.25%), and teenagers and infants (8% each).[3] According to a study in Pune, the commonest age group affected was in the third and fourth decades.[4] Dagdia et al reported that 77.33% of BC were in patients between 21 and 80 years.[2] In a study of BC in children conducted by Katoch et al, the commonest age group affected (42%) was between 11 and 15 years.[8] These variations may be attributed to differences in the population being studied, geographic distributions, and periods of observations. Though the frequency of BC in children is relatively low, they are not entirely spared.

In India, BC is more common in males than females.[3,5] In our study, the majority were male (55.8%) with a male-to-female ratio of 1.3:1. This finding is similar to most of the available literature in India. Foreign studies suggest that gender distribution is not different from the Indian scenario. Sarbay reported that 56.2% of BC patients were males.[6] Kato et al from Japan reported that 70.7% of study subjects were male.[9] The higher incidence of BC in males may be due to male preponderance in malignancies, personal habits such as alcohol abuse, and relatively more outdoor exposure to infections than females.

The Pattern of Bicytopenia in Various Groups

In the present study, the most prevalent type of BC was found to be anemia with thrombocytopenia (69.8%), followed by anemia with leukopenia (27.9%) and leukopenia with thrombocytopenia (2.3%). These findings align with the results reported by Naseem et al, who also observed that anemia with thrombocytopenia was the most common type of BC (77.5%), followed by anemia with leukopenia (17.3%) and leukopenia with thrombocytopenia (5.5%).[5]

Malignant conditions such as acute leukemia presented with anemia and thrombocytopenia in 78.6% of cases. It is well known that infiltration of bone marrow with immature progenitor cells leads to relative suppression of erythroid and megakaryocyte series, resulting in peripheral blood anemia with thrombocytopenia.

Anemia with leukopenia was most common (27.9%) in malignant etiology. Nine cases were seen in various organ malignancies of the breast, cervix, ovary, and colorectum. This may be due to decreased immunity in these cancer patients. Hematological malignancies such as subleukemic acute myeloid leukemia (AML), Hodgkin lymphoma, and non-Hodgkin lymphoma also presented with anemia with leucopenia.

Leukopenia with thrombocytopenia was equally prevalent (50% each) in nonmalignant and infectious etiologies. The only infectious etiology in this group was dengue fever. Dengue virus causes the destruction or suppression of myeloid progenitor cells, which leads to leukopenia and peripheral destruction of platelets or destruction of bone marrow megakaryocytes by the virus, resulting in decreased platelet count.[10]

Microcytic hypochromic anemia was the most common morphological subtype of anemia (41.5%) in malignant etiology. Dimorphic and macrocytic anemia (43.3%) were common in

nonmalignant and normocytic normochromic anemia (50%) in infectious etiology.

Macrocytic anemia in chronic liver disease (CLD) may be caused by increased cholesterol deposition on the membranes of circulating red blood cells. This deposition effectively expands the erythrocyte's surface area. Peripheral smear shows nonmegaloblastic macrocytosis displaying round macrocytes characteristic of CLD.[11] Viral or bacterial infections can also result in anemia through mechanisms such as mild idiopathic hemolysis and marrow inhibition.[12]

Bone Marrow Examination

In our study, a bone marrow examination was performed on eight patients with BC. It was done in three cases of multiple myeloma, two cases of immune thrombocytopenic purpura (ITP), one case of Burkitt's lymphoma, one case of AML (M5), and one case of chronic myeloid leukemia—blast phase.

Few studies of BC in adults and children have been conducted in bone marrow examination. In a study conducted by Dagdia et al, they reported that the most common finding in bone marrow examination was megaloblastic anemia (29.3%) observed in all age groups except between 61 and 80 years, followed by aplastic anemia, AML, and myelodysplastic syndrome (22.22%) in 61 to 80 years.[2] A study by Katoch et al in children showed that bone marrow examination helped diagnose six cases of acute lymphoblastic leukemia (ALL) and one case of AML. It also helped in diagnosing nonmalignant conditions such as aplastic anemia (two cases), megaloblastic anemia (two cases), ITP and iron deficiency anemia (one case each).[8]

Bone marrow examination is indicated in various neoplastic and nonneoplastic diseases. In cases of leukemia, further studies such as fluorescence in situ hybridization can be done on bone marrow samples for subtyping. It is necessary to diagnose and initiate the proper treatment, management, and prognostic purposes.

Symptoms and Signs

In our study, the most common symptom reported at the time of presentation was fever (41.95%), followed by generalized weakness (30.2%), abdominal pain (25.6%), vomiting (17.4%), bleeding (14.0%), and cough (10.5%). Fever was observed predominantly in infectious etiology (47.2%). These findings are similar to the study done by Katoch et al.[8]

Fever is a physiological reaction to infectious, inflammatory, and autoimmune diseases. It involves the secretion of chemical mediators, which activate the hypothalamic thermoregulatory center and elevate body temperature.[13]

Pallor was the most prevalent sign (36.0%), followed by icterus (12.8%), hepatomegaly (8.1%), lymphadenopathy (7.0%), and splenomegaly (4.7%). Pallor was most common in malignant conditions (21.5%) such as multiple myeloma, ALL, adenocarcinoma of the rectum, ovarian cancer, and cutaneous T cell lymphoma, which had anemia and thrombocytopenia. Icterus (13%), hepatomegaly (9.3%), and splenomegaly (5.6%) were common signs in nonmalignant conditions such as chronic liver disease, chronic pancreatitis, and splenomegaly with splenic abscess. Lymphadenopathy was a common sign in malignant conditions such as Hodgkin lymphoma, non-Hodgkin lymphoma, carcinoma of the left breast, and cutaneous T cell lymphoma.

Katoch et al, in their study, also reported that pallor (86%) was the most common sign, followed by hepatomegaly (64%), lymphadenopathy (60%), and splenomegaly (58%).[8] In a study done by Thakur et al, hepatomegaly was found in 14.8% of bicytopenic patients, splenomegaly (9.6%), whereas lymphadenopathy was found in 12.6% of bicytopenic patients.[4]

Extramedullary infiltration of blasts causes splenomegaly, lymph node enlargement, gum involvement, and diffuse skin infiltration in AML.[14]

Bleeding manifestations are due to thrombocytopenia, fatigue, and weakness due to anemia. Fever is due to increased susceptibility to infections due to decreased levels of neutrophils. Signs such as hepatosplenomegaly and lymphadenopathy are attributed to malignant etiology such as leukemia.

Etiologies

Nonmalignant etiology emerged as the predominant cause of BC in our study (37.2%), followed by malignant conditions (32.5%), infectious cases (25.6%), and drug-induced cases (4.7%). Few studies of BC have been done in children and few in adults.

A study conducted by Thakur et al in adult patients presenting with BC reported that the most common etiology was infectious cases (77.8%), followed by nonmalignant (17%), drugs (3%), and malignant (2.2%).[4]

These findings diverge from a study conducted by Naseem et al, where malignant etiology was reported as the most common cause of BC in children (69.5%), followed by nonmalignant cases (18.4%) and nonspecific causes (12.1%).[5]

The variations could be because the present study included all age groups who were presented with BC.

Nonmalignant Conditions

Among the nonmalignant cases, chronic alcoholic liver disease was found to be the most common nonmalignant cause, accounting for 12.8% of the cases, followed by ITP and coronary artery disease (2.3% each). These patients had anemia with thrombocytopenia.

A study conducted by Vijay et al also found chronic alcoholic liver disease as the predominant nonmalignant cause of BC.[15]

CLD leads to progressive liver damage, impacting the synthesis of proteins and clotting factors, detoxification processes, and bile excretion. This deterioration results in hematological complications such as cytopenias (BC) and coagulation irregularities. Conditions such as megaloblastic anemia, iron deficiency anemia, double deficiency anemia, aplastic anemia, marrow failure, and spleen cell sequestration can contribute to cytopenias in individuals with CLD. Furthermore, diminished production of thrombopoietin by the liver is a factor in decreased platelet counts.[16]

Singh et al conducted a study that revealed alcoholic liver disease as the second most prevalent nonmalignant cause of BC, following ITP.[3]

CLD is not cited as a cause in studies on BC in children.[3] In our study, a maximum number of patients were in the age group between 40 and 69 years, which could be the reason for increased cases of alcoholic liver disease.

There were two cases of ITP presented with BC in our study. Their peripheral smear showed anemia (dimorphic anemia) with thrombocytopenia. These women were 43 and 53 years old and presented with bleeding, fever, and overall weakness. Bone marrow aspiration showed hypercellular marrow with both erythroid and megakaryocytic hyperplasia (►**Fig. 1**).

Naseem et al reported that the most common etiology of BC was ITP (5.2%).[5]

One case of chronic kidney disease (CKD) was encountered in this study. His peripheral smear showed microcytic hypochromic anemia with leucopenia. CKD causes BC, most commonly anemia, and leucopenia, via complex mechanisms. CKD-related kidney damage reduces erythropoietin production, leading to anemia due to decreased red blood cell formation. Concurrently, accumulated uremic toxins affect bone marrow function, impairing red and white blood cells production and resulting in leucopenia.[17]

Megaloblastic anemia causes anemia and low platelet count by hampering DNA synthesis due to vitamin B12 or folate deficiencies. This disruption affects the bone marrow's red blood cells and platelet maturation, producing enlarged immature red cells (megaloblasts), causing anemia, and impeding platelet formation. The impaired DNA replication alters platelet production, reducing count alongside anemia.[18] We had one case of megaloblastic anemia who had macrocytic anemia with thrombocytopenia (►**Fig. 2**). One case of splenomegaly with splenic abscess was seen in an 87-year-old man.

Malignant Conditions

In the current study, malignant conditions (32.5%) were further subdivided into hematological causes (16, 51.6%) and nonhematological causes (15, 48.4%). The most common hematological malignant etiology of BC was multiple myeloma (25%), followed by AML (18.8%) and Hodgkin lymphoma (12.5%). The most common nonhematological malignant etiology of BC was carcinoma of the breast and ovarian cancer (16.7% each).

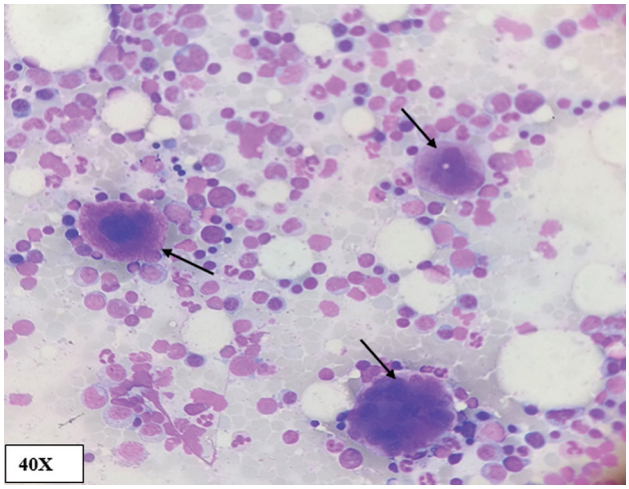

Fig. 1 Bone marrow aspiration showing increase in megakaryocytes (thick arrow), ×40, Leishman's stain.

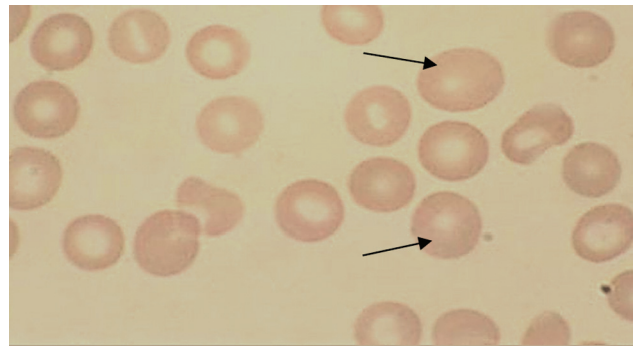

Fig. 2 Peripheral blood smear showing macrocyte (black arrow), ×100, Leishman's stain.

In a study conducted in Belgaum, the most frequent malignant etiology of BC was observed to be AML, with a prevalence of 4.75%, followed by ALL with a prevalence of 2.5%.[3] Conversely, another study conducted in Chandigarh on BC/pancytopenia in a pediatric population reported that acute leukemia was the most common cause, accounting for 66.9% of cases.[5]

BC in multiple myeloma stems primarily from bone marrow infiltration by malignant plasma cells, disrupting the normal production of red blood cells and platelets. Multiple myeloma patients presented with anemia and thrombocytopenia. Plasma cells were increased (88%) in bone marrow aspiration. (►**Fig. 3**).

BC in AML commonly occurs due to bone marrow infiltration by rapidly proliferating leukemic blasts, suppressing the normal production of red blood cells and platelets. In the current study, AML patients presented with anemia and thrombocytopenia. The myeloblasts ranged from 10 to more than 20% in peripheral blood smears, varying between cases, while they exceeded 20% in bone marrow smears. Myeloblast has enlarged irregular round to oval nuclei, fine chromatin, three to five nucleoli, and basophilic agranular cytoplasm. A few can show Auer rods (►**Fig. 4**).

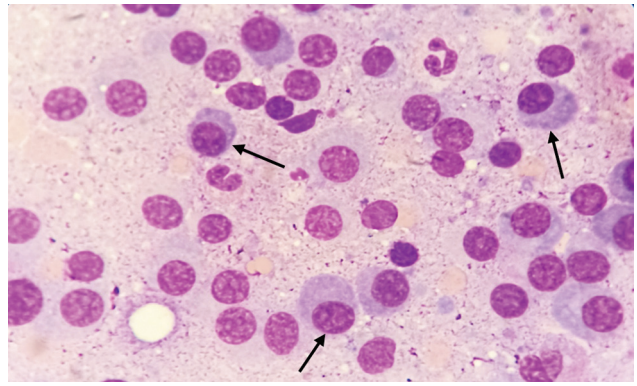

Fig. 3 Bone marrow aspiration showing increase in plasma cells (thick arrow), ×100, Leishman's stain.

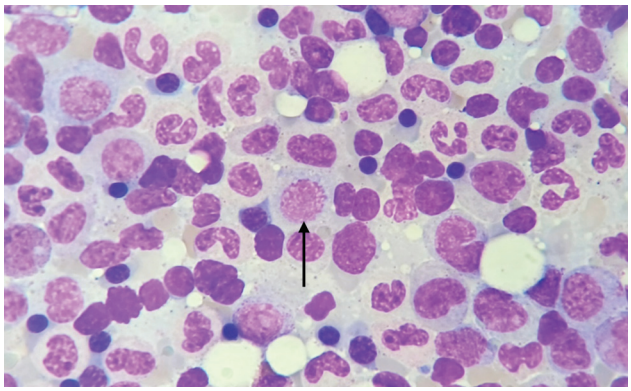

Fig. 4 Bone marrow aspiration showing myeloblasts (black arrow), ×100, Leishman's stain.

Ours is a tertiary care hospital; hence, the number of patients with malignancies visiting our center is also high on a day-to-day basis, which could have led to increased cases of malignant etiology in our study.

Infectious Conditions

The present study identified infectious etiology as the third most prevalent cause of BC, comprising 25.6% of the cases.

Leptospirosis was the most prevalent infectious etiology, accounting for 3.5% of the cases, followed by neonatal sepsis and COVID-19 infection (2.3% each). All the cases of leptospirosis presented with anemia and thrombocytopenia.

Leptospirosis causes anemia with thrombocytopenia by triggering bone marrow suppression and immune-mediated destruction of red blood cells and platelets.

Infectious etiology was the most common cause of BC, accounting for 61.8% of the cases in a study by Thakur et al, who reported dengue fever as the most common infectious cause of BC.[4] In the present study, one case of dengue fever presented as leukopenia with thrombocytopenia. Serology was positive for nonstructural protein 1 antigen. Atypical lymphocytes were found in the peripheral smear (►**Fig. 5**).

Drug-Induced

The drug-induced etiology showed the least number of cases causing BC in the current study (4.7%). The most common drug-induced etiology was chemotherapy for AML (2.3%) with arasid and daunorubicin injection, followed by chemotherapy for squamous cell carcinoma of the oral cavity (1.2%) and chemotherapy for Burkitt's lymphoma (1.2%). Chemotherapy for AML presented anemia with thrombocytopenia, whereas the latter two cases presented with anemia with leukopenia.

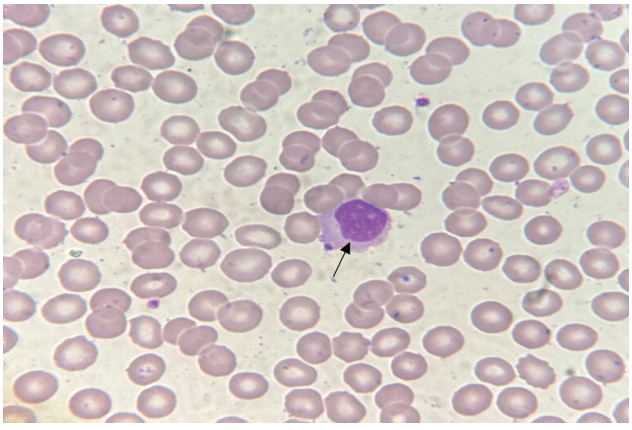

Fig. 5 Peripheral smear showing atypical lymphocyte in dengue fever (arrow), ×100, Leishman's stain.

Singh et al found retroviral disease patients and certain nonhematological malignancies such as lung carcinoma and cervical carcinoma on chemotherapy as the most frequent cause of drug-induced BC.

Drugs which cause BC are antiretroviral drugs such as zidovudine and efavirenz, antipsychotic drugs, benzodiazepine abuse, antidepressants, and anti-epileptic drugs.[3] Certain drugs cause isolated thrombocytopenia. Drugs such as quinine, cephalosporins, L-Dopa cause thrombocytopenia by binding to antibody and platelet membrane glycoprotein, promoting antibody response and formation of autoantibodies, respectively.[19]

Many studies have been done on BC only in children or adults separately. Our study covers the etiological spectrum of BC across all age groups. It also categorizes the malignant causes into hematological and nonhematological malignant causes, offering better insights to existing literature.

Limitations of this study included a restricted timeline for sample collection, resulting in a small sample size. Not all leukemic patients' samples were subjected to advanced tests such as flow cytometry and cytogenetics due to financial constraints.

Conclusion

This study assessed the clinicohematological profile in patients with BC. Anemia with thrombocytopenia emerged as the predominant form of BC in nonmalignant etiology. Most of the patients in the malignant etiology group, particularly with nonhematological malignancies, were presented with anemia with leukopenia. The infectious etiology group showed the highest occurrence of leukopenia with thrombocytopenia. The most prevalent morphological subtype of anemia was microcytic hypochromic anemia. Nonmalignant etiology accounted for the majority of cases of BC.

Neonatal sepsis emerged as the most prevalent cause of BC in the age group younger than 10 years. In the age group of 10 to 39 years, viral fever was the most frequent cause of BC. In the age group of older than 70 years, T cell ALL was identified as the most common cause and CLD in patients aged between 40 and 69 years.

Evaluating patients with BC will provide valuable insights into the underlying causes of BC and help the clinicians in diagnosing underlying conditions promptly, in selecting appropriate treatments, monitoring complications, and improving patient outcomes.

Conflict of Interest
None declared.

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