ORIGINAL ARTICLE

PATTERN OF BASIC HEMATOLOGICAL PARAMETERS IN ACUTE AND CHRONIC LEUKEMIAS

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ABSTRACT

Objective: To determine pattern of basic hematological parameters in leukemias, thus highlighting their diagnostic significance.

Material and method: This cross sectional descriptive study was done in Khyber Teaching Hospital , from January 2015 to July 2017. Cases of acute and chronic leukemias were included in the study by Non probability purposive sampling technique. Patients whose aspirates were inadequate were excluded from the study. Complete blood counts were done by Sysmex analyzer. CBC findings were recorded and results were drawn . Mean and standard deviation were used for quantitative data, while frequency and percentages were used for qualitative data .

Results: Out of 117 cases of Leukemia, 8 cases were excluded due to inadequacy of their aspirate sample. Remaining 109 cases were included in the study. Mean age of study sample was 49 ± 19 years . Changes in blood counts were as increased TLC (in 52%, 66.6%, 87.5%, and 66.6% cases of ALL, AML,CML and CLL respectively), and low hemoglobin level (in 82%, 97.4%, 87.5%, and 100% cases of ALL, AML, CML and CLL). The platelet count was low (in 88%, 92.3%, and 58% cases of ALL, AML and CLL), but high in CML (in 62.5% cases).

Conclusion: Anemia , raised white cell count and thrombocytopenia is characteristic in all leukemias, except chronic myeloid leukemia where platelet count is raised. Careful study of these parameters give idea about underlying leukemia.

Keywords: Blood counts, Acute lymphoid leukemia, Acute myeloid leukemia, Chronic lymphocytic leukemia, Chronic myelogenous leukemia.

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INTRODUCTION

Leukemia is a white blood cell disorder involving the bone marrow [1]. It is a malignant disorder of hematopoietic tissue that is associated with uncontrolled abnormal proliferation of malignant white blood cells in the bone marrow [1,2]. The malignant white blood cells cause infiltration of the bone marrow stroma , accumulate there , spill into the circulation , and thus infiltrate other tissues of the body as well [2]. The infiltration of the tumour cells into the bone marrow causes the replacement of other normal hematopoietic cells like erythroid precursor cells and megakaryocytes by abnormal tumour cells referred to as blasts [2]. This leads to decreased production of red blood cells and platelets , manifesting as anemia and thrombocytopenia in patients of leukemia [1,2].

The incidence of leukemia is gradually increasing in Pakistan as reported in several studies [2,3,4,5]. In Northern areas of Pakistan, leukemias are reported to be the second commonest cancer [5]. Most cases of leukemia commonly develop in the male population [3]. Acute myeloid leukemia (AML) is common in adults, while acute lymphoblastic leukemia (ALL) is common in children [3,6,7]. Incidence of AML is 3–4 persons per 100,000 individuals[8]. The median age of diagnosis of AML is reported to be around 70 years [8,9,10]. The world wide incidence of ALL is about 3 per 100,000 population [6] .The median age of ALL patients in Pakistan is 6 years [11,12] . The incidence of Chronic lymphocytic leukaemia (CLL) is 1 - 5.5 per 100,000 population worldwide [13]. Leukemias are generally classified into two categories i.e acute leukemias and chronic leukemias [14]. The acute leukemias are then further classified into acute myeloid leukemia (AML) and acute lymphoblastic leukemia (ALL) [14]. Chronic leukemias are further subclassified into chronic lymphocytic leukemia (CLL) and chronic myeloid leukemia (CML) [15].World health organization (WHO) classified acute leukemias on the basis of immunophenotypes and cytogenetic studies [15].The WHO classification of Leukemias is of prognostic importance and is followed till date all over the world. Routine investigations in laboratory that are performed for leukemia

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include performing a complete blood count (CBC), peripheral blood film examination ,and review of the bone marrow aspiration [16]. More advanced investigations include flow cytometry analysis and cytogenetic studies [16]. Complete blood count is a simple first line test that is advised by the clinician when suspecting leukemia [17]. There are certain basic hematological parameters in CBC , which include total leukocyte count (TLC), Hemoglobin (Hb) and platelet count . CBC report is almost always abnormal in leukemic patients ,and that too in a specific way . Therefore , the clinician should be aware of the way in which the basic hematological parameters change in leukemias . The pattern of CBC findings in leukemic patients reported in literature is raised white cell count , decreased hemoglobin and a decreased platelet count [17,18]. No study has been done so far to determine the changes in basic hematological parameters in all leukemias collectively in our setup . So the present study was done in order to determine pattern of changes in basic hematological parameters in all leukemias in our population .

MATERIAL AND METHODS

This Cross Sectional Descriptive study was done in Khyber Teaching Hospital , Peshawar, from January 2015 to July 2017. All patients referred to the Pathology department for bone marrow aspiration ,having blasts or atypical cells on blood smear or with suspicion of leukemia on history or examination were included in the study. Patients who were already on chemotherapy for treatment of leukemias and those whose aspirates were inadequate for comment were excluded from the study. Non probability purposive sampling technique was used .The complete blood counts were done by Sysmex hematology analyzer. Normal ranges for TLC, Hb and platelet count taken were 4-11x10^9/mm^3, 11.5-13 gm/d L, and 150-400x10^9/mm^3 respectively [24]. Bone marrow aspirate and biopsy was done in all patients. Samples were obtained from posterior superior iliac spine under local anesthesia. Slides were prepared , stained with Giemsa stain and examined under microscope by haematologists. To differentiate AML from ALL, slides were stained with myeloperoxidase stain .The diagnoses of leukemias was made . Variables included age and gender of patients, subtype of leukemia, and basic hematological parameters including hemoglobin level, total leukocyte count, and platelet counts . Data regarding these variables were recorded in proforma , analysed , and the results were drawn accordingly. Mean and standard deviation were used for quantitative data like age, while frequency and percentages were used for qualitative data like gender.

RESULTS

A total of 109 cases of acute and chronic leukemias were included in the study. About 61(56%) cases were males and 48(44%) cases were females. Male to female ratio was 1.27 :1. Changes in the hematological parameters in cases of leukemias are shown in Table 1 and figure 1-4.

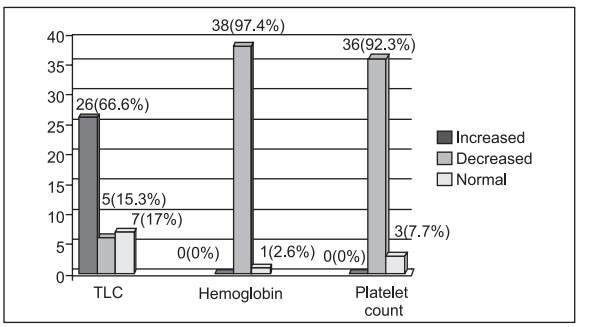

Fig 1: Pattern of basic hematological parameters in 39 cases of acute myeloid leukemia

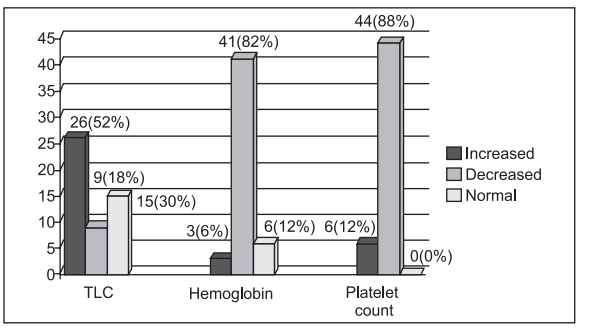

Fig 2: Pattern of basic hematological parameters in 50 cases of acute lymphoid leukemia

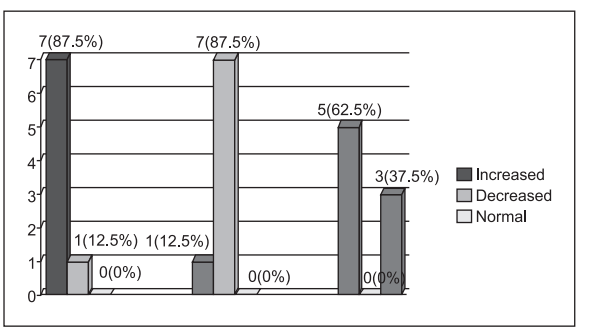

Fig 3: Pattern of basic hematological parameters in 8 cases of chronic myeloid leukemia

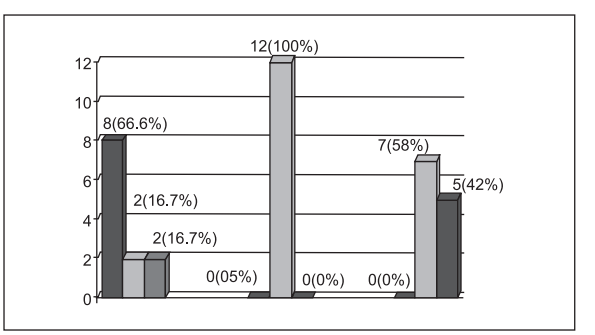

Fig 3: Pattern of basic hematological parameters in 8 cases of chronic myeloid leukemia

Table 1: Hematological parameters in cases of acute and chronic leukemias (n=109)

	Total Leukocyte Count (x10^3/ μL)		Haemoglobin (gm/d L)		Platelet count (x10^3/ μL)	
	Range	Mean ± SD	Range	Mean ± SD	Range	Mean ± SD
Acute Myeloid Leukemia	1.3-270	61.75±15.4	4-11	7.4±1.86	5.2-215	48±12
Acute Lymphoid Leukemia	0.7-206	26.5±6.6	5.2-12	8.3±2.09	3-404	62.9±15.7
Chronic Myeloid Leukemia	2-268	112±28	6-15.1	9.6±2.4	148-1828	698±174
Chronic Lymphocytic Leukemia.	1-162	26±6.5	4-10	7.7±1.9	9-366	147±37

DISCUSSION

Leukemia is a hematological disorder that is prevalent worldwide. Mutations, ionizing radiations , exposure to chemicals like benzene and pesticides and infections are important risk factors for leukemia [19,20]. On the other hand, studies suggest that atopic conditions like allergy, asthma, hay fever, and maternal use of folate are associated with a reduced risk of developing leukemia[21,22,23].

CBC is the first test done in patients suspected of having leukemia [17]. CBC is the reflection of the changes in the bone marrow caused by the leukemic cells . Findings in the CBC are so characteristic that a good physician can confidently narrow down his differential diagnoses to specific type of leukemia [17].Thus it is important to recognize the changes in CBC early in order to do further confirmatory tests like bone marrow and flow cytometry [18]. Early diagnosis leads to timely treatment ,which in turn decreases the morbidity and mortality

The changes in the bone marrow due to leukemia are reflected in the CBC [17]. Leukemic cells proliferate in an uncontrolled manner in the bone marrow and replace normal hematopoietic cells [1,2].The excessive abnormal leukocytes spill in to the peripheral blood , and this is manifested as increased TLC in CBC [17,18]. Replacement of marrow by the malignant cells causes decreased erythropoiesis, which is manifested as anemia or reduced Hb on CBC [17,18,24]. Anemia is a significant finding in almost all leukemias whether acute or chronic, and has prognostic importance [24,25,26]. Thrombocytopenia or reduced platelet count is either due to bone marrow replacement by the blast cells or splenomegaly [25]. It is common finding in almost all leukemias [25,26]. So the CBC findings in leukemias correspond to underlying pathogenetic mechanism of leukemia. Acute lymphoid leukemia (ALL) is the commonest leukemia of all leukemias [17].In the present study ,the basic hematological parameters in cases of ALL were as raised TLC, low Hb and low platelet (in 52%, 82% and 88% cases of ALL respectively) .This pattern is same as that reported in literature [24,28]. Similar findings were reported in another study done by Naeem S on ALL patiens in 2015 from Lahore ,i.e TLC was raised in 58% cases, Hb was low in 74% cases, but the low platelet count was seen only in 12% cases of all.

Rest of them have normal platelets [28]. Similar findings were reported from Iran by Moussavi F in 2014, who reported anemia and thrombocytopenia (in 89.7% cases each) in ALL patients , yet a raised TLC was seen only in 39% cases[17]. Similar findings were reported from Spain by Perez JCJ in 2018 [18]. Thus , the constellation of raised TLC, low Hb and low platelet count is a diagnostic clue that should prompt a physician to keep Acute leukemia in differential diagnoses and it should not be missed. Many cases of infections may show anemia and raised TLC, but in that case, platelet count is not decreased, as is in acute leukemias. So all the three hematological parameters i.e TLC, Hb , and platelet count should be considered to avoid missing the diagnostic clue.

Chronic myeloid leukemia (CML) is a chronic myeloproliferative disease common in adults [25]. The disease has three phases i.e chronic, accelerated and blast crises [25].In the present study , the changes in the basic hematological parameters were found to show raised TLC (in 87.5% cases) and a low Hb (in 87.5% cases), just like other leukemias. But the platelet count was found to be raised rather than decreased. Similar findings were seen in a study done by Amer AH in 2017, reporting a raised TLC in total 100% cases of CML, anemia in 92% cases and a raised platelet count in 94.6 % cases of CML [25]. Thus in CML , the CBC findings are anemia , leukocytosis and thrombocytosis (rather than thrombocytopenia). The reason for raised platelet count in CML is that it is a myeloproliferative disorder. So, all the hematopoietic cells are proliferating and so

are the megakaryocytes [25]. The raised platelet count in CML is therefore characteristically different from all other leukemias, where platelet counts is low [25,27]. This specific CBC picture along with clinical sign symptoms act as a diagnostic clue to diagnosis of CML. Clinicians should be aware of this particular finding.

Chronic Lymphocytic Leukemia (CLL) is a malignancy of B-lymphocytes [27]. Anemia is a common finding in CLL .It has a prognostic significance as it is associated with increased morbidity [27]. There are multiple reasons for development of anemia in CLL i.e marrow infiltration , anemia of chronic disease, nutritional deficiencies and immune mediated [27]. In the present study , the prevalence of anemia was very high (in 100% cases) as compared to that 26.7% in study done by Zeeshan , and 15.1% in study done by Dhodhi [27,28].

Salawuet et al from Nigeria reported prevalence of anemia to be 74.4% in CLL patients in their study, which is somewhat close to that in the present study [29].Thrombocytopenia in CLL is a bad prognostic factor[27]. In the present study , thrombocytopenia was seen in 58% cases of CLL .This is quite high rate as compared to that reported by Zeeshan in 2015 ,where about 21.7% cases of CLL had thrombocytopenia [27]. A lower rate of 18% is reported in a study from Thailand [30].

So , most of patient in our setup present with bad prognostic factors i.e anemia and thrombocytopenia . Both these are markers of advanced disease [27].This means that our patients have a high disease burden , and this may be due to late presentation to the clinician. So, the changes in the CBC findings can provide a diagnostic clue if tailored to the history, age of the patient , and sign symptoms of the patients[17].Anemia and thrombocytopenia in CLL has a prognostic significance , and hence gives clues about outcome of the disease in patient. Although , further evaluation like bone marrow biopsy and flow cytometry is done anyways to confirm the diagnoses of leukemia, yet the clues on CBC are equally significant and must not be missed.

LIMITATION

of the present study was that data was taken from single tertiary centre. Thus , the results may not be truly representative of whole population in our setup.

CONCLUSION

Knowledge of pattern of basic hematologic parameters in leukemia i.e a low hemoglobin and platelet count , and a raised white cell count (except in chronic myelogenous leukemia, where the platelet count is raised) is necessary as it narrows down the differential diagnosis to know the subtype of leukemia.

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AUTHOR'S CONTRIBUTION

Following authors have made substantial contributions to the manuscript as under:

Munir AH: Discussion, Result Compilation.

Khan MI: Main Author.

Authors agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.