Original Article

Serum D-dimer Level in Patients with Acute Leukemia in a Tertiary Care Hospital

*Amit MNH[1], Rahman MM[2], Hossain ML[3], Hasan MR[4], Ali MH[5], Talukder KC[6], Ullah AZMA[7], Sultana MS[8]

Abstract

D-dimer is a molecule, formed by the breakdown of excessive fibrin from the activation of coagulation system. Ample evidence suggests that increased activation of coagulation system in patients with acute leukemia (AL) leads to higher D-dimer levels. Considering shortage of evidence in our perspective, the study was designed to observe the D-dimer level in acute leukemia in different morphological types and phases among the patients admitted in a tertiary care hospital. This hospital based cross-sectional study was conducted at the Department of Medicine and Department of Hematology in Dhaka Medical College Hospital, for a period of 6 months following approval of this protocol. Patients with New case (NC) of AL, at complete remission (CR) and in patient's wither lapsed (R) AL were included in the study. Purposive sampling methods were followed for sample selection. Written informed consents were taken from the all study subjects and ethical issues were ensured. Data were collected by interview using a structured questionnaire. All study population were subjected to details history taking, physical examination and relevant investigations of D-dimer level. Collected data were analyzed by the SPSS version 20.0. Among 50 patients, 58% were males and 42% were females. Mean age was 34±5.6 SD years and the height number of patients (40%) belonged to age group 21-30 years. Three fourth of the patient (76%) had diagnosed as AML and rest of them 24% had ALL. The most common subtype of Acute Myeloblastic Leukemia M3 (AML) was 47, 37% and most common subtype of ALL L2 was 50%. Most of the respondents were found as new case (80%) followed by in decreasing order complete remission case 14% and relapse case 6%. Overall, D-dimer level was 3.69 mg/dl (0.1mg/dl-40 mg/dl), and D-dimer level is slightly higher in AML group than ALL patient (4.26 vs 2.18mg/dl). Moreover, new cases have higher level of D-dimer (4.2 mg/dl) in comparison with complete remission (1.2 mg/dl) or relapse case (2.7 mg/dl). It was also found that APL patients has higher D-dimer level than other form of leukemia. D-dimer level in acute leukaemia patients 3.69 mg/dl. Higher value of AML was found in patients than ALL and increased D-dimer level is also evident in newer case particularly APL. D-dimer level rises in acute leukemia patients. However, further study is recommended with appropriate study design.

Keyword: *Serum D-dimer, acute leukemia (AL), coagulation system, acute myeloblastic leukemia (AML)*

1 *Dr. Mohammad Nafees Hussain Amit, Medical Officer, Department of Medicine, Dhaka Medical College Hospital (DMCH), Dhaka. E-mail: nafees.hussain@gmail.com
2 Dr. Mohammad Mizanur Rahman, Medical Officer, Department of Medicine, DMCH
3 Dr. Md. Liakat Hossain, Medical Officer, Department of Medicine, DMCH, Dhaka.
4 Dr. Md. Rashedul Hasan, Consultants, Department of Medicine, Sheikh Hasina Medical College Hospital (SHMCH), Tangail
5 Dr. Md. Haidar Ali, Assistant Professor, Department of Medicine, SHMCH, Tangail
6 Dr. Kshitish Chandra Talukder, Medical Officer, Department of Medicine, BIRDEM General Hospital, Dhaka
7 Dr. A.Z.M Ahsan Ullah, Consultants, Department of Cardiology, Colonel Malek Medical College Hospital, Manikgonj
8. Dr. Mst.Siddika Sultana, Asst. Professor(gynae and Obs), NIRCH Mohakhali. Dhaka
* For correspondence

INTRODUCTION

With a high mortality rate acute leukemia (AL) is a malignant tumor of the blood system and frequently occurs in children, three quarters of the cases are Acute Lymphoblastic Leukemia (ALL).[1,2] While Acute Myeloblastic Leukemia (AML) is more common in adults.[3] Initially acute leukemia was classified based on morphology, French American British Classification (FAB) which classifies AL mainly in AML and ALL, their subtypes are as follows: (1) AML- M0: minimally differentiated, M1: without maturation, M2: with maturation, M3: promyelocytic, M4: myelomonocytic, M5: (a) monoblastic, (b) monocytic, M6: erythroleukemia and M7: megakaryoblastic; (2) ALL- L1: small, monomorphic, L2: large, heterogenous and L3: Burkitt-cell type. Classification of acute leukemia has evolved in recent years, from based purely on morphology [French-American-British (FAB) classification] to also include immunophenotyping, cytogenetic and molecular analysis in classification algorithm (WHO classification).

The important differences in the WHO classification compared with the FAB classification included (a) lowering of the threshold for the percentage of blast cells to 20 per cent in the blood or bone marrow, based on the fact that survival patterns for cases with 20-30 per cent blasts is similar to cases with >30 per cent blasts in the bone marrow; (b) the recognition of acute cases of leukemia with an even lower blast count if specific acute leukemia associated cytogenetic or molecular genetic abnormalities are present; (c) inclusion of AML with cytogenetic abnormalities, AML with myelodysplasia related features, and therapy related AML as distinct categories. D-dimer levels increase in AL patients at initial diagnosis. These are indicative of activated coagulation systems in AL, as reported by authors from several developed countries.[4,5] Acute Myeloid Leukemia and Acute Lymphoblastic Leukemia commonly manifest with elevated peripheral blood blast counts and in some instances, derangements of coagulation parameters.[6] Acute Promyelocytic Leukemia (APL) is well known to be associated with Disseminated Intravascular Coagulation (DIC).[7] Acute Promyelocytic Leukemia (APL) is a clinically distinct form of AML that occurs as a result of specific cytogenetic abnormality resulting in fusion of promoyelocytic leukemia (PML) and retinoic acid receptor-α gene products, which disrupts normal differentiation. Rarely, translocations involving chromosome 17 and 11 or 5 may also result in a similar clinical picture. Patients with APL are at increased risk of bleeding with or without thrombosis because of the procoagulant activity of the granules released by the APL blasts. Despite high cure rates, approaching almost 70-80 per cent in the APL, early deaths occur due to this coagulatizon abnormalities, making it a medical emergency that needs early attention. Besides supportive care and attempt to confirmation of the diagnosis by polymerase for PML-RARα fusion products, it is important to start treatment with all-trans retinoic acid (ATRA), which induces differentiation in the APL blasts. Likewise, ALL can also present with DIC, as can subsets of non-APL AMLs.[8] Formal determinations of DIC involves assessment of coagulation parameters including D-dimer levels, prothrombin time, fibrinogen concentration, and platelet counts. To assess for schistocytes, a useful morphologic feature that may be present in DIC, the morphology of red blood cells in a peripheral blood smear is frequently evaluated.[9,10] However, in a recent study of 35 patients with DIC related to neoplastic and non-neoplastic etiologies, an increase in schistocytes did not appear to be sensitive indicator of DIC found by author.[11] These parameters are reported to be independent in univariate analysis and interdependent in multivariate analysis.[8] During the treatment process of ALs, DIC occurred in one-third of non-M3 AML patients[12] and thrombotic events (TE) appeared more often in cases of APL than in other ALs, with the reported prevalence ranging from 2% to 10-15%.[13] APL may be distinguished from other AML subtypes by core markers of DIC including D-dimer.[14] DIC can also be frequently triggered or aggravated by chemotherapy induction. [12] Although no single test is sufficient to confirm or deny the diagnosis of DIC, D-dimer is still viewed as a reference of DIC diagnostic indicators.[15] As a specific product of the degradation of fibrin clots, D-dimer is regarded as a specific biomarker of fibrin formation and stabilization.[16] When hyperfibrinolysis took place, elevated D-dimer levels were detected in 91% of AML patients.[17] D-dimer was generally recognized as a good reflection of the incidence of thrombotic events and many studies showed that elevation of D-dimer values predicted adverse outcomes in AMLs.[18] APL has evolved from being a deadly to a highly curable disease, due to targeted molecular therapy with all-trans retinoic acid (ATRA). As a result, the incidence of early hemorrhagic deaths for which APL is notorious has reduced to 5-10% as reported in clinical trials.[19] These results are not replicated outside of clinical trials as is evident from recent population-based registries. High incidence of early hemorrhagic deaths remains the greatest contributor to treatment failure in this otherwise curable leukemia.

OBJECTIVES

General Objectives:

To observe D-dimer level in acute leukemia in different morphological types and phases

Specific Objectives:

To assess the demographic profile of the patients to identify APL through D-Dimer level

MATERIALS AND METHODS

This was a cross sectional observational study by selected purposive sampling method. Total 50 cases were taken for this study, 58% were males and 42% were females. Selected patients with new case of AL (NC), complete remission (CR) and in patients with relapsed (R) AL attending at the Department of medicine and hematology in Dhaka Medical College Hospital (DMCH), Dhaka, Bangladesh.

The research work was done during August 2018 to February 2019.

Inclusion Criteria

Patients labelled as new case AL (NC), at complete remission (CR) and in patients with relapsed AL (R) attending the Department of Medicine and Hematology in DMCH. Both sexes by taking informed consent, patients will be included in the study.

Study Procedure

The present study evaluated data from 50 patients that were newly diagnosed with AL or at complete remission or in relapse and were admitted into the Department of Medicine and Department of Hematology in Dhaka Medical College Hospital between August 2018 and February 2019. After initial assessment and treatment, all patients were described about the objective of the study. Informed written consent was taken from each participant. For classification of the patients, FAB classification was followed. Data were collected by interview using a structured questionnaire. All study population was subjected to details history taking, physical examination and relevant investigations. Blood samples were taken from the antecubital vein and placed in plastic tubes containing 3.8% trisodium citrate or ethylenediaminetetraacetic acid (EDTA)·K2 anticoagulant. For plasma separation, blood was centrifuged at 2,500 × g for 15 min at 4°C; blood samples were obtained prior to the initiation of any treatment for AL. Before sample collection, aseptic procedure was followed. Then the patients would be examined by the researcher and all collected data were recorded into the case record form. After completion of data collection, all data were put into the statistical software. Final analysis was done with SPSS 20 with help of a statistician.

Ethical Clearance

The ethical clearance of this study was taken from research & review committee of Dhaka Medical College Hospital (DMCH).

Data Processing &Analysis

After collection of all the required data, these were checked, verified for consistency and then tabulated into the computer using the Package for Social Sciences (SPSS Inc., Chicago, IL, and version 20.0 for Windows). Statistical analysis was carried out using Statistical tests. Normality of data was checked by measures of Kolmogorov–Smirnov tests of normality. For normally distributed data, means were compared using Student's t-test for two groups. Qualitative or categorical variables were described as frequencies and proportions. All statistical tests will be two-sided and performed at a significance level of $p < 0.05$.

RESULTS

Table I shows the distributions of respondents in age group of Acute Leukemia. Among 50 patients 40% was in age group 21-30 years, followed by in decreasing order, 31-40 years 28%, 13-20 years 22%, 41-50 years (8%), 51-60 years 2% and 61-70 years 2%. Mean age was 34±5.6 SD (years).

Table I: Distribution of patients by age (n=50)

Age in year	n	%
13-20 yrs.	11	22.0
21-30 yrs.	19	38.0
31-40 yrs.	14	28.0
41-50 yrs.	4	8.0
51-60 yrs.	1	2.0
61-70 yrs.	1	2.0
Age Mean ± SD	34±5.6	

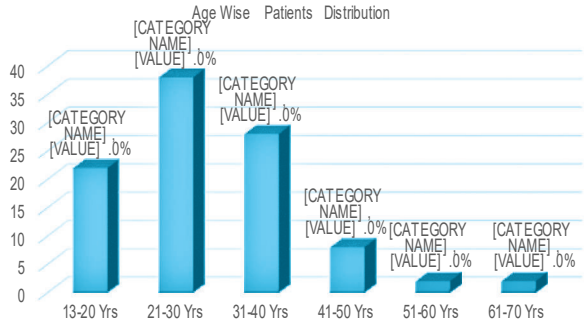

Figure 1: *Distribution of patients by age (N=50)*

Table II shows sex distribution of participants, where male 58% and 42% was female.

Table II: Distribution of respondents by gender (n=50)

Sex	n	%
Male	21	42.0
Female	29	58.0
Total	50	100.0

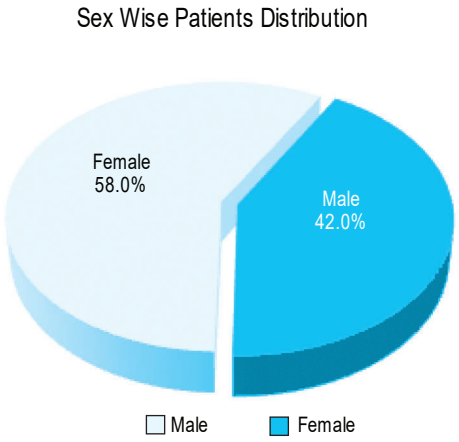

Figure 2: *Distribution of patients by Sex (N=50)*

Table III shows the respondents diagnosed as a case of Acute Myeloid Leukemia (AML) 76% and rest 24% was suffering from Acute Lymphoblastic Leukemia.

Table III: Distribution of respondents by prevalence of AML and ALL (n=50)

AML and ALL	n	%
AML	38	76.0
ALL	12	24.0

Table IV shows the total patients suffering from ALL were 12. ALL was L2 (50%) followed by in decreasing order L1 with 33.33% and L3 with 17.67%.

Table IV: Distribution of respondents by subtype of ALL (n=12)

Type of ALL	n	%
L1	4	33.3
L2	6	50.0
L3	2	16.7

Table V shows the total patients suffering from AML (38). AML M3 was 47.37% followed by in decreasing order M2 21.05%, M1 10.52%, M4 7.89%, M5 5.26%, M0 5.25%, M6 2.16% and M7 2.16%.

Table V: Distribution of respondents by subtype of AML (n=38)

Type of AML	n	%
M0	2	5.3
M1	4	10.5
M2	8	21.1
M3	17	44.7
M4	3	7.9
M5	2	5.3
M6	1	2.6
M7	1	2.6

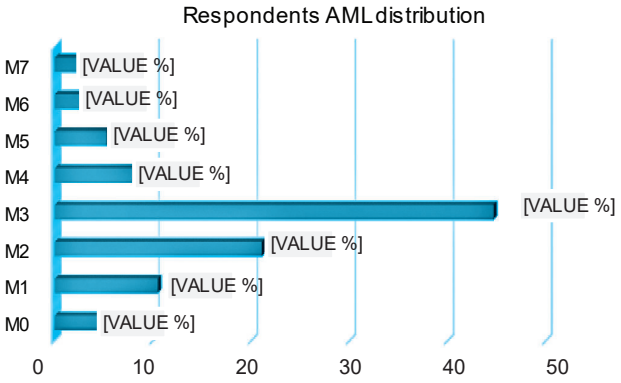

Figure 3: *Distribution of respondents by subtype of AML (n=38)*

Table IV shows the AML patients in age group, here 34% was in 21-30 years followed by 31-40 years and others. Among ALL 16% was in age group 13-20 years.

Table VI: Age wise distribution of AML and ALL diagnosed patient. (n=50)

Age group	ALL (%)	AML (%)	Total (%)
13-20 yrs.	8(16.0)	3(6.0)	11 (22.0)
21-30 yrs.	3(6.0)	17(34.0)	20(40.0)
31-40 yrs.	0(0.0)	14(28.0)	14(28.0)
41-50 yrs.	1(2.0)	2(4.0)	3(6.0)
51-60 yrs.	0(0.0)	1(2.0)	1(2.0)
61-70 yrs.	0(0.0)	1(2.0)	1(2.0)
Total	12(12.0)	38(38.0)	50(100.0)

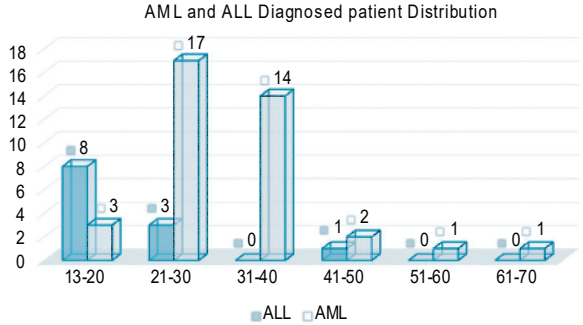

Figure 4: *Age wise distribution of AML and ALL diagnosed patient(n=50)*

Table VII shows the respondents were divided into three disease phases- New case, Relapse case and complete remission case. Respondents were found as new case 80% followed by in decreasing order complete remission case 14% and relapse case 6%.

Table VII: Distribution of AL in relation to phases of disease. (n=50)

Type of AL	M0	M1	M2	M3	M4	M5	M6	M7	ALL	Total
New Case	2(4.0)	3(6.0)	7(14.0)	16(32.0)	3(6.0)	1(2.0)	0(0.0)	0(0.0)	8(16.0)	40(80.0)
Complete Remission	0(0.0)	0(0.0)	0(0.0)	1(2.0)	0(0.0)	1(2.0)	1(2.0)	1(2.0)	3(6.0)	7(28.0)
Relapse	0(0.0)	1(2.0)	0(0.0)	1(2.0)	0(0.0)	0(0.0)	0(0.0)	0(0.0)	1(2.0)	3(12.0)
Total	2(0.0)	4(8.0)	7(14.0)	18(36.0)	3(6.0)	2(4.0)	1(2.0)	1(2.0)	12(12.0)	50(100.0)

Table VIII shows the distrbution of complaints; fever 76% was followed by pallor 32%, bleeding disorders 22%, generalized body aches 18%, abdominal pain/distension 14%, lymph node enlargement 12%, weight loss 8% and weakness 6%. Other presenting complaints which were present in less than 5% of patients included vomiting, cough, shortness of breath, easy fatigability, headache, sore throat, flank pain, fits, amenorrhea, urinary incontinence/retention, anorexia, constipation, lacrimal gland enlargement and loss of consciousness.

Table VIII: Percentage of presenting complaints among respondents (n=50)

Presenting Complaint	n	%
Fever	38	76.0
Pallor	16	32.0
Bleeding Disorder	11	22.0
Generalized body aches	9	18.0
Abdominal Pain/distention	7	14.0
Lymph node enlargement	6	12.0
Weight loss	4	8.0
Weakness	3	6.0

Table IX shows the median value of D dimer level, it was 3.69 mg/dl ranging from .1mg/dl to 40 mg/dl. D dimer level found in ALL patient was 2.18 mg/dl ranging from .1mg/dl to 14.6 mg/dl. For AML it was 4.26 mg/dl ranging from 0.1mg/dl to 40mg/dl.

Table IX: D-dimer level in AML and ALL patients. (n=50)

Category of respondents	Count Median value of D-dimer level	Range
Total	3.69 mg/dl	0.1mg/dl-40 mg/dl
ALL	2.18 mg/dl	0.1 mg/dl-14.6mg/dl
AML	4.26 mg/dl	0.1mg/dl-40mg/dl

Table X shows the, mean value of WBC which was found around 11.4 x 10^9/l among new cases, 4.8x10^9/l among complete remission cases and 5.8x10^9/l among relapse cases. Mean Haemoglobin level was found in same chronology 75 g/l, 105 g/l and 92 g/l. Mean value of platelet was 31.1x10^9gm/l, 180x10^9gm/l and 32x10^9 gm/l respectively. Mean value of prothrombin time was 14.6 seconds, 13.7 seconds and 14.6 seconds respectively. Mean value of activated partial thromboplastin time was 36.8 seconds, 38.8 seconds and 39.8 seconds respectively. Mean value of fibrinogen value was 3.4 g/l, 3.7 g/l and 2.9 g/l.

Table X: Hematological measurements in respondents at various stages of AL.(n=50)

Hematological value	New Case	Complete Remission Case	Relapse Case
WBC, x10^9/l	11.4 (0.1-632.4)	4.8 (2.1-13.2)	5.8 (0.1-328.0)
Hb, g/l	75.0 (34.0-149.0)	105.0 (64.0-155.0)	92.0 (45.0-148.0)
PLT, x10^9/l	31.0 (5.0-235.0)	180.0 (6.0-460.0)	32.0(4.0-167.0)
PT, sec	14.6 (12.5-33.6)	13.7 (11.7-18.1)	14.6(11.9-22.8)
aPTT, sec	36.8 (26.6-75.5)	38.8 (29.1-58.8)	39.8 (25.9-59.6)
FIB, g/l	3.4 0.2-9.1	3.7 (0.6-8.5)	2.9 (0.8-8.4)

Table 11 showed the, mean value of D- dimer which was found 4.2 mg/l among new cases ranging from .54 mg/l to 7.0 mg/dl. Among complete remission cases it was found 1.2 mg/l ranging from .1mg/l to 7.2 mg/l. The value was found 2.7 mg/l among relapse cases ranging from .3 mg/l to 40 mg/l.

Table XI: D dimer level among respondents according to different disease stage. (n=50)

	New case	Complete Remission	Relapse
D dimer level	4.2 (0.54-7.0)	1.2 (0.1-7.2)	2.7 (0.3-40.0)

Table XII showed the, significant difference between D-dimer level of new cases of APL (AML, M3) and new cases of other types of AL excluding APL. It shows increased D-dimer level in APL patients.

Table XII: D-dimer level in different stage of disease. (n=50)

Characteristics	All respondents			Respondents excluding APL		
	New Case	Complete Remission	Relapse	New Case	Complete Remission	Relapse
D-dimer, mg/l	4.2* (0.54-7.0)	1.2 (0.1-7.2)	2.7 (0.3-40.0)	2.2* (0.5-10.4)	0.6 (0.1-1.6)	1.6 (0.3-17.4)

DISCUSSION

Relapsed AL remains to be associated with a dismal prognosis, despite the outstanding improvements made over the past decade regarding our knowledge of acute leukemia (AL). Acute leukemia (AL) is a clonal disease that progressively produces novel sub-clones, which exhibit altered phenotypic and cytogenetic traits. AL is divided into acute lymphoblastic leukemia (ALL) and acute myeloid leukemia (AML). AML is the most frequent type of leukemia in adults. Acute promyelocytic leukemia (APL) is a distinct subtype of AML characterized by coagulopathy and signs of disseminated intravascular coagulation.[20] Acute myeloid leukemia (AML) and acute lymphoblastic leukemia (ALL) commonly manifest with elevated peripheral blood blast counts and in some instances, derangements of coagulation parameters.[21-23] acute promyelocytic leukemia (APL) is well known to be associated with disseminated intravascular coagulation, as evidenced by abnormal coagulation parameters and low platelet counts, which can prove fatal if not rapidly treated. Likewise, ALL can also present with disseminated intravascular coagulation (DIC) as can subsets of non-APL AMLs.[24,25] While formal determination of DIC involves assessment of coagulation parameters including D-dimer levels, prothrombin time, thrombin time, fibrinogen concentration, and platelet counts, the morphology of red blood cells in a peripheral blood smear is frequently evaluated to assess for schistocytes, as a useful morphologic feature that may be present in DIC. However, to date, a large-scale statistically powered systematic evaluation of major coagulation parameters in addition to the morphologic features of red blood cells in peripheral blood specimens from patients with acute leukemia has not been performed.[26-28] This study was carried out in Medicine and Hematology department of a tertiary care hospital. Fifty patients were taken who had been diagnosed as cases of various types of acute leukemia. Patients of all disease phase were included. In this study out of 50 respondents, 40% belonged to age group 21-30 years, 28% belong to 31-40 years, 22% belong to 13-20 years, 6% belong to 41-50 years, and 2% belong to each 51-60 years and 61-70 year's group. A study by Niessen et al. on hematological malignancies found majority cases belong to 20-29 year's age group.[29] Here the age range is 13-70 which is not similar to other related studies like the study by Jill M Gore et al.[30] That study found the age range for all types of leukemia from 2-90 years old.[62] but in present study our sample was taken from 'Hematology' and 'Medicine' department of a tertiary care hospital where patients aged less than 13 years old are not usually admitted. In this study female preponderance was found with a percentage of 58% female and 42% male. This finding also differ with similar type of other studies.[28,31,32] found higher male to female ratio. Small sample size and non-probability purposive sampling method may be the reason of this dissimilarity.[31-34] 68% respondents came from urban area and 32% respondents came from rural area. 69% of them belong to middle economic class, 15% to upper class and 16% to lower class. In this study majority of the respondents were suffering for AML with a percentage of 76%. 24% respondents were diagnosed as cases of ALL. A study by Linet et al.[35] found that the frequency of AML is two times higher than that of ALL in Bangladesh. They also found that the incidence of AML is relatively common

in North America, Europe, and Oceania, while adult AML is rare in Asia and America.[35] An another study by Singh et al. [36] found Acute lymphoblastic leukemia (ALL) with a percentage of 29.7% and acute myeloid leukemia (AML) with 37.3% among all hematological malignancies.[36] Total patients suffering from ALL were 12. The most common subtype of ALL was L2 with 50% followed by in decreasing order L1 with 33.33% and L3 with 16.67%. In ALL, L2 was the most common subtype in our study. Similar L2- ALL predominance was observed by Nasim et al however Humayun et al and Gupta showed L1 as the most common subtype.[37-39] Usually ALL subtype is more prevalent in children younger than 15 years old. Study by Shah et al. found L1, L2 and L3 constituted 54.3%, 43.7 % and 2% respectively.[40] As all of our respondents were aged more than 13 years old, real scenario may come out altered here. Total patients suffering from AML were.[41] The most common subtype of AML was M3 with 47.37% followed by in decreasing order M2 with 21.05%, M1 with 10.52%, M4 with 7.89%, M5 with 5.26%, M0 with 5.25%, M6 with 2.16% and M7 with 2.16%. AML-M3 was most common AML subtype in our study which is consistent with findings of study by Nasim et al.[37] However Humayun et al found M1 as most common subtype.[38] Gupta et al and observed M2 subtype as most common in AML cases.[39] One aim of our study was to compare D-dimer level between APL (M3) patients and other AL patients. So, during sample selection, we chose non-probability purposive sampling to pick up more APL patients. Among AML patients, majority found in 21-30 years followed by in decreasing order 31-40 years and others. Among ALL majority patients found in 13-20 years. In a study by Singh et al,[36] a total 105 leukemia cases were diagnosed in children (≤15 years), in which ALL subtype was the most prevalent (n=69 cases).[36] This similar finding was observed with other studies.[37,39] While total respondents were 132, maximum cases were found as AML in adult who were 102 in number as compared to children with a number of 30 in our study. Same observation also found in studies conducted by Paul B et al.[42] Usually AML is generally a disease of older people and is uncommon before the age 45. The average of people when they are first diagnosed with AML is about.[36] ALL occurs both in children and adults with highest rates seen between the ages three and seven years.[43] This study finding [44] shows dissimilarity due to sampling method and sample size. In this study Fever (76%) was the most common presenting complaint followed by pallor (32%), bleeding disorders (22%), generalized body aches (18%), abdominal pain/distension (14%), lymph node enlargement (12%), weight loss (8%) and weakness (6%). Gore et al[45] found easy bruising, prolonged bleeding, gingival bleeding, epistaxis, or menorrhagia as frequent presenting complaint. Among 50 respondents, 80% were found as new case, 14% after complete remission and 6% as relapse case. A study by Takahashi et al. states that standard intensive chemotherapy induces complete remission in 60-80% of cases. But a significant number of patient's experience relapse of the disease.[43] In this study, we found elevated D-dimer levels in acute leukemia patients at initial diagnosis. Authors reports from several developed countries are indicative of activated coagulation systems in acute leukemia patients. Athale et al [4] reported a mean D-dimer level of 2,766 (SD 2,385.8) ng/mL in newly diagnosed case of ALL in children while Giordano et al.[5] reported a mean of 299 (SD 32) ng/ mL in children with ALL.[4,5] Comparing the incidence of elevated D-dimer level in ALL, our finding was lower than Athale's but almost similar with the result of Giordano et al [5] Another studies reported that 80% of their subjects with ALL had elevated D-dimer levels. Chojnowski et al [46] also found that 85% of AML subjects had elevated D-dimer levels. In this study, comparative blood routine and coagulation measurements were done between APL and other forms of AL. No significant changes found in median range of Hb, PLT, PT, aPTT and FIB level. WBC level was found to be raised in other forms of AL excluding APL. Statistically significant difference found in D-dimer level where D-dimer level increased in APL. Study by Shahmarvand et al, Wangqiang et al and Jawed et al. found similar findings.[43,47,48]

LIMITATION OF THE STUDY

This was a single center study. Sample size was small but large number of sample could provide more information regarding D-dimer level in acute leukaemia.

CONCLUSION

In this study, it was observed that D-dimer level raised in acute leukemia patients and higher value is noted in acute myeloid leukemia patients than acute lymphoblastic leukemia patients. Considering the treatment status, it is more prominent in new cases than complete remission cases and relapse cases. Furthermore, the level also increased in APL than other variety of leukemia. However, further larger cohort study is needed to finalize the findings.

REFERENCES

1. Mohammad SH, Mamtaz B, Md Mahmuduzzaman M: Epidemiology of childhood and adolescent cancer in Bangladesh, 2001–2014. BMC Cancer. 2016; 16: 104.
2. Afiqul I and Tim E: Brief report on pediatric oncology in Bangladesh. South Asian J Cancer. 2013; 2(2): 105–106.
3. Hossain MS, Iqbal MS, Khan MA et al. Diagnosed hematological malignancies in Bangladesh - a retrospective analysis of over 5000 cases from 10 specialized hospitals. BMC Cancer. 2014; 14:438.
4. Athale U, Moghrabi A, Nayiager T, et al. von Willebrand factor and thrombin activation in children with newly diagnosed acute lymphoblastic leukemia: an impact of peripheral blasts. Pediatr Blood Cancer. 2010; 54:963-9.
5. Giordano P, Molinari AC, Del Vecchio GC, et al. Prospective study of hemostatic alterations in children with acute lymphoblastic leukemia. Am J Hematol. 2010; 85:325-30.
6. Weinberg OK, Ohgami RS, Ma L, et al. Acute myeloid leukemia with monosomal karyotype: morphologic, immunophenotypic, and molecular findings. Am J Clin Pathol 2014; 142:190-5.
7. Nur S, Anwar M, Saleem M, et al. Disseminated intravascular coagulation in acute leukaemias at first diagnosis. Eur J Haematol 1995; 55:78-82.
8. Uchiumi H, Matsushima T, Yamane A, et al. Prevalence and clinical characteristics of acute myeloid leukemia associated with disseminated intravascular coagulation. Int J Hematol 2007; 86:137-42.
9. Zini G, d'Onofrio G, Briggs C, et al. ICSH recommendations for identification, diagnostic value, and quantitation of schistocytes. Int J Lab Hematol 2012;34: 107-16.
10. Kaneko T, Wada H. Diagnostic criteria and laboratory tests for disseminated intravascular coagulation. J Clin Exp Hematop 2011; 51:67-76.
11. Lesesve JF, Fenneteau O, Zini G. Schistocytes. Transfusion 2014; 54:1459.
12. Uchiumi H, Matsushima T, Yamane A, et al. Prevalence and clinical characteristics of acute myeloid leukemia associated with disseminated intravascular coagulation. Int J Hematol 2007;86(2):137-42.
13. Mitrovic M, Suvajdzic N, Elezovic I, et al. Thrombotic events in acute promyelocytic leukemia. Thromb Res 2015;135(4):588-93.
14. Lee HJ, Park HJ, Kim HW, et al. Comparison of laboratory characteristics between acute promyelocytic leukemia and other subtypes of acute myeloid leukemia with disseminated intravascular coagulation. Blood Res 2013;48(4):250-3.
15. Bakhshi S, Arya LS. Diagnosis and treatment of disseminated intravascular coagulation. Indian Pediatr 2003;40(8):721-30.
16. Tripodi A. D-dimer testing in laboratory practice. Clin Chem 2011;57(9): 1256-62.
17. Speiser W, Pabinger-Fasching I, Kyrle PA, et al. Hemostatic and fibrinolytic parameters in patients with acute myeloid leukemia: activation of blood coagulation, fibrinolysis and unspecific proteolysis. Blut 1990;61(5):298–302.
18. Geng Y, Jian C, Yang S et al. The Prognostic Value of D-Dimer in De Novo Acute Myeloid Leukemia. Am J Med Sci.2016;352(2):129-33
19. Choudhry A and DeLoughery TG. Bleeding and thrombosis in acute promyelocytic leukemia, Am. J. Hematol.2012; 87:596-603.
20. Deschler B and Lübbert M: Acute myeloid leukemia: Epide- miology and etiology. Cancer 107: 2099-2107, 2006.1
21. Weinberg OK, Ohgami RS, Ma L, Seo K, Ren L, Gotlib JR, Seetharam M, Cherry A, Arber DA. Acute myeloid leukemia with monosomal karyotype: morphologic, immunophenotypic, and molecular findings. Am J Clin Pathol 2014; 142:190-5.
22. Ribeiro RC, Pui CH. The clinical and biologi- cal correlates of coagulopathy in children with acute leukemia. J Clin Oncol 1986;4: 1212-8.
23. Barbui T, Falanga A. Disseminated intravas- cular coagulation in acute leukemia. Semin Thromb Hemost 2001; 27:593-04.

24. Uchiumi H, Matsushima T, Yamane A, Doki N, Irisawa H, Saitoh T, Sakura T, Jimbo T, Handa H, Tsukamoto N, Karasawa M, Miyawaki S, Murakami H, Nojima Y. Prevalence and clinical characteristics of acute myeloid leukemia associated with disseminated intravascular coagulation. Int J Hematol 2007; 86:137-42.

25. Zini G, d'Onofrio G, Briggs C, Erber W, Jou JM, Lee SH, McFadden S, Vives-Corrons JL, Yutaka N, Lesesve JF; International Council for Standardization in Haematology (ICSH). ICSH recommendations for identifi- cation, diagnostic value, and quantitation of schistocytes. Int J Lab Hematol 2012;34: 107-16.

26. Kaneko T, Wada H. Diagnostic criteria and laboratory tests for disseminated intravascu- lar coagulation. J Clin Exp Hematop 2011; 51:67-76.

27. Franchini M, Di Minno MN, Coppola A. Disseminated intravascular coagulation in hematologic malignancies. Semin Thromb Hemost. 2010 Jun;36(4):388-403. doi: 10.1055/s-0030-1254048. Epub 2010 Jul 7. PMID: 20614391.

28. Salkar AB, Patrikar A, Bothale K, Malore S, Salkar A, Modani S. Clinicohematological evaluation of leukemias in a tertiary care hospital. IOSR-JDMS. 2014; 13:126-34

29. Niessen LW, Rahman M, Mottalib A, Khan MA, Dipta TF, Khatun H, et al. Diagnosed hematological malignancies in Bangladesh-a retrospective analysis of over 5000 cases from 10 specialized hospitals. BMC Cancer. 2014;14(1):1-7.

30. Gore JM. Acute leukemias. JAAPA J. 2014;27(5): 47-8.

31. Harani MS, Adil SN, Shaikh MU, Kakepoto GN, Khurshid M. Frequency of FAB subtypes in acute myeloid leukemia patients at Aga Khan University Hospital Karachi. J Ayub Med Coll Abbottabad. 2005; 17:26-9.

32. Ullah K, Ahmed P, Raza S, Satti TM, Chaudhry QU, Akhtar F, Kamal MK, et al. Management of acute myeloid leukemia- 5 years' experience at Armed Forces Bone Marrow Transplant Centre. Rawalpindi.

33. Salkar AB, Patrikar A, Bothale K, Malore S, Salkar A, Modani S. Clinicohematological evaluation of leukemias in a tertiary care hospital. IOSR-JDMS. 2014; 13:126-34

34. Braham-Jmili N, Sendi-Senana H, Labiadh S, Ben Abdelali R. Hematological characteristics, FAB and WHO classification of 153 cases of myeloid acute leukemia in Tunisia. Ann Biol Clin. 2006; 64:457- 65.

35. Linet MS, Devesa SS, Morgan GJ: The leukemias. In Cancer epidemiology and prevention. 3rd edition. Edited by Schottenfeld D, Fraumeni J Jr. New York: Oxford University Press; 2006:841-871. 200

36. Singh G, Sen R, Singh S, Parmar P, Kataria S. Spectrum of acute and chronic leukemia at a tertiary care hospital, Haryana, India. Int J Res Med Sci. 2016;4(4):1115-8.

37. Nasim N, Malik K, Malik NK, Mobeen S, Awan S, Mazhar M. Investigation on the prevelance of leukemia at a tertiary care hospital, Lahore. Biomedica. 2013; 29:19-22.

38. Humayun M, Khan SA, Muhammad W. Investigation on the prevalence of leukemia in North West Frontier Province of Pakistan. TJC. 2005;35(3):119-22.

39. Gupta R, Kaul KK, Dewan D. Clinicomorphological profile in acute leukemias: experience from a tertiary care centre in Jammu. Indian J Res. 2015; 4:4-6. tertiary care hospital, Haryana, India. Int J Res Med Sci. 2016;4(4):1115-8.

40. Sah K, Shrestha P. Acute Lymphoblastic Leukemia: Fourteen Years' Experience of a Single Institution. J Nepal Paediatr Soc. 2014;34(1):1-6.

41. Shahmarvand N, Oak JS, Cascio MJ, Arber DA, Zehnder JL, Ohgami RS, et al. A study of disseminated intravascular coagulation in acute leukemia reveals markedly elevated D-dimer levels are a sensitive indicator of acute promyelocytic leukemia. Int Jnl Lab Hem. 2017; 39:375-83.

42. American Cancer Society. Cancer Facts & Figures 2019. Atlanta, Ga: American Cancer Society; 2019.

43. Takahashi, Whijae Roh, and Farhad Ravandi. Clonal evolution of acute myeloid leukemia relapsed after 19 years of remission. Koichi

44. Hoffbrand, Victor; Moss, Paul; Pettit, John (31 October 2006). Essential Haematology. Wiley. pp. 192–196. ISBN 978-1-4051-3649-5. Archived from the original on 21 March 2015. Retrieved 14 September 2013.

45. Gore JM. Acute leukemias. J Am Acad Physician Assist. 2014;27 (5):47-8.

46. Chojnowski K, Wawrzyniak E, Trelinski J, Niewiarowska J, Ciemiewski C. Assessment of coagulation disorders in patients with acute leukemia before and after cytostatic treatment. Leuk Lymphoma. 1999; 36:77-84.

47. Shahmarvand N, Oak JS, Cascio MJ, Alcasid M, Goodman E, Medeiros BC, et al. A study of disseminated intravascular coagulation in acute leukemia reveals markedly elevated D-dimer levels are a sensitive indicator of acute promyelocytic leukemia. Int J Lab Hematol. 2017;39 (4):375-83.

48. FAREED J, Hoppensteadt DA, Reddy VB, KUMAR A, Harold R. S, Walenga JM, et al. Global and Molecular Hemostatic Markers in Acute Myeloid Leukemia. Am J Clin Pathol. 2016;94(4):397-4