

Coagulation profile (Prothrombin Time, Activated Partial Thromboplastin Time, D-dimer) in Chronic Lymphocytic Leukemia in Sudanese patients

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Abstract:

Background: *chronic lymphocytic leukemias are a heterogeneous group of conditions characterized by an increased number of small, mature appearing lymphocytes in the blood. Haemostasis disorders are complications of chronic lymphocytic leukemia which could be diagnosed by coagulation profile (D-dimer, PT and APTT).*

Objective: *The purpose of this study was to evaluate the haemostatic property among chronic lymphocytic leukemia patients in Sudan by determining D-dimer level, prothrombin time (PT) and activated partial thromboplastin time (APTT).*

Materials and Methods: *50 cases were included in this study with Chronic Lymphocytic Leukemia and 25 individuals as control group, All of them were Sudanese, we evaluated to determine D-dimer was measured using VEDALAB EASY READER, PT and APTT were measured by semi automated coagulometer, among in the two group.*

Result: *The result of the patients D-dimer level mean was 565.96 ± 474.22 ng/ml and control mean was 102.44 ± 33.86 ng/ml (p -value 0.000), patients PT mean was 15.14 ± 9.16 second and control*

group mean was 12.20 ± 1.68 second (p -value 0.032), and mean APTT for patients was 53.86 ± 27.95 second and control group was 31.44 ± 8.09 second (p -value 0.000).

Conclusion: Our study confirms the hypercoagulable state among chronic lymphocytic leukemia in Sudan, which has been determined by elevated D-dimer, PT and APTT.

Key words: D-dimer level, Chronic lymphocytic leukemia, Sudan

INTRODUCTION:

The chronic lymphocytic leukemias are a heterogeneous group of conditions characterized by an increased number of small, mature appearing lymphocytes in the blood, It is uncommon below the age of 40 years; however, onset in the early thirties is not unheard of. Chronic lymphocytic leukemia is 1.5 to 2 times more common in men than women.

Thrombocytopenia is important prognostic features in CLL and form part of the information used for staging (1).

Both experimental and clinical studies have evidenced an association between cancer and haemostasis (2). It has been estimated that approximately 15% of all cancer patients thrombosis develops during the course of their disease (3). In fact, the occurrence of cancer is usually associated with various clinical thrombotic syndromes, including local and systemic venous and arterial thrombosis. (4)

By far the most common is a proliferation of small B cells that express the T cell-associated antigen CD5; the term chronic lymphocytic leukemia (CLL) refers to this entity unless specified otherwise. This type of CLL is closely related to B-cell diffuse small lymphocytic lymphoma (SLL).

Mature T-cell lymphoproliferations occur, but these are rare. B-cell chronic lymphocytic leukemia/small lymphocytic lymphoma (CLL) is the most common adult leukemia in the

United States and Western Europe (~30% of adult leukemias). Chronic lymphocytic leukemia is predominantly a disease of older ages; the median age at diagnosis is ~55 to 65 years.

PT test measures clotting time of plasma in the presence of an optimal concentration of tissue extract (thromboplastin) and indicate the overall efficiency of the exterinsic clotting (factor VII). Although originally thought to measure prothrombin, the test is now known to depend also on reaction with factor V, X, prothrombin and fibrinogen. It can be expressed as the INR.

APTT measures the clotting time of plasma after the activation of contact factors but without added tissue thromboplastin and also indicate the overall efficiency of the interinsic pathway. (5)

D-dimer (or D dimer) is a fibrin degradation product (or FDP), a small protein fragment present in the blood after a blood clot is degraded by fibrinolysis. It is so named because it contains two Crosslinked D fragments of the fibrin protein.

D-dimer concentration may be determined by a blood test to help diagnose thrombosis. Since its introduction in the 1990s, it has become an important test performed in patients with suspected thrombotic disorders. (6)

MATERIALS AND METHODS:

Seventy five subjects were enrolled in this case control study: fifty were diagnosed with chronic lymphocytic leukemia which diagnosed by flow cytometry ,both gender above 40 years old, and Sudanese patients attending to radiation and isotope center(Khartoum),and twenty five normal subjects as control group ,patient with history of chemotherapy and new case.

2.5 ml of venous blood was collected from each subjects in 0,25 trisodium citrate containers, evaluated to determine D-

dimer was measured using VEDALAB EASY READER ,PT and APTT were measured by semi automated coagulometer. This study was approved by ethical committee of ministry of health, and informed consent was obtained from each participant before sample collection.

Statistical analysis was performed using statistical package for social science (SPSS) software.

RESULTS :

In total of 50 patients were diagnosed with chronic lymphocytic leukemia, and twenty five health individual as control group, All subjects were tested for D-Dimer level, PT, and APTT. Mean D-dimer level for the patients was 565.96 ± 474.22 ng/ml, the level were elevated in 64% ,Mean level of control group was 102.44 ± 33.86 (p value 0.000). Mean PT for the patients was 15.14 ± 9.16 second, and mean of control group was 12.20 ± 1.68 second (p value 0.032). And the mean of APTT of patients was 53.86 ± 27.95 second and mean of control group was 31.44 ± 8.09 second (p value 0.000) (table1). Percentage of abnormal D-dimer(64%), PT(44%) and APTT(68%) in patients compared to normal ranges of above-mentioned tests (fig 1). Moreover ,we compared between the mean of D-dimer, PT and APTT in new cases and cases under treatment, we found in new cases D-dimer mean was (735.73 ± 285.73) and cases under treatment D-dimer mean was (489.88 ± 411.73) (p-value0.044). PT mean in new cases was (9.21 ± 14.73) and in case under treatment PT mean was (66.50 ± 35.35) (p-value0.236), and APTT mean (66.50 ± 35.35) in new cases and in case under treatment APTT mean was (48.25 ± 22.91) (p-value0.063)(table2).

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Table 1: Mean of D-dimer, PT, and APTT in patients and Control group

	Group	N	Mean	Std. Deviation	P-value
D-dimer	Case	50	565.96	474.22	0.000
	Control	25	102.44	33.86	
PT	Case	50	15.14	9.16	0.032
	Control	25	12.20	1.68	
APTT	Case	50	53.86	27.95	0.000
	Control	25	31.44	8.09	

Fig (1): The frequency of abnormal D-dimer, PT and APTT in patients:

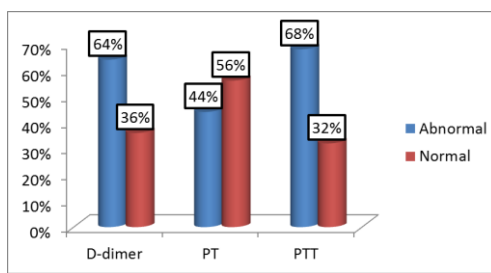


Table 2: D-dimer, PT and APTT in new cases and cases under treatment

	Grouping	N	Mean	Std. Deviation	P-value
D-dimer	new-Case	15	735.73	285.19	0.044
	Under-Treatment	35	489.88	411.73	
PT (second)	new-Case	15	14.73	9.21	0.236
	Under-Treatment	35	15.41	9.38	
APTT (second)	new-Case	15	66.50	35.35	0.036
	Under-Treatment	35	48.25	22.91	

DISCUSSION:

In this study we utilized a quantitative approach for the determination of D-dimer level, PT and APTT. We observed higher D-dimer levels among CLL patients when compared with the normal healthy control. Similar findings, with higher D-Dimer level had previously been reported (AY C et al, Vienna, 2009) (8). D-dimer is the major breakdown fragment of fibrin and a good biochemical marker of thrombogenesis and fibrin turnover, increased D-dimer level in plasma is an indirect

marker of hypercoagulation activation and thrombolysis. Elevated plasma D-dimer levels can be seen in cancer patients because procoagulant factors in various types of cancer lead to constitutive activation of the coagulation cascade which results in thrombin generation and fibrin formation (9). Mean PT and APTT of patients were significantly prolonged compared to healthy control (P-value 0.032 and 0.000 respectively) ,This finding is in agreement with other study(Mohammed MR et al,2013) (10),In this study ,we found abnormal APTT in (68%) of CLL patients and the lower percent was found in abnormal PT (44%). We found , in this study that is no relationship between the mean of PT when compared between new cases and cases under treatment , whereby this was a difference between mean of D-dimer and APTT between new cases and cases under treatment.

CONCLUSION:

This study evaluated the haemostatic properties among Chronic lymphocytic leukemia patients in Sudan, PT and APTT were prolonged compared to control group as well as the D-dimer. APTT and D-dimer showed difference in the mean between new cases and cases under treatment but this difference was not significant in PT. Those finding suggest hypercoagulable state among chronic lymphocytic leukemia patients.

RECOMMENDATION:

We recommend that the coagulation profile (D-dimer, PT and APTT) should be requested as routine investigation to screen for the hemostatic disorder that can occur in chronic lymphocytic leukemia patients so as to prevent complications.

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