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Determination of PT, APTT and D- dimer among Sudanese patient with acute Leukemia in Khartoum State, Sudan 2017

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Abstract:

Background: *Leukemia is a progressive malignant disease of the blood. Both the clinical and experimental should have studies association between acute leukemia and homeostasis. Acute leukemia is usually aggressive disease in which malignant transformation occur in the haemopoietic stem cell or early progenitor cell. Acute leukemia is defined as presences of over 20% of blast cell in the peripheral blood and /or bone marrow at clinical presentation.*

Aim: *we conducted our study to evaluate coagulation profile (PT, APTT & D- dimer) in Sudanese Patients with acute leukemia.*

Method: *This is a prospective analytical case control study was conducted to evaluate coagulation profile in 80 Sudanese population,40 of them with acute leukemia; study was performed to determination of PT, APTT and D-dimer , patients who attended to Radiation isotopes center of Khartoum (RICK) at Khartoum state, and enrolled 40 healthy individual during 2015…2017.*

Results: *In disease, group males are 33(82.5%) and females are 7 (17.5%), most of participant in case group in age group between (20-30) years. The case group in our study was divided into two subgroups based on type of leukemia ALL was 26 (65%), AML 14(35%).*

There is significant correlation between case and control group in PT, PTT, and D-dimer (P values < 0.05) ***(Table 2).***

Conclusion: *We conclude that there were significant variations in PT, PTT, and D-dimer between case and control group.*

Key words: D dimer level, Acute leukemia, Sudan, 2017.

INTRODUCTION

Acute leukemia is characterized by a rapid increase in the number of immature blood cells. The crowding that results from such cells makes the bone marrow unable to produce healthy blood cells. Immediate treatment is required in acute leukemia because of the rapid progression and accumulation of the malignant cells, which then spill over into the bloodstream and spread to other organs of the body. Acute forms of leukemia are the most common forms of leukemia in children [(1).] The main types of acute leukemia are: Acute lymphocytic (lymphoblastic) leukemia (ALL) seen in both children and adults, but its incidence peaks between ages 2 and 5 years. The causation of ALL considered as multi-factorial, including exogenous or endogenous exposures, genetic susceptibility, and chance. The survival rate of pediatric ALL has improved to approximately 90% with risk stratification by biologic features of leukemic cells and response to therapy [(2).] ALL arises from hematopoietic precursors of the lymphoid lineage. It is the most common leukemia in pediatrics, accounting for up to 80% of leukemia's in this group and 20% of leukemia's in adults. Acute myeloid leukemia (AML) accounts for approximately 15–20% of all childhood leukemia's, and despite dramatic improvements in treatment outcome, only approximately 70% of children with AML cured. AML results from collaborating genetic aberrations in at least two different classes; Type-I aberrations, inducing uncontrolled cell proliferation and or survival, and type-II

aberrations inhibiting cell differentiation [3]. All subtypes of AML probably share abnormalities in common pathways that regulate proliferation, differentiation, and cell death.

D-dimer is a biomarker that globally indicates the activation of hemostasis and fibrinolysis. It is a degradation product of fibrin, which produced when cross-linked fibrin is degraded by plasmin-induced fibrinolytic activity. As D-dimer, plasma levels are elevated after clot formation, the measurement of D-dimer routinely used in conjunction with clinical parameters in the initial assessment of suspected acute VTE [4] Various solid tumor patients, including lung, prostate, cervical, and colorectal cancer patients found with elevated D-dimer level in the plasma. In patients with colorectal cancer, D-dimer level has been shown to correlate with depth of tumor invasion at the time of surgical excision. Abnormal coagulation activation promotes endothelial adhesion and metastatic spread, as well as tumor cell growth and tumor cell survival [5]. It is widely recognized that the majority of cancer patients present with one or more abnormalities of laboratory coagulation tests. The most frequent abnormalities include increased levels of fibrinogen, factors V, VIII, IX, X, fibrin (ogen) degradation products (FDPs) and thrombocytosis [6]. the modern hemostasis laboratory performs a large number of distinct tests, often using a variety of methodologies. All hemostasis laboratories perform routine coagulation tests comprising the prothrombin time (PT), international normalized ratio (INR) and the activated partial thromboplastin time (APTT), sometimes supplemented by specific fibrinogen assays, and occasionally thrombin time (TT) assays. Most routine test laboratories also perform D-dimer assays. These tests are variably performed to investigate hemostasis in patients suspected of having a potential dysfunction in the secondary hemostasis pathway, either congenital like hemophilia) or acquired like DIC. This is

because PT/INR, APTT, and TT are sensitive to deficiencies or defects in various procoagulant factors. Thus, the PT/INR is sensitive to factors (F) I, II, VII, V, and X, and the APTT to F I, II, V, VIII, IX, X, XI, and XII [(7).]

METHODOLOGY

80 samples were enrolled in this case control study, 40 patients with acute leukemia attending (RICK) Radiation and isotope center with different age compared with 40 normal adult subject as control with history of new case acute leukemia patient receiving and anticoagulant excluded the standard was used. Informed consent was obtained from each subject before enrollment in the study. venous blood sample 2.5 mL in 3.8% trisodium citrate (9:10 kept on ice until centrifugation at 2000 for 15 min to pre pare plate late poor plasma (PPP) remove the supernatant plasma 4oc plasma sample were immediately frozen and stored at - 80°C for subsequent coagulation analysis. Laboratory analysis was performed at the Department of Haematology, Faculty of Medical Laboratory Sciences, Alneelain University. D-dimer was measured using i-CHROMATM system APTT and PT were measured using coagulometer (Sysmex CA 50) which rely on scattered light detection method.

D. dimer was measured by CHROMA System.

Immunodetection method by D. dimer bound with antibody in buffer. The antigen antibody complex captured by antibodies that have been immobilizes on the test strip as sample mixture migrate through nitro cellulose matrix the of intensity florescence. On defection an antibody reflects the auraut of antigen and processed by CHROMA reader to show the concentrations of D.dimer.

Statistical analysis

Data were entered and analyzed by SPSS programmer (version: 21.0). All demographic data of the study population were presented as mean and SD in the text and P.value (< 0.01, < 0.000, < 0.000 respectively for, PT , APTT and D .Dimer .)was used for detecting the power of relationship between the determinant and the outcome and 95% confidence interval was calculated. [8]

Quality control

Depending on pilot study in the quality control results (that saved in the Q.C of Coaglometer and CHROMA System).

RESULTS

This case control study conducted in RICK during the period from 2015 to 2017, to compare coagulation parameters between patient attending RICK and healthy individuals. The participants included 80 subjects. 40 Out of them, was already diagnosed with leukemia and 40 healthy. In case group gender wise males are 33(82.5%) and females are 7 (17.5%) There is significant correlation between case and control group in PT, PTT, and D-dimer (P values < 0.05).

Table (1) Distribution demographic data of according to their Age, Sex and disease

Variable	Frequency	Percent %
Age		
Less than 20	8	20
20__30	21	52.5
30__40	4	10
40__50	6	15
More than 50	1	2.5
Total	**40**	**100**
Sex		
Male	33	82.5

Female	7	17.5
Total	**40**	**100**

Type		
All	26	65
Aml	14	35
Total	**40**	**100**

Table (2): Comparison of means of PT, AAPT and D.dimer in The Test group and the control group

Variable	Test group N=40	Control group N=40	P value
PT	15.3± 4.5 (9.8 - 32)	12.2± 1.6 (10 - 15)	< 0.01
APTT	64± 28.2 (36 – 137)	30± 4.4 (22 – 36)	< 0.000
D.dimer	1075± .95 (250– 3650)	101.9± 30.4 (60 – 180)	< 0.000

The table shows the mean ± SD (mini - max) and probability (P)
T-test was used for comparison.
P value ≤ 0.05 was considered significant.

DISCUSSION

Cancer can confer a prothrombotic or hypercoagulable state through an altered balance between the coagulation and fibrinolytic systems [(9).] Many studies have been conducted to assess the function of the haemostatic system in patients with cancer. In this study we utilized a quantitative approach for the determination of D-dimer level, APTT, and PT. The study included 40 Sudanese acute leukemia patients, their D-dimer levels, APTT and PT were measured and compared with 40 age and sex matched normal subjects as controls. We observed higher D-dimer levels among cancer patients (1075± .95) when compared with the normal healthy controls (101.9± 30.4). Similar findings, with higher D-Dimer level had previously been reported the p.value (< 0.000) considered significant different [(10-12)]. 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 hyper coagulation activation and thrombolysis [10]. 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 [13]. D-dimer levels have been found to rise proportionally to the extent and severity of disease in patients with various types of malignancy [13, 14], and has been suggested as a measure of disease status in patients with malignant neoplasms [10, 11, 15, 16].

Mean APTT and mean PT were significantly higher in malignancy cases (64± 28.2), (15.3± 4.5) respectively when compared to healthy controls, and p.value also were significant different (< 0.000) and were directly associated with D-Dimer levels. This finding is in agreement with other study [17] (Mohammed et al., 2013) (D-dimer 45%, n=18, PT 27.5%, n=11, APTT 25%, n=10). This finding most probably is explained by the competition of the FDP for the fibrinogen binding sites of thrombin, and thus slows down clot formation by preventing the conversion of fibrinogen to fibrin leading to prolonged plasma clotting times.

CONCLUSION

We conclude that there were significant increase in PT, PTT, and D.dimer between acute leukemia patients and control group.

Recommendation

We recommend designing cohort study for acute leukemia to determination of PT, APTT & D.dimer also we recommend increasing sample size.

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