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RESEARCH ARTICLE

ASSESSMENT OF LIVER AND RENAL FUNCTION TESTS AMONG PATIENTS WITH ACUTE LYMPHOID AND MYELOID LEUKEMIAS IN KHARTOUM STATE-SUDAN

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ABSTRACT

Leukemia one of the malignancies starts in blood but extend to other body organs as blood is the major of body supply of oxygen and nutrients. Leukemia can be divided according to many considerations but the important on is the set of the disease to acute and chronic and then type of cell involved in its occurrence to myeloid and lymphoid type. This study concerned about acute leukemia in Khartoum state and the status of renal and liver function tests. The study involved 100 patients 42% females and 58% males. After approval and formal consent obtained by Alneelain University, Khartoum Nuclear and Radiology hospital and patients of acute leukemias, blood samples were used to measure urea and creatinine as renal parameters and liver function tests included bilirubin, protein and enzymes. All parameters among acute leukemia patients presented increased than normal range. Patients were in different age levels and still abnormality of measured parameters presented

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INTRODUCTION

The leukemias are a group of disorders characterized by the accumulation of malignant white cells inthe bone marrow and blood. These abnormal cellscause symptoms because of: (i) bone marrow failure (i.e. anemia, neutropenia, and thrombocytopenia) and (ii) infiltration of organs (e.g. liver, spleen, lymphnodes, meninges, brain, skin or testes. Acute leukemia is defined as the presence ofover 20% of blast cells in the blood or bone marrowat clinical presentation. It can be diagnosed with evenless than 20% blasts if specific leukemia-associated cytogenetic or molecular genetic abnormalities arepresent. It is further subdivided into acute myeloid leukemia (AML) and acute lymphoblastic leukemia (ALL) on the basis of whether the blasts are shownto be myeloblasts or lymphoblasts (Hoffbrand, 2006). The incidence of AML increases with age and AML is the most common types of adult leukemias (Bruguera, 2007). These alterations disrupt normal differentiation and/or cause excessive proliferation of abnormal immature leukemic cells known as blasts. As the disease progresses, blast cells accumulate in the bone marrow, blood, and organs and interfere with the production of normal blood cells. This leads to fatal infection, bleeding, or organ infiltration in the absence of treatment within 1 year of diagnosis (Bruguera, 2007; Lowenberg, 1999). Acute lymphoid leukemia (ALL), like cancer in general, is likely to arise from interactions between exogenous or endogenous exposures, genetic (inherited) susceptibility, and chance. These factors account for the approximately 1 in 2000 risk of childhood (0–15 years) ALL. The challenge is to identify the relevant exposures and inherited genetic variants and to decipher how and when they contribute to the multi-step natural history of ALL from its initiation (usually in utero) through its largely covert evolution to overt disease (Shipley, 2009) While acute myeloid leukemia (AML) is a heterogeneous disorder characterized by clonal expansion of myeloid progenitors (blasts) in the bone marrow and peripheral blood. Previously incurable, AML is now cured in approximately 35%–40% of patients younger than age 60 years old (Döhner, 2015). Most of acute leukemia patients have organs enlargement as splenomegaly and hepatomegaly, this might be caused by infiltration of leukemic cells, which are seen in some cases of leukemia (Mohammed Elbossaty, 2017). Acute liver failure considers as the initial manifestation of acute leukemia, also it is extremely rare, it is difficult to diagnose due to the rapid progression (Sharma, 2017). It has been described in acute lymphoblastic leukemia far more than

in acute myeloid leukemia this due to blasts infiltration in ALL more than in AML (Bruguera, 2007; Margolin *et al*., 2001). Other organ can be affected due to acute leukemia is kidney, but renal failure is a rarely a presenting symptom in ALL (Larsen, 1996; Suh, 2007). Renal involvement can present as renal enlargement due to leukemic infiltrates or as renal failure due to uric acid nephropathy (Basker *et al*., 2002; Appleyard, 1971). The reason why some patients develop hyperuricemia in the absence of significant tumor load still remains unclear. It is presumed that tumors with a high mitotic index may predispose to more spontaneous lysis and cell deaths. Although leukemic infiltration of kidney may present in all types of leukemia, it more often occurs with lymphoblastic leukemia. Leukemic infiltrates may lead to significant impairment of renal function if it is bilateral and diffuse and in particular involves the cortical region (Sengul *et al*., 2008).

MATERIALS AND METHODS

This cross sectional study involved 100 patients with acute leukemia, myeloid and lymphoid, attended to Khartoum Nuclear Atomic hospital, where they take regular follow up and treatment, 50 of them were diagnosed with acute myeloid leukemia (AML) with age mean$\pm$SD as 26.3$\pm$16.5 years and the other 50 were diagnosed with acute lymphoid leukemia (ALL) with age mean$\pm$SD as 31.3$\pm$16.8 years. Under hygienic conditions, blood samples withdrew in heparinized blood containers, plasma used for measurement of renal parameters, urea and creatinine and liver function tests, as total bilirubin, direct bilirubin, total protein, albumin, alkaline phosphatase, aspartate transaminase and alanine transaminase. Device and reagents for chemical parameters were used were Mindray trade mark, Chinese manufacturer, laboratory measurements were conducted at laboratory section of Khartoum Radio Atomic hospital. Data obtained analyzed with the statistical package of social science program (SPSS) version 21.

RESULTS

Chemical measurements were conducted on plasma samples of one hundred (100) acute myeloid and lymphoid leukemia patients in Khartoum state's oncology hospital; they were 42% females and 58% males as in Figure 1. Measuring RFT and LFT parameters for AML and ALL and comparing their mean+SD of each with the reference value reveals significant difference of all parameters urea and creatinine as renal parameters and liver function tests ; total bilirubin(TB), direct bilirubin (DB), total protein (TP), albumin (ALB), alkaline phosphatase (ALP), aspartate transaminase (AST) and alanine transaminase (ALT) except alkaline phosphatase (ALP) as in Table 1. Comparison of RFT and LFT parameters of AML and ALL brought insignificant difference for RFT parameters, while some of LFT parameters presented with significant difference such as TB (total bilirubin), DB (direct bilirubin) with p value 0.000 and ALT (alanine transaminase) with p value 0.021, while the rest did not bring significant difference form comparison as in Table 2. Sorting leukemia to AML and ALL, each one measurements be evaluated separately according to the reference value, AML parameters brought significant difference for all except the alkaline phosphatase total bilirubin and ALP and the rest showed high p value 0.000 as in Table 3. Acute lymphoblastic leukemia (ALL) measured parameters revealed significant difference when compared to the reference value except for alkaline phosphatase as in Table 4.

Correlation of RFT and LFT parameters for both ALL and AML subjects with their age brought negative correlation for urea, albumin and liver enzymes, while the rest presented with positive correlation as in Table 5. While correlation with duration of the disease and measured parameters levels brought negative correlation with total bilirubin, direct bilirubin, albumin and alkaline phosphatase and the rest of the parameters presented with positive correlation as in Table 6. Considering gender, comparing RFT and LFT parameters has no significant difference between parameters of both genders

DISCUSSION

Most of acute leukemia patients have organs enlargement as splenomegaly and hepatomegaly, this might be caused by infiltration of leukemic cells, which are seen in some cases of leukemia[16]. Acute liver failure considers as the initial manifestation of acute leukemia, also it is extremely rare, it is difficult to diagnose due to the rapid progression (Sharma, 2007). It has been described in acute lymphoblastic leukemia far more than in acute myeloid leukemia this due to blasts infiltration in ALL more than in AML (Bruguera, 2007), and acute renal failure has been reported as complicated feature in many of leukemia cases (Toblem, 1980). Multiplication and overgrowth of malignant cells increase rate of turn over nucleic acid and this can cause acute renal failure due to the release of urate salts, which may deposited in renal tubule and cause blocking it (Freireich *et al*., 1982). Also, high cell turnover may be causes elevated lactate dehydrogenase. However, leukemia patients characterized with infection and inflammation this may be reason for elevated the rate of erythrocyte sedimentation (Mohammed Elbossaty, 2017). In this study, renal function tests included just urea and creatinine beside liver function tests involved total bilirubin, direct bilirubin, total protein, albumin and hepatic enzymes ALP.AST and ALT, were analyzed among ALL and AML patients.

For AML patients, urea and creatinine brought increased significant difference according to the reference value, and LFT also presented with significant difference for all parameters except total bilirubin and alkaline phosphatase, while ALL data revealed significant difference for all renal and liver parameters except alkaline phosphatase, these findings in partial agreement of study conducted among both acute leukemia myeloid and lymphoid, as the significant difference obtained for all measured parameters include renal and hepatic with increased p value manner as 0.000 for most of them was obtained (Mahmood Rasool *et al*., 2015). Also partial agreement with an Egyptian study conducted on four case of acute leukemia, presented with acute renal and hepatic failure due accumulation of blast cells in their organs (Walaa Fikry Elbossaty, 2017). Renal function tests outcome for this study shows indicator for renal damage, but as data of patients situation and therapy program were not goals, it hardly to sort these patients to what level of disorder kidney status could be, but overall renal deviation from normality occurred and that similar to finding of study concerned about renal status among acute leukemia and renal failure sorted out due to measureable parameters and treatment program as well (Reinhold Munker, 1998). While other study mentioned that renal failure can be due to organ infiltration among acute lymphoid leukemia even before treatment administration starts (Erkan Sengul, 2008).

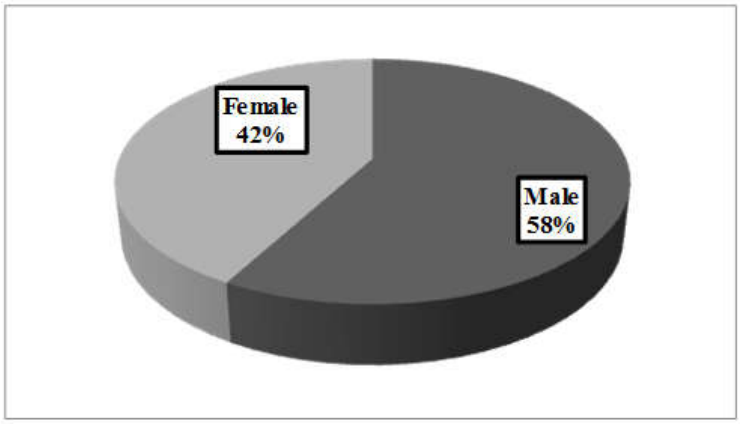

Table 1. Mean concentration and standard deviation of study parameters comparison with normal range

Parameters	Mean±SD	*Mean (R.V)*	*P-value*
Urea	46.70±28.16	10-50 (30)	0.000
Creatinine	1.58±0.97	Up to 1	0.002
TB	2.13±0.98	Up to 1	0.000
DB	1.15±1.17	Up to 0.25	0.000
TP	6.22±1.76	7-9.5 (8.25)	0.001
ALB	3.32±1.06	3.5-5 (4.25)	0.001
ALP	99.51±53.27	44-147 (95.5)	0.453
AST	69.99±56.37	4-45 (24.5)	0.000
ALT	74.43±31.43	4-45 (24.5)	0.000

Significant difference p value < 0.05.

Table 2. Mean concentration and SD of RFT and LFT for AML and ALL patients according to gender

Parameters	AML (Mean±SD)	ALL (Mean±SD)	*P-value*
Urea	49.14±27.82	44.26±28.56	0.389
Creatinine	1.60±0.95	1.57±1.01	0.855
TB	0.91±0.39	3.34±1.97	0.000
DB	0.48±0.33	1.82±1.31	0.000
TP	6.30±1.67	6.13±1.87	0.620
ALB	3.15±0.88	3.49±1.20	0.111
ALP	97.62±35.0	101.40±67.09	0.725
AST	67.32±51.29	72.66±61.44	0.638
ALT	63.34±49.71	85.53±47.11	0.021

Significant difference p value < 0.05.

Table 3. Mean concentration of study parameters AML comparison with normal range

Parameters	AML (Mean±SD)	*Mean (R.V)*	*P-value*
Urea	49.14±27.82	10-50 (30)	0.000
Creatinine	1.60±0.95	Up to 1	0.000
TB	0.91±0.39	Up to 1	0.110
DB	0.48±0.33	Up to 0.25	0.000
TP	6.30±1.67	7-9.5 (8.25)	0.000
ALB	3.15±0.88	3.5-5 (4.25)	0.001
ALP	97.62±35.0	44-147 (95.5)	0.670
AST	67.32±51.29	4-45 (24.5)	0.000
ALT	63.34±49.71	4-45 (24.5)	0.000

Significant difference p value < 0.05.

Table 4. Mean+SD of study parameters ALL comparison with normal range

Parameters	ALL (Mean±SD)	*Mean (R.V)*	*P-value*
Urea	44.26±28.56	10-50 (30)	0.000
Creatinine	1.57±1.01	Up to 1	0.001
TB	3.34±1.97	Up to 1	0.000
DB	1.82±1.31	Up to 0.25	0.000
TP	6.13±1.87	7-9.5 (8.25)	0.000
ALB	3.49±1.20	3.5-5 (4.25)	0.001
ALP	101.40±67.09	44-147 (95.5)	0.665
AST	72.66±61.44	4-45 (24.5)	0.000
ALT	85.53±47.11	4-45 (24.5)	0.000

Significant difference p value < 0.05.

Table 5. Correlation between study parameters and age

Variables	*R-value*	*P-value*
Urea	-0.024	0.809
Creatinine	0.006	0.950
TB	0.099	0.326
DB	0.089	0.379
TP	0.043	0.672
ALB	-0.026	0.800
ALP	-0.056	0.578
AST	-0.095	0.348
ALT	-0.163	0.104

Pearson correlation significance between -1 and +1.

Table 6. correlation between study parameters and duration of the disease

Variables	*R-value*	*P-value*
Urea	0.175	0.082
Creatinine	0.234*	0.019
TB	-0.054-	0.592
DB	0.047	0.639
TP	-0.134-	0.183
ALB	-0.075-	0.456
ALP	-0.078-	0.441
AST	0.030	0.767
ALT	0.053	0.603

Pearson correlation significance between -1 and +1

According to age of acute leukemia patients, negative correlation found with urea, albumin, ALP, AST and ALT, that partially in agreement of outcome of a study conducted among patients with acute myeloid leukemia, as it showed decreased in albumin level among younger than adults (Amit Lahoti *et al*., 2010).

Conclusion

Acute leukemia patients presented with abnormal renal function tests as well as liver function tests with exception of certain parameters such as alkaline phosphatase, among both myeloid and lymphoid.

Recommendation

Extra considerations should be set as part of follow up program to ensure delay of organ damage as possible to increase chance of survival time for acute leukemia patients.

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