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Full Length Research Paper

Assessment of Liver Functions among Sudanese Leukemic Patients in Khartoum State

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Background: Leukaemia is a malignant disorder of the bone marrow and it's in a heterogeneous group of neoplasm arising from transformation of uncommitted or partial committed hematopoietic cells. This study was conducted at Khartoum state Sudan during October to December 2015. Aim: The aim of the study was to assess liver functions in leukemic patients. Methods: In this study (100) blood samples were tested, 50 samples for known patients with leukaemia and 50 samples from healthy persons as control group. Liver biochemical tests and enzymes were analyzed by auto-analyzer (BS-200 Chemistry Analyzer, Mindray). Results: The study demonstrated significant increasing of liver enzymes, aspartate aminotransferase (AST), alanine aminotransferase (ALT), alkaline phosphatase (ALP), gamma-glutamyltransferase(GGT) and globulins in leukemic patients, the mean levels were (54.32U/L), (43.10U/L), (116.10U/L, 33.4U/L,3.94g/dl) respectively, p.value (0.000, 0.000, 0.000, 0.000, 0.006), respectively. Also this study demonstrated insignificant variation of total proteins, albumin and globulin. In addition the study showed that the liver enzymes AST, GGT and albumin were increased significantly p.value (0.000, 0.008, 0.037) in the female leukemic patients rather than in male leukemic patients when compared according to sex. Moreover, ALT and GGT were significantly increased in the age group less than 40 years and decreased in the age group more than 40 years when compared according to age, p.value (0.001, 0.003). There was statistical significance increased in liver enzymes AST, ALT, ALP, and GGT in acute leukaemia (AML and ALL), p.value was (0.000, 0.002, 0.000, 0.000), respectively, while the enzymes decreased in chronic leukaemia (CML and CLL), when compared according to type of leukaemia.

Key words: AST, ALT, ALP, GGT, TP, ALB, GLB and leukaemia.

INTRODUCTION

The leukaemia are a heterogeneous group of neoplasm arising from transformation of uncommitted or partial committed hematopoietic cells (Hasse *et al.,* 1995; Conway *et al.,* 2010) there are four common types of leukaemia, chronic myeloid leukaemia (CML):which effect myeloid cells and usually grows slowly at first, it accounts for nearly 5,000 new cases of leukaemia.

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It mainly affects adults (Bruce *et al.,* 2010). About 50% of patients with CML showed mild to moderate hepatomegaly at presentation, with no liver function abnormalities (Cervantes and Rozman, 1982). At the time of blastic crisis, however, liver sinusoidal infiltration by immature cells may lead to liver enlargement and elevated serum ALP level (Ondreyco *et al.,* 1981) Chronic lymphocytic leukaemia (CLL): effect lymphoid cells and usually grows slowly (Bruce *et al.,* 2010) patient with (CLL) often showed mild to moderate liver enlargement and extensive lymphocytic infiltration in the

portal tract, with functional impairment of the liver in late stages (Schwartz and Shamsuddin, 1981; Wilputte *et al.,* 2003). Acute lymphocytic leukaemia (ALL): affects lymphoid cells and grows quickly, it is the most common type of leukaemia in young children. (Ondreyco *et al.,* 1981) acute myeloid leukaemia (AML): which effect myeloid cells and grows quickly, hepatic involvement in acute leukaemia's is usually mild and silent at the time of diagnosis.(Bruguera and Miguel, 2007) Some study showed liver infiltration in 95% of ALL and 75% of AML patients (Thiele DL, 2002) in ALL, infiltration was confined to the portal tract , whereas in AML, infiltration was observed in both portal tract and sinusoids, massive leukemic cells infiltration of the liver may present as fulminant hepatic failure (Litten *et al.,* 2006) The aminotransferases are normally present in the serum in low concentration, these enzymes are released in to the blood in greater amounts when there is damage to the liver cell membrane resulting in increased permeability (Eugene *et al.,* 2001; Anderson *et al.,* 2001), The activation of ALP and GGT are elevated in hepatic infiltration by leukemic cells (Shimizu *et al.,* 2006.)

There is limited information on the effect of leukaemia on the liver functions. Some studies showed that elevation of the liver enzymes such as AST, ALT, ALP, GGT in leukemic patients due to infiltration of the leukemic cell that leads to liver damage, while other studies demonstrated limited effect of leukaemia in the liver functions, Therefore the present study was undertaken to assess the level of AST, ALT, ALP, GGT, TP, ALB and GLB in leukemic patients.

MATERIALS AND METHOD

Study design: Cross-sectional study was conducted at National centre for radiotherapy and nuclear medicine during the period from October to December 2015, leukemic patients (50) with age between 20-80 years and control (50).

Sampling: Vein puncher blood samples were collected from all participant, samples were left at room temperature and then serum were obtained by centrifugation at 3000 rpm for 10 min, serum used for measure of AST, ALT, ALP, GGT, total proteins and albumin.

Ethical consideration: The study was approved by the local ethics committee of Al-Neelain University. All participants were informed by the aim of study after signed written informed consent. Sample and clinical information's were used anonymously.

Analytical analysis: BS-200 Chemistry Analyzer (Mindray) was used for estimation of all parameters.

Measurement of AST: In assay reaction, the AST catalyzes the reversible transamination of L-aspartate and alpha-oxoglutarate to oxaloacetate is then reduced malate in the presence of malate dehydrogenase with NADH being oxidized to NAD+. The rate of the photometrically determined NADH decrease is directly proportional to the rate of formation of oxaloacetate and thus the AST activity.

Measurement of AST: In assay reaction, the AST catalyzes the reversible transamination of L-aspartate and alpha-oxoglutarate to oxaloacetate is then reduced malate in the presence of malate dehydrogenase with NADH being oxidized to NAD+. The rate of the photometrically determined NADH decrease is directly proportional to the rate of formation of oxaloacetate and thus the AST activity.

Measurement of ALT: In assay reaction, the ALT catalyzes the reversible transamination of L-alanine and alpha-oxoglutarate to pyrovate and L-glutamate. The pyrovate then reduced to lactate in the presence of lactate dehydrogenase (LDH) with the concurrent oxidation of reduce beta- NADH to beta-NAD. This change in absorbance is directly proportional to the activity of ALT in the sample.

Measurement of ALP: by the action of ALP and magnesium ions, P-Nitrophenyl phosphate is catalyzed to p-Nitrophenol, and the absorbency increase is directly proportional to the activity of ALP.

Measurement of GGT: GGT transfers the gamma- glutamyl group of gamma-glutamyle-3-carboxy-4-nitroanilide to glycyl-glycine with production of p-nitroaniline. The amount of 5-amino-2-nitrobenzoate results in the elevated absorbance which is directly proportional to the activity of GGT in the sample.

Measurement of Total proteins: At an alkaline solution (PH>12) copper ions combine with protein to produce a blue – violet colour complex. The absorbency increase is directly proportional to the concentration of proteins.

Estimation of ALB (Albumin): At a slightly acid pH (pH=4.2), serum albumin combines with bromcresol green to produce a glaucous complex. The absorbency increase is directly proportional to the concentration of albumin.

Statistical analysis: Data from all patients were presented as percentage and (mean±SD), difference between mean of patients and control group were considered statistically significant with p-value threshold <0.05 using independent T-test.

RESULTS

Table 1 presented the mean concentrations of liver enzymes and biochemical levels (AST, ALT, ALP, GGT, TP, Alb and Glb) in leukemic patients versus the control group. There is significant increasing of liver enzymes, aspartate aminotransferase (AST), alanine aminotransferase (ALT), alkaline phosphatase (ALP), gamma-glutamyltransferase (GGT) and globulins in Leukemic patients when compared with means of control group, the mean levels were (54.32U/L), (43.10U/L), (116.10U/L, 33.4U/L,3.94g/dl) respectively, p.value (0.000, 0.000, 0.000, 0.000, 0.006), respectively.

Table 2 represented the comparison of mean levels of AST, ALT, ALP, GGT, TP, ALb and Glb in leukemic patients

Table 1: Demonstrated the concentration of mean levels of AST, ALT, ALP, GGT, TP, ALb and Glb in leukemic patients versus the control group.

Measured units	Means ± SD		*p-value
	Patients No. =(50)	Control No. =(50)	
AST	54.32±30.60	21.96±3.87	0.000
ALT	43.10±43.69	29.06±5.67	0.000
ALP	116.10±51.32	87.52±17.02	0.000
GGT	33.44±22.06	19.30±4.86	0.000
TP	7.62±.89	6.59±.52	0.164.
Alb	3.76±.50	4.18±.52	0.862
Glb	3.94±.81	2.97±.47	0.006.

*The P<0.05 were considered significant.

according to the gender. The liver enzymes AST, GGT were increased significantly p.value (0.000, 0.008) in the female leukemic patients rather than in male leukemic patients when compared according to sex.

Table 3 showed the comparison of liver mean biochemical and enzymes levels among the leukemic patients according to the age. ALT, GGT and Alb were significantly increased in the age group less than 40 years when compared according to age, p.value (0.001, 0.003, 0.037). Table 4 demonstrated the comparison of the mean levels of AST, ALT, ALP, GGT, TP, ALb and Glb in leukemic patients according to the type of the leukemia. AST, ALT, ALP, and GGT were significantly increased in acute leukemia (AML and ALL), p.value was (0.000, 0.002, 0.000, 0.000), respectively.

DISCUSSION

This study included (100) samples, 50 samples as study group and the other 50 as control which were analyzed for liver biochemical and enzymes. In this study, the average concentration of AST enzyme was 54.32U/L in leukemic patients, while it was 21.96U/L in control group, there is significant increase in AST level with p-value (0.000), when compared with the level of control group, this finding agreed with previous study reports (11, 12), who said that, the infiltration of leukemic cells caused liver damage which lead to an increased in the level of AST. Also the mean level of ALT enzyme was 43.10U/L in leukemic patients, and it was 29.06U/L in control group there was highly significant increase of ALT level in leukemic patients with p-value (0.000) this finding agreed with previous study which report that, the infiltration of leukemic cells causing hepatocellular damage which lead to increasing the level of ALT and other liver enzymes. (11, 12) also the mean concentration of ALP was 116.10U/L in leukemic group, and it was 87.52U/L in control group, there was a significant increase in ALP mean level. These findings agreed with past work (13, 14), who had mentioned, in some hematological disorders like leukemia causing hepatocellular damage which lead to high level of ALP. Moreover, the mean concentration of GGT was 33.44U/L while it was 19.30U/L in control group, with statistical significance difference p-value (0.000), this finding in consistent to the past study (Shimizu *et al.,* 2006), who reported that, the infiltration of leukemic cells causing liver damage and increase the level of GGT enzyme concerning the average concentration of total proteins, albumin and globulins in leukemic group, their mean concentrations were insignificant when compared versus controls, p.value (0.164, 0.862, 0;355), respectively (table 1). Regarding the leukemic group according to sex, AST was found significantly high among female group rather than males, p.value (0.000), whereas the mean level of ALT enzyme was found insignificant p.value (0.08), meanwhile the average concentration of ALP was 103.16U/L in male, and it was 135.50U/L in female with p-value 0.111, and the mean levels of GGT in male was 28.16U/L and 41.35U/L in female group with p-value 0.008. our result findings according to sex revealed that there is, high significant increase of AST level in female, insignificant variation in ALT, insignificant variation in ALP level, and significant decreased of GGT level in male, as well as the biochemical of the liver (T.p,Alb,Glb) in the two groups did not revealed significant difference. Our result findings presented that, ALT, GGT and Albumin were significantly increased in the age group less than 40 years when compared with the age group greater than 40 years, p.value (0.001, 0.003, 0.037), respectively, while the other enzymes and biochemical tests were statistically not different in the two groups (Table 3).In this study results, the liver enzymes AST, ALT, ALP, and GGT were significantly increased in acute leukemia (AML and ALL),in comparison with chronic leukemia (CML, CLL), p.value was (0.000, 0.002, 0.000, 0.000), respectively (Table 4). These findings typically agreed with elsewhere study (15) who noticed that, the liver infiltration in 95% of ALL and up to 75% of AML patients which lead to elevated liver enzymes. The present study found that, there was insignificant variation in mean concentration of total proteins, albumin, and globulin in comparison between types of leukemia.

CONCLUSIONS

The present study concluded that the level of AST, ALT, ALP and GGT were increase in leukemic patients, also these enzymes were increased in female leukemic patients and decrease in male leukemic patients when compared according to sex, ALT, GGT and Albumin were increased in the age group less 40 years, while decreased in

Table 2: Demonstrated the comparison of mean levels of AST, ALT, ALP, GGT, TP, Alb and Glb in leukemic patients according to the gender.

Measured units	Means ± SD		*p- value
	Male No. =(30)	Female No. =(20)	
AST	41.63±13.69	73.35±38.64	0.000
ALT	30.93±34.11	61.35±50.63	0.08
ALP	103.16±35.61	135.50±64.79	0.111
GGT	28.16±15.826	41.35±27.62	0.008
TP	7.67±0.66	7.54±1.182	0.168
Alb	3.76±0.51	3.76±0.49	0.466
Glb	3.92±0.868	3.97±0.736	0.355

*The P<0.05 were considered significant.

Table 3: demonstrated the comparison of mean levels of AST, ALT, ALP, GGT, TP, Alb and Glb in leukemic patients according to the age.

Measured units	Means ± SD		*p- value
	Less than 40 years No. =(31)	More than 40 years No. =(19)	
AST	58.67±35.68	47.21±18.44	0.074
ALT	48.74±53.27	33.89±17.95	0.001
ALP	122.22±58.14	106.10±36.98	0.080
GGT	39.45±25.44	23.63±9.06	0.003
TP	7.64±1.05	7.57±0.58	0.177
Alb	3.74±0.57	3.78±0.36	0.037
Glb	4.02±0.88	3.81±0.67	0.073

*The P<0.05 were considered significant.

Table 4: demonstrated the comparison of the mean levels of AST, ALT, ALP, GGT, TP, Alb and Glb in leukemic patients according to the type of the leukemia.

Measured units	Means ± SD				*p- value
	AML No =(10)	CML No= (17)	ALL No=(20)	CLL No=(3)	
AST	101.80±35.64	44.23±15.92	41.30±10.53	40.00±1.73	0.000
ALT	87.50±61.43	31.23±15.51	34.05±40.21	22.66±2.30	0.002
ALP	176.60±56.88	106.00±37.95	99.45±39.47	82.66±6.35	0.000
GGT	65.60±26.87	23.76±9.23	28.10±11.73	16.66±2.88	0.000
TP	7.57±1.74	7.57±0.61	7.68±0.55	7.63±0.11	0.983
Alb	3.73±0.64	3.75±0.37	3.74±0.56	4.03±0.05	0.824
Glb	4.23±1.17	3.84±0.70	3.94±0.73	3.60±0.17	0.579

*The P<0.05 were considered significant.

the age group more than 40 when compared between leukemic patients according to age, AST, ALT, ALP and GGT was increased in acute leukemia (AML and ALL), while decreased in chronic leukemia, total proteins, albumin and globulin levels were normal in leukemic patients.

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