Saudi Journal of Medical and Pharmaceutical Sciences **ISSN 2413-4929 (Print)**
Scholars Middle East Publishers **ISSN 2413-4910 (Online)**
Dubai, United Arab Emirates
Website: https://saudijournals.com/ DOI: 10.36348/sjmps.2016.v02i02.004

Original Research Article

Assessment of Liver Biochemical Parameters in Sudanese Patients with Myeloid Leukemia

Mutaz A. Alamin[1], Salih Abdelgadir Elmahdi[2], Gad Allah Modawe[3], AbdElkarim A. Abdrabo[1]
[1]Department of Clinical Chemistry, Faculty of Medical Laboratory Sciences, Al-Neelain University, Khartoum, Sudan.
[2]Department of Clinical Chemistry, Faculty of Medical Laboratory Sciences, The National Ribat University, Khartoum, Sudan
[3]Department of Biochemistry, Faculty of Medicine, Omdurman Islamic University, Omdurman, Sudan

***Corresponding Author:**
AbdElkarim A. Abdrabo
Email: abdrabokarim@gmail.com

Abstract: The effect of myeloid leukemia therapy has been widely noticed especially in acute myeloid leukemia mainly of liver enzymes. The objective of this study was to estimate the concentrations of some liver biochemical parameters (enzymes and proteins) including total protein, albumin, globulins, AST, ALT, ALP, and GGT, as well as to study correlation between these parameters in myeloid leukemia patients. This is a cross-sectionalstudy conducted in Institute of Nuclear Medicine and Oncology in Wad Madani City, Gezira Stateduringthe period from October to November 2015. The blood samples were obtained from 110 patients, 60 newly diagnosed myeloid leukemia with nottreated yet, and 50 patients treated with chemotherapy, all biochemical parameters were assessed using reagent kits, spectrophotometric method (BioSystem, Spain-Bercelona) was used. The mean of AST, ALT, GGT showed statistical significant increase, p. values (0.01,0.005, 0.026, 0.04), respectively compared to reference values.Mean levels of AST, ALT were higher in pretreatment <20years when compared with post-treatment <20 years, p.values (0.008, 0.025), respectively, as well as in pre and post treatment >20 years group also they observed significance values (0.000, 0.001), respectively. ALP enzyme level was significantly elevated in only the post treatment >20 years group, p.value (0.03). Pearson's correlationsbetween (age/disease, AST/ALT, AST/ALP, ALT/ALP) of the pretreatment group was found significant positiver. values (0.438, 0.886, 0.540, 0.492) p.value (0.000), while in post treatment group r.values were (0.272, 0.511, 0.960, 0.512), respectively and p.value for each (0.000). This study revealed that, thechemotherapy of myeloid leukemia in patients causes significant change in serum liver enzymes AST, ALT and GGT. There was a positive correlation between the myeloid leukemia disease and elevation of liver enzymes of pre and post treatment patients groups.
Keywords: leukemia, liver function test, Gezira state, serum proteins, chemotherapy.

INTRODUCTION

Leukemia is cancer of the blood forming cells; it occurs when immature or mature cells multiply in bone marrow [1]. And then blood stream accumulated of malignant white blood cells in bone marrow and blood. It has different criteria of classifications, according to cellular origin to lymphoid or myeloid [2]and either to acute, signifying rapidly progressing disease with a predominance of highly immature (blastic) cells[1], which infiltrate bone marrow, blood and other organs[3], or chronic, which denotes slowly progressing disease with greater numbers of more mature cells [1]. leukemia can be caused by various reasons include radiation, genetic and congenital factors, as Philadelphia chromosome in chronic myeloid leukemia, drugs and chemicals; exposure to certain ones can increase the predisposing of acute myeloid leukemia as petroleum derivatives, and infection with certain viruses [1]. Signs and symptoms can include A pale complexion from anemia, Signs of bleeding caused by a very low platelet count, Mild fever, Swollen gums, Frequent minor infections, such as perianal sores, Loss of appetite and weight loss, Discomfort in bones or joints, Enlarged spleen and Enlarged liver [4]. Although it was incurable 50 years ago, AML is now cured in 35 to 40% of adult patients who are 60 years of age or younger and in 5 to 15% of patients who are older than 60 years of age [3]. AML treatment includes Induction therapy with certain drugs; some of them in more adult subjects can bring side effects after remission [5]. And consolidation therapy after remission which can includes conventional chemotherapy as well as hematopoietic cell transplantation [3, 6]. Liver involvement with AML is rarely reported [7]. While in CML in chronic phase, approximately 50% of patients with CML show mild to moderate hepatomegaly at presentation, with no liver function abnormalities [8]. At the time of plastic crisis, however, liver sinusoidal infiltration by immature cells may lead to liver enlargement and elevated serum ALP levels [9]. The objective of this research to compare the concentrations of some biochemical parameters such as total protein, Albumin and globulins and also measures

the activity of liver enzymes AST, ALT, ALP, and GGT in myeloid leukemia patients, of both pre and post treatment.

MATERIAL AND METHOD

Reagents

All chemical reagents were purchased from (Biosystem, Spain, Bercelona Company for Analytical Material and Chemical Reagents).

Study population

This is a cross-sectional study conducted in Institute of Nuclear Medicine and Oncology, Wad Madani City, Gezira State, central Sudan. During from October to November 2015. The blood samples were obtained from 110 patients, 60 newly diagnosed myeloid leukemia with no treatment, and 50 patients were already diagnosed and under chemotherapy treatment.

Leukemic patients subdivided to pre and post-treatment,and also divided into acute myeloid leukemia(CMA) and chronic myeloid leukemia(CML). Ethical clearance was obtained from an ethical review board of Elneelein University, College of Medical Laboratory Sciences and appropriate informed consent from patients and their legal guardians.

Inclusion criteria

Myeloid leukemia patients

Exclusion criteria

Patients diagnosed with other types of cancer, hematological disorders and any malignant disease using chemotherapy.

Blood samples

From each participant leukemicpatient involved in this study, five mls of blood samples were collected in lithium heparin containers. The blood was centrifuged at 4000 rpm. For 10 minutes then plasma was separated,and kept at -20 and biochemical parameters were directly quantitatively measured**,** reagent kits purchased from Biosystem Company following the manufacturer's guidelines using spectrophotometer(BTS, Spain, Bercalona).

Statistical analysis

All the results were analyzed by statistical analysis, using statistical packaged of social sciences (SPSS). T-test was used to compare between means of parameters measured, and ($P<0.05$) value was considered significant.

RESULTS

Selected leukemic patients were categorized into two groups pre-treatment and post-treatment. Liver enzymes levels AST, ALT and GGT when compared with the two patients groups revealed statistical significant difference p.values (0.01, 0.005, 0.026, 0.04), respectively and plasma total proteins, albumin, globulins and ALP enzyme levels in the two patients groups were not different (table 1). The subgroups of the myeloid leukemia patients classified into pre-treatment 60(55%) and post-treatment 50(46%).

In this study myeloid leukemia was classified into two types acute myeloid leukemia represents 21% and the chronic one represents 79% among the studied patients.

Leukemic patients were categorized according to age into two groups (<20 years, >20 years) and to pre-treatment and post-treatment. The means of the enzymes in patients(pre-treatment group <20 years), with an elevated enzymes AST, ALT, ALP, and GGT was(2, zero, 11, zero), respectively, whereas among >20 years was (10, 5, 13, zero), respectively (table 2). Moreover the distribution of patients with elevated enzymes AST, ALT, ALP, GGT was (2, 1, 3, zero), respectively, among (post-treatment <20 years), and was (14, 10, 22, zero) among those of age >20 years of the same group.The elevated enzymes in the two patients groups revealed statistical significance values (table 3). In this study we found that all the 3 liver enzymes collectively were increased in about 13 patients (26%) of the post-treatment group, and increased in only I (1.6%) patients of the pre-treatment group.

Pearson's correlations between (T.protein/albumin, AST/ALT, ALT/ALP, AST/ALP, GGT/ALP) r.values (0.759, 0.886, 0.492, 0.540, 376) p.value (0.000, 0.000, 0.000, 0.000, 0.007), respectively,whereas in post treatment group r.values were (0.880, 0.333, 0.960, 0.0511, 0.512), and p.value (0.000, 0.018, 0.000, 0.000, 0.000), respectively, corresponding to (T.p/alb, ALP/alb, AST/ALT, AST/ALP, ALT/ALP. Extra positive correlations were found, among post treatment group between (GGT/AST, GGT/ ALP), r.value (0.601, 0.536), p.values were (0.000, 0. 000).

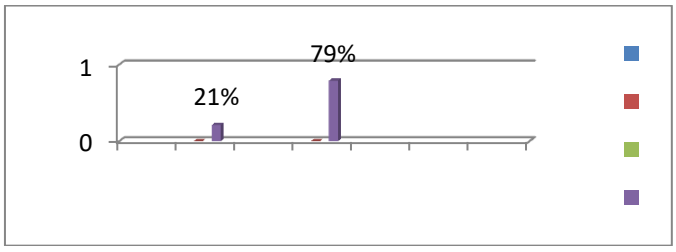

Fig.1: types of leukemia included in the study, AML represented 21% and CML represented 79%.

Table 1: shows (mean± SD) of Biochemical parameters in the study population.

Parameters	**Pre-treatment No 60**	**Post-treatment No 50**	***P* value**
Age (years)	30.7±14.2*	32.3±12.2*	0.01
T. protein g/dl	7.6±1.7	6.6±2.1	0.11
Albumin g/dl	3.3±1.5	3.2±1.1	0.72
Globulins g/dl	3.7±0.9	3.52+0.98	0.35
AST U/L	29.9±18.6*	54.1±62.2*	0.005
ALT U/L	25.6±25.1*	44.3±58.1*	0.026
ALP U/L	158.5±142.8	189.5±192.9	0.075
GGT U/L	10.4±3.7*	13.1±9.5*	0.04

Table 2: shows distribution of patients with an elevated enzymes levels in pre and post treatment <20 years group

Liver enzymes (Mean in U/L)	**Pre<20 years**	**Post <20 years**	**P.value**
AST No (%)	23.8 2(3.3%)	72.5 2(4%)	0.008
ALT No (%)	20.75 zero	60.75 1(2%)	0.025
ALP No (%)	264.1 11(18.3%)	292.0 3(6%)	0.51

Table 3: shows distribution of patients with an elevated enzymes levels in pre and post treatment >20 years group

Liver enzymes (Mean in U/L)	**Pre>20 years**	**Post >20 years**	**P.value**
AST No (%)	29.4 10(16.6%)	52.5 14(28%)	0.000
ALT No (%)	24.1 5(8.3%)	42.8 10(20%)	0.001
ALP No (%)	127.9 13(21.6%	180.5 22(44%)	0.03

Table4: shows correlations between liver enzymes and other factors in pre and post treatment groups.

Correlation between parameters	**r.value**	**p.value**
AST pre/ ALT	0.886	0.000
AST pre/ ALP	0.540	0.000
ALT pre/ ALP	0.492	0.000
AST post/ ALT	0.511	0.000
AST post/ ALP	0.960	0.000
ALT post/ ALP	0.512	0.000
Age pre/ Disease	0.438	0.001
Age post/ Disease	0.272	0.05
ALP/ GGT	-0.576	0.007
T.p/Alb	0-759	0.000

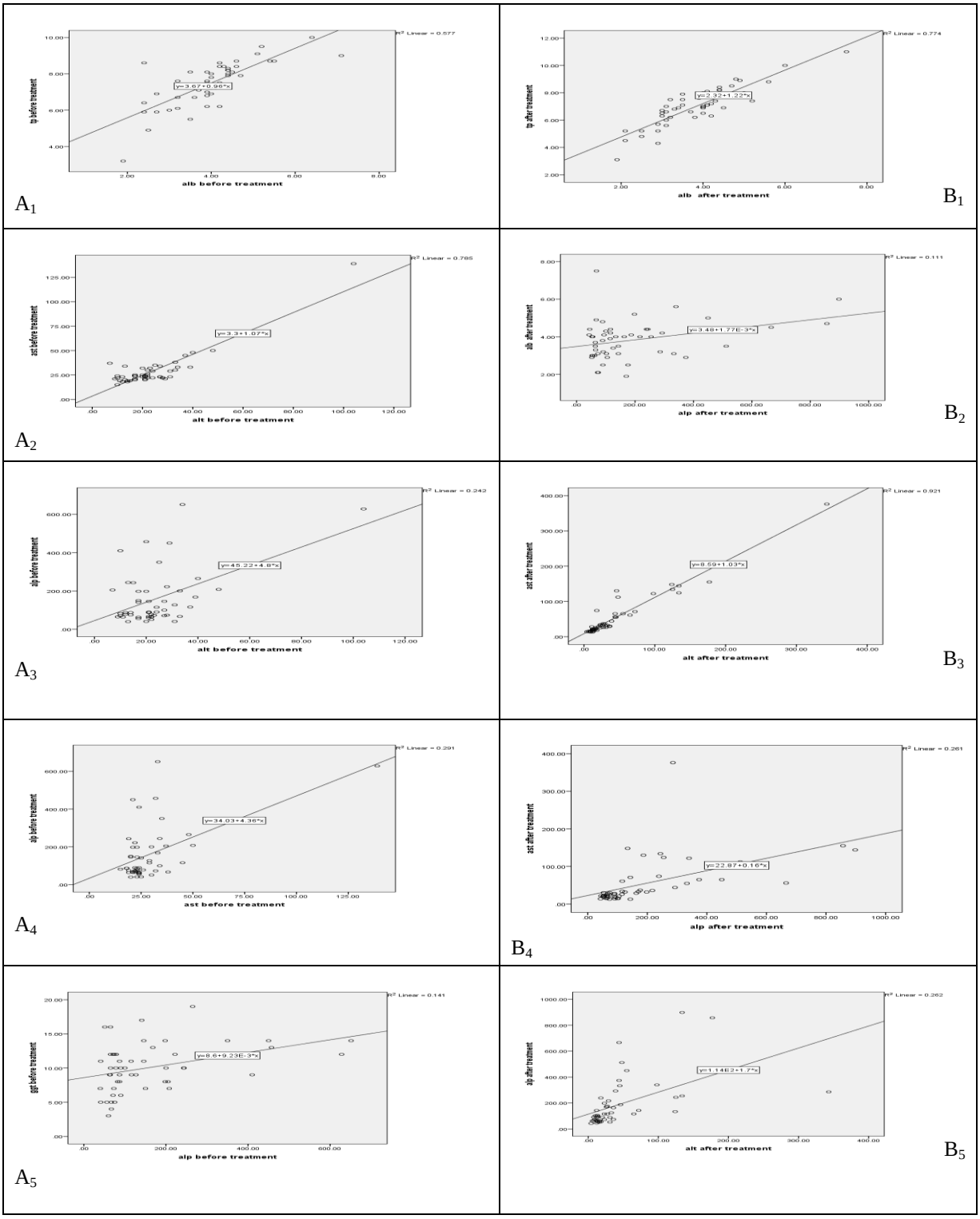

Fig. 2: shows correlations of (pre and post treatment groups) between different parameters and liver enzymes among the leukemic patients. Pretreatment A1-A5, post treatment B1-B5

DISCUSSION

This study involved 110 patients of myeloid leukemia, treated and un treated, aged between 5 and 70 years, 76(69%) male and 34(31%) females showed in fig(1). In this study the main consideration was the treatment, so levels of total protein. Albumin, globulins, and ALP of post treatment patients were not different from those of pre-treatment patients, while the mean levels of AST, ALT and GGT brought a significant difference when compared with post-treatment as shown in (Table1).There was a significant different in age groups, indicate that myeloid leukemia can occur at any age regardless of acute or chronic onset (Table1). This study showed that most biochemical tests of the liver

(T.proteins, albumin, globulins, GGT) were increased but within the normal range, however enzymes (AST, ALT, ALP) were significantly increased among CML post treatment group. These findings weren'tin agreement with study [8]whosuggested that about 50% of patients with CML show mild to moderate hepatomegaly at presentation, with no liver function abnormalities, while the higher levels of the enzymes obtained from the CML, agreed with the past study research [9] who said, at the time of blastic crisis, however, liver sinusoidal infiltration by immature cells may lead to liver enlargement and elevated serum ALP levels [11]. For AML pretreatment, data obtained disagree with study [12], which suggested that there were elevation in liver parameters in newly diagnosed subjects before treatment, and in agreement of other study considering post-treatment consequences [13]. Our result findings reveals a considerable elevations of AST,ALT enzymes 12(20%), 6(10%), in pretreatment <20 years and in 16(32%), 12(24%), respectively of the post treatment <20 years patients, while ALP were elevated in 14(23%) of the same pretreatment group and were elevated in about 25(50%) of the post treatment group, (table 2). These findings were in consistent with the report findings of Stefen et al., 2006 [14]who found liver function test abnormality elevation in ALT, AST of the patients, and in most cases these were transient and would resolve after a few days. Another research study done by Wandroo et al., 2004[15]also agreed with our result findings where AST, ALP increased.In the same context our research results of liver enzymes AST, ALT, ALP, of the post treatment >20 years were statistically significantly higher than pretreatment group, p.value (0.000, 0.001, 0.03), respectively and only ALP enzyme was presented with highermean levels than the normal reference value in both groups (Table 3). Our study may not revealed enough significant in certain parameters whether in pre or post treatment states, may be due to many causes as considering treatment program without diagnosed othertypes of disease lead to hidden findings that may later show up as significant difference, as ALP, which was presented later in each leukemic phase, apparent manner, that may be due to involved AML subjects who were younger ages, and the ALP elevated normally in their systems, moreover, calculation of means from data included high levels of ALP, would lead to hidden abnormal calculated means, as expressed here in our results by similar patients number of ALP that elevated in 24 patients of pretreatment and 25 of post treatment. Multi correlations of the variables were performed, although there is no such correlations were seen published. correlations analysis reveals a positive correlations between liver enzymes and biochemical variables of the pretreatment group was found positive between (T.p/albumin, AST/ALT, ALT/ALP, AST/ALP, GGT/ALP) r.values (0.759, 0.886, 0.492, 0.540, 376) p.value (0.000, 0.000, 0.000, 0.000, 0.007), respectively (fig 2), while in post treatment group r.values were (0.880, 0.333, 0.960, 0.0511, 0.512), and p.value (0.000, 0.018, 0.000, 0.000, 0.000), respectively, corresponding to (T.p/alb, ALP/alb, AST/ALT, AST/ALP, ALT/ALP.Furthermore extra positive correlations were found,among post treatment group between (GGT/AST, GGT/ ALP), r.value (0.601, 0.536), p.values were (0.000, 0.000).

I recommended that, regular assessment of the activity of enzyme especially under chemotherapy treatment, because the chemotherapy caused the liver dysfunction.

CONCLUSION

In conclusion, our study revealed that high levels of liver biochemical parameters were higher in post treatment subjects than pretreated ones but within the normal reference values, in both AML and CML Sudanese subjects involved in the study, the chemotherapy of myeloid leukemia patients caused significantly changed of liver enzymes AST, ALT and GGT). Target treatment of leukemia, helps most of time in getting healthy state process, but later patients suffer from consequences leading to death after remission from the original disease.

REFERENCES

1. Leonard, B. (1998). *Leukemia: a research report*. DIANE Publishing.p- 6.
2. Hoffbrand, A.V., & Moss, P.A.H (2011). Essential Hematology 6th edition, p-179.
3. Döhner, H., Estey, E. H., Amadori, S., Appelbaum, F. R., Büchner, T., Burnett, A. K., ... & Lo-Coco, F. (2010). Diagnosis and management of acute myeloid leukemia in adults: recommendations from an international expert panel, on behalf of the European LeukemiaNet. *Blood*, *115*(3), 453-474.
4. Karp, J(2011). Acute myeloid leukemia, p- 8.
5. Juliusson, G., Lazarevic, V., Hörstedt, A. S., Hagberg, O., & Höglund, M. (2012). Acute myeloid leukemia in the real world: why population-based registries are needed. *Blood*, *119*(17), 3890-3899.
6. Sorror, M. L., Storb, R. F., Sandmaier, B. M., Maziarz, R. T., Pulsipher, M. A., Maris, M. B., ... & Estey, E. (2014). Comorbidity-age index: a clinical measure of biologic age before allogeneic hematopoietic cell transplantation. *Journal of Clinical Oncology*, JCO-2013.
7. Goor, Y., Goor, O., Michalewitcz, R., & Cabili, S. (2002). Acute myeloid leukemia presenting as obstructive jaundice. *Journal of clinical gastroenterology*, *34*(4), 485-486.
8. Cervantes, F., & Rozman, C. (1982). A multivariate analysis of prognostic factors in chronic myeloid leukemia. *Blood*, *60*(6), 1298-1304.
9. Ondreyco, S. M., Kjeldsberg, C. R., Fineman, R. M., Vaninetti, S., & Kushner, J. P. (1981). Monoblastic transformation in chronic myelogenous leukemia: presentation with massive hepatic involvement. *Cancer*, *48*(4), 957-963.

10. Cervantes, F., & Rozman, C. (1982). A multivariate analysis of prognostic factors in chronic myeloid leukemia. *Blood*, *60*(6), 1298-1304.
11. Ondreyco, S. M., Kjeldsberg, C. R., Fineman, R. M., Vaninetti, S., & Kushner, J. P. (1981). Monoblastic transformation in chronic myelogenous leukemia: presentation with massive hepatic involvement. *Cancer*, *48*(4), 957-963.
12. Byrd, J. C., Mrózek, K., Dodge, R. K., Carroll, A. J., Edwards, C. G., Arthur, D. C., ... & Koduru, P. R. (2002). Pretreatment cytogenetic abnormalities are predictive of induction success, cumulative incidence of relapse, and overall survival in adult patients with de novo acute myeloid leukemia: results from Cancer and Leukemia Group B (CALGB 8461). *Blood*, *100*(13), 4325-4336.
13. Príncipe, F, Ferreira, J. S., & Sobrinho-Simões, M. (1988). Acute myeloid leukemia followed by hepatic leiomyosarcoma. A case report. *Acta Médica Portuguesa*, *1*(1), 87-89.
14. Faderl, S., Verstovsek, S., Cortes, J., Ravandi, F., Beran, M., Garcia-Manero, G., ... & Giles, F. J. (2006). Clofarabine and cytarabine combination as induction therapy for acute myeloid leukemia (AML) in patients 50 years of age or older. *Blood*, *108*(1), 45-51.
15. Wandroo, F. A., Murray, J., Mutimer, D., & Hubscher, S. (2004). Acute myeloid leukaemia presenting as cholestatic hepatitis. *Journal of clinical pathology*, *57*(5), 544-545.