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# Assessment of Serum Level of Electrolytes and Trace Elements in Leukaemia Patients in Sudan

**Eiman A. A. Elshaygi[1], Abdalsalam A. Dafaala[2] and Amel O. Bakheet[3]**

1. College of Science, Al- Jouf university, Saudi Arabia kingdom
2. Department of Chemistry, College of Science
3. Deanship of Scientific Research, Sudan University for Science and Technology.

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**ABSTRACT**

Electrolyte and trace elements disturbances frequently occur with leukaemia patients that complicate their management and prolong patients' hospitalization, due to leukemic processes, organ infiltration, and cell death or to adverse effects of cytotoxic drugs. This research work investigated the interrelationship among different types of leukaemia with concentration of electrolytes and trace elements in Sudanese patients attended the Radiation and Isotope Center (KRIC) Khartoum, Sudan. 201 subjects (79 control participants and 122 were suffering from leukaemia). Patients were divided into four groups; acute lymphoid leukemia (ALL), acute myeloid leukaemia (AML), chronic myeloid leukaemia (CML), chronic lymphoid leukaemia (CLL). Some electrolytes and trace elements zinc (Zn), copper (Cu), manganese (Mn) and cobalt (Co). Results obtained showed that a significant decrease in serum level of Cu ($p < 0.001$), Mn ($p < 0.05$) and cobalt ($p < 0.05$) was observed in all groups. Zinc and calcium showed lower levels in CLL, CML and ALL ($p< 0.05$). The results also showed significantly higher serum level of Zn in AML group than CML group ($p<0.05$). Magnesium reported higher level in CML, AML and ALL ($p< 0.01$). The concentration of Mg was significantly lower in CLL ($p<0.05$) compared to CML, AML and ALL patients. The concentration of sodium was significantly lower in CML than the ALL patients ($p<0.05$). There is no significant difference between the levels of Na, K and $PO_4^{3-}$ in leukaemia patients and control. Data revealed positive correlation between sodium and potassium ($p = 0.000$), positive correlation between calcium and phosphorus but not significant ( $p = 0.195$). It could be concluded that Ca, Cu, Zn, Mn and Co showed lower level and Mg reported higher level in leukemia patients.

## INTRODUCTION

Cancer is becoming a global health problem and the number of cancer cases in Africa is rising. Being an African country, Sudan has its share of cancer burden (Intisar *et al.,* 2014). Sudan, the largest and most diverse country in Africa, is experiencing a growing cancer problem but it is little known on tumors patterns, cancer epidemiology and ethnic or environmental risk factors (Awadelkarim *et al.,* 2012). There were 322 children with cancer in Sudan from hospital registry for the period 1999 to 2007, 83.26% are diagnosed as leukemic (Abuidris *et al.,* 2008). Leukaemia is defined as the uncontrollable production of white blood cells caused by a Failure of normal differentiation of haemopoietic stem cells and progenitors into mature cells (Salman *et al.,* 2013).

Leukemias are divided into two categories; lymphocytic and myelogenous leukemias. Cancerous production of lymphoid cells, which is beginning in a lymph node or other lymphatic tissue is characteristic of lymphocytic leukaemia, usually it spreads to all of the body. The second kind of leukemia begins with cancerous production of young myelogenous cells in the bone marrow and then spreads throughout the body so that white blood cells are produced outside the bone marrow in extramedullary tissues especially in the lymph nodes, spleen, and liver (Hall, 2011). Trace elements have an important role within human body such as protection against cellular oxidative stress, production of proteins and synthesis and structural stabilization of nucleic acids. Over recent years many studies were done to tests if the trace elements have any effect in the etiology of neoplastic disease and in alteration of antioxidants levels (Atieh *et al*., 2012).

This study was conducted to determine serum levels of some electrolytes and trace elements, to define the relation between their levels and leukaemia patients in Sudan.

## MATERIALS AND METHODS

The control group consisted of 79 healthy subjects (55 male and 24 female). The study group included 122 who diagnosed as leukemic patients (78 males and 44 females), their age ranged from less than one year to over 45 years. Serum samples were collected from patients coming to the Radiation and Isotope Center at Khartoum (RICK), Khartoum State. All the patients enrolled in the study were receiving treatment before the analysis was made. Among these patients, 72 of them had acute lymphoid leukemia (ALL), 17 patients had acute myeloid leukaemia (AML) ,27 patients had chronic myeloid leukaemia (CML), and six patients had chronic lymphoid leukaemia (CLL).

Venous blood sample (5 ml) was collected from the Leukaemia patients and healthy group. Samples with signs of hemolysis were discarded. Blood samples allowed to clot then centrifuged for 15 minutes at 3000 rpm to extract the serum. The serum transferred to 5 ml

polystyrene tube, and stored at -5 ºC until analysis.

Atomic absorption spectrophotometer (210VGP Buck Scientific) double beam manufactured by United States of America was used in measuring the serum concentrations of Cu, Zn, Co and Mn in both patients and controls (AAS, 1994). Operational standards were maintained and checked frequently according to recommendations of the manufacturer. For the determination of serum copper, the samples were diluted with an equal volume of deionized water. For the determination of serum zinc the samples diluted 1:5 with deionized water.

For the determination of serum manganese and cobalt the samples were diluted 1: 9 with $HNO_3$. Different Standard solutions of elements were prepared by dilution of standard stock solution of copper, zinc, manganese and cobalt immediately before their use. Ultra pure water was used throughout the work. Measurement of the level of serum electrolytes, sodium and potassium was conducted using potentiometric method; ion selective electrode direct method (EasyLyte analyzer, Medica Corporation, USA). Magnesium, calcium and phosphorus level was measured by spectrophotometer instrument by using kits from Biosystems chemical company.

***Statistical analysis***: SPSS was used for statistical analysis. Results were expressed by mean and standard error and the correlations between various parameters and different subgroups were also determined. $P < 0.05$ was considered as statistical significance.

**RESULTS**

The leukemic subjects were classified into different sub-type and showed a highly significant difference among themselves and with control. The results are summarized in Table1.

According to the present study result shows that serum magnesium level in leukaemia patients was significantly higher in CML, AML and ALL ($P > 0.01$) when compared to the control. CLL group showed significantly lower Mg ($p<0.05$) compared to CML, AML and ALL patients. Serum levels of calcium were significantly lower with CML, CLL and ALL than in control ( $p < 0.001$, $p < 0.05$ and $p < 0.05$ respectively).

The concentration of sodium was significantly lower in CML than the ALL patients ($p$ <0.05), while no significant difference in sodium and potassium concentration between leukaemia groups and control.

In the current study serum phosphate level in different groups of leukemia patients showed non-significant difference when compared to the control group. In this study observed decrease serum zinc concentration in the leukemic group (CLL, CML and ALL) ($p< 0.05$) compared with control. The results also showed significantly higher serum level of Zn in AML group than CML group ($p < 0.05$). The present study observed

decrease in copper, manganese and cobalt concentrations ($p < 0.01$, $p < 0.05$ and $p < 0.05$ respectively) in all types of leukaemia compared to control.

**Table 1:** Level of electrolytes and trace elements in different types of leukemia

| Parameters | Control | Different types of leukaemia | | | |
|---|---|---|---|---|---|
| | | CLL | CML | AML | ALL |
| Na (mmol/l) | 141.07 $^{a\,b}$ ±0.57 | 134.78$^{ab}$±0.66 | 137.49$^{a}$±0.86 | 143.18$^{b}$±2.22 | 142.41$^{ab}$±1.94 |
| K (mmol/l) | 3.95$^{a}$±0.04 | 4.27 $^{a}$±0.85 | 4.13 $^{a}$± 0.13 | 4.19 $^{a}$±0.17 | 4.03 $^{a}$±0.09 |
| Ca (mg/dl) | 9.62 $^{a}$±0.14 | 8.82 $^{b}$ ±0.70 | 8.40 $^{c}$±0.13 | 9.48 $^{a\,b}$±0.25 | 9.03 $^{b}$ ±0.19 |
| Mg (mg/dl) | 2.15 $^{a}$ ±0.03 | 1.83 $^{a}$±0.14 | 2.73 $^{b}$±0.10 | 2.52 $^{b}$±0.10 | 2.48 $^{b}$±0.08 |
| P (mg/dl) | 3.74 $^{a}$±0.10 | 3.89 $^{a}$±1.01 | 4.14 $^{a}$±0.16 | 3.82 $^{a}$±0.23 | 4.03 $^{a}$±0.15 |
| Cu (mg/l) | 0.89 $^{a}$ ±0.02 | 0.46 $^{b}$±0.14 | 0.53 $^{b}$±0.06 | 0.53 $^{b}$±0.08 | 0.62 $^{b}$±0.04 |
| Zn (mg/l) | 0.57 $^{a}$ ±0.02 | 0.30 $^{cb}$±0.00 | 0.37 $^{cb}$±0.03 | 0.54 $^{a\,b}$±0.14 | 0.44 $^{b}$±.03 |
| Mn (mg/dl) | 0.34 $^{a}$ ±0.03 | 0.22 $^{b}$±0.02 | 0.21 $^{b}$±0.03 | 0.20 $^{b}$±0.03 | 0.26 $^{b}$±0.02 |
| Co (mg/dl) | 0.46 $^{a}$ ±0.02 | 0.14 $^{b}$±0.05 | 0.12 $^{b}$±0.02 | 0.22 $^{b}$±0.04 | 0.15 $^{b}$±0.02 |

Means with the same letter are not significantly different from each other ($p<0.05$).
The data presented as the Mean ± SE.

All parameters were correlated using Bivariate correlation, Pearson coefficient, two tailed test of significant. Correlations for leukaemia patients were outlined in Table 2.

**Table 2:** Correlation among various electrolytes and trace elements in different types of leukaemia

| Group | Correlation coefficient (r) | *P* - value |
|---|---|---|
| Na vs. K | 0.492** | 0.000 |
| K vs. Mn | -0.152$^{*}$ | 0.032 |
| K vs. Co | -.0176$^{*}$ | 0.013 |
| Ca vs. Co | 0.236** | 0.001 |
| Mg vs. Cu | -0.152$^{*}$ | 0.031 |
| Mg vs. Mn | -0.151$^{*}$ | 0.032 |
| Mg vs. Co | -0.205** | 0.004 |
| P vs. Mn | 0.260** | 0.000 |
| P vs. Co | 0.147$^{*}$ | 0.037 |
| Cu vs. Co | -0.200** | 0.004 |
| Zn vs. Mn | -0.153$^{*}$ | 0.031 |
| Mn vs. Co | 0.308** | 0.000 |

**. Correlation is significant at the 0.01 level (2-tailed).
*. Correlation is significant at the 0.05 level (2-tailed).

## DISCUSSION

Leukaemia patients in this study were having higher magnesium level, this agrees with Study conducted by Merza *et al*. (2009) found increased in serum Mg in some leukemia patients while other patients recorded normal and lower level. Although the increased level of serum magnesium was statistically significant in this study, but it was not considered as case of hypermagnesmia (more than 3.5 mg/dl). Also O'Regan *et al*. (1977) reported serum magnesium was elevated as a result of its release of

malignant cells after cytotoxic therapy or its accumulation due to urate nephropathy.

Lower level of calcium was found in leukaemia patients, this result was in agreement with that achieved by Randy and Ursula (2014) who reported: lower level of calcium (hypocalcemia) in hematologic malignancy and might be results from various factors, including hypoalbumine-mia, malabsorption, malnutrition, vitamin D deficiency. Also this finding was similar to that obtained by Liamis *et al*. (2016) who reported hypocalcaemia in patients with malignancies is associated with the using of anticancer drugs.

No significant difference in concentration of sodium and potassium was found, this results disagree with Filippatos *et al.,* (2005) and Milionis *et al.,* (1999) finding, which showed a low serum level of sodium (hyponatremia) and potassium (hypokalemia). One study by O'Regan *et al.,* (1977) reported that patients in remission usually have normal serum electrolyte concentrations.

In agreement with the observations of other studies conducted by Reisi *et al*. (2015) and Salman *et al.,* (2013), serum phosphate level in different groups of leukemia patients in the current study show non significant difference when compared to the control group.

Leukaemia patients in this study were having decreased levels of serum zinc concentration. This in an agreement with Ursula *et al*. (2006) who reported that the general trend in malignant diseases towards slight decrease in zinc concentrations, implying that zinc deficiency is associated with the etiology of cancer. Similar finding by Zuo *et al*., (2006) who reported decreasing of serum zinc in all groups of leukaemia patients have been related to general nutrition.

Copper concentration was decreased in all types of leukaemia in the current study. This finding of Cu levels is in agreement with study conducted by Rafallah, (2015). Some investigators combined between copper deficiency and haematological and neurological abnormalities. They consider copper deficiency as an established cause of haematological abnormalities but is frequently misdiagnosed (Thorvardur *et al.,* 2008).

Manganese (Mn) is necessary for optimal biological function that is required as a cofactor for many enzymes (Parmalee and Michael, 2016). In the current study, serum manganese showed significantly lower concentration. This finding was agree with a study done by Cengiz *et al.* (2011) who reported : significant decrease in the serum concentration of Mn in leukaemia patients. Ana Bela *et al*. (2012) showed that when Mn level was decreased the concentration of an antioxidant enzymes also decreased and low levels of oxidative stress so increasing free radicals generation, stimulate cellular proliferation and involved in the pathogenesis of human leukaemia.

In this study there was low cobalt level in serum of leukemic patients. This disagrees with Cengiz *et al.* (2011) who reported no significant difference in serum level of cobalt between leukaemia patients and control. While Sheppard *et al*. (2007) suggested that in study conducted in Nevada they a temporal correspondence between the onset of excessive childhood leukaemia and elevated levels of tungsten and cobalt. Lingamaneni *et al.* (2015) said that the deficiency of cobalt leads to decreased

availability of B12, and developed many symptoms and problems attributed to B12 deficiency, particularly pernicious anemia, nerve damage and a significant increase in the incidence of lymphatic and hematopoietic malignancies.

**CONCLUSION**:

This study concluded that, leukaemia patients in Sudan recorded significant decrease in serum levels of copper, manganese and cobalt. Most of them showed higher magnesium levels and lower concentration of zinc and calcium.

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