ABSTRACT

Background: A number of studies have been published in recent years showing a significant association between leukemia and low plasma cholesterol levels. Objectives: We measured lipids profile which includes plasma total cholesterol, low density (LDL) and high density (HDL) lipoproteins in patients with leukemia in comparison with age and sex matched controls. Materials and Methods: The study included 50 normal healthy controls and 100 patients with leukemia (64 acute and 36 of them are chronic). Cholesterol profile was estimated using spectrophotometer method. Results: Mean ± SD of total cholesterol, LDL and HDL in leukemic patients were (120.86 ± 23.04, 29.47 ± 10.76, 29.38 ± 8.45mg/dl) respectively, while the mean ± SD of healthy person were (168.00 ± 14.73, 61.94 ± 14.64, 62.50 ± 10.60mg/dl) respectively. This result show highly significant difference which was lower in the leukemic patients compared to the control with P value (0.000). Conclusion: This study concluded that the strong association between leukemia and plasma cholesterol can be used as markers for bad prognosis, degree of maturation of leukemic cells and follow up of treatment. Also LDL may be used as a carrier targeting lipophilic cytotoxic drugs to leukemic cells.

KEYWORDS: Leukemic patients, Cholesterol, Spectrophotometer, Sudanese.
INTRODUCTION

In Sudan approximately 10% of all cancer cases are hematological malignances among both men and women\textsuperscript{[1,2]}, the most common type of hematological malignancies is leukemia. Exactly how genetic mutations accumulate in haemopoietic malignancies is largely unknown. As in most diseases, it is the combination of genetic background and environmental influence that determines the risk of developing a malignancy. However, in the majority of individual cases neither a genetic susceptibility nor an environmental agent is apparent.\textsuperscript{[3]}

Leukemia is a bone marrow disorder that arises when one abnormal white blood cell begins to continuously replicate itself. These cells do not function normally, they do not fight infection, do not die at the same rate as other WBCs. As they accumulate, they inhibit the production of the other normal blood cells in the marrow, leading to anaemia, bleeding, and recurrent infections. Over time, the leukemic cells spread through the bloodstream where they continue to divide, sometimes forming tumors and damaging organs such as the kidney and liver.\textsuperscript{[4]}

Hypocholesterolemia is a common finding in patients with leukemia and in other types of malignancies. It is unclear whether it is a risk factor for the development of malignancy or secondary to the cancer.\textsuperscript{[5]} Although the presence of high cholesterol has been linked strongly with cardiovascular disease, a defect in the body's production of cholesterol (hypocholesterolemia) can lead to adverse consequences as well, because cholesterol is an essential component of mammalian cell membranes and is required to establish proper membrane permeability and fluidity.\textsuperscript{[6]}

The high-affinity degradation of low-density lipoprotein (LDL) is enhanced 3- to 100-fold in leukemic blood cells from patients with acute myeloid leukemia (AML), suggesting an increased cellular LDL receptor expression.\textsuperscript{[7]}

In patients with leukemia conversion of cholesterol to bile acids was suppressed a phenomenon that may result in a decreased intestinal absorption of cholesterol and subsequent hypocholesterolemia.\textsuperscript{[8]}

Plasma lipid and lipoprotein changes before and after induction of treatment in acute myeloid leukemia (AML) and in acute lymphocytic leukemia (ALL) this show relationship with disease activity and prognostic relevance. AML and ALL patients at diagnosis are associated
with significantly low levels of all lipid parameters compare with those who respond to effective chemotherapy. The present study was aimed to assess cholesterol profile in Sudanese adult patients with both acute and chronic leukemia.

MATERIALS AND METHODS

Study design: It is a case control –hospital based study, and a structural interviewing questionnaire was designed to maintain all valuable informations of each case examined.

Study area and duration: This study was carried out at Khartoum state in private clinic centers at patients already diagnosed as leukemic, during the period from December 2014 to February 2015.

Study population: The subjects for the present study comprised of 150 samples (50 healthy adults of both sex with an age group ranged between (25 - 80 years) and 100 adults with 64 acute and 36 chronic leukemia, age and sex were matched).

Blood Sample: Venous blood specimens (5ml) were collected using vacutainer systems and were drawn into lithium heparin container, centrifuged at 4000 rpm for 3 minutes, and then plasma samples were stored at -20°C until analysis.

Lipids profile included estimations of plasma total cholesterol, low density lipoprotein (LDL) cholesterol and high density lipoprotein (HDL) cholesterol. All estimations were done using reagents purchased from Biosystems company. Total cholesterol, LDL and HDL were estimated by enzymatic and precipitating method using Biosystems spectrophotometer BS 302-Spain.

Statistical analysis: All statistical analyses were performed using SPSS software for Windows, version 17.0. Independent t.test was used for calculation of mean and standard deviation. The level of significance was expressed as P value < 0.05 for significant.

RESULTS

Table (1): Mean ± SD of Total cholesterol, LDL and HDL in study population

<table>
<thead>
<tr>
<th>Variable</th>
<th>Control group n= 50</th>
<th>Cases group n=150</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>T.cholesterol (mg/dl)</td>
<td>168.00 ± 14.73</td>
<td>120.86 ± 23.04</td>
<td>0.000</td>
</tr>
<tr>
<td>LDL cholesterol (mg/dl)</td>
<td>61.94 ± 14.64</td>
<td>29.47 ± 10.76</td>
<td>0.000</td>
</tr>
<tr>
<td>HDL cholesterol (mg/dl)</td>
<td>62.50 ± 10.60</td>
<td>29.38 ± 8.45</td>
<td>0.000</td>
</tr>
</tbody>
</table>
Table (3) Mean ± SD of Total cholesterol, LDL and HDL in types of leukaemia

<table>
<thead>
<tr>
<th>Variable</th>
<th>Total cholesterol (mg/dl)</th>
<th>LDL-cholesterol (mg/dl)</th>
<th>HDL-cholesterol (mg/dl)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Acute lymphoid leukaemia (n=46)</td>
<td>118.78 ± 20.38</td>
<td>28.39 ± 11.80</td>
<td>30.04 ± 8.22</td>
</tr>
<tr>
<td>Acute myeloid leukaemia (n=18)</td>
<td>133.22 ± 24.18</td>
<td>32.66 ± 9.69</td>
<td>29.66 ± 11.33</td>
</tr>
<tr>
<td>Chronic lymphoid leukaemia (n=16)</td>
<td>116.50 ± 14.23</td>
<td>28.06 ± 7.15</td>
<td>26.93 ± 6.69</td>
</tr>
<tr>
<td>Chronic myeloid leukaemia (n=20)</td>
<td>136.00 ± 27.88</td>
<td>30.20 ± 11.61</td>
<td>29.55 ± 7.48</td>
</tr>
</tbody>
</table>

Also results reveal that there is positive correlation between T.cholesterol, HDL cholesterol and duration of leukaemia with significance value 0.03 and 0.00 respectively, while no correlation observed with LDL-cholesterol, P. value of 0.09.

DISCUSSION

In the current study the assessment of cholesterol profile in leukemic patients were found to be as follows: plasma total cholesterol showed significantly decreased levels (p<0.00) in leukemic patients than in normal. These results agreed with the results of the studies done by Naik et al[5] and Zyada[10] and Tatidis.[8]

In the department of biochemistry, Tata Memorial Hospital, Parel, Mumbai India, Naik et al demonstrated that plasma cholesterol, HDL & LDL cholesterol were found to be inversely associated with incidence of cancer. In Egypt Zyada demonstrated that there is a relation between hypocholesterolemia and the degree of maturation of leukemic blast cells in acute myeloid leukemia. In Sweden Tatidis et.al reported the conversion of cholesterol to bile acids was suppressed in leukemic patients.

Also the study showed that the concentration of plasma LDL cholesterol was highly significant lower in cases than control group with (p<0.00). These results agreed with the results of the studies done by Zyada[10] and Vitols and Peterson in Sweden[11] who demonstrated that hypocholesterolemia in cancer patients may be caused by elevated LDL receptor activities in malignant cells.

The high-affinity degradation of low-density lipoprotein (LDL) is enhanced 3- to 100-fold in leukemic blood cells from patients with acute myeloid leukemia (AML), suggesting an increased cellular LDL receptor expression.[7]
Also since bile acids are major excretion products of cholesterol, the hepatic degradation of cholesterol to bile acids was investigated in leukemic patients by analyzing a circulating marker for bile acid synthesis, the plasma levels of 7-alpha-hydroxy-4-cholesten-3-one, reflecting bile acid production, were markedly lower in patients with leukemia than in healthy controls.\[5\]

The conversion of cholesterol to bile acids was suppressed in patients with leukemia a phenomenon that may result in a decreased intestinal absorption of cholesterol and subsequent hypocholesterolemia.\[8\]

Also there is significant lowering in HDL in cases compare with control group with (p<0.00), which agreed with the results of the studies done in Brazil by Gonçalves et.al\[12\] who found that there is higher maximal velocity rates in lymphoblasts and myeloblasts compared to normal cells.

Plasma lipid and lipoprotein changes before and after induction treatment in acute myeloid leukemia (AML) and in acute lymphocytic leukemia (ALL) this show relationship with disease activity and prognostic relevance. AML and ALL patients at diagnosis are associated with significantly low levels of all lipid parameters compare with those who respond to effective chemotherapy.\[9\] This study recommended that cholesterol profile should be added to the list of monitoring tests that performed to leukemic patients.

CONCLUSION
The results strongly suggest that low cholesterol and low HDL cholesterol levels together with low LDL cholesterol were the most prominent features being consistently present in all cancer patients with leukemia. The inverse association between cancer and plasma cholesterol may reflect a physiological response to the early stages of cancer and marker to monitor chemotherapy.

REFERENCES
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4. American Association for Clinical Chemistry.