INTRODUCTION

Thyroid diseases are principally situations that influence the number of thyroid hormones being formed (Rabeh, 2016). Though the levels of trace elements are small in an individual body, they have a vital task in many biological processes and are well-known to influence hormones at levels of action. In contrast, hormones control trace metals metabolism at numerous levels of action, including excretion and transport of trace elements (Henkin, 1976). Chiefly, zinc (Zn) is necessary for the appropriate function of the enzyme 1,5'- deiodinase, which stimulates the change of body thyroxine (T4) to its active form triiodothyronine (T3) and lowers the metabolic rate (Ezzat Aziz, 2016). In the human body, copper is the third most abundant mineral, has a significant role in thyroid metabolism, expressly in hormone formation and absorption. It stimulates the production of the T4 and prevents over absorption of it in the blood cells by controlling the body's calcium levels. Additionally, copper is requisite for the synthesis of phospholipids, which are necessary for the stimulation of the thyroid-stimulating hormone (Mohammed, 2015).

The studies concerning the responsibility of trace elements in hypothyroidism and hyperthyroidism is not fine recognized in the literature; hence, we attempt to do this study with the plan to evaluate concentrations of zinc and copper in hypothyroidism and hyperthyroidism and to find the probable associations between trace elements and thyroid hormones.

MATERIALS AND METHODS

This cross-sectional study was conducted in Sudan, Khartoum state during the period from April to June 2017. The scientific committee of the clinical chemistry department of the Faculty of Medical Laboratory Science at Alneelain University approved this study. One hundred individuals were included in this study patient (35 hyperthyroidism, 35 hypothyroidism, 35 healthy individuals) age was matched between 25 to 50 years. The automated analyzer system estimated triiodothyronine (T3), thyroxin (T4) and thyroid-stimulating hormone (TSH). Atomic Absorption Spectrophotometers estimated zinc and copper and the data were analyzed by SPSS version 19.0. Results: A significant decrease in serum zinc level among hyperthyroidism and hypothyroidism patients were found, when compared with the control group (P-value <0.05). The copper level was significantly increased among hyperthyroidism and hypothyroidism patients when compared with the control group (P-value < 0.05). There was an insignificant correlation of copper level with a duration of disease (r= -0.020, P=0.869), with a significant positive correlation of copper with the age of patients (r=0.318, P=0.001). Whereas a significant inversely correlation was observed between zinc level and age of patients and duration of disease (r= -0.424, P= 0.006) respectively. Conclusion: Study results revealed that patients with hypothyroidism or hyperthyroidism have abnormal levels of copper and zinc.

ARTICLE INFO

Article History:
Received 10th December, 2019
Accepted 19th February, 2020
Published online 30th March, 2020

ABSTRACT

Background: Trace elements are well-known to affect hormones at levels of action, as well as binding to the target tissue, hormone secretion, and activity. Objective: This study aimed to evaluate the serum levels of copper and zinc among hypothyroidism and hyperthyroidism Sudanese patients. Material and Methods: One hundred participants were enrolled in this cross-sectional study. Thirty-five hyperthyroidism patients, 35 hypothyroidism patients, and 30 normal healthy individuals were taken as control, with aged-matched 25 to 50 years. The automated analyzer system estimated triiodothyronine (T3), thyroxin (T4) and thyroid-stimulating hormone (TSH). Atomic Absorption Spectrophotometers estimated zinc and copper and the data were analyzed by SPSS version 19.0. Results: A significant decrease in serum zinc level among hyperthyroidism and hypothyroidism patients were found, when compared with the control group (P-value <0.05). The copper level was significantly increased among hyperthyroidism and hypothyroidism patients when compared with the control group (P-value < 0.05). There was an insignificant correlation of copper level with a duration of disease (r= -0.020, P=0.869), with a significant positive correlation of copper with the age of patients (r=0.318, P=0.001). Whereas a significant inversely correlation was observed between zinc level and age of patients and duration of disease (r= -0.424, P= 0.006) respectively. Conclusion: Study results revealed that patients with hypothyroidism or hyperthyroidism have abnormal levels of copper and zinc.
After obtaining informed consent from all participants, the demographic data were obtained by the questionnaire, clinical information of the patients, and results of T3, T4, and TSH were obtained from records, then 5 ml of blood was collected from the vein by standard vein puncture technique without venous stasis. Blood samples were drawn in a plain container after the formation of the clot then for 3 minutes centrifuged at 3000 RPM to obtain serum. The serum was stored at -20 °C until the time of analysis of copper and zinc.

Methods: Serum samples were diluted 1:5 times with de-ionized water; the analysis was then performed against standards prepared in glycerol to approximate the viscosity characteristics of the diluted sample. The determination of copper and zinc was done by using Atomic Absorption Spectrophotometers 220GF GRAPHITE FURNACE & 220AS AUTOSAMPLER.

Statistical Analysis: All obtained and recorded results were analyzed by SPSS version 19.0, t-test was used to compare zinc and copper levels between patients group (hypothyroidism or hyperthyroidism) and control group (healthy individuals), Pearson’s correlation test was used to study the association between zinc and copper levels and thyroid hormones in addition to studying variable (age, duration of disease). $P$-value was considered significant when $<0.05$ in all used statistical tests.

RESULTS

Table 1 shows the statistics measured of zinc and copper levels among hyperthyroidism, hypothyroidism and control group, which indicate that results were found to be significantly decreased of serum zinc level in hyperthyroidism and hypothyroidism when compared to control group ($P = 0.001$), and significantly increased of serum copper level in hyperthyroidism and hypothyroidism when compared to control group ($P = 0.001$ and 0.038 respectively). Table 2 shows Person’s correlation results which reflect statistically insignificant correlation between duration and copper level ($r = -0.020, P = 0.869$), whereas there was significant inversely correlation between duration and zinc level ($r = -0.424, P = 0.006$). Also, there was a significant inverse correlation between age and zinc level ($r = 0.227, P=0.023$) and a significant positive correlation between age and copper ($r=318, P=0.00$).

Table 3 shows Person’s correlation results among patients with hyperthyroidism which reflect statistically insignificant correlation between TSH and zinc level ($r = 0.164, P=0.347$) and significant positively correlation between TSH and copper level ($r=0.425, P=0.008$). Also there was significant inversely correlation between zinc and T3 and T4 ($r = -0.439, P= 0.008$) and ($r = -0.320, P= 0.012$) respectively, and significant positively correlation between copper and T4 ($r = 0.318, P= 0.034$), but there was insignificant correlation between copper and T3 ($r = 0.075, P= 0.669$). Table 4 shows Person’s correlation results among patients with hyperthyroidism which reflect statistically significant inversely correlation between TSH and zinc level ($r = 0.490, P=0.007$) and insignificant correlation between TSH and copper level ($r = 0.140, P=0.421$). Also there was significant inversely correlation between zinc and T3 and insignificant correlation with T4 ($r = -0.388, P= 0.010$) and ($r = -0.201, P= 0.147$) respectively, and also shows significant positively correlation between copper and T4 ($r = 0.371, P= 0.030$), but there was insignificant correlation between copper and T3 ($r = 0.125, P= 0.475$).

DISCUSSION

Normal thyroid hormone metabolism needs several mineral and trace elements, and co-existing deficiencies of these elements are leading causes of thyroid dysfunction (Zimmermann, 2002). Several studies reported that Zinc levels are lower in hypothyroidism Baltaci et al. point out a relationship between Zinc and thyroid gland (Baltaci et al., ). The present study results showed a significant decrease in zinc content in the serum of hypothyroidism and hyperthyroidism patients. This result comes online with results of different previous studies (Mohammed et al., 2015; Baloch et al., 2013; Al-Juboori 2009; Ali et al., 2008; Jinger et al., 2015; Rashid, 2010; Manisha, 2018; Sinha, 2015; Yoshida , 1990). The possible mechanism for the lowing level is the tubular excretion of zinc. It may also be secondary to the sequestration of metallothioneins in the liver as a response of increased production of interleukin-6 (IL-6) produced during inflammation in hyperthyroidism patients (Sinha et al., 2015; Yoshida, 1990), while the decreasing level occurred due to impairment of gastrointestinal zinc absorption in hypothyroidism patients (Baltaci et al., 2013; Aihara et al., 1984). Copper acts as a cofactor for tyrosinase, a requisite for the biosynthesis of tyrosine, which in turn needed for the synthesis of the thyroid hormones (Manisha et al., 2018). The current study results revealed a significant increase in serum copper levels in hyperthyroidism and hypothyroidism patients, which agreed with the results of studies performed on hyperthyroidism patients (Sinha et al., 2015; Aihara 1984). While the results of an elevated level of copper in hypothyroid disagreed with results reported by some authors (Jinger et al., 2015; Rashid, 2010; Manisha et al., 2018). It is very known from the literature that most plasma Copper is bound to ceruloplasmin (Lindsey, 2000). Hence, the increase in serum copper may be due to the increase in ceruloplasmin, which was reported to be elevated in patients with hyperthyroidism (Sinha, 2015).

According to results revealed by this study regarding patients of hypothyroidism, there is a negative correlation between zinc level and both T3 and TSH, but no correlation was found with T4 as well as no significant correlations were found between copper level and thyroid hormones. These results come in line with what reported by Rashid et al. (2010) but disagreed with the results of other authors (Aihara et al., 1984). The negative correlation of zinc with T3 may be due to decreased activity of hepatic deiodinase which reported to be decreased as a result of zinc deficiency (Kralik et al., 1996). Another cause is that T3 receptor is supposed to need zinc to implement its biologically active conformation, so the levels of T3 decreased accordingly when zinc is deficient, so the concentration of T3 may be decreased when the level of Zn is decreased (Freak et al., 2001). Results of the current study concerning patients with hyperthyroidism showed that copper level was positively correlated with TSH and T4 and no correlation was found with T3, a result which agreed with previous reports (Sinha et al., 2015), the possible justification is that ceruloplasmin, a known acute phase reactant that increases in response to inflammation, and accordingly leads to elevation of copper and TSH and T4 in hyperthyroid (Sinha et al., 2015). In contrast, the zinc level was negatively correlated with T4 and T3, and no correlation was found with TSH. According to the remarks of our study, we can theorize that zinc decline may lead to the development of hyperthyroidism and highlighting the necessity of zinc supplementation to patients with thyroid disorders.
Table 1. Comparison of the means of plasma levels of copper and zinc of the test groups and the control group

<table>
<thead>
<tr>
<th>Variable</th>
<th>Test group n = 35</th>
<th>Control Group n = 30</th>
<th>P. Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hyperthyroidism</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>S. Copper (mg/L)</td>
<td>1.98 ± 0.42</td>
<td>0.83 ± 0.11</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>S. Zinc (mg/L)</td>
<td>0.50 ± 0.12</td>
<td>0.83 ± 0.11</td>
<td>0.038</td>
</tr>
<tr>
<td>Hypothyroidism</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>S. Copper (mg/L)</td>
<td>0.97 ± 0.13</td>
<td>0.72 ± 0.22</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>S. Zinc (mg/L)</td>
<td>0.49 ± 0.11</td>
<td>0.72 ± 0.22</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

P-value based on Student’s t-test: significant at (p<0.05)

Table 2. Correlation between (duration and Age) and (S. Copper and S. Zinc levels) in the study group respectively

<table>
<thead>
<tr>
<th>Variables</th>
<th>Duration (Years)</th>
<th>Age (Years)</th>
<th>R. Value</th>
<th>P. Value</th>
<th>R. Value</th>
<th>P. Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>S. Copper (mg/L)</td>
<td>-0.020</td>
<td>0.869</td>
<td></td>
<td>0.318</td>
<td>0.001</td>
<td></td>
</tr>
<tr>
<td>Zinc (mg/L)</td>
<td>-0.424</td>
<td>0.006</td>
<td></td>
<td>-0.227</td>
<td>0.023</td>
<td></td>
</tr>
</tbody>
</table>

Pearson’s correlation test was used, P-value considered significant when < 0.05

Table 3. Correlation between (T₃, T₄, and TSH) and (S. Copper and S. Zinc levels) among patients with hyperthyroidism respectively

<table>
<thead>
<tr>
<th>Variables</th>
<th>T₃ (ng/ml)</th>
<th>T₄ (ng/ml)</th>
<th>TSH (μU/ml)</th>
</tr>
</thead>
<tbody>
<tr>
<td>S. Copper (mg/L)</td>
<td>0.075</td>
<td>0.318</td>
<td>0.425</td>
</tr>
<tr>
<td>Zinc (mg/L)</td>
<td>-0.439</td>
<td>-0.320</td>
<td>0.164</td>
</tr>
</tbody>
</table>

Pearson’s correlation test was used, P-value considered significant when < 0.05

Table 4. Correlation between (T₃, T₄, and TSH) and (S. Copper and S. Zinc levels) among patients with hypothyroidism respectively

<table>
<thead>
<tr>
<th>Variables</th>
<th>T₃ (ng/ml)</th>
<th>T₄ (ng/ml)</th>
<th>TSH (μU/ml)</th>
</tr>
</thead>
<tbody>
<tr>
<td>S. Copper (mg/L)</td>
<td>-0.125</td>
<td>0.371</td>
<td>-0.140</td>
</tr>
<tr>
<td>Zinc (mg/L)</td>
<td>0.388</td>
<td>-0.201</td>
<td>-0.490</td>
</tr>
</tbody>
</table>

Pearson’s correlation test was used, P-value considered significant when < 0.05

Conclusion

Patients with hypothyroidism or hyperthyroidism have increased in serum copper level and decreased in serum zinc level when compared to healthy individuals; this may due to defect in the metabolism of zinc and copper in hyperthyroidism and hyperthyroidism diseases. Zinc supplementation may improve the condition. Furthermore, studies must be done to verify these results and determination of the level of Copper and Zinc routinely, especially in patients with hypothyroidism and hyperthyroidism disease.

Acknowledgement: Our appreciation and gratefulness to all who were contributed to the success of this study.

Declaration of Conflict of Interest: Regarding this information, all authors were declared that they have no conflict of interest

Funding source: This research funded by the author’s own budget and there is no funds received from any outside source.

REFERENCES

Hypothyroidism with Special Reference to Zinc and Copper”. Biomed J Sci & Tech Res. 62: 5190-5194.

*****