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Evaluation of Copper and Zinc among Hyper and Hypo Thyroidism Patients

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Abstract:

Background: *Thyroid disorder is an epidemic disease in most countries and in the Sudan. The objective of this study is to shed more light on the role of trace elements and their mode of action in thyroid disorders. The content of the trace elements (Zn and Cu) in the serum of patients was determined and compared to that of normal subjects.*

Materials and Methods: *Cross-sectional study was conducted at Nyala and kassala teaching hospitals during the period from March to May 2015. Thyroid disorders patients 180 with aged between 25-80 years classified as, hypothyroidism 60 hyperthyroidism 60, and control 60.*

Results: *The study showed that, in hypothyroid patients the serum levels of zinc is ($p<0.013$) were significantly decreased compared*

to controls. In hyperthyroid patients the serum levels of zinc is (p<0.000) were significantly decreased compared to controls.

Conclusion: *Study concludes that, serum zinc is lower in patients with hypo and hyper thyroidism, which may exaggerate the complication on hypo and hyper thyroidism***.**

Key words: triiodothyronine, tetraiodithyronine, copper, zinc

Introduction:

The thyroid gland regulates a wide range of physiological functions in the body including growth, metabolism and energy homeostasis, via the secretion of thyroid hormone (1, 2).

Thyroid gland produces triiodothyronine called T3 & tetraiodithyronine (thyroxine or T4), these hormones play a critical role in cell differentiation during development and help to maintain thermogenic, mineral, metabolic homeostasis in the adult. Hypothyroidsm subnormal activity of thyroid gland that leads mental and physical slowing because of decrease is the basal metabolic rate (3). Hyperthyroidsm excess activity of thyroid gland that leads mental and physical slowing because of increases the basal metabolic rate The mean annual incidence rate of hypothyroidism is up to 4 per 1000 women, 1 per 1000 men, 1 in 4000 inborns. The prevalence of overt hypothyroidism increases with age (4).

Thyroid hormone is essential for normal growth and maturation of the skeleton. (5,6)

Deficiency of thyroid hormone in early life leads to both delay in the development of bone and stippled appearance of epiphysial centers of ossification, this result possible dwarfism. In hypothyroidism there is a depressed turnover due to impaired mobilization of calcium into the bone than leads to decrease the blood calcium level (7). In hyperthyroidism there is poor mobilization of calcium than leads to increases the blood calcium level.

In hypothyriodism increased production of thyroid calcitonine (7). In hyperthyroidism decreased production of thyroid calcitonine (7).

The prevalence of thyroid dysfunction increases with age and diagnosis may be complicated in the older age group due to concomitant disease or therapy. Early diagnosis and management of thyroid disease are crucial however, since it is associated with increased morbidity and mortality, especially in the elderly (8).

Copper is the third most abundant mineral in the human body. Copper is present in the body combined with various enzymes to form metallo-enzymes such as ceruloplasmin, SOD, These enzymes play a major role in redox reactions, such as superoxide dismutase which plays key role in antioxidant defense (9). It is known that copper plays an important role in the development and maintenance of immune system function (10).

Copper plays an important role in thyroid metabolism, especially in hormone production and absorption. Copper stimulates the production of the thyroxine hormone T4, and prevents over absorption of T4 in the blood cells by controlling the body's calcium levels (11).

Besides this, copper is also required for the synthesis of phospholipids, that are found in the myelin sheaths that insulates nerves to protect them. Phospholipids are required for the stimulation of thyroid stimulating hormone. Therefore correct level are needed to prevent thyroid problems and can be used in treatment of thyroid disease (11).

Zinc is an intracellular element it can influences the development and normal growth of tissues. Zinc too is needed to prevent hypothyroidism. Zinc is involved the process that converts inactive hormone T4 into active hormone T3 and decreases the metabolic rate. In hypothyroidism the tubular excretion of zinc leads to low levels of plasma zinc (12,13)

Zinc Just as copper is important for thyroid function, zinc too is needed to prevent thyroid problems. Zinc is involved in the processes that convert inactive hormone T4 into active hormone T3. An excess of inactive thyroid hormone in the body can lead to an under active thyroid gland. An Italian study showed that patients suffering with hypothyroidism gained improved thyroid function by supplementing their diet with extra zinc (11). It appears that adequate levels of both copper and zinc help I improving thyroid health, and even in the treatment of thyroid diseases (11).

The biological effects of zinc are remarkably diverse. It is a constituent of >300 enzymes, representing all six classes described by the International Union of Biochemistry (14). In addition, 30% of cellular zinc is found within the nucleus (15) and a large number of proteins that play a role in the regulation of gene expression have been either shown or suspected to contain zinc (16). The biological effects of thyroid hormones are also remarkably diverse (17). The active hormone is triiodo-L-thyronine T3 derived through peripheral deiodination from thyroxine T4, the major secretory product of the thyroid gland. T3 actions in its target tissues are initiated by binding of the hormone to specific thyroid hormone receptor proteins within the nucleus (18). There are two T3-receptors genes (α and ß), and multiple products are derived from these genes, although not all retain the ability to bind hormone. T3 receptors are closely related to the receptors of other nuclear acting agents, including those for steroid hormones, retinoic acid and vitamin D (19). Together, they form the steroid/thyroid nuclear receptors superfamily, sharing similar mechanisms of action and considerable sequence homology. T3 receptors bind to specific sequences in target genes known as thyroid response elements, probably as heterodimers with another member of the nuclear receptor family, the retinoid X receptor, whose ligand is 9-cis retinoic acid (20).

2. Materials and Methods

2.1 Study design: Cross-sectional study was conducted at Nyala and Kassala teaching hospitals during the period from March to May 2015. Thyroid disorders patients (180) with aged between 25-80 years classified as hypothyroidism (60), hyperthyroidism (60), and control (60).

2.2 Sampling: Veinpencher Blood samples were collected from all participants, samples were left at room temperature and then serum were obtained by centrifugation at 3000 rpm for 10 min, serum used for measure of T3, T4, TSH copper and zinc.

2.3 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 were used anonymously.

2.4 Measurement of T3: Goat Anti – mouse IgG is coated onto microtiteration wells. Test sera are applied along with antibody Reagent. T3 enzyme Conjugate is added which competes with the serum T3 for available binding sites on the solid phase. After incubation, the wells are washed to remove any unbound T3 or T3 enzyme Conjugate. On addition of the substrate (TMB), a colour will develops only in those wells in which the enzyme is present, indicating a lack of serum T3. The reaction is stopped by the addition of dilute Hydrochloric acid and the absorbance is then measured at 450nm. (21, 22, 23).

2.5 Measurement of T4: Specific anti – T4 antibodies are coated onto microtiteration wells. Test sera are applied. T4 with Horseradish Peroxidase enzyme (Conjugate) is added which competes with the released serum T4 for available binding sites

on the solid phase. After incubation, the wells are washed with water to remove any unbound T4 or T4 enzyme Conjugate. On addition of the substrate (TMB), a colour will develops only in those wells in which the enzyme is present, indicating a lack of serum T4. The reaction is stopped by the addition of dilute Hydrochloric acid and the absorbance is then measured at 450nm (21, 22).

2.6 Measurement of TSH hormone: Specific anti – TSH antibodies are coated onto microtiteration wells. Test sera are applied. Then goat anti – TSH labelled with Horseradish Peroxidase enzyme (Conjugate) is added if human TSH is present in the sample it will combine with the antibody on the well and the enzyme Conjugate, resulting in the TSH molecule being sandwiched between the solid phase and the enzyme linked antibodies. After incubation, the wells are washed to remove unbound labelled antibodies. On addition of the substrate (TMB), a colour will develop only in those wells in which the enzyme Conjugate is present, indicating the presence of TSH. The enzyme reaction is stopped by the addition of dilute Hydrochloric acid and the absorbance is then measured at 450nm (24, 25, 26).

2.7 Estimation of copper by atomic absorption: Principle: The electron of the atom promoted to higher orbital's (excited state) for a short period of time by absorbing a defined quantity of energy. The amount of energy (wave length) is specific to a particular electron transition in a particular element. The radiation measured by using detector and the absorbance is converted to analyze concentration or mass using Bear Lamber low (27). For determination of cupper 1ml of serum diluted with 1ml of distal water wave length 324.8 nm.

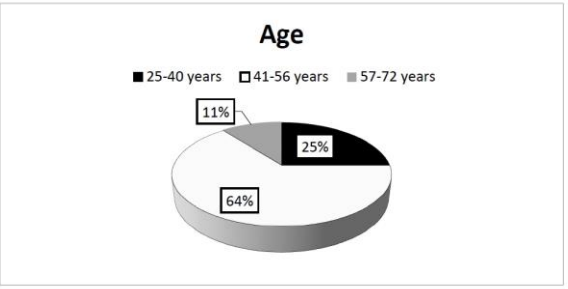
2.8 Estimation of zinc by atomic absorption: Principle: The electron of the atom promoted to higher orbital's (excited state)

for a short period of time by absorbing a defined quantity of energy. The amount of energy (wave length) is specific to a particular electron transition in a particular element. The radiation measured by using detector and the absorbance is converted to analyte concentration or mass using Bear Lamber low (27). For determination of zinc 1ml of serum diluted with 5 ml of distal water wave length 213.9 nm.

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

3. Results

3.1 Graf of Concentration of age Thyroid Disordered patients.



3.2 Table (1) concentration of T3, T4, TSH, copper and zinc in Hyperthyroidism patients.

Variable	Case	Control	P value
	Mean±SD	Mean±SD	
zinc	0.43±0.09	0.84±0.27	**0.000**
copper	1.17±0.23	1.07±0.22	**0.245**
T3	3.96±0.79	1.01±0.27	**0.000**
T4	24.60±12.60	9.60±2.00	**0.034**
TSH	0.15±0.05	2.47±0.60	**0.000**

*Results expressed as means ± SD

*significant different consider as *P*.value ≤ 0.05

3.3 Table (2) concentration of T3, T4, TSH, copper and zinc in Hypothyroidism patients versus control group.

Variable	Case	Control	*P* value
	Mean±SD	Mean±SD	
zinc	0.38±0.09	0.84±0.27	**0.013**
copper	1.16±0.19	1.07±0.22	**0.061**
T3	0.16±0.05	1.01±0.27	**0.000**
T4	1.75±0.64	9.56±2.00	**0.000**
TSH	10.90±2.51	2.47±0.59	**0.000**

*Results expressed as means ± SD

*significant different consider as *P*.value ≤ 0.05

3.4 Table (3) concentration of T3, T4, TSH, copper and zinc in Hypothyroidism patients in Kassala and Nyala.

Variable	Kassala	Nyala	P value
	Mean±SD	Mean±SD	
zinc	**0**.37±0.08	**0**.39±0.09	0.816
copper	1.17±**0**.18	1.15±**0**.20	0.734
T3	**0**.17±0.05	0.14±0.05	0.769
T4	1.74±0.60	1.76±0.70	0.201
TSH	10.43±2.60	11.33±2.36	0.838

*Results expressed as means ± SD

*significant different consider as *P*.value ≤ 0.05

3.5 Table (4) concentration of T3, T4, TSH, copper and zinc in Hyperthyroidism patients in Kassala and Nyala.

Variable	Kassala	Nyala	P value
	Mean±SD	Mean±SD	
zinc	**0**.43±0.08	**0**.44±0.09	0.198
copper	1.19±0.26	1.15±0.20	0.210
T3	3.98±0.81	3.93±0.80	0.811
T4	24.73±2.80	24.50±2.43	0.388
TSH	**0**.16±0.04	**0**.15±0.05	0.098

*Results expressed as means ± SD

*significant different consider as *P*.value ≤ 0.05

3.6 Table (5) concentration of T3, T4, TSH, copper and zinc in Hypothyroidism patients in male and female.

Variable	Male	Female	P value
	Mean±SD	Mean±SD	
zinc	0.40 ±0.08	0.35 ±0.10	0.216
copper	1.17 ±0.19	1.14 ±0.19	0.780
T3	0.16 ±0.06	0.15± 0 .05	0.502
T4	1.70 ±0.62	1.88 ±0.69	0.992
TSH	10.81 ±2.06	11.06 ±3.47	0.026

*Results expressed as means ± SD

*significant different consider as *P*.value ≤ 0.05

3.7 Table (6) concentration of T3, T4, TSH, copper and zinc in Hyperthyroidism patients in male and female.

Variable	Male	Female	P value
	Mean±SD	Mean±SD	
zinc	0.41 ±0.09	0.46 ±0.07	0.458
copper	1.190 ±0.22	1.15 ±0.24	0.594
T3	3.83 ±0.78	4.10±0.78	0.772
T4	24.43 ±2.78	24.82 ±2.42	0.463
TSH	0.16 ±0.06	0.16 ±0.05	0.300

*Results expressed as means ± SD

*significant different consider as *P*.value ≤ 0.05

4. Discussions

Zinc and copper are important for thyroid function, and they are needed to prevent thyroid problems. Zinc is involved in the processes that convert inactive hormone T4 into active hormone T3. An excess of inactive thyroid hormone in the body can lead to an under activation thyroid hormones. Which increase active thyroid hormones inhibit the production of the thyroid hormone from the gland. Also supplementation of zinc improved the function of the thyroid in hypothyroidism patients (11).

Main causes of hyperthyroidism about 70% are graves' disease and about 70% of hypothyroidism are hashimoto's disease both autoimmune disease prevalence beginning after 35 years old, the present study found that the frequency of the

thyroid the is high present of thyroid among 41-56 about 65% following by 57-72 about 25% and 25-40 about 11%.

The present study found that, there was significant decrease in mean concentration of zinc in patients with hyperthyroidism in comparison with control groups with *P*-value 0.000. This finding agreed with previous study which report that, serum zinc and albumin were significantly lower in hyperthyroidism patients than normal volunteers(24). Because it seems likely that, albumin acts as the major transporter protein for zinc in plasma. Moreover our finding contradict previous study report that, inhyperthyroidism there is a low renal blood flow and decreased clearance of zinc is observed, leading high levels of zinc causing higher zinc values (28) .

The study revealed that, there was significant decrease in mean concentration of zinc in patients with hypothyroidism in comparison with control groups with *P*-value 0.013. This finding agreed with previous study which report that, in hypothyroidism the tubular excretion of zinc leads to low levels of plasma zinc (17, 18).

The results of present study revealed that, there was insignificant difference between mean zinc levels of hypothyroidism and hyperthyroidism patients in comparison with control group among Kassala and Nyala, hypothyroidism with *P*-value 0.816 and hyperthyroidism with *P*-value 0.198 respectively.

The present study revealed that, there was insignificant difference between mean zinc levels of hypothyroidism and hyperthyroidism patients in comparison with group among male and female, hypothyroidism with *P*-value 0.216 and hyperthyroidism with *P*-value 0.458 respectively.

The study revealed that, there was insignificant difference between mean copper levels of hypothyroidism patients in comparison with control groups with *P*-value 0.061. The results of present study showed that, there was insignificant difference between mean copper levels of

hyperthyroidism patients in comparison with control groups with *P*-value 0.245.

The present study found that, there was insignificant difference between mean copper levels of Hypothyroidism and Hyperthyroidism patients in comparison with group among Kassala and Nyala, hypothyroidism with *P*-value 0.734 and hyperthyroidism with *P*-value 0.210 respectively.

The results of present study revealed that there was insignificant difference between mean copper levels of Hypothyroidism and Hyper thyroidism patients in comparison with group among male and female, hypothyroidism with *P*-value 0.780 and hyper thyroidism with *P*-value 0.594 respectively.

5. Conclusion

Study concludes that, serum zinc is lower in patients with hypo and hyper thyroidism, which may exaggerate the complication on hypo and hyper thyroidism.

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