

Correlation of Serum Ceruloplasmin in Patients with Hypothyroidism

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Abstract

In this study, 120 individuals with subclinical hypothyroidism (group I) and 120 healthy controls (group II) participated. The outcomes were contrasted with 120 healthy, age-matched controls of either sex (group II). Serum ceruloplasmin, serum FT3, serum FT4, and serum TSH were measured. Subclinical hypothyroid individuals (group I) had a slightly lower mean serum FT3 level than healthy controls (group II), although the difference was statistically significant ($P<0.0001$). Subclinical hypothyroid individuals (group I) had a slightly lower mean serum FT4 level than healthy controls (group II), although the difference was statistically significant ($P<0.0001$). Subclinical hypothyroid individuals (group I) had a mean serum TSH level that was significantly higher ($P<0.0001$) than

controls (group II). Mean serum Ceruloplasmin levels were considerably lower in subclinical hypothyroid participants than in healthy subjects ($p<0.0001$). The study's overall results so confirm that the participants with subclinical hypothyroidism had considerably lower serum ceruloplasmin levels.

Nevertheless, more observational and experimental research is required to demonstrate the function of serum ceruloplasmin in subclinical hypothyroidism. Verification of serum ceruloplasmin levels in subclinical hypothyroidism may make it possible to start treatment for certain patients and disease groups, such as atherosclerosis and cardiovascular disease that coexist with advanced age hypothyroidism.

Keywords: Ceruloplasmin, Cerebellarataxia, Hypothyroidism, Thyroid, TSH Levels

Introduction

An endocrine condition called hypothyroidism is brought on by a thyroid hormone shortage. It is frequently the main cause of the thyroid gland's inadequate thyroid hormone production. It can also be secondary, meaning that there is insufficient thyroid hormone secretion as a result of either insufficient pituitary thyrotropin (TSH) secretion or insufficient thyrotropin-releasing hormone (TRH) secretion from the hypothalamus (secondary or tertiary hypothyroidism). The patient may look asymptomatic or, in rare cases, in a coma with multisystem organ failure (myxoedema coma). The incidence of thyroid disease in the general population appears to be precisely determined by the Whickham survey^{1,2,3,4,5}. A condition known as subclinical hypothyroidism (SCH) is characterized by normal serum free thyroxine (FT4) levels and elevated serum thyroid stimulating hormone (TSH) levels (less than 10 μ IU/L). Subclinical hypothyroidism is now a prevalent biochemical finding in the general population. Subclinical hypothyroidism affects between 3% and 8% of the population. Additionally, it has been discovered that SCH is more common in the old population⁶, particularly in women. It also rises with age and is more common in the white population than in the black population⁷.

Generally asymptomatic, subclinical hypothyroidism (SCH) can develop into overt hypothyroidism⁸. It might be linked to symptoms that treatment can monitor⁹. However, 30% of patients may exhibit signs of thyroid hormone deficit^{10,11,12}. Muscle cramps, constipation, puffy eyes, cold intolerance, hoarseness of voice, fatigue, depression, neuromuscular symptoms, and irregular menstruation are some possible symptoms¹³.

Particularly in individuals with higher TSH levels, SCH may be associated with a slight increase in the risk of coronary heart disease and mortality. Hyperlipidemia and dyslipidemia in SCH have been documented in certain investigations¹⁴. Atherogenicity is accelerated by dyslipidemia, as demonstrated by the SCH¹⁵. The presence of an inflammatory marker (CRP) is also linked to the illness. Patients with SCH have significantly increased hs-CRP levels, according to several studies.

Ceruloplasmin: The CP gene in humans encodes the ferroxidase enzyme ceruloplasmin. The essential blood protein that carries copper, ceruloplasmin, is also involved in iron metabolism. 1948 saw the first description of it. Hephaestin, another protein, is highly similar to ceruloplasmin and is involved in the metabolism of iron and possibly copper. Rare mutations in the ceruloplasmin gene (CP) can cause aceruloplasminemia, a hereditary disorder characterized by hyperferritinemia with iron excess. Characteristic neurologic signs and symptoms, including cerebellarataxia, progressive dementia, and extrapyramidal indications, may result from this iron overload in the brain. Additionally, too much iron can accumulate in the pancreas, liver, and retina, causing endocrine problems, cirrhosis, and blindness, respectively.

The role of serum apelin and ceruloplasmin in subclinical hypothyroidism has been the subject of conflicting findings in various investigations. Numerous studies have demonstrated alterations in blood apelin and ceruloplasmin levels in subclinical hypothyroidism; nevertheless, the relationship between serum apelin and ceruloplasmin in subclinical hypothyroidism is not entirely clear, necessitating more investigation. In order to ascertain serum apelin and ceruloplasmin levels in

subclinical hypothyroidism, the current investigation was conducted.

Sub clinical hypothyroidism occurs when thyrotropin (TSH) levels elevated but thyroxin(T4) and triiodothyronine (T3) levels are regular (Ochs et al.,2008)

Although, subclinical hypothyroidism is generally asymptomatic, potential risk which are associated with this condition includes progression to overt hypothyroisim, cardiovascular effects, hyperlipidemia and neuropsychiatric effects(Cooper,2001).

Other terms for this condition are mild hypothyroidism, preclinical hypothyroidism, biochemical hypothyroidism, and depleted thyroid reserve. The TSH elevation in such patients is modest, with values typically between 5 and 15 mU/L. This syndrome is most often seen in patients with early Hashimoto's disease and is a common phenomenon, occurring in 7% to10% of older women.

Goals and Objectives

The current study's goals are to:

1. Examine serum ceruloplasmin levels in patients with subclinical hypothyroidism who have been detected early.
2. To compare the groups' serum ceruloplasmin levels.

Material and Methods

Study type: It is a cross-sectional, observational descriptive study conducted at a hospital.

The goal of this research is to assess serum ceruloplasmin levels in patients with subclinical hypothyroidism who have been detected early and to determine whether there may be a connection between them.

Study Design: The current study was carried out on 120 newly diagnosed patients with subclinical

hypothyroidism, ages 20 to 50, of both sexes, who were visiting the Department of Medicine's outpatient department. The diagnosis of thyroid disorder was made using the criteria suggested by the European Thyroid Association Guidelines-2013. The outcome was compared to 120 euthyroid people who were matched for age and gender and served as controls. Participants' ages, medical histories, and addictions have all been thoroughly recorded.

Exclusion Criteria

- Persons with diabetes or those with stroke
- Persons with Thyroid supplementation and antithyroid agents.
- Persons with coronary artery disease
- Smokers/alcohol users
- Persons using drugs that affect Serum apelin and ceruloplasmin level.
- Pregnant women

Serum Ceruloplasmin Estimation Using The Enzyme Linked Immunosorbent Assay Method (ELISA):

Total ceruloplasmin in human plasma, serum, urine, milk, saliva, and cell culture supernatants can be quantitatively determined with this Human Ceruloplasmin ELISA assay.

Principle: The affinity purified capture antibody placed on the microtiter plate will bind to human ceruloplasmin. Biotin-labeled anti-human ceruloplasmin polyclonal antibody attaches to the collected ceruloplasmin following the proper washing procedures.

After removing any extra antibody, bound polyclonal antibody is reacted with streptavidin conjugated with peroxidase. TMB substrate is utilized for color development at 450 nm after another washing stage. Human ceruloplasmin dilutions are used to construct a standard calibration curve and the samples to be

analyzed. The amount of total ceruloplasmin in the sample is closely correlated with color development. Normal blood concentration of ceruloplasmin in humans is 20–50 mg/dL.

Observations

Table 1: Anthropometric parameters of Subclinical Hypothyroidism and healthy subjects (controls)

Parameters	Group-I	Group-II
	Subclinical Hypothyroidism subjects Mean \pm SD (n=120)	Healthy subjects (controls) Mean \pm SD (n=120)
AGE (yrs)	40.25 \pm 11.8	39.50 \pm 10.8
WEIGHT (kg)	60.27 \pm 3.8	52.58 \pm 5.0
HEIGHT (cm)	156.0 \pm 4.9	154.8 \pm 4.5
BMI (kg/m ²)	24.5 \pm 2.6	21.9 \pm 2.8

Table 2: Biochemical parameters of Subclinical Hypothyroidism and healthy subjects (controls)

Parameters	Group-I	Group-II
	Subclinical Hypothyroidism subjects Mean \pm SD (n=120)	Healthy subjects (controls) Mean \pm SD (n=120)
FT3(pg/ml)	1.820 \pm 0.51	2.31 \pm 0.60
FT4(ng/dl)	0.68 \pm 0.11	0.80 \pm 0.14
TSH (μ IU/ml)	8.95 \pm 2.0	3.14 \pm 1.60
S. Apelin (ng/ml)	6.2 \pm 1.80	3.1 \pm 1.4
S. ceruloplasmin (mg/dl)	14.6 \pm 2.1	26.8 \pm 6.1

Table 3: Comparison of Serum Thyroid Function (TSH, FT3, FT4 level) of Subclinical Hypothyroidism subjects and healthy subjects (controls)

Parameters	Group-I	Group-II	T statistic (‘p’ value)
	Subclinical Hypothyroidism subjects Mean \pm SD (n=120)	Healthy subjects (controls) Mean \pm SD (n=120)	
FT3(pg/ml)	1.820 \pm 0.51	2.31 \pm 0.60	6.816 (<0.0001)
FT4(ng/dl)	0.68 \pm 0.11	0.80 \pm 0.14	7.383 (<0.0001)
TSH (μ IU/ml)	8.95 \pm 2.10	3.14 \pm 1.60	24.107 (<0.0001)

*p – value <0.0001 Highly Significant (HS) p – value<0.01 Significant (S) p – value>0.05 Non significant (NS)

Table 4: Comparison of S. Ceruloplasmin levels of Subclinical Hypothyroidism subjects and healthy subjects (controls)

Parameters	Group-I Subclinical Hypothyroidism subjects Mean \pm SD (n=120)	Group-II Healthy subjects (controls) Mean \pm SD (n=120)	T statistic Value*	'p'
S. ceruloplasmin (mg/dl)	14.6 \pm 2.1	26.8 \pm 6.1	20.716 (<0.0001)	

*p – value <0.0001 Highly Significant (HS) p – value<0.01 Significant (S) p – value>0.05 Non significant (NS)

Summary and Conclusion

In this study, 120 individuals with subclinical hypothyroidism (group I) and 120 healthy controls (group II) participated. The outcomes were contrasted with 120 healthy, age-matched controls of either sex (group II). Estimates were made of serum FT3, FT4, TSH, Apelin, and ceruloplasmin. Subclinical hypothyroid individuals (group I) had a slightly lower mean serum FT3 level than healthy controls (group II), although the difference was statistically significant (P<0.0001). Subclinical hypothyroid individuals (group I) had a slightly lower mean serum FT4 level than healthy controls (group II), although the difference was statistically significant (P<0.0001). A highly significant increase (P<0.0001) in mean Serum TSH level has been observed in subclinical hypothyroid subjects (group-I) when compared to controls (group- II). In subclinical hypothyroid subjects, mean serum Apelin levels were found to be significantly Higher in comparison to healthy subjects (p<0.0001). Mean serum Ceruloplasmin levels were considerably lower in subclinical hypothyroid participants than in healthy subjects (p<0.0001). According to the study's overall results, people with subclinical hypothyroidism have significantly higher serum Apelin levels and significantly lower serum Ceruloplasmin levels.

Nevertheless, more observational and experimental research is required to demonstrate the function of serum ceruloplasmin in subclinical hypothyroidism. Verification of serum ceruloplasmin levels in subclinical hypothyroidism may make it possible to start treatment for certain patients and disease groups, such as atherosclerosis and cardiovascular disease that coexist with advanced age hypothyroidism.

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