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A CROSS-SECTIONAL STUDY TO ASSESS THE ROLE OF SERUM HEPCIDIN LEVEL IN IRON HOMEOSTASIS OF POSTMENOPAUSAL FEMALES WITH AND WITHOUT HYPOTHYROIDISM

Medical Biochemistry

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ABSTRACT

Hepcidin has emerged as the central regulatory molecule of systemic iron homeostasis and the iron metabolism is very intricately connected to thyroid hormone metabolism. Therefore, this study was planned to estimate the level of serum hepcidin in hypothyroid postmenopausal and healthy postmenopausal females. In this study, 150 postmenopausal females without hypothyroidism and 150 cases of hypothyroidism were evaluated. They were compared for serum hepcidin level. Postmenopausal females with hypothyroidism showed a highly significant ($p<0.0001$) relationship in serum hepcidin level when results were compared with healthy postmenopausal females without hypothyroidism.

KEYWORDS

Hepcidin, Post-menopause, Hypothyroidism

INTRODUCTION

Hepcidin has emerged as the central regulatory molecule of systemic iron homeostasis. It is a 25-amino acid peptide hormone that is produced and secreted predominantly by hepatocytes, circulates in the bloodstream, and is excreted by the kidneys.[1]

Acute phase protein hepcidin is the master regulator of iron homeostasis. Hepcidin binds to ferroportin, the only known iron export protein, which results in internalization and degradation of this transporter, which then blocks iron export from enterocytes and macrophages to the circulation. Finally, measurement of serum hepcidin concentration is important for the monitoring of novel therapies for iron disorders that target hepcidin, its up-stream regulators, or its downstream receptor ferroportin.[2]

Iron is an important part of the thyroid hormone function in the body cells and lack of it can lead to poor of thyroid hormone leading to deficient metabolic activity of hypothyroid even in presence of normal FT_3 levels casing produce a thyroxine resistance and prevent T_3 to T_4 conversion by reducing the stimulate heme–containing thyroid peroxidase activity for thyroid hormone synthesis and then reducing thyroid hormone levels.[3]

Thyroid diseases are very common in middle-aged and older post-menopausal women. Hypothyroidism is one of the diseases most commonly associated with long-term prescription drug use and is the most common hormone deficiency disease. It affects people all over the world of every age, sex, race and level of wealth and education. It is more common in women; the incidence is 5 to 20 times higher in women than in men.

Menopause symptoms are similar to symptoms of hypothyroidism. It has also been observed that menopausal symptoms are more intense in patients with hypothyroidism. There is likelihood of symptoms of hypothyroidism in this age group being misinterpreted as menopausal symptoms and hypothyroidism remaining undetected. If hypothyroidism remains undetected and untreated, it can lead to health hazard like hyperlipidemia, atherosclerosis and heart disease.

Outcomes of the study may implicate role of serum hepcidin level in iron homeostasis of postmenopausal females with and without hypothyroidism. Thus it will change the management of treatment for postmenopausal hypothyroid females.

MATERIALS AND METHOD

The study was conducted on 150 postmenopausal females with hypothyroidism of 45-60 years of age groups and results were compared with 150 postmenopausal females without hypothyroidism attending Out Patient Department in the Department of Gynaecology and Obstetrics, Umaid Hospital for Women and Children and MDM Hospital, Jodhpur.

An informed consent was taken from all the healthy control groups and study groups who participated in the study for physical examination and biochemical procedures after apprising them the nature and objective of the study.

Test for serum hepcidin was estimated by ELISA method in the clinical laboratory of the Department of Biochemistry at Dr. S. N. Medical College, Jodhpur.

RESULTS

The present study had been conducted on 300 postmenopausal females of same age group (45-60 years), comprising of 150 clinically established postmenopausal females and equal number of postmenopausal females with hypothyroidism.

The mean serum hepcidin of the hypothyroid postmenopausal females was 38.88±17.48 ng/ml; which varies from 10.22 ng/ml to 80.31 ng/ml. It was 161.0±39.88 ng/ml in postmenopausal females without hypothyroidism which varies from 101.20 to 277.0 ng/ml. (Table 1)

A statistically highly significant difference ($p<0.0001$) was observed in serum hepcidin of hypothyroid postmenopausal females ($t=34.350$) when results were compared with the postmenopausal females without hypothyroidisms. (Table 2)

Table 1: Mean Serum Hepcidin level (ng/ml) of the subjects studied

Group Studied	Serum Hepcidin (Mean±SD) [Range]
Postmenopausal females with hypothyroidism	38.88±17.48 [10.22 - 80.31]
Postmenopausal females without hypothyroidism	161.0±39.88 [101.20 - 277.0]

Table 2: Statistical analysis of serum hepcidin among the groups studied

Group Compared	t – value	p – value
Postmenopausal females with hypothyroidism Vs Postmenopausal females without hypothyroidism	34.350	p<0.0001 (HS)

* HS= Highly Significant

DISCUSSIONS AND CONCLUSIONS

Hepcidin-25 plays a key role in the regulation of iron metabolism in humans by controlling the absorption of iron from the intestine. It is mainly synthesized in the liver as an 84 amino acid preprohormone which is converted to an active 25-amino acid peptide hormone detectable in serum and urine. Mammalian iron homeostasis is concertedly regulated through hepcidin and ferroportin that govern iron absorption, transport, storage and utilization. In several diseases, hepcidin over-expression leads to iron-restricted anemia. Conversely, decreased expression of hepcidin leads to iron overload conditions such as haemochromatosis, β-thalassaemia or congenital

dyserythropoietic states. Since hepcidin has been identified as a possible contributor in other autoimmune diseases, it should also be considered as one of the factors increasing the risk of anemia in the course of hypothyroidism.

In this study, serum hepcidin level showed a highly significant relationship between both the groups studied.

Hernik A et al (2019)[4] study observed that the mean serum hepcidin levels was lower (07.75±5.07 ng/ml) in hypothyroid postmenopausal female subjects as compared to control groups (17.70±02.95 ng/ml) and it showed a highly significant difference ($p<0.002$) when both of the groups were compared. The level of hepcidin is regulated by Fe ions in the serum and by numerous stimulating and inhibiting factors. In the majority of situations, a decrease in Fe concentration (for examples, haemolysis or haemorrhage) causes a decrease in hepcidin production. Conversely, states of acute inflammation mediated via IL-6, cancers and chronic and autoimmune disease lead to an increase in hepcidin levels.[5]

A similar result was found in a study of Matta RA et al (2022)[6], that the mean values of serum hepcidin level in hypothyroid postmenopausal female (12.80 ± 3.80 ng/ml) were lower than that in control groups (122.09 ± 19.04 ng/ml). A statistically significance difference ($p<0.001$) was found between cases and comparison groups.

According to study of Zhang H et al (2021)[7], the ages of candidates were 62.31±5.79 years, with average serum hepcidin and ferritin concentrations being 26.01±10.35 (pg/ml) and 205.13±98.39 (ng/ml), in hypothyroid postmenopausal females. Comparing the data of the two groups, it was found that serum hepcidin in the hypothyroid group (T-score < -2.5) was significantly lower than that in the non-hypothyroid group (T-score > -2.5), ($p<0.05$).

Summary

In view of the results obtained from the current study and considering the previous studies, there is a possibility of a shift in the activities of thyroid hormones with age. Considering the improved life expectancy and the fact that the activities of thyroid hormones could influence the reproductive, postmenopausal state and other metabolic pathways, it is important for us to have a better understanding of the activities of thyroid hormones as a person ages for appropriate management. Also, there is a need to understand the baseline thyroid function by measuring the activities of thyroid hormones in euthyroid women at various climacteric stages of life.

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