Hepcidin mRNA and Endocrine Risk in β-Thalassemia

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Background

Beta-thalassemia major (BTM) is a severe transfusion-dependent disease complicated by secondary hemosiderosis, leading to organ damage in the heart, liver, and endocrine glands. Endocrine disorders are among the most frequent complications, significantly reducing quality of life (Albu & Albu, 2018).

Hepcidin, a 25–amino acid peptide encoded by the HAMP gene, is the master regulator of systemic iron homeostasis. It binds ferroportin on enterocytes and macrophages, inducing its degradation and thereby reducing iron efflux (Katsarou & Pantopoulos, 2018). Hepcidin expression increases with iron overload and inflammation, while hypoxia, iron deficiency, and erythropoiesis suppress it. In BTM, ineffective erythropoiesis and iron overload cause dysregulated hepcidin expression (Ayatollahi et al., 2020).

Thalassemia-related endocrine disease (TED) commonly involves multiple glands (Carsote et al., 2022). Reported prevalences include hypogonadotropic hypogonadism (50–100%), hypothyroidism (6–35%), impaired glucose tolerance/diabetes (10–24%), and hypoparathyroidism (1–19%) (De Sanctis et al., 2013; Cappellini et al., 2022)

Aim and Objectives

1. To evaluate circulatory levels of mRNA expression of hepcidin gene in BTM adult patients.
2. To assess the predictive value of circulatory levels of mRNA expression of hepcidin gene as a marker for pituitary-gonadal-thyroid axes dysfunction in adult patients (BTM).

Methods

A Cross-sectional study in which the expression levels of hepcidin gene mRNA were investigated, Sixty adults were studied: 40 with β-thalassemia major (20 with and 20 without pituitary–gonadal–thyroid dysfunction) and 20 healthy controls matched for age and sex. Clinical history, endocrine profile (LH, FSH, testosterone/estrogen, TSH, fT4), and iron indices (serum ferritin) were obtained.

Hepcidin mRNA expression was quantified in peripheral blood mononuclear cells using qRT-PCR with GAPDH as a reference and ΔΔCT for analysis.

Results

A statistically significant difference in hepcidin gene expression levels among the studied groups ($p < 0.001$) was demonstrated, with the lowest levels in the group with endocrine complications.

Serum hepcidin mRNA expression showed strong prognostic value. ROC analysis distinguished BTM patients from controls at a cutoff of 1.0 (AUC = 0.938, 95% CI: 0.881–0.995; sensitivity = 90%, specificity = 80%; $p<0.001$).

It also differentiated BTM patients with endocrine complications from those without at a cutoff of 0.65 (AUC = 0.801, 95% CI: 0.684–0.917; sensitivity = 90%, specificity = 65%; $p<0.001$).

Conclusions

Serum hepcidin mRNA expression is a reliable prognostic biomarker in β-thalassemia major, effectively distinguishing patients from healthy controls and identifying those at higher risk of endocrine complications.

Keywords

β-thalassemia major, Hepcidin mRNA, Endocrine dysfunction, Biomarker, ROC analysis