

## Which is the best biomarker for restless leg syndrome: Hepcidin or ferritin?

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**Objectives:** To compare serum hepcidin and ferritin levels between patients with primary restless legs syndrome (RLS) and healthy controls, and to assess the relationship with RLS severity, dopaminergic drug intake, and augmentation of symptoms.

**Method:** One hundred and two drug-free RLS patients (age 58.91 [24.50-77.22], 63 women), and 73 controls (age 56.85 [23.46-76.65], 45 women) underwent a clinical examination and one night polysomnography. A second assessment was performed in 34 RLS patients under dopaminergic treatment. Serum hepcidin and ferritin levels were measured by ELISA and electrochemiluminescence assays.

**Results:** A low ferritin level (<50µg/l) was found in 15 (14.7%) patients and 18 (25%) controls. Hepcidin levels were higher in drug-free RLS patients compared to controls in a dose dependent manner, even after adjustment for confounding factors, and after excluding participants with low ferritin levels. Conversely, serum ferritin levels did not differ between RLS patients and controls. No between-group differences were found for either ferritin and hepcidin levels between treated and untreated patients, or between those with (n=17) or without a recent history of augmentation. Ferritin and hepcidin correlated with age, BMI, and periodic legs movements of sleep. The highest hepcidin levels were associated with older age, older age at RLS onset, less sleepiness, familial RLS and potentially with RLS severity.

**Conclusion:** Serum ferritin levels did not differ between RLS patients and controls. Conversely, we found higher serum hepcidin levels in RLS, not influenced by dopaminergic treatment and augmentation. Hepcidin may be a relevant biomarker in RLS diagnosis and more reliable than serum ferritin levels.