

# Hepcidin: A review on Potential Mediator between Obesity and Iron Deficiency

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## ABSTRACT

Hepcidin is a small peptide hormone secreted by the liver and by adipocytes. Hepcidin is suppressed in iron deficiency, allowing increased absorption of dietary iron and replenishment of iron stores. According to the World Health Organization (WHO) more than 1 billion adults are overweight and at least 300 million of them are obese. Experimental and clinical studies indicate that there is a relationship between iron metabolism and weight status. Iron deficiency is significantly more prevalent among obese individuals compared to non-obese ones. Recently, hepcidin expression in adipose tissue has been described and shown to be increased in patients with severe obesity. The effect of obesity on hepcidin serum levels and treatment outcome of iron deficiency anaemia in children is assessed. Finally, it is concluded that obesity increased hepcidin levels and was associated with diminished response to oral iron therapy in childhood iron deficiency anaemia.

**Key words:** *Hepcidin, Anaemia, Hormone, Overweight, Metabolism.*

## INTRODUCTION

According to recent WHO data, more than 1 billion adults are overweight and at least 300 million of them are obese. Moreover, the prevalence of obesity among children and adolescents is increasing at an alarming rate. Data from the National Health and Nutrition Examination Survey (NHANES) revealed that since 1980, the prevalence of obesity among school children and adolescents in the United States has tripled (Ogden et al., 2006; Ogden et al., 2008).

Both iron deficiency (ID) and obesity are global epidemics affecting billions with regional disparities. It has become clear that iron deficiency and obesity do not merely represent the coincidence of two frequent conditions but are molecularly linked and mutually affect

each other. The interaction of iron homeostasis with obesity represents a Janus-faced clinical condition. On the one hand, obesity may promote iron deficiency by inhibition of dietary iron uptake from the duodenum. On the other hand, a condition termed “dysmetabolic iron overload syndrome (DIOS)” has become the most frequent differential diagnosis for elevated ferritin concentrations, affecting approximately one-third of subjects’ with non-alcoholic fatty liver disease (NAFLD) or metabolic syndrome (MetS).

Obesity is associated with low-serum iron concentrations. The inverse relationship between iron status and adiposity was first reported in 1962, when (Wenzel et al, 1962) found significantly a lower mean serum iron concentration in obese compared with non-obese

adolescents. Most subsequent studies in podiatric and adult samples have shown similar results. For example, in a large study using National Health and Nutrition Examination Survey- I (NHANES-I) data, (Micozzi et al,1989)found that higher body mass index (BMI) was significantly associated with lower serum iron in women, and that transferrin saturation was significantly lower in the highest BMI quartile for both men and women.

Hepcidin is a recently identified as a peptide hormone. Human hepcidin gene (HAMP) is located on human chromosome 19q13 and encodes a precursor protein consisting of 84 amino acids. Hepcidin is released into the blood circulation as a peptide containing 20, 22 or 25 amino acids. This protein is synthesized mainly in the liver, but also in the heart, pancreas, kidney, spleen and adipose tissue (Leong and Lönnerdal, 2004).

## DISCUSSION

Phinas-Hamiel and coworkers, (2003) described a greater prevalence of iron deficiency (ID) in overweight and obese children and adolescents from Israel. In this study, iron deficiency (ID) was defined as iron concentration  $< 8 \mu\text{mol/l}$ , and iron deficiency anaemia (IDA) was defined as a haemoglobin level below 2 standard deviations (SDS) for age and gender. Subsequently, a large study confirmed those findings where it was demonstrated that overweight children were twice as likely to be iron deficient as normal weight children (Nead et al., 2004).

Richardson and coworkers (2009) described a low iron status in obesity is associated with the inflammation process. They evaluated high sensitivity CRP (hs-CRP), iron metabolism parameters (serum iron, ferritin and transferrin saturation) and weight status (BMI) in a group of 107 children and adolescents between 2-19 years of age. The BMI and serum iron were negatively correlated with hs-CRP, after age and gender adjustment. It is concluded that chronic inflammation due to obesity results

in a low iron status. The relationship between obesity and iron deficiency has been investigated mainly in children and adolescent by Wenzel et al., 1962; Seltzer and Mayer, (1963) and observed that lower serum iron concentration in obese compared with normal weight adolescents (11-19 years of age). In this study, obese children with IDA had significantly higher serum hepcidin levels ( $p < 0.01$ ); in comparison to non-obese children with IDA and healthy control group ( $P < 0.01$ ). In contrast, non-obese children with IDA had significantly lower serum hepcidin levels, compared to obese children with IDA and healthy control children ( $P < 0.01$ ).

Furthermore, Zimmermann et al, (2008) stated that adiposity in young women predicted not only lower iron absorption but also reduced response to iron supplementation, possibly due to increased hepcidin production. Finally, we can conclude that obesity increased hepcidin levels and was associated with diminished response to oral iron therapy in childhood iron deficiency anaemia. Further studies in larger groups will be required to verify these findings and to assess the value of weight reduction in refractory IDA of obese children.

Obesity and iron deficiency are two of the most common nutritional disorders worldwide. Several studies have consistently found the higher rates of iron deficiency in obese children and adolescents. Particularly, two epidemiological studies published in the early 1960s noted an association between overweight status among children and adolescents and iron deficiency. More recently, data from the American National Health and Nutrition Examination Survey III as well as data obtained in children from transition countries (Morocco and India) have suggested that among children, the prevalence of iron deficiency increases as body mass index (BMI) increases from normal weight to at risk for obesity to obesity.

## CONCLUSION

Obesity increased hepcidin levels and was associated with diminished response to oral iron therapy in childhood iron deficiency anaemia. In obese patients, increased hepcidin production, at least partly leptin mediated, can represent the missing link between obesity and disrupted iron metabolism. Overweight children demonstrated an increased prevalence of iron deficiency. The association between iron deficiency and overweight may have important public health and clinical implications. The hypoferrremia of obesity appears to be explained both by true iron deficiency and by inflammatory-mediated functional iron deficiency. Obesity induces a depletion of hepatic iron. Increased SAA (?) levels and a higher ratio of hepatic hepcidin mRNA expression to iron content demonstrate that the lower hepatic iron status in obese animals is associated with inflammation.

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