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Original Research Article

Assessment of iron status and its correlation with hepcidin in obese adults – A prospective case-control study

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ABSTRACT

Background: Obesity, broadly refers to increased body fat, which has become an important public health problem. Its prevalence continues to increase worldwide. In the World Health Survey, the prevalence of physical inactivity in India was 9.3% in men and 15.2% in women. Adipose tissue being an endocrine organ secretes several cytokines such as Interleukin-6, TNF-α and adipokines such as adiponectin, hepcidin, resistin. This study is to compare ferritin to iron and hepcidin with normal and obese men.
Methods: This case-control study was conducted at a multispecialty centre in Chennai, Tamil Nadu between 2013 and 2015, including 80 subjects of South Indian population. The biochemical parameters which were measured included the levels of hepcidin, ferritin, iron, Total Iron Binding Capacity and Hemoglobin.
Results: The results were statistically analyzed. Mann whitney U test performed to check for the statistical significance for differences in mean between the groups. The mean hepcidin values for the control group was 800.55 ± 503.50 and the study group was 1106.68 ± 826.25 and was found to be statistically significant with a p-value of 0.03. There was positive correlation of hepcidin with ferritin and Transferrin Saturation.
Conclusion: Hepcidin is recognized as the key regulator of systemic iron homeostasis. The measurement of hepcidin in biological fluids is therefore a promising tool in the diagnosis and management of medical conditions in which iron metabolism is affected.

1. Introduction

Obesity, broadly refers to increased body fat, which has become an important public health problem.[1] The WHO has stated Obesity as the most ignored general medical conditions, influencing many regions globally.[2] The overall commonness of stoutness has almost multiplied somewhere in the range of 1980 and 2008. More than a quarter of the world's adult population (1.4 billion adults) are physically inactive.[3] Obesity has arrived at pestilence extent in India with sullen stoutness influencing 5% of nation's population. In the World Health Survey, the prevalence of physical inactivity in India was 9.3% in men and 15.2% in women.[4] The study by Anjana et al. in 2005[4] reported that there is absence of recreational activity by 88.4%, 94.8%, 91.3% and 93.1% of the subjects in Chandigarh, Jharkhand, Maharashtra and Tamilnadu respectively.

Globally, data suggests that the prevalence of obese and overweight males is higher than that of females in some regions.[5] Obesity-related subclinical inflammation and its effects on hepcidin levels seem to be the most plausible explanation for the link between Iron Deficiency and obesity.[6]

Hepcidin, a 25 amino acid peptide present in human serum and urine, acts as a key regulator of iron homeostasis by binding to the iron transporter ferroportin, thereby resulting in internalization and lysosomal degradation.[7]

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Hepcidin is primarily expressed in the liver but few studies have reported its expression in subcutaneous as well as visceral adipose tissue; albeit at much lower levels.[8] There was a close correlation between the hepcidin gene expression in subcutaneous adipose tissue and BMI increasing the possibility that adipose tissue could contribute significantly to overall hepcidin pool in morbidly obese patients.[7,8]

Adipose tissue is a complex endocrine organ with an intricate role in whole body homeostasis. Adipokines and cytokines are the signaling factors from adipose tissue which play a key role in maintaining health, but are also the causative factors pathologies associated with obesity.[9] As the pace of Obesity climbs, weight related infections and conditions follow with increased medical expenses.[10]

2. Materials and Methods

This case-control study was conducted at a multispecialty centre at Chennai between 2013 and 2015, including 80 subjects of South Indian population, of male sex, non-smoking, non-alcoholic, in the age group of 20 to 45 years comprising 40 subjects in each of two groups A (BMI between 18 and 24.9) and B (BMI 30 and above) respectively. Any pre-existing diseases like T2DM, Systemic hypertension and coronary artery disease were excluded from the study.

A written informed consent was obtained from every participant in this study who were interviewed for a full medical history including age, sex, occupation and family history. The biochemical parameters include serum hepcidin and ferritin measured by Enzyme Linked Immunosorbent Assay (ELISA), serum iron and Total Iron Binding Capacity (TIBC) by Ferrozine method. Other parameters such as Triglyceride (TG), total cholesterol, High-density Lipoprotein (HDL) and Low-density Lipoprotein (LDL) were also measured and Transferrin Saturation (TSAT) calculated as [(Serum Iron / TIBC) X 100], Body Mass Index (BMI) was calculated as weight/ height in metres^2. The study was conducted after obtaining the clearance from Institutional Human Ethics Committee.

3. Results

The outcomes acquired were genuinely investigated utilizing JASP software version 0.14.1. Mean and Standard deviation were calculated for all parameters. Mann-whitney U test were performed to check for the statistical significance for differences in mean between the groups. Pearson correlation coefficient was done to correlate hepcidin and other iron parameters such as ferritin, iron, TIBC and TSAT and Hb.

The mean hepcidin values for the control group and study group was 800.55 ± 503.50 and 1106.68 ± 826.25 respectively, showing statistically significance with a p-value of 0.03 as shown in Table 1. The mean ferritin values were 20.48 ± 11.20 and 15.03 ± 5.43 respectively with a p-value of 0.01, which were also statistically significant (Table 1).

There was no factual importance among the groups for serum iron, TIBC, TSAT and furthermore for hemoglobin.

Pearson correlation of Hepcidin with Ferritin and TSAT showed positive correlation as shown in Table 2 Iron had negative correlation with TIBC and positively correlated with TSAT as shown in Table 2. There was a positive correlation of TSAT with Hb but TIBC showed negative correlation TSAT as shown in Table 2.

4. Discussion & Conclusion

The predominance of obesity has expanded drastically lately and is related with a few constant sicknesses like CAD, hypertension, metabolic disorder and type 2 diabetes mellitus.[11] Fat tissue is a functioning endocrine organ that deliveries a few cytokines, for example, IL-1, IL-6 TNF-α and adipokines, for example, leptin, adiponectin, hepcidin and resistin,[12] which contributes to the development of a low-grade systemic inflammation. The second rate aggravation in fat and dysmetabolic iron over-burden disorder patients is related with expanded hepcidin focuses, prompting helpless iron assimilation along these lines causing Anemia of Chronic Disease.[13] In constant gentle provocative conditions, like overweight or the metabolic disorder, even a gentle hepcidin overabundance might be adequate to modify the harmony between iron misfortune and iron take-up prompting iron insufficiency. The peptide chemical hepcidin assumes a focal part in controlling dietary iron retention and body iron appropriation.[14] Numerous human illnesses are related with changes in hepcidin focuses.

Hepcidin is overwhelmingly delivered by hepatocytes and furthermore in fat tissue, as a 25 amino-acid peptide that is discharged available for use.[15] Hepcidin is currently perceived as the vital controller of fundamental iron homeostasis.[16] The estimation of hepcidin in organic liquids is in this way a promising instrument in the finding and the executives of ailments wherein iron digestion is influenced.[17,18]

The correlation between overweight, hepcidin and iron status have been concentrated by different specialists globally since its disclosure in the year 2000.[19] Anyway, extremely restricted studies have been done dependent on South Indian population. So, this research is an endeavor to study the serum hepcidin levels in non-obese and obese male individuals, without any pre-existing disease, in the south Indian population, with other related parameters of iron status such as serum ferritin, serum iron, serum TIBC, calculated TSAT and Hb. The mean value of hepcidin in control group was 800.55 ± 503.50 ng/mL which correlated well with the values reported by Tomas Ganz et al.[20] Similar

Table 1: Hepcidin and Ferritin in control & study group

Parameter	Control Group N = 40	Study Group N = 40	p-value*
Hepcidin	800.55 ± 503.50	1106.68 ± 826.25	0.03
Ferritin	20.48 ± 11.20	15.03 ± 5.43	0.01

*p ≤ 0.05 is considered significant

Table 2: Correlation matrix of Hepcidin, Ferritin, Iron, TIBC, TSAT and Hb

Variable	Hepcidin	Ferritin	Iron	TIBC	TSAT
Ferritin	0.398+				
Iron	0.116	0.013			
TIBC	-0.100	-0.066	-0.595+		
TSAT	0.282*	0.143	0.251*	-0.406+	
Hb	0.089	-0.024	0.017	-0.059	0.248*

* Correlation is statistically significant at the p< 0.05 level.
+ Correlation is statistically significant at the p< 0.01 level;

methods of estimation of serum hepcidin by ELISA were also reported by Vasiliki koliaraki et al.[21] and the reference range was 10 – 1500 ng/mL.

When comparing the control and study groups (1106.68 ± 826.25), it was statistically significant with a p-value of 0.03. This outcome verified well with the results of Tomas Ganz et al.[20] Ferritin values between control and obese group were also statistically significant (Table 1). The difference within the mean values of serum iron, TIBC, TSAT and Hb between control and study group were not statistically significant in this study, which could be due to other confounding factors like, dietary iron intake, iron supplements, inherent individual variation in the iron homeostasis. The findings correlated well with the investigations reported by Young et al[16] and Dallalio et al.[22]

In this study, Pearson's correlation showed a positive correlation of serum hepcidin with ferritin and TSAT (Table 2). The correlation, observed between serum hepcidin and serum ferritin could be due to the effect of obesity, a chronic inflammatory condition, on the ferritin level.[23,24]

Hepcidin has also been proposed to have a role in counter regulating increased body iron concentration by decreasing absorption and releasing Iron from macrophages. Iron had negative correlation with TIBC whereas positively correlated with TSAT. These data correlate well with the study reported by Culafic et al.[25]

TIBC showed a negative relation with serum hepcidin which corresponds to the observation that TIBC increases whenever iron status decreases. This may be due to unknown reasons in which one reason could be both hepcidin and ferritin acting as an acute phase reactants. Similar results have been observed in the study conducted by Roe et al.[26] and Galesloot et al.[27] Other studies have also demonstrated the role of hepcidin as a positive acute phase response peptide.[28–30] Pearson's correlation of serum hepcidin with iron, TIBC, TSAT and Hb showed no correlation due to unknown reasons.

The study has several limitations. First being the relatively small sample size and the second is study design excluding women where we need to additionally investigate waist circumference and other anthropometry indicators. The other ratios that can be comparatively studied would have been hepcidin to ferritin ratio[31] might provide a good index of liver iron concentration. Limited research is available with respect to these ratios.

5. Conclusion

Serum Hepcidin is a strong regulator of Iron homeostasis and its analysis in biological fluids will be an identified tool in the prophylaxis and treatment of disorders related to iron metabolism and also in many other inflammatory conditions. Being secreted in adipose tissue, its role in adipose tissue metabolism needs to be well explored. Evaluating the ratios of Hepcidin to Ferritin and Ferritin to iron can further pave ways to comprehend Iron metabolism much better. The measurement of hepcidin in biological fluids is therefore a promising tool in the diagnosis and management of medical conditions in which iron metabolism is affected. Being a small sample size and only men included in this study, inclusion of women and recording the history of oral intake of iron or any other drugs would be helpful for planning future studies related to Iron disorders, obesity and hepcidin.

6. Source of Funding

None.

7. Conflict of Interest

The authors declare that there is no conflict of interest.

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