

## IS HEPCIDIN INDUCED ANEMIA IN OBESE INDIVIDUAL

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### **Abstract**

Iron deficiency anemia is common within obese human, increment level of hepcidin was notice in obese which considers as systemic regular for homeostasis the iron ,it limits iron absorption rate from intestine.

**Objectives:** The purpose is to explore hepcidin role in induced iron deficiency anemia in obese individuals.

**Method:** A 240 participants were entered in this work,121 were normal weight and 119 were obese .The iron- status parameters, serum hepcidin and inflammatory marker were calculated.

**Results:** IL-6, C-RP, TIBC in addition to hepcidin were significantly higher and the data demonstrate significantly lower serum iron in the obese group and male than those non obese and female correspondingly. While Hb and ferritin establish non-significant variation among these group .

**Conclusions:** The study resolved, High hepcidin level in obese subject involve in exacerbation iron deficiency anemia.

**Key words :** Anemia , Obesity, Hepcidin

### **Introduction**

Iron deficiency anemia is frequent type of anemia, iron is most abundant trace element in the body ,Obesity consider as a risk agent for different complications and comorbidities, it has negative affect on iron status and causing iron deficiency anemia (ID) through disrupt iron homeostasis, (1,2).Hepcidin is a hormone can synthesis by hepatocyte, macrophage, and adipocyte and it suggest as a indicator of inflammation, is considered as a sensitive hormone to inflammatory stimuli and an important role in anemia association to inflammation ,it involved in regulation of iron absorption (3).

Different studies identified that the obese individual associated with low and poor iron concentrations and absorption in relation to non-obese. Further, research indicated that obese were a twice as likely to be anemic than non-obese although they had normally dietary iron intakes and bioavailability (4).

Sex variation in iron parameter was noticed and suggested that ,the men is at a higher exposure of iron deficiency than women (5) .

Obesity is a low-grade of chronic inflammation which enhance inflammatory cytokine releasing, such as C-reactive protein (CRP) , tumor necrosis factor (TNF- $\alpha$ ), interleukin-6 (IL-6), and, these cytokines are direct promotion hepcidin rate expression . (6,7)

The adipose tissue synthesis these proinflammatory cytokines .The inflammatory process caused by such cytokine is believe to play significant role in the development different illness link to obesity such as ID (8). Heparin is one of these adipokines which is involve in iron homeostasis , erythropoiesis regulator A great level of hepcidin observed in obese human. This proposed that ,ID anemia recognized in obese may be due to hepcidin- linked mechanism (9).

## Method

A case control study of one hundred nineteen obese and one hundred twenty one of non-obese where comprised in this research. They collect from out -clinics of Nutritional care center ,the purpose to verification the influence of hepcidin associated obesity on iron status, Farther classification depend on the gender for obese participants in to two subclass included 60 obese-male and 59 obese- female .

Participant supplemented with iron therapy, blood transfusion , subject with bleeding such as gastric bleeding ,female with menstrual cycle and pregnant woman were excluded. Another questioner about vitamin C or calcium supplementation .

Ethical consideration: The approval was obtained from the director of the Nutritional care Unit . Al so approval was obtained from faculty of pharmacy, Jabir Ibn - Hayyan , Medical University Ethical Committee. All participants in our study were informed. Confidentiality and privacy any participant was considered.

S. iron, ,Hb ,S. ferritin and TIBC value estimated. Serum hepcidin, (IL-6), (CRP) were measurement for all participants .

## Bio-statistical analysis:

The results were express as mean  $\pm$  SD, Student's t-test applied to verify the implication of obesity in iron deficiency anemia. The significant differences was accept when P-value less than 0.05.

## Result :

The data of obese individual exhibit significant higher level TIBC( $332.4 \pm 47.1$ ,  $P < 0.0001$ ) , hepacidin ( $7.8 \pm 4.9$  , $P < 0.0001$ ), CRP ( $13.3 \pm 6.9$ ,  $P < 0.0001$ )and IL-6 ( $9.35 \pm 3.33$ ,  $p=0.0001$ ) and significant low level for serum iron( $48.4 \pm 28.1$ , $p= 0.0001$ ) , while the data didn't demonstrate significant differences for ferritin and Hb value among both group. While the data depend on the obese-gender display significant higher level TIBC( $340.11 \pm 39.4$ , $p= 0.02$ ) , hepacidin ( $9.8 \pm 3.6$ , $p=0.022$ ) , CRP ( $14.8 \pm 7.1$ , $p=0.024$ ) and IL-6 ( $11.84 \pm 5.31$ , $p=0.034$ ) and significant low level for serum iron( $39.01 \pm 25.3$ , $p=0.044$ ) for male in compares to female.

**Table 1:.Clinical data of iron status among non-Obese and Obese individuals**

Parameters	Non-Obese	Obese	P-value
NO	121	119	.....
Age (year)	37.9 ± 3.4	38.4 ± 3.2	0.24
BMI (kg/m <sup>2</sup> )	21.2 ± 2.9	32.71 ± 2.1	P < 0.0001
Hb (g/dl)	9.1±1.2	8.8±1.4	0.076
S. iron(µg/dL)	62.8 ± 26.2	48.4 ± 28.1	0.0001
S. ferritin (ng/mL)	35.2 ± 20.3	39.6 ± 18.3	0.079
TIBC (µg/dL)	274.3 ± 42.5	332.4 ± 47.1	P < 0.0001

**Table 2.: Data of inflammatory marker among non-Obese and Obese individuals**

Parameters	Non-Obese	Obese	P-value
NO	121	119	
Hepcidin (ng/mL)	3.4 ± 2.1	7.8 ± 4.9	P < 0.0001
Interleukin-6 (pg/mL)	4.66±1.69	9.35±3.33	0.0001
CRP (mg/L)	4.1 ± 1.2	13.3± 6.9	P < 0.0001

**Table 3.: Clinical data for iron status for Male and Female Obese individuals**

Parameters	Obese Male	Obese Female	P-value
NO	60	59	.....
Age (year)	38.2 ± 4.4	39.1 ± 2.2	0.16
Hb (g/dl)	8.5 ± 1.3	8.7±1.11	0.37
S. iron(µg/dL)	39.01 ± 25.3	47.9 ± 22.3	0.044
S. ferritin (ng/mL)	38.3 ± 17.2	36.6 ± 19.2	0.61
TIBC (µg/dL)	340.11 ± 39.4	322.9 ± 40.3	0.02

**Table 4: Data of inflammatory marker among Male and Female Obese individuals**

Parameters	Obese Male	Obese Female	P-value
NO	60	59	.....
Hepcidin (ng/mL)	9.8±3.6	8.13±4.2	0.022
Interleukin -6 (pg/mL)	11.84±5.31	10.11±3.21	0.034
CRP (mg/L)	14.8± 7.1	12.1± 5.7	0.024

### Discussion

Obesity is correlated with a low-grade of chronic inflammatory process (10). The adipose tissues secrete many pro-inflammatory cytokines, such as IL6 and TNF alpha. about 33% of IL-6 with in circulation produced from the adipose tissue (11). The basis mechanism which relationship between the obesity and ID is low-grade -systemic inflammation, which noted in those obese population (12).

Physiologically, hepcidin is reactively up regulated or down regulated by high or low serum iron, respectively. Measurement concentration of hepcidin might consider a auspicious indicator for evaluation iron metabolism( 13) . The presence of high levels of IL-6 can induce hepcidin synthesis, iron deficiency, and lower of Hb levels(14).

So will discuss these association between these parameter and there implication on anemia through effect on iron status

Our results demonstrate significant higher level for Hepcidin , IL -6 and CRP and significant low level for iron in obese compare to non-obese group while Hb and ferritin exhibit higher but not significant level. ferritin values is not great parameter for monitor ID. It suggested the ferritin level can elevated during inflammation from white adipose- tissue (15) There for we depend on other parameter such as hepcidin. Our result compatible with Amira S. Nassar who study verified that serum ferritin, TIBC and CRP were significantly higher in obese woman (16).

It was observed that the level of IL6 and Hepacidin were higher value in abnormal BMI than normal BMI(17,18). The IL6 usually stimulated this hormone to syntheses from liver (19) . Several data decided ,the obese people demonstrated higher hepcidin value, excess inflammation level, decrement iron, and lowing absorption of iron in compares to normal body mass index (20).

The CRP in our study was good indicator in coordinated with IL -6 , there was a positive correlation with highly statistically significant for it ,this means that CRP increased in obese compare to non-obese . These results are in accordance with the study of Lee (2017) which show that there is significant positive correlation between obesity and CRP levels(21,22).

Several searching studied the causes of anemia in obese and overweight, finally they decided that the increment of inflammatory markers were implicated in anemia due to iron depletion which combined with inflammation and elevated hepcidin value (23, 24). Additionally, Humphreys *et al* evaluated serum hepcidin among obese and normal body mass index women ,He observed a higher hepcidin in serum obese relative to non-obese woman (25). A converse study detected iron, inflammation and hepcidin for obese -women and terminated that, iron deficiency anemia not coupled to hepcidin or inflammation (26).

Know we discuss the difference of iron status, hepcidin and inflammatory marker among male and female, Since Iron metabolism is influenced by gender, were females generally having lower serum hepcidin than males (27). So we will verify the impact of gender on these parameter which influenced on iron status and resulting ID in obese individual .

Our data not exhibits difference in ferritin and Hb in obese class in relation to sex as in table 3, Al so other study reported higher but non-significant ferritin values in male obese then female obese and this may be due to the effect of testosterone and this compatible with our data (28).

The result in table 4 show significant elevated hepcidin ,CRP and TNF levels in obese male compare to female and this lead to inhibition iron- absorption and avoid iron liberation from macrophages

and hepatocytes ,resulting so called hypoferremia as show in table 3 ,The hepcidin has ability to impairment iron absorption (29). and this associated with elevated serum ferritin .Serum hepcidin positively correlate with level of ferritin and inversely with serum iron (30,31).

Our observation was certify in the malty- analysis after adjustment for various variables, that men was associated with high value of hepcidin and low TFR-F -index in compare to that noted in female (32,33).

In male with obesity, serum interleukin-6 was significantly higher than female. anemia characterize by lowering the total iron body but there is enhancing in storage of ferritin . while IL-6 level is increase and this lead to excitation the liver expression of hepcidin. And the last causes decrease intestinal absorption of iron through degradation of ferroportin in combined decreases iron liberation from macrophages. (34).

A recent research has been agreement with our observation which summarized by in obese male there are higher inflammatory, hepcidin, decrement iron levels, lower iron absorption (2) many article suggestion that obesity has negative effect on iron status and cause iron deficiency anemia because increase low-grade inflammation plus hepcidin.

Thus the data emphasize the convincing for monitor and treated ID in the population with obesity. Initial checking to iron parameter for obese one seeking for medical nutritional therapy for losing the weight might may has an beneficial in clinical setting, and also the significant correlation between Hb level and waist hip ratio suggested the significant role of these anthropological indices for the development of anemia. Further controlled studies are needed to prove these suggestions.

#### **Recommendation :**

Farther biochemical investigation like soluble- transferrin -receptor must be examine to check iron status precisely, hence this receptor do not impressed by inflammation process, so it could be utilized to diagnose iron- deficiency anemia .

#### **Conclusion :**

Obesity associated with high level of Hpcidin which affected negatively on serum iron and is associated with inflammatory process as illustrate by higher of CRP and IL- 6 levels and consequence iron deficiency anemia will develop.

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