Available online at **www.ijmrhs.com**

ISSN No: 2319-5886

International Journal of Medical Research & Health Sciences, 2022, 11(11): 9-14

Physiological and Inflammatory Markers Alteration in Obesity-Related Iron Deficiency in Adults

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Received: 21-August-2022, Manuscript No. ijmrhs-22-72515; **Editor assigned:** 22-August-2022, PreQC No. ijmrhs-22-72515(PQ); **Reviewed**: 22-October-2022, QC No. ijmrhs-22-72515(Q); **Revised**: 28-October-2022, Manuscript No. ijmrhs-22-72515(R); **Published**: 10-November-2022, J-invoice: J-72515

ABSTRACT

Homeostasis of iron, an essential micronutrient, is crucial to many physiological functions in the human body, such as cellular activity, erythropoiesis, and innate immunological response. So Iron deficiency anemia may occur from obesity's ability to disturb iron homeostasis. Increased hepcidin levels caused by chronic inflammation may be the cause of the link between obesity and iron insufficiency. This study aimed to investigate the associations between iron parameters, hepcidin, and inflammation markers in obese adults. For this cause, this current experiment is designed to investigate the iron profile and some hematological and inflammatory parameters in adults in Kurdistan region-Iraq. The cross-sectional study was designed within the setting of a medium private laboratory with participants being common people involved, two hundred adults were participated in this study and allocated into two groups according to BMI (control group (BMI ≤ 29.9): N=100 and obese group (BMI >30): N=100). Oxygen saturation (SpO_2) and pulse rate were assessed. Blood sera (once) was obtained for iron profiles (s. Iron, Ferritin, Hepcidin) and inflammatory levels (C-Reactive Protein (CRP), Interleukin 6 (IL-6)). Our findings highlighted that all inflammatory markers increased significantly in the obese groups in both sexes and positive correlation with BMI with a significant decrease of iron in the obese group. This research reveals that hepcidin levels in adult obese people contribute to the development of iron deficiency anemia due to increased inflammation because obesity and visceral adiposity are positively correlated with higher cytokine levels, lowering these risk factors is crucial for preventing cytokine level increases.

Keywords: Adults, Iron profiles, Inflammation markers, Obesity

INTRODUCTION

Over the past 50 years, obesity has become a global epidemic in terms of prevalence [1]. It is one of the most critical public health issues of the twenty-first century, according to public health professionals. Most of the world now stigmatized obesity (particularly in the Western world) [2]. Concern over morbidity and mortality linked to obesity is on the rise. High-sensitivity C-Reactive Protein (hs-CRP) is a newly discovered inflammatory marker that also serves as a predictor of ischemic heart disease and diabetes [3]. In addition, Iron deficiency anemia is a condition in which the body is unable to store enough iron, leading to reduced red blood cell production, One-third of the global population suffers from anemia, with iron deficiency anemia being the main cause [4,5]. Early in the 1960s, the first account of a probable relationship between obese people's iron status and obesity occurred, Four decades later, cross-sectional research completed in 2003 revealed that overweight and obese children and adolescents had a greater prevalence of iron insufficiency, According to a research that used data from the National Health and Nutrition Examination Survey (NHANES III), American children who were overweight had a double the likelihood of being iron deficient than children who were of normal weight, Similar to this, Yanoff et al. (2007) showed that the prevalence of iron insufficiency increased among obese people, who had considerably lower blood iron levels and greater levels of soluble transferrin receptor than non-obese persons, In a different study, Menzie et al. (2008) discovered that when obese people were compared to non-obese adults, the level of serum iron and transferrin saturation was considerably lower in the obese adults [6-9]. The endocrine organ adipokine, which is secreted by adipokine-producing adipose tissue, plays a role in inflammatory processes. As a result, obesity might be seen as a pre-inflammatory condition with mild, ongoing systemic inflammation. This inflammatory state, particularly iron deficiency, may be crucial in the etiology of illnesses linked to obesity [10]. Additionally, a strong negative predictor of serum iron content was discovered to be fat mass [11]. Previous population-based surveys reported that 18.0% of men and 32.9% of women aged 18 to 49 were overweight or obese, respectively, while 31.5% of children under the age of five and 31.5% of women aged 15 to 49 were found to be anemic [12]. Homeostasis of iron, an essential micronutrient, is crucial to many physiological human functions, such as cellular activity, erythropoiesis, and innate immunological response [13]. So Iron deficiency anemia may occur from obesity's ability to disturb iron homeostasis. Increased hepcidin levels caused by chronic inflammation may be the cause of the link between obesity and iron insufficiency. A little peptide hormone called hepcidin controls the intestinal absorption of iron negatively. Significant body weight loss improves iron status by increasing iron absorption in overweight and obese people by reducing chronic inflammation and serum hepcidin levels. To verify this impact, more randomized controlled studies are necessary [6]. Interleukin-6 (IL-6) produced by macrophages in response to inflammatory stimuli encourages hepatocytes to generate acute-phase proteins such as C-Reactive protein (CRP) and hepcidin. This inflammatory condition might result in prolonged hypoferremia and anemia [14].

METHODS

The cross-sectional study was carried out from Nov 2021 to Feb 2022. In this study, two hundred adults were participated and allocated into two groups according to body mass index (BMI) (control group (BMI ≤ 29.9): N=100 and obese group (BMI >30):N=100). The ages of the participant started from twenty-five and above, and both

genders male and female were included. The physiological markers like oxygen saturation (SpO_2) and pulse rate were measured by using a pulse oximeter (American Diagnostic Corporation, China). The techniques commonly used clinically, whether in focused thought or a medical procedure. Blood samples (10 mL) were collected from each participant and were divided into EDTA tubes for hematological parameters and Gel tubes for serological tests. Blood was gathered in gel container tubes, centrifuged at 15000 rpm for 5 min then serum separated. A fully automated chemical analyzer (Roche Cobas Integra 400 plus (Germany) has been used to estimate Iron and CRP parameters. A microplate reader (Lab, China) has been used to estimate serum IL-6 and Hepcidin.

Data were analyzed using the statistical package for Social Sciences (SPSS, version 21). One-way analysis of variance (ANOVA) was used in the study. A p-value of <0.05 was considered statistically significant.

RESULTS

The results of the current study showed that the level of oxygen saturation (PO_2) decreased significantly in the obese group for both males and females when compared to the control in male and female groups respectively.

The rate of heartbeat per minute was increased non-significantly in the obese group when compared with those of the control groups in both sexes as shown in Table 1.

Table 1 Physiological parameters comparison in control and obese groups about sex

Gender		**Male**		**p-value**	**Female**		**p-value**
BMI		**Control**	**Obese**		**Control**	**Obese**	
Statistics		**Mean ± S.D***	**Mean ± S.D**		**Mean ± S.D**	**Mean ± S.D**	
Physiological marker	O_2 (%)	98.41 ± 2.47	94.71 ± 2.45	0.047	98.65 ± 2.27	95.96 ± 2.73	0.044
	Pulse(beat/minute)	84.41 ± 11.15	87.6 ± 10.39	0.147	85.09 ± 9.58	86.73 ± 8.58	0.724
*S.D: standard deviation							

Table 2 demonstrates a significant increase ($p<0.05$) in white blood cell counts and a significant decrease in hemoglobin levels in the obese groups when compared with those of the control groups in both sexes, while other hematological parameters showed non-significant changes in the obese group when compared to the control group in both sexes.

Table 2 Hematological parameters comparison in control and obese groups about sex

Gender		**Male**		**p-value**	**Female**		**p-value**
BMI		**Control**	**Obese**		**Control**	**Obese**	
Statistics		**Mean ± S.D**	**Mean ± S.D**		**Mean ± S.D**	**Mean S.D**	
Hematological tests	RBC (10^{12}/l)	4.95 ± 0.43	5.1 ± 0.61	0.164	4.38 ± 0.46	4.51 ± 0.35	0.091
	WBC (10^9/l)	6.93 ± 1.69	7.8 ± 1.98	0.021	7.02 ± 2.31	8.64 ± 1.17	0.026
	HGB (g/dl)	14.21 ± 1.16	12.79 ± 1.5	0	12.38 ± 1.19	11.87 ± 1.34	0.046
	HCT (%)	43.45 ± 3.37	44.33 ± 4.39	0.262	37.21 ± 4.08	38.56 ± 3.45	0.074
	MCV (fl)	84.57 ± 15.51	87.15 ± 7.74	0.313	82.27 ± 14.38	79.97 ± 17.4	0.476
	MCH (pg)	31.78 ± 12.37	28.42 ± 3.11	0.05	30.12 ± 12.39	32.8 ± 17.87	0.392
	PLT (10^9/l)	223.65 ± 63.58	228.06 ± 51.92	0.709	271.84 ± 94.29	263.8 ± 62.9	0.61

Table 3 revealed a significant decrease in serum iron levels in the obese group in comparison to the control group in both sex groups. Regarding the Ferritin level, the obese group showed increases non-significantly ($P \geq 0.05$) in Ferritin levels in comparison to the control group in both male and female groups.

The level of Hepcidin was increased significantly in the obese group as compared with the control group in both male and female groups.

Table 3 Iron profile markers in control and obese groups about sex

Gender		Male		p-value	Female		p-value
BMI		Control	Obese		Control	Obese	
Statistics		Mean ± S.D	Mean ± S.D		Mean ± S.D	Mean ± S.D	
Iron profile	S. IRON (mg/dl)	108.73 ± 31.25	93.68 ± 27.04	0.025	94.83 ± 21.83	79.75 ± 31.78	0.014
	FERRITIN (µg/l)	145.1 ± 103.02	165.09 ± 107.08	0.347	163.94 ± 64.77	161.34 ± 79.88	0.846
	Hep (pg/ml)	402.57 ± 194.52	475.98 ± 158.82	0.043	402.26 ± 124.06	487.32 ± 128.1	0.037

Table 4 showed a significant increase in inflammatory markers in the obese groups in comparison to the control group, the highest level of C-reactive protein and interleukin-6 was found in the obese group in both male and female groups when compared with these of the control groups respectively.

Table 4 Inflammatory markers in obese groups about sex

Gender		Male		p-value	Female		p-value
BMI		Control	Obese		Control	Obese	
Statistics		Mean ± S.D	Mean ± S.D		Mean ± S.D	Mean ± S.D	
Inflammatory markers	CRP (mg/dl)	3.48 ± 2.9	5.77 ± 7.44	0.04	4.23 ± 4.68	6.47 ± 6.37	0.049
	IL-6 (ng/ml)	47.37 ± 10.22	52.36 ± 13.48	0.035	65.9 ± 37.04	77.94 ± 37.24	0.002

DISCUSSION

Physiological Parameters

The results of this study demonstrated a significant reduction in blood oxygen saturation with non-significant elevation in heartbeat per minute in the obese group when compared to the control group in both male and female groups. The results of the current investigation are confirmed with these previous studies [15-18]. This previous study suggests that despite having a comparable magnitude of association with SpO_2 levels, the effects of obesity on gas exchange in adults may be underappreciated in comparison to other clinical entities that are frequently associated with hypoxemia (such as smoking, heart failure, and obstructive lung disease) [16]. If the BMI is over 30, hypercapnia and hypoxia in arterial blood can happen in someone who is dangerously overweight. 90% of people with a BMI over 30 have sleep difficulties and have lower nighttime oxygen saturation [17].

Hematological Parameters

In this study, a significant increase in the WBC counts was seen in the obese group in both sexes with a significant decrease in hemoglobin level. Previous studies found the alteration of hematological parameters in obese individuals with increasing leukocyte count [19-21]. It is previously reported that leukocytes are thought to have a significant part in the low-grade inflammation that has been defined as the state of obesity. According to Salma et al., obese

people with a high WBC count have insulin resistance [21]. In obese persons, platelets, Red Blood Cells (RBCs), and hemoglobin are linked to cardiorespiratory disorders and the association between BMI and hematological parameters are mediated by their associations with abdominal fat and insulin resistance markers [22].

Iron Profile Markers

The results revealed reducing serum iron significantly in the obese group in both sexes with a non-significant increase of serum ferritin and a significant increasing of hepcidin in the obese group in both sex groups, this is indicated by the parallel correlation of hepcidin with body mass index. Several previous studies showed that the hepcidin level increase with the BMI in the obese population and this lead to some issues in the body such as iron deficiency anemia [6,23]. A link between obesity and iron status is suggested by the high prevalence of obesity along with the incidence of iron deficiency seen across different age and sex groups [24]. Iron deficiency anemia may occur from obesity's ability to disturb iron homeostasis. Increased hepcidin levels caused by chronic inflammation may be the cause of the link between obesity and iron insufficiency [6].

Inflammatory Markers

The present study showed a significant increase of both inflammatory markers CRP and IL-6 in the obese group when compared to the control group in both sexes. The results conducted by previous studies that obesity, particularly visceral obesity, is increasingly thought of as a low-grade inflammatory illness because of raised serum levels of a variety of Inflammatory Markers (IM), such as C-Reactive protein (hs-CRP) and Interleukin-6 (IL-6) [3,25,26]. Another study backed up our finding that generally, there was a significant relationship between weight, BMI, waist-hip ratio, hip circumference, and serum concentrations of CRP, TNF, and IL-6. CRP and IL-6 are substantially linked with visceral adipose tissue, waist circumference, and BMI in obese people [3]. CRP was strongly correlated with BMI according to multiple regression analysis, but IL-6 was significantly correlated with visceral adiposity in obese participants. Because obesity and visceral adiposity are positively correlated with higher cytokine levels, lowering these risk factors is crucial for preventing cytokine level increases [25]. Obesity most likely plays a major role in the etiology of chronic diseases by causing the establishment of low-grade chronic inflammation both locally and systemically in adipose tissue. The molecular processes that initiate the inflammation linked to obesity are distinct from those that initiate the traditional inflammatory response brought on by infections and involve distinct signaling pathways. A lack of nutrition leads to quantitative and qualitative changes in the lipid content of adipose tissue as well as the production of several chemicals that act as endogenous ligands to activate immune cells, which in turn sets off the inflammatory process in obese persons [26].

CONCLUSION

This research revealed that hepcidin levels in adult obese people contribute to the development of iron deficiency anemia due to increased inflammation because obesity and visceral adiposity are positively correlated with higher cytokine levels, lowering these risk factors is crucial for preventing cytokine level increases. In addition, Increase in obesity-associated anthropometric measurements (BMI) is associated with relative leukocytosis within the

physiological range. Physiologically, decreased oxygen saturation significantly with non-significant elevation in heartbeat in the obese group may be due to other clinical features. Further experiments for physiological parameters could support finding the correlation between obesity and iron deficiency anemia.

DECLARATIONS

Conflict of Interest

The author(s) declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

Ethical Clearance

This work was supported by Sulaimani Polytechnic University (Iraq). Experimental Protocol was approved by the Ethics Review Committee of Health and Medical Technology College in Sulaimani, Iraq. (Approval no: MLD00075)

Source of Funding:

Self-funding (Brwa Zahid)

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