Al-Kindy College Medical Journal (KCMJ)

Research Article

Alterations in some Physiological and Inflammatory Markers in Iron-Deficient Obese Adults in the Kurdistan Region, Iraq

Brwa Zahid[1], Kaniaw R. Khafar[1*], Mariwan A. Hama Salih[1]

[1] Department of Medical Laboratory, College of Health and Medical Technology, Sulaimani Polytechnic University, Sulaimani, Iraq
*Corresponding author: kaniaw.khafar@spu.edu.iq

ABSTRACT

Background: Iron homeostasis is crucial to many physiological functions in the human body, such as cellular activity, erythropoiesis, and the innate immune response. Iron deficiency anemia may occur from obesity's ability to disturb iron homeostasis. Obesity may be seen as a pre-inflammatory condition with mild, ongoing systemic inflammation. Additionally, an increase in hepcidin levels by chronic inflammation causes iron insufficiency in obese people. For this reason, this current experiment is designed to investigate the iron profile and some hematological and inflammatory parameters in obese adults in the Kurdistan region-Iraq.

Subjects and Methods: The cross-sectional study was designed within the context of a medium private laboratory with participants being common people involved, 200 adults participated in this study and were allocated into two groups according to BMI (control group (BMI $\leq$ 29.9): N=100 and obese group (BMI >30): N=100). Oxygen saturation (SpO2) 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)).

Results: Our findings highlighted that all inflammatory markers increased significantly in the obese groups in both sexes and a positive correlation with BMI and a significant decrease in iron in the obese group.

Conclusions: This research reveals that hepcidin levels in obese adult people contribute to the development of iron deficiency anemia due to increased inflammation.

Introduction

Over the past 50 years, obesity has become a global epidemic in terms of prevalence. It is one of the most critical public health issues of the twentieth century, according to public health professionals. Most of the world is now stigmatizing obesity (particularly in the western world) (1). 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 (2), One-third of the global population suffers from anemia, with IDA being the main cause (3). In the 1960s, the first account of a probable relationship between the iron status of obese people and obesity occurred (4), Four decades later, cross-sectional research completed in 2003 revealed that overweight and obese children and adolescents had a high 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 of normal weight (5), Similar to this, Yanoff et al. (2007) showed that the prevalence of iron deficiency increased among obese people, who had considerably lower blood iron levels and higher levels of soluble transferrin

receptor than non-obese persons (6), In another 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 obese adults (4). The study aimed to investigate the associations between iron parameters, hepcidin and inflammation markers in obese adults in Kurdistan region-Iraq.

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. Additionally, a strong negative predictor of serum iron content was discovered to be fat mass (7). Homeostasis of iron, an essential micronutrient, is crucial to many physiological human functions, such as cellular activity, erythropoiesis, and innate immunological response (8). 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 (4). 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 could result in prolonged hypoferremia and anemia (9).

Subjects and Methods

The cross-sectional study was carried out from Nov 2021 to Feb 2022. In this study, 200 adults were included and allocated in to two groups according to BMI (control group (BMI ≤ 29.9): N=100 and obese group (BMI >30): N=100). The ages of the participant started from 25 and above, and both males and females were included. The physiological markers like oxygen saturation (SpO2) and pulse rate were measured by using a pulse oximeter (American Diagnostic Corporation, China). Techniques are commonly used clinically, whether in focused thought, or a medical procedure. Blood samples (10ml) were collected from each participant and 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 the 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). In the study, a one-way analysis of variance (ANOVA) was used. A P-value of < 0.05 was considered statistically significant.

Results:

The results of the current study showed that the level of oxygen saturation (PO2) was significantly reduced in the obese group for both males and women compared to the control in the 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			Female		
	BMI	Control Mean± S.D	Obese Mean± S.D	p-value	Control Mean± S.D	Obese Mean± S.D	p-value
	Statistics						
physiological marker	O2 (%)	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

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			Female		
	BMI	Control	Obese	p-value	Control	Obese	p-value
	Statistics	Mean± S.D	Mean± S.D		Mean± S.D	Mean± S.D	
hematological tests	RBC	4.95±0.43	5.1±0.61	0.164	4.38±0.46	4.51±0.35	0.091
	WBC	6.93±1.69	7.8±1.98	0.021	7.02±2.31	8.64±1.17	0.026
	HGB	14.21±1.16	12.79±1.5	0.000	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	84.57±15.51	87.15±7.74	0.313	82.27±14.38	79.97±17.4	0.476
	MCH	31.78±12.37	28.42±3.11	0.05	30.12±12.39	32.8±17.87	0.392
	PLT	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 level in the obese group in comparison to the control group in both sex groups. Regarding the Ferritin level, the obese group showed nonsignificant increases (P ≥ 0.05) in Ferritin levels compared to the control group in both male and female groups.

The level of hepcidin increased significantly in the obese group compared to the control group in both male and female groups.

Table 4 showed a significant increase in inflammatory markers in the obese groups compared 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 compared to these control groups, respectively.

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

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

Table 4: Inflammatory markers in obese groups regarding sex

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

Discussion

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 greater than 30 have sleep problems and have lower nighttime oxygen saturation (10). 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) (11). Some previous studies confirmed that hypoxia and a decrease in heartbeat per minute have been recorded in obese people (12).

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. (13), obese people with a high WBC count have insulin resistance. In obese people, platelets, red blood cells (RBC), and hemoglobin are associated with cardiorespiratory disorders (13) and the association between BMI and hematological parameters is mediated by their associations with abdominal fat and insulin resistance markers (14). Previous studies found the alteration of hematological parameters in obese individuals with an increase in leukocyte count (15).

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 (16). 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 (4). Previous studies showed that the level of hepcidin increases with BMI in the obese population, which leads to some issues in the body such as iron deficiency anemia (4, 17).

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. These 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) (18-20). Another study supported our finding that there was a significant

relationship between weight, BMI, waist-hip ratio, hip circumference, and serum CRP, TNF, and IL-6 concentrations. CRP and IL-6 are substantially linked with visceral adipose tissue, waist circumference, and BMI in obese people (19). 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 (18). 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 obesity-lined inflammation are different from those that initiate the traditional inflammatory response caused by infections and involve different signaling pathways. 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 starts the inflammatory process in obese people (20).

Conclusion:

This research revealed that hepcidin levels in obese adult 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 to prevent increases in cytokine levels . Also, an increase in obesity-associated anthropometric measurements (BMI) is associated with relative leukocytosis within the physiological range. Physiologically, the decrease in oxygen saturation significantly with a nonsignificant increase in a heartbeat in the obese group may be due to other clinical features. Further experiments on physiological parameters could support the finding of the correlation between obesity and iron deficiency anemia.

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).

Conflict of Interest

No conflict of interest

References

[1] Medina FX, Solé-Sedeno JM, Bach-Faig A, Aguilar-Martínez A. Obesity, Mediterranean diet, and public health: A vision of obesity in the Mediterranean context from a sociocultural perspective. International journal of environmental research and public health. 2021;18(7):3715.

[2] Paul P, Maiti D, Adhikary T. Iron deficiency anemia-An updated overview. International Journal of Research in Pharmacy and Pharmaceutical Sciences. 2021;6(4):28-33.

[3] Kumar P, Shah P, Awasthi V, Khera B, Agarwal M, Lakhtakia M, et al. Anemia in Pregnancy: A knowledge, Attitude and Practice Survey Amongst Obstetricians and Gynaecologists in

India. The Journal of Obstetrics and Gynecology of India. 2022:1-7.

[4] Alshwaiyat NM, Ahmad A, Wan Hassan WMR, Al‑Jamal HAN. Association between obesity and iron deficiency. Experimental and Therapeutic Medicine. 2021;22(5):1-7.

[5] Nead KG, Halterman JS, Kaczorowski JM, Auinger P, Weitzman M. Overweight children and adolescents: a risk group for iron deficiency. Pediatrics. 2004;114(1):104-8.

[6] Yanoff L, Menzie C, Denkinger B, Sebring N, McHugh T, Remaley A, et al. Inflammation and iron deficiency in the hypoferremia of obesity. International journal of obesity. 2007;31(9):1412-9.

[7] Stoffel NU, El-Mallah C, Herter-Aeberli I, Bissani N, Wehbe N, Obeid O, et al. The effect of central obesity on inflammation, hepcidin, and iron metabolism in young women. International Journal of Obesity. 2020;44(6):1291-300.

[8] Weyh C, Krüger K, Peeling P, Castell L. The role of minerals in the optimal functioning of the immune system. Nutrients. 2022;14(3):644.

[9] Wieczorek M, Schwarz F, Sadlon A, Abderhalden LA, de Godoi Rezende Costa Molino C, Spahn DR, et al. Iron deficiency and biomarkers of inflammation: A 3-year prospective analysis of the DO-HEALTH trial. Aging clinical and experimental research. 2022;34(3):515-25.

[10] Manuel AR, Hart N, Stradling JR. Correlates of obesity-related chronic ventilatory failure. BMJ Open Respiratory Research. 2016;3(1):e000110.

[11] Kapur VK, Wilsdon AG, Au D, Avdalovic M, Enright P, Fan VS, et al. Obesity is associated with a lower resting oxygen saturation in the ambulatory elderly: results from the cardiovascular health study. Respiratory care. 2013;58(5):831-7.

[12] Saechee J, Wannasamai K, Jaimanee P, Pinkeaw D, Chinda K, Inthachai T. Effects of general obesity on heart rate variability in Thai people with physical inactivity. Chulalongkorn Medical Journal. 2019;63(3):187-92.

[13] Sait S, Alqassas M, Othman S, Shihon S, Alqalayta L, Alqusair S, et al. Obesity correlates with neutrophilia. Hematol Transfus Int J. 2016;3(2):159-62.

[14] Park Y-M, Zhang J, Steck SE, Fung TT, Hazlett LJ, Han K, et al. Obesity mediates the association between Mediterranean diet consumption and insulin resistance and inflammation in US adults. The Journal of nutrition. 2017;147(4):563-71.

[15] Raghavan V, Gunasekar D, Rao KR. Relevance of haematologic parameters in obese women with or without metabolic syndrome. Journal of clinical and diagnostic research: JCDR. 2016;10(5):EC11.

[16] Smith L, Toussaint L, Micoli A, Lynch B. Obesity, putative biological mediators, and cognitive function in a national sample of children and adolescents. Preventive Medicine. 2021;150:106659.

[17] Langer AL, Ginzburg YZ. Role of hepcidin- ferroportin axis in the pathophysiology, diagnosis, and treatment of anemia of chronic inflammation. Hemodialysis International. 2017;21:S37-S46.

[18] Delgado C, Chertow GM, Kaysen GA, Dalrymple LS, Kornak J, Grimes B, et al. Associations of body mass index and body fat with markers of inflammation and nutrition among patients receiving hemodialysis. American Journal of Kidney Diseases. 2017;70(6):817-25.

[19] Lavanya K, Ramamoorthi K, Acharya RV, Madhyastha SP. Association between Overweight, Obesity in Relation to Serum Hs-CRP Levels in Adults 20-70 Years. Journal of Clinical & Diagnostic Research. 2017;11.(١٢)

[20] Varì R, Scazzocchio B, Silenzi A, Giovannini C, Masella R. Obesity-associated inflammation: does curcumin exert a beneficial role? Nutrients. 2021;13(3):1021.

To cite this article: Zahid B, Khafar KR, Salih MAH. Alterations in some Physiological and Inflammatory Markers in Iron-Deficient Obese Adults in the Kurdistan Region, Iraq. Al-Kindy College Medical Journal. 2022;18(3):233–6.