Original Article

Study of Oxidative Stress and Relationship with Se(selenium), cu(copper), cd(cadmium) and pb(lead) levels in Obese Patients with diabetes and Hypertension

Ruaa. K. Abbas and Jamal Harbi Hussein Alsaadi

ABSTRACT

Objective: The current study was aimed at investigating the changes in MDA (Malondialdehyde), some trace elements, and heavy metals in serum of obese patients with Type-2 diabetes and hypertension in Thi-Qar province, Iraq.

Study Design: Observational and Case series study

Place and Duration of Study: This study was conducted at the "Al-Nasiriya Teaching Hospital in Thi-Qar Governorate" and "biochemistry Laboratory" in the "College of science" in the duration between August 2024 to March 2025.

Methods: There are 140 subjects (male and female) in the study, 105 patients diagnosed with obese (BMI ≥30) among them, and 35 as control with (BMI <25) and their ages range from (35–65) years. They divided into four groups as the following: **Cont**. group: included (35) normal healthy, **Obes**. group: Included (35) Just obese patients, **ODM** group: Included (35) obese diabetes patients and **OHTN** group: Included (35) obese hypertensive patients.

Results: The results in this study indicated a significant increase (P≤0.05) in MDA, Cu, Cd and Pb levels and a significant decrease in Se level in all patients' groups in comparison with the control group, whereas no significant change (p≤0.05). While there was no significant difference in each serum MDA, Se, Cu, Cd, and Pb levels between the obese-DM group and the obese-HTN group compared to the obese group (p ≤0.05).

Conclusion: This study concluded that the obese patients with T2DM and with HTN had high significant level of MDA, Cu and heavy metals (Pb and Cd) and low significant level of Se than control group.

Key Words: Obesity, Oxidative Stress, Trace Elements.

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INTRODUCTION

Obesity-related oxidative Stress is responsible for the disturbance of internal environment homeostasis, which is characterized by oxidative stress responses. Oxidative stress (OS) is a condition of cellular disparity, "persistent imbalance between the production of oxidizing agents and the antioxidant defense," in which there is an excessive number of free radicals and reactive oxygen species (ROS). The mechanisms of the metabolic syndrome and their comorbidities help a promote pro-oxidative state, which contributes to cell and tissue damage, and thus metabolic disorders occur[1].

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The obesity-associated fat accumulation leads to inflammation, hypertrophied adipocytes, and hypoxia. Moreover, OS worsens inflammation and alters adipokine secretion. Many of these phenomena activate the monocyte infiltration in adipose tissue that worsens the inflammatory processes [2]. Malondialdehyde. It is the most common marker used to investigate the presence of oxidative stress in a biological system. it's the end products of polyunsaturated fatty acids after degradation by ROS, indicating the overall lipid peroxidation level in human blood and tissue samples[3].

Trace Elements: are considered pivotal components of redox metabolism and the immune system, obesity and trace elements are related in a complicated, multifaceted manner. The development of obesity is assumed to be influenced by metabolic dysfunction, inflammation, and oxidative stress, which are all thought to be caused by trace element deficits. Additionally, obesity itself may change the metabolism of trace elements, aggravating deficits, Se, Zn and Cu are key components of many antioxidant enzymes.[4] Cu metabolism is changed in diabetic patients and may play particular functions in the progression of diabetes and its complication[5]. Study had shown that the content

of Cu in patients with hyperglycemia, hypertension, and obesity is higher than that in ordinary people. Numerous essential biological functions, including hormone production and the regulation of ROS concentrations, depend on selenium. Maintaining adequate amounts of selenium is crucial since low or high levels can negatively impact cardiovascular health. On the other hand, severe toxicity and deadly cardiac symptoms can result from consuming too much selenium[6]. **Heavy metals,** "non-essential or toxic elements" such as Lead and Cadmium are persistent environmental contaminants as heavy metals cannot be degraded or destroyed, they have been connected to a number of detrimental health consequences, such as a higher risk of stroke and CVDs. According to biological data, Pb and Cd exposure causes oxidative stress, inflammation, and endothelial dysfunction, which eventually results in atherosclerosis, elevated blood pressure.[7]

METHODS

Study was conducted at the "Al-Nasiriya Teaching Hospital in Thi-Qar Governorate" and "biochemistry Laboratory" in the "College of science" in the duration between August (2024) to March (2025). 140 study case were included in this study, 105 patients which divided into three groups (obese, obese diabetic and obese hypertensive patients) each group 35 subjects, with control group of the normal healthy individuals (350), The overall mean age of study subjects was (48.84 ± 8.50).

Exclusion Criteria: The study excludes any participant taking drugs that cause obesity or an increase in body weight, such as steroids and chemotherapy, and pregnant women. Furthermore, the smokers and patients with other chronic diseases, such as "kidney diseases, liver failure, thyroid disease, and immunological diseases," were excluded.

Blood Samples: About (5 ml) of blood samples were collected from healthy subjects and the patients at the morning, the blood samples were collected in gel tubes, then left for half an hour and centrifuged at 3000 rpm for 15 minutes, the serum samples were separated and stored at (-20ºC)

Statistical Analysis: All statistical analyses were performed using SPSS-23, Windows version 23.0.

RESULTS

1. Clinical and Characteristic Features of the Studies Groups: The mean BMI of case patients was (39.62±4.38 kg/m²) and (23.96 ± 1.21 kg/m²) for the normal healthy individuals.

Table (1) shows characteristics of case and control subjects. There were non-significant comparisons between case and control in each (age and sex) (p value ≤ 0.05), While significant comparisons by BMI. Characteristic information is presented in following Table for all studied groups.

Table No.1: Descriptive data for all studied groups

Groups	No.	Sex (M/F)	Age (years) Mean ± SD	BMI (kg/m^2) Mean ± SD
Cont.	35	15/20	48.03 ± 8.01	23.96 ± 1.21
Obes.	35	13/22	47.57 ± 7.84	38.92 ± 4.24
ODM	35	12/23	50.00 ± 9.23	39.33 ± 4.33
OHTN	35	12/23	48.94 ± 8.42	40.60 ± 4.58
			P-value = 0.534$^{Non.\ sig}$	**P-value = 0.000^{Sig}**

*** P-value ≤ 0.05 consider significant.**
*** At the 0.05 level, the mean difference is significant.**

2. Oxidative Stress

2.1 Serum Malondialdehyde Levels: The MDA concentration in the obese-DM and obese-HTN groups where significantly higher than those obese group and control group, as indicated by Table (3) and Figure (1). Additionally, the MDA concentration in the obese group significantly higher than in the control groups (p≤0.05). While there was no significant difference in MDA levels between obese-DM and obese-HTN groups (p≤0.05).

Table No.2: Serum MDA values of studied groups

Groups	No.	MDA (µmol/l) Mean ±SD
Cont.	35	2.34 ± 0.59 ^{c}
Obes.	35	3.96 ± 0.55 ^{b}
ODM	35	4.47 ± 0.65 ^{a}
OHTN	35	4.37 ± 0.64 ^{a}
P- value		< 0.001 **
LSD		0.29

*** P-value ≤ 0.05 consider significant.**
*** At the 0.05 level, the mean difference is significant.**
(a, b, c): "indicates having various letters in same column have been significantly differed (P <0.05) The different letters refer to a significant difference. The same letters refer to a non-significant difference".

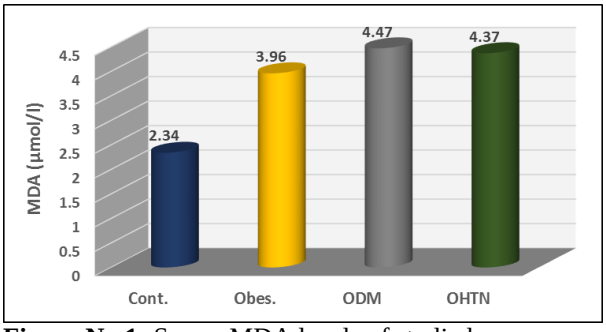

Figure No.1: Serum MDA levels of studied groups

3. Evaluation of Serum Trace Elements Levels:

The results of trace elements point to a significant decrease in Se levels in all patients' groups in

comparison with the control group ($p \leq 0.05$). While there was a significant increase in the Cu levels between all patients' groups in comparison with the control group ($p \leq 0.05$). Table 3 and Figures 2 & 3.

Table No.3: Serum Se and Cu concentrations of studied groups

Groups	No.	Se (ppb) Mean ±SD	Cu (ppm) Mean ±SD
Cont.	35	29.17 ± 5.70 [a]	4.83 ± 2.16 [b]
Obes.	35	18.04 ± 2.63 [b]	7.08 ± 2.32 [a]
ODM	35	17.01 ± 1.89 [b]	6.13 ± 1.81 [a]
OHTN	35	17.68 ± 3.39 [b]	6.25 ± 2.26 [a]
P- value		< 0.001 **	< 0.001 **
LSD		1.75	1.01

*** P-value ≤ 0.05 consider significant.**
*** At the 0.05 level, the mean difference is significant.**

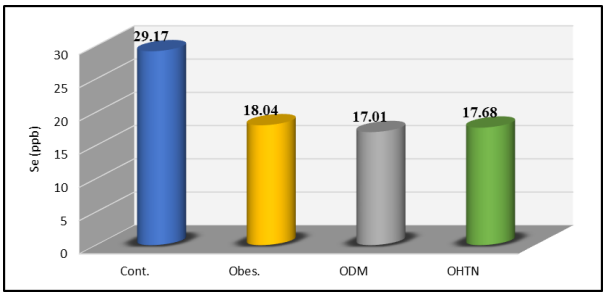

Figure No.2: Serum Se levels of studied groups

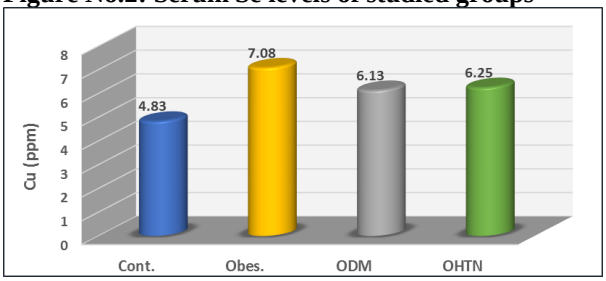

Figure No.3: Serum Cu levels of studied groups

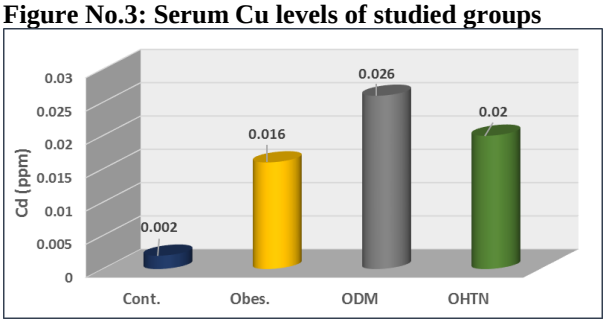

Figure No.4: Serum Cd levels of studied groups

4. Serum Heavy metals Levels: Cd and Pb concentration a significant increase in all patients' groups in comparison with the control group ($p \leq 0.05$). While there was no significant difference in each Cd and Pb concentration between the obese-DM group and the obese-HTN group compared with the obese group ($p \leq 0.05$). As shown in Table 4 and Figures 4 & 5.

Table No.4: Serum Cd and Pb concentrations of studied groups

Groups	No.	Pb (ppm) Mean ±SD	Cd (ppm) Mean ±SD	
Cont.	35	0.041 ± 0.009 [b]	0.002 ± 0.007 [b]	85% of cases were BDL
Obes.	35	0.048 ± 0.005 [a]	0.016 ± 0.025 [a]	63% of cases were BDL
ODM	35	0.046 ± 0.008 [a]	0.026 ± 0.030 [a]	54% of cases were BDL
OHTN	35	0.047 ± 0.007 [a]	0.020 ± 0.031 [a]	68% of cases were BDL
P-value		0.001 **	0.001 **	
LSD		0.003	0.014	

*** P-value ≤ 0.05 consider significant, BLD: Below detection limit.**
*** At the 0,05 level, the mean difference is significant.**

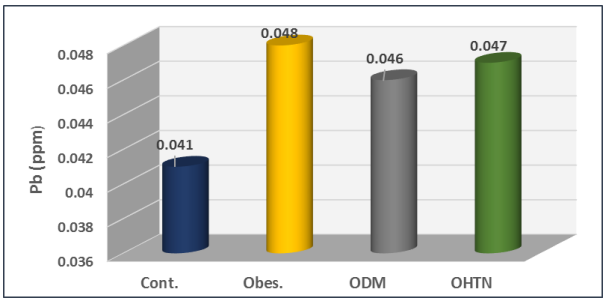

Figure No.5: Serum Pb levels of studied groups

DISCUSSION

Evaluation of Serum Malondialdehyde Levels: The present results showed that the MDA level was increased in all patient groups in comparison with control group, these results agreed with a study by Abu Khadra et al. (2024)[8], Serum MDA levels are significantly connected with obese DM and obese HTN groups, possibly due to the detrimental effect of oxidative stress on vascular endothelial dysfunction, which is strongly linked to elevated blood pressure produced by poor vasodilation[9]. Recent research reveals that oxidative stress plays a critical role in the development of various metabolic disorders including T2DM, have been suggesting several hypothesized mechanisms including oxidative stress[10]. The biomarkers of oxidative damage are higher in individuals with obesity and correlate directly with BMI. Moreover, an increase in the MDA levels in association with increased BMI was obtained indicating that obesity could predispose to free radical-mediated lipid peroxidation [11].

Adipose tissue in obesity builds up and releases adipokines, which in turn trigger the creation of pro-

inflammatory cytokines and, eventually, more reactive oxygen species (ROS), which can harm cellular constituents and cause inflammation and chronic illnesses [12]. Balancing the redox state of adipose tissue may be a feasible treatment target for obesity, as research has demonstrated that elevated oxidative stress in adipose tissue is a precursor to metabolic syndrome [13]. an alternative inflammatory pathway replaces the traditional lipolytic pathway in obesity. ROS and RNS can influence these pathways at different levels. adipose tissue primarily undergoes structural and functional alternations as a result of sever and protected lipolysis, or lipotoxicity. The weakening of insulin sensitivity marks the conclusion of the physio pathogenic cascade, Finelly, we stress how crucial antioxidants are to reestablishing the internal environment balance [14]. Reduced biogenesis, changed membrane potential, because overproduction of free radicals in obesity. In addition to the overabundance of nutrients, the result is the overburdening of the mitochondrial respiratory chain and the Krebs cycle. This is the process that triggers mitochondrial malfunction, which leads to the production of more ROS.[15].

Evaluation of Serum Trace Elements Levels: This study was conducted that a significant increase in Cu levels and significant decrease in Se levels in all patients' groups in comparison with the control group. Our results agree with the Tagar study, which found that Cu is elevated in obese populations [16]. Obese participants' elevated serum Cu levels support the meta-analysis's conclusion that there is a positive correlation between elevated serum Cu and obesity [17]. High serum Cu levels were also found to be associated with increased BP in obese HTN patients, as well as there were positive associations between BMI and Cu ($p<0.05$), according to Darroudi et al [18]. Copper can influence oxidative stress, which is a fundamental mechanism in the development of obesity, "Positive association between Cu status and atherogenic lipid profile and be mediated through the impact of Cu on lipid metabolism." [17]. Similarly, another study has also shown that serum Cu levels were significantly higher in overweight and obese patients than in those of normal weight. Our results corelates with the study by Tinkov et al, suggesting that the obese women Se levels in both serum or hair samples were found to be inversely linked with obesity, obese subjects' serum Se levels were much lower than the normal ranges needed for normal selenium function, while Cu levels positively linked with obesity [18]

Evaluation of Serum Heavy metals Levels: Epidemiologic studies have suggested a role for the toxic metals lead (Pb), cadmium (Cd), and mercury (Hg) in the development of metabolic syndrome. All three elements have been shown to interact with obesity in various ways, like substituting for essential trace elements or increasing the risk for developing DM and HTN. When these elements take the place of vital micronutrients like iron and Zinc, they may catalyze oxidative stress responses and harm cells, enzymes, and genes. Pb leads to oxidative stress, which destroys sections of cell components. On the other hand, metal neurotoxicity on brain function and signaling linked to appetite and satiety may potentially play a role in the development of obesity, since brain development is affected by both Pb and Cd. Additionally, it damages the body by acting as endocrine disruptors which change physiological processes and induce chronic inflammation[19]. By substituting Fe and Cu in cytoplasmic and membrane proteins, Cd may indirectly produce free radicals by raising the concentrations of weakly or unattached Cu and Fe. Additionally, Cd may replace zinc in metalloproteins and enzymes, leading to buildup and dysfunction in soft tissues like the kidney and liver. Pb is associated with higher blood concentrations of soluble adhesion molecules. Changes in contractility, interruption of blood flow, arterial stiffness, and HTN are all consequences of these changes in vascular function· Despite that, published studies on the correlation between BMI and toxic metals have shown ambiguous results. However, found a negative correlation between BMI and 'whole blood and urine Pb and Cd' these inverse relations have been difficult to explain, but seem to bein dependent of age and gender.[19]

Abbreviations:

Symbol	Meaning
AT	Adipose Tissue
BMI	Body Mass Index
BDL	Below detection limit.
BP	Blood Pressure
Cd	Cadmium
Cont.	Normal healthy group
Cu	Copper
CVDs	Cardiovascular diseases
DM	Diabetes Mellitus
F	Female
Hg	mercury
HTN	Hypertension
LSD	least significant difference
M	Male
No.	Number of subjects
Obes.	Just obese patients' group
ODM	Obese diabetes patients' group
OHTN	Obese hypertensive patients' group
OS	Oxidative stress
Pb	lead
Se	Selinum
SD	Standard deviation
SPSS	Statistical Package for the Social Sciences
T2DM	Type 2 Diabetes Mellitus
Zn	Zinc

CONCLUSION

This study concluded that the obese patients with T2DM and with HTN had high significant level of

MDA, Cu and heavy metals (Pb and Cd) and low significant level of Se than control group.

Limitations: The major limitation of this study was in the small sample sizes of the Obese, HTN, T2DM and control groups. In addition, this study was only a one province study. As a next step, we are planning to expand the sample size and conduct multi-provinces research. Additionally, well-designed, each gender-separately specific prospective studies are needed to evaluate the role of trace elements and heavy metals in the development of obese complications.

Author's Contribution:

Concept & Design or acquisition of analysis or interpretation of data:	Ruaa. K. Abbas, Jamal Harbi Hussein Alsaadi
Drafting or Revising Critically:	Ruaa. K. Abbas, Jamal Harbi Hussein Alsaadi
Final Approval of version:	All the above authors
Agreement to accountable for all aspects of work:	All the above authors

Conflict of Interest: The study has no conflict of interest to declare by any author.

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