Evaluation Iron (Fe) and lad (Pb) effect on Diabetes mellitus2 patients in Erbil Governorate

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Abstract

Diabetes mellitus (DM) is a complex, chronic illness requiring continuous medical care with multifactorial risk-reduction strategies beyond glycemic control to preventing acute complications and reducing the risk of long-term complications. Therefore, Iraq is one of the 19 countries and territories of the International Diabetes Federation (IDF)The target of present work is to study some cases of people evaluation Iron (Fe) and led (Pb) effect on DM2 patients in Erbil governorate lead was estimated by using Flam atomic absorption spectrophotometry (FAAS) and the estimation of iron by used randox manual kit, while the grafite Furnace Atomic Absorption Spectrophotometry (GFAAS) was used in the estimation of chromium and Estimation of iron using RANDOX kit which based on colorimetric method. Data were revised, coded, and analyzed using the "Statistical Package of Social Science(SPSS) version 26.0. These results In patient group lower serum iron concentration have been found compared to healthy Lead raises the oxidative pressure on living organisms,and may potentially contribute to diabetes

Keywords: *DMII patients, Iron (Fe), lad (Pb), toxic heavy element.*

تقييم تأثير عنصري الحديد والرصاص على مرضى السكري النوع الثاني في محافظة اربيل

أ.م.د. احمد سعدي حسن

الخلاصة

مرض السكري (DM) هو مرض مزمن معقد يتطلب رعاية طبية مستمرة مع استراتيجيات للحد من المخاطر متعددة العوامل تتجاوز السيطرة على نسبة السكر في الدم للوقاية من المضاعفات الحادة وتقليل مخاطر حدوث مضاعفات طويلة الأجل. لذلك ، يعد العراق واحدًا من 19 دولة ومنطقة تابعة للاتحاد الدولي للسكري .(IDF) الهدف من العمل الحالي هو دراسة بعض حالات تقييم الأشخاص لتأثير الحديد (Fe) والقيادة (Pb) على مرضىالسكري النوع الثاني DM2 في محافظة أربيل. تم تقديره باستخدام مطياف الامتصاص الذري باللهب (FAAS) وتقدير الحديد بواسطة مجموعة راندوكس اليدوية المستخدمة ، بينما تم استخدام مقياس الطيف بالامتصاص الذري لفرن الجرافيت (GFAAS) في تقدير الكروم وتقدير الحديد باستخدام مجموعة RANDOX التي تعتمد على طريقة القياس اللوني . تم مراجعة البيانات وترميزها وتحليلها باستخدام "الحزمة الإحصائية للعلوم الاجتماعية (SPSS) الإصدار 26.0. هذه النتائج وُجد أن تركيز الحديد في مصل الدم أقل في مجموعة المرضى مقارنةً بالرصاص الصحي يرفع ضغط الأكسدة على الكائنات الحية ، وقد يساهم في الإصابة بمرض السكري.

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الكلمات المفتاحية: مرضى السكري من النوع الثاني , الحديد , الرصاص , سمية المعادن الثقيلة .

Introduction

Diabetes mellitus (DM) is a metabolic disorder with heterogeneous aetiologies, which is characterized by chronic hyperglycaemia and disturbances of carbohydrate, fat and protein metabolism resulting from defects in insulin secretion, insulin action or both. Diabetes may present with characteristic symptoms such as thirst, polyuria, polydipsia, blurred vision, weight loss and sometimes polyphagia. However, often, symptoms are not severe or may be absent, and consequently in the absence of routine biochemical screening, hyperglycaemia sufficient to cause pathological and functional changes may be present for a long time before the diagnosis is made. Several pathogenic processes are involved in the development of diabetes. These include processes that impair or destroy the function of the pancreatic beta cells, with consequent insulin deficiency, and others that result in resistance to insulin action [1].

The term trace elements refer to very small quantities of chemical elements found in the natural material. In biochemistry, a trace element is the dietary mineral essential for the proper growth, development and physiology of the organism in very minute quantities [2]. Trace elements play an important role in the maintenance of an organism's healthy state. As a consequence, disruptions in homeostasis of trace elements can lead to the development of diseases and pathologic states. Such a deficit frequently occurs due to increased requirements of an organism or inadequate trace element content in foods. Conversely, excessive entry of toxic metals in to the organism are directly related to adverse environmental conditions [3]. Trace metals are important for normal human homeostasis in the right proportion and concentration. Analysis of trace elements in human tissues has been of great interest because of their role in normal physiological and biochemical processes. Some trace metals are believed to be carcinogenic and able to cause a toxic effect by forming free radicles and acting as cofactors in the oxidative damage of the biological macromolecules and DNA. The general public is exposed to non-essential heavy toxic metals at various concentrations by consuming polluted food and water or through contact with contaminated air, soil, smoking tobacco and alcoholic drinks [4]. The toxic heavy metal can affect human health through oxidizing cell stress, neurological or renal injury, damage to DNA or altered glucose. There is emerging evidence that diabetes leads to imbalances in trace element homeostasis such as zinc and copper. Iron is a chemical element with an atomic number 26 and with(Fe) symbol. It is the most abundant metal in human body. The body content of Fe is about 3-4 g, which corresponds almost to a concentration of 40-50 mg per kilogram of body weight [5]. About 2/3 of total iron in the body is incorporated in the hemoglobin. Red blood cells, muscles, liver and bones are rich in iron. The optimal daily intake of

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iron is 10-20 mg, while the toxic level is 200 mg and the lethal dose is 7-35 g. Red meat, liver beans, peas, lentils, nuts, seafood, seeds, fish, poultry, leafy vegetables are rich sources of dietary Fe. It has been found that Fe in meat is absorbed more easily than Fe in the vegetables [6]. Iron is absorbed from diet when there is need and ferritin is the iron transport form. Iron absorption is enhanced when the stores in body are depleted. Hepcidin is the peptide hepatic hormone is important for systemic iron regulating. It regulates intestinal iron absorption, tissue iron distribution and plasma iron concentrations via inducing degradation of its receptor and cellular iron producer ferroportin. Ferroportin exports the iron into plasma from absorptive enterocytes, from macrophages that recycle iron from the senescent erythrocytes, and from iron-storing hepatocytes [7]. Hepcidin deficiency causes hemochromatosis. Deficiency of this important trace element will cause severe disorders, most important of them is iron deficiency anemia, tiredness, Microcytic hypochromic RBC's, impaired attention, irritability atrophy of epithelium, and lowered memory are some of the features of iron deficiency anemia. While prolonged or chronic accumulation of iron in the body occurs there is a hepatic failure, testicular atrophy, diabetes, arthritis, cardiomyopathy, hyperpigmentation, and peripheral neuropathy [8]. Fe is the essential element of organisms, a constituent of various enzymes and proteins. It is currently believed that overload of iron strongly associates with resistance to insulin, hyperglycemia and increased risk of Diabetes mellitus2. Many researchers think that Fe causes diabetes through oxidative stress and direct damage to pancreatic β cells. Increased dietary heme iron and the high stores of body iron, as measured by serum ferritin, are combined with an increased risk of T2DM and other insulin resistance states. A common disorders of the iron overload complication such as hemochromatosis is diabetes mellitus. In hemochromatosis, iron accumulates into pancreatic cells, where it is believed to have a direct toxic effect on β cells through inducing oxidative stress, apoptosis and thereby impairing the insulin secretion, however iron overload have toxic effects on liver and causes insulin resistance. In secondary overload of iron everywhere hepcidin is upregulated and the expression of ferroportin is reduced, iron accumulates into adipocytes and contributes to insulin resistance via reducing production of insulin-sensitizing hormone adiponectin [9].

Lead is the most important toxic heavy element in the environment. It was the first element that was characterized by its type of toxicity with symbol Pb (from Latin: Plumbum, meaning“the liquid silver”). Human exposure to the pb and its compounds occurs mostly in a lead related occupations with different sources like leaded gasoline, industrial processes such as smelting of lead and its combustion, pottery, lead based painting, boat building, lead containing pipes, battery recycling, printing of books. pb is a metal with high poisonous effect every organ in the body [10].

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Studies comparing the levels of essential trace elements in biological samples of patients with type 2 diabetes mellitus with those of non-diabetic subjects have shown that deficiency and accumulation of some essential trace metals that play a role in the development of diabetes mellitus [11]. Particularly, individuals live in poor urban areas with older housing stocks, are at high risk of pollution from lead. There are few studies available about incidence of chronic metabolic disease like DM T2 due to an effect of lead exposure. Pancreatic beta-cells appear to be extremely sensitive to the reactive oxygen species (ROS). Several antioxidants, which includes N-acetyl cysteine, lipoic acid and vitamin C, reduced resistance to insulin in type 2 diabetes. It is still to be determined if antioxidant medication can prevent or slow the development of T2DM and to identify the signaling pathways that can be modulated to reduce the volume of oxidative stress in pancreatic islets. Recent studies show a strong correlation of blood lead with oxidative stress markers in general population and indicate that Pb induced oxidative stress should be consideration given to developeing lead mediated illness. Pb is toxic to most organs in human body and interfering with metabolism and cellular function. The human body does not have any mechanism for excreting heavy metals like Pb and it can accumulate in the body that lead to develpe health problems [12].

Finally, there is no such analysis, to the best of our knowledge performed where the trace factor, heavy metal and resistin, leptin hormone are analyzed together and the findings are often contradictory in separate studies. The aim of this analysis is to highlight conflicting serum lead, zinc, copper, chromium, Iron, resistin and leptin level in DM T2 patient [13]. This study aimed Determination the concentration of Iron (Fe) and lead (Pb) in the blood of male and female with type 2 diabetic patient and healthy control Correlation between selected (Fe) element and (pb) that are estimated among cases.

Material and Method

This resent study was carried out at main medical facilities in Erbil and National Center for Teaching Laboratories, Poisoning Consultation Center / Specialized Surgeries Hospital, Iraq during the period from 2020. It included 50 participants; divided into 2 groups (25 patients with type 2 diabetes and 25 healthy control) and 2 subgroups. The type 2 diabetic patient group were subdivided into (male, female) with age (30-65years) and healthy control group subgroup (male, female) with age (30-65 years). Estimation of Lead 2.5 ml of Trichloroacetic acid (TCA) was added to (2.5) ml of whole blood then mixed well with a wooden stick, and centrifuged for 10 minutes at 3000 rpm to remove cellular debris. The supernatant was transferred to a clean plane tube and directly aspired to

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the flames (FAAS). The prepared standard concentration (0.0,0.5,1.0,1.5) µg / dl was used to determine a standard curve.

Range of Lead (0-25) µg/dl, Estimation of iron

About 250 µl of serum was used to estimate serum iron by using RANDOX kit which based on colorimetric method.

Results and Discussion

Age characteristics of patients and control

This study included the type 2 diabetic patient group were subdivided into (male, female) with age (30-65) years and healthy control group subgroup (male, female) with age (30-65) years from Erbil respectively.

With a mean± SD. of (49.40±9.461) and (45.30±8.87) years respectively as shown in table (3-1). The age rang for male and female patients group was (30-64) and (30-65) years respectively with a mean ± SD. Of (47.00±10.17) and (53.00±8.86) years respectively.

Table (3-1) :(Mean± SD) of study groups (Male and Female) According to Age (years).

		Male		Female		Total	
		Range	**Mean± SD.**	**Range**	**Mean± SD.**	**Range**	**Mean± SD.**
Age years	Control	30-65	49.44± 9.87	30-65	47.60±9.51	30-65	42.30±8.87
	Patients	30-64	47.30±10.17	30-65	53.28±8.86	30-65	44.40±9.461

These result were compatible with a study done in Baghdad Alaa.S.H. who reported that the T2DM most frequently during the fourth and fifth decades of male and female life [14]. Decreased pancreatic islet activity and increased risk of T2DM are associated with advancing.

Similarly, these result were compatible with El Omri, et al. supporting the T2DM which frequently occurred through the fifth decade of age**)**. Metabolic disorders including cardiovascular disease and DMT2, decline in lean body mass and increase fat in the body, especially visceral adiposity, which often accompanies aging and may contribute to insulin resistance development. As for the type 2 diabetes mechanism, it is understood that aging causes a reduction in insulin sensitivity and alteration

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or inadequate compensation of the functional mass of beta cells in the face of increased insulin resistance. Aging is associated with a decreased proliferation of beta-cells capacity and enhance the sensitivity to apoptosis**.**

- Body mass index (BMI) of patients and control

The mean BMI for patients and control groups was (34.90±4.59 Kg/m^2) and (28.96±4.88 Kg/m^2) respectively as shown in table (3-2) and figure (3-1). Male patients had mean BMI of (30.86±4.51) Kg/m^2, while female patients had mean BMI of (34.93±4.52) Kg/m^2. The mean BMI for male and female control was (31.96±5.16) and (32.91±4.59) Kg/m^2 respectively.

Table (3-2): Descriptive Statistic of BMI in Study Groups.

		Male	Female	Total
		Mean± SD.	**Mean± SD.**	**Mean± SD.**
BMI Kg/m^2	**Control**	(28.21±5.16)	(34.91±4.27)	31.96±4.88
	patient	(31.86±4.51)	(33.93±4.52)	32.91±4.59

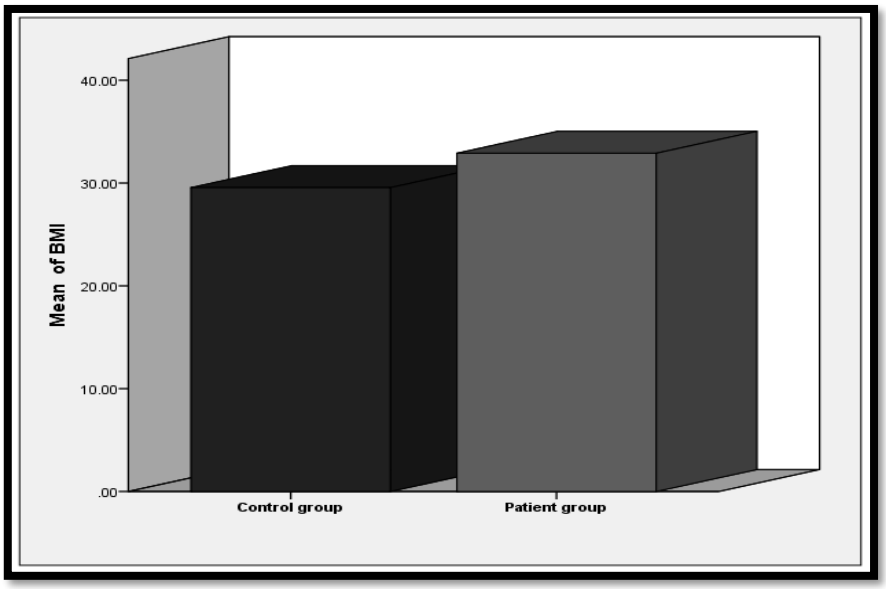

Fig. (3-1): Mean value of BMI among study groups (patient &control).

These study findings are compatible with a study by Asiimwe. *et al*. who observed that the incidence of T2DM was more frequent in overweight people [16]. Epidemiological studies have improved our understanding better for environment ,psychological and biological risk factors for T2DM.

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Rising adiposity is the single most significant risk factor for T2DM ,as reflected by higher BMI rates Increase body weight is a diabetes risk factor and therefore a containing factor complication risk factor for those with demonstrated diabetes.

A Zunt et al. study suggested BMI as one of the reason that increased a diabetes incidence in almost all of countries**.**

- The Level of serum (Fe) in patients and healthy control groups according to gender

The result summarized in table (3-3) and figure (3-2) and showed that the total mean of serum serum iron concentration in control group (136.939±12.492ug/dl) was significantly higher than that in the patients group (95.632±24.581ug/dl). In addition, there was significantly higher serum iron concentration in male control (142.436±9.910ug/dl) than that of female control (120.668±18.781 ug /dl). On the other hand, female patients had significantly lower mean serum iron concentration than that of male patients (86.340±17.855and 102.524±27.901 ug/dl respectively). mean serum iron in female control was significantly higher than female patient (128.442±12.548 and 87.640±17.855 ug/dl) respectively. Highly significant difference between male patients and male control)102.524±27.901 and140.436±9.910 ug/dl) respectively.

Table (3-3): Comparison of serum (Fe) concentration among studied Groups in relation to gender.

Fe (ug/dl)	Total (Mean± SD.) ug/dl	Male (Mean± sD.) ug/dl	Female (Mean± SD.) ug/dl	t-test	P-Value	C.S
Control	136.939±12.492	142.436±9.910	128.442±12.548	2.938	.001	P<0.01 (HS)
Patient	95.632±24.581	102.524±27.901	87.640±17.855	2.443	.018	P<0.05 (S)
t-test	9.988	6.202	9.476			
P-Value	.000	.000	.000			
C.S	P<0.01 (HS)	P<0.05 (HS)	P<0.01 (HS)			

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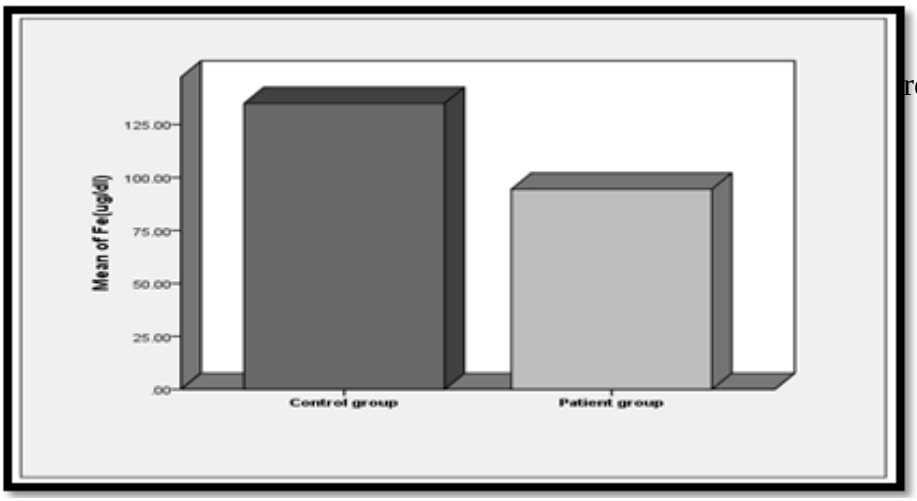

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Fig. (3-2): Mean value of Fe among study groups (patient and control)

In patient group lower serum iron concentration have been found compared to healthy subject confirming result demonstrated by Pechlaner, et al., which also well reported in our study Moreover these result compatible with Ahmed, et al., who was reported lower serum iron level in patient with T2DM compared to control [17]. These result were compatible with Atalay et al., who was reported that serum iron significantly lower in women with T2DM patient compared to the healthy controls. Iron concentration in healthy men is higher than women, menstruation is the major cause of iron loss in women [18].

Considered hyperglycemia lead to increase oxidative stress, which reduced circulation of free iron, and elevated hepcidine that is a negative regulator in metabolism of iron during chronic disease such as T2DM that lead to inhibition of iron intestinal absorption [19].

- **The Level of of blood lead in patient and control groups according to gender**

patients (23.38±3.63 as shown in table (3-4) and figure (3-3) the mean of total blood lead in ug/dl) was significantly higher than that of the control group (16.38±3.09 ug/dl). There was a highly significant difference between males and females in the patient group (P<0.01). In addition, there was a highly significant difference between (male and female) in the healthy control groups (18.300±2.121and 12.960±2.615µg/dl). Male patient was significantly higher than male control with mean (23.940±2.911 and17.200±2.121µg/dl). Also female patient have higher blood lead level than female control (18.920±2.170 and 12.960±2.615 respectivelyµg/dl).

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Table (3-4): Comparison of blood (Pb) concentration among studied groups in relation to gender.

Pb (ug/dl)	Total (Mean± SD.) ug/dl	Male (Mean± SD.) ug/dl	Female (Mean± SD.) ug/dl	t-test	P-Value	C.S
Control	16.38±3.09	18.300±2.121	12.960±2.615	5.405	.000	P<0.01 (HS)
Patient	23.38±3.63	23.940±2.911	18.920±2.170	7.051	.000	P<0.01 (HS)
t-test	10.384	10.606	9.063			
P-Value	.000	.000	.000			
C.S	P<0.01 (HS)	P<0.01 (HS)	P<0.01 (HS)			

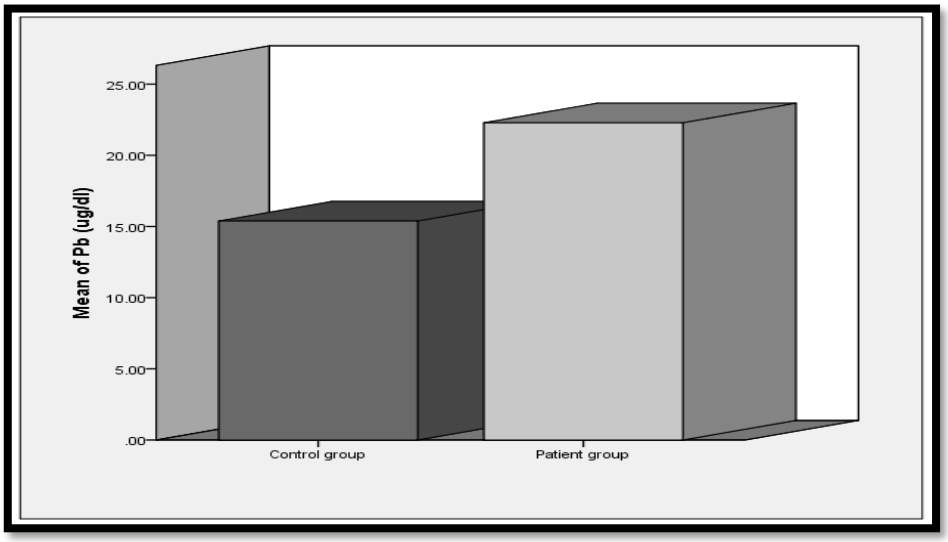

Fig.(3-3): Mean value of blood Pb among study groups (patient and control).

These results were in agreement with Al-Anbari,et al., who was indicated a higher concentration of blood lead in T2DM patient compared to healthy control **[**20] **.** Recent study indicated a astrong association between Pb and oxidative stress markers in the general population and suggested that oxidative stress should be taken into account when developing and mediated diseases . Lead raises the oxidative pressure on living organisms,and may potentially contribute to diabetes, because Pb is a pro-oxidant and oxidative stress is thought to stimulate the diabetes mellitus by having direct effects on cell signaling pathways affecting signaling of insulin Male sex, older age ,smoking, lead in paints and pipes , moonshine drinking , urban residence, low socioeconomic and housing in older building are factors that are related to high levels of blood lead .Our result showed higher level of blood lead

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in the blood of males compared to the females, and in agreement with Kelsall, et al., who showed that the mean blood lead level for males was significantly higher (p<0.001) than the level for females [21].

These results are also in agreement with a study conducted in Saudi Arabia, where the concentration of blood lead in males was higher than in females, this could be explained by a greater prevalence of smoking in male participants in addition with their more outdoor activities with greater exposure to sources of pollution from lead.

3.5. The correlation coefficient between BMI and (Fe, pb) among groups

Data in table (3-5) showed that there was a positive sigificant correlation between iron and BMI in healthy control. While there was no significant correlation between BMI and the other selected elements(Pb) in both patients and control groups.

Table (3-5): Simple correlation coefficient between BMI and (Fe, pb) among groups.

	Patient(n=50)		**Control(n=50)**	
	R	**P (C.S)**	**R**	**P(C.S)**
Fe (µg/dl)	-0.121	.503 (NS)	0.303	.043 (S)
Pb(µg/dl)	-0.227	.212 (NS)	-0.188	.200 (NS)

Obesity is a risk factor for many illnesses including T2DM, hypertension, cardiac disorder, stroke, dyslipidemia osteoarthritis, gynecological complications, sleep apnea and difficulties with the breathing. Studies have suggested that obesity adversely affects the iron status.

A study by [22] was found a negative significant correlation coefficient between BMI and serum iron **(Huang, *et al*.,2015)**. This difference may be due to the difference in the diet or the small size of the sample, as well as.

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