

Serum iron levels in correlation with serum lead, and serum calcium levels in diabetic patients

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الخلاصة:

أكدت البحوث الطبية الحديثة ان هناك احتمالية وجود ربط بين مستويات الحديد ومرض السكري وتهدف هذه الدراسة الى قياس مستويات الحديد في مرضى السكري ومقارنتها مع الاصحاء، ولقد شملت هذه الدراسة ايضا قياس مستويات كل من الكالسيوم والرصاص في مصل الدم لدى مرضى السكري لغرض تقييم علاقتها مع المرض وعلاقتها مع مستويات الحديد.

هذه الدراسة تضمنت 30 مريضا بالسكري احيلوا الى العيادة الخارجية في مستشفى بغداد التعليمي هؤلاء المرضى يختلفون في اعمارهم (30-70 سنة) ومدة المرض (1-22 سنة) مقارنة ب 20 من الاصحاء ظاهريا (غير مصابين بالسكري) لهم نفس المدى العمري.

تقييم الكالسيوم والرصاص والحديد انجز بواسطة طريقة الامتصاص الذري.

في هذه الدراسة لم تكن هناك فروقات معنوية في كل من مستوى الرصاص والحديد في مصل دم مرضى السكري مقارنة بالاصحاء في حين هناك زيادة معنوية في مستوى الكالسيوم في المرضى مقارنة بالاصحاء. ($p < 0.0001$)

هناك علاقة عكسية بين مستوى الكالسيوم والحديد ($r = -0.398$) وعلاقة ضعيفة عكسية بين مستوى الرصاص والحديد ($r = -0.069$) وهناك ايضا علاقة ضعيفة مباشرة بين مستوى الرصاص والكالسيوم ($r = 0.027$) وجدت في المرضى .

ان دور الحديد في تطور مرض السكري لايزال غير واضح وعلى المرضى اللذين يستخدمون الادوية المدعمة بالحديد ان يستخدموها بحذر وخصوصا المرضى المصابين بالسكري لفترة طويلة.

Abstract:

Recent medical researches suggest that there may be a link between iron levels and diabetes . The objective of this study is to measure serum iron levels in diabetic patients and compared with healthy controls .The study also include the measurement of both serum calcium ,and serum lead levels in diabetic patients and the correlation between these two elements and the disease ,and the correlation between these elements and iron level in diabetic patients.

This study included 30 patients had diabetes were submitted to the out patients clinic of Baghdad Teaching Hospital. Those patients were varying in their ages (30-70 years) and duration of disease (1-22 years) compared with 20 apparently healthy controls (non diabetic), with the same range of age. Calcium, lead, and iron estimation were done by atomic absorption method.

In this study there is no significant changes were found in both serum lead levels of the patients compared with the controls and serum iron levels of the patients compared with the controls , While there is a significant changes in serum calcium levels of the patients compared with the controls $p < 0.0001$. Also there is inverse correlation between serum calcium and serum iron ($r=-0.398$) , a weak inverse correlation between serum lead and serum iron ($r=-0.069$),and a direct weak correlation between serum calcium and serum lead($r=0.027$) were found in the patients.

The role of iron in diabetes development still unclear, and the patients should carefully use iron supplements particularly patients with long duration of the disease.

Keywords: Diabetes, Iron, Calcium, Lead.

Introduction:

There is an increasing concern about the relationship between iron status and diabetes^[1].

The role of micronutrients in the etiology of diabetes is not well established, several lines of evidences suggest that iron may play arole in the pathogenesis of diabetes and have an association with the risk of type 2 diabetes^[2].Excessive body iron is found to be associated with diabetes^[3].

It was found that elevated iron levels can damage cells and interfere with the function of organs, which may affect the body use of insulin^[4].

Diabetes affect 30%-60% of patients with hereditary hemochromatosis ,due primarily to iron induced β cell failure^[5].

Iron is a transition metal that can easily become oxidized and thus act as an oxidant. The general effect of catalytic iron is to convert poorly reactive free radicals, such as H_2O_2 , into highly reactive ones, such as the hydroxyl radical. Increased accumulation of iron affects insulin synthesis and secretion in the pancreas^[6] and interferes with the insulin-extracting capacity of the liver^[7]. Iron deposition in muscle decreases glucose uptake because of muscle damage^[8]. Conversely, insulin stimulates cellular iron uptake through increased transferrin receptor externalization^[9]. Thus, insulin and iron can mutually potentiate their effects, leading, after a vicious cycle, to insulin resistance and diabetes. Others^[10] have described a relationship between serum ferritin and several components of the insulin resistance syndrome in seemingly healthy subjects. Serum ferritin was

proportional to serum glucose concentration, and insulin resistance^[11]. In fact, the higher the ferritin levels, the higher the incidence of type 2 diabetes in recent epidemiological studies^[12].

It increasingly recognized that iron influence glucose metabolism ,even in the absence of significant iron over load in the general population ,and body iron stores are positively associated with development of glucose intolerance ,and type2 diabetes.^[13] Iron metabolism is closely associated with the clinical presentation of numerous systemic disease such as diabetes^[14].

Iron can modify hepatocytes insulin sensitivity by interfering with insulin receptors and intracellular insulin signaling^[15].A study found that the effect of iron depletion is possibly related to an improvement of insulin signaling and increase insulin receptors binding^[16], therefore Blood letting resulted in 50% reduction in serum ferritin concentration which improve hyperglycaemia and insulin sensitivity in diabetic patients,and Phlebotomy is followed by areduction in insulin resistance and an increased insulin release in diabetic patients^[17].It was found that there is low iron status and enhanced insulin function in vegetarians^[18].

Blood donation is simultaneously associated with increased insulin sensitivity and decreased iron stores, stored iron seems to impact negatively on insulin action even in healthy people associated with increased insulin sensitivity and not just in classic pathologic conditions associated with iron overload (hemochromatosis and hemosiderosis),^[19].

It was found that diabetes is a common complication in individuals with massive iron over load, this lead to speculation that high iron stores increase the risk of developing type 2 diabetes, and the dietary intake is the major source of body iron stores and accumulation with age in men^[20].

Transferrin and iron induce insulin resistance of glucose transport in adipocytes, therefore this finding may further explain the association between body iron store and risk of type2 diabetes^[21].

Iron chelating agents and blood donation can prevent the development of type2 diabetes^[22].

Glycaemic control was also correlated with excess iron and improvement in glycaemic control achieved by iron reduction support adirect role for iron and strengthens the call for chelation in patients with excess iron^[23].

Materials and Methods:

Thirty diabetic patients enrolled in this study, they were submitted to the out patients clinic of Baghdad Teaching Hospital. Those patients were varying in their ages (30-70) and duration of disease (1-22 years) compared with 20 apparently healthy controls (non diabetic), with the same range of age.

Calcium, iron and lead were estimated by atomic absorption method.

Statistical analysis were done by Microsoft Excel 2007 using Student t-test, considering $p < 0.01$ as significant value, and correlation test.

Results:

The mean \pm SD for the patients and controls were shown in (Table 1 and 2). There was a significant changes in serum calcium levels of the patients compared with the controls $p < 0.0001$ (Table-3), while no significant changes were found in both serum lead levels of the patients compared with the controls and serum iron levels of the patients compared with the controls.

Age	Duration of the disease	Pb (Pmm)	Ca (Pmm)	Fe (Pmm)
47.266 \pm 11.063	6.216 \pm 6.068	0.106 \pm 0.128	0.148 \pm 0.061	0.054 \pm 0.016

Table-1: Mean \pm SD for patients

Age	Pb(Pmm)	Ca (Pmm)	Fe (Pmm)
45.05 \pm 10.205	0.090 \pm 0.094	0.086 \pm 0.027	0.055 \pm 0.024

Table-2: Mean \pm SD for controls

	Controls Mean \pm SD	Patients Mean \pm SD	p-value
Pb(Pmm)	0.090 \pm 0.094	0.106 \pm 0.128	0.6 NS
Ca(Pmm)	0.086 \pm 0.027	0.148 \pm 0.061	0.0001
Fe(Pmm)	0.055 \pm 0.024	0.054 \pm 0.016	0.9 NS

Table-3: The changes in serum lead, calcium, and iron in controls and patients.

NS not significant

There were inverse correlation between serum calcium and serum iron ($r = -0.398$), a weak inverse correlation between serum lead and serum iron ($r = -0.069$), and a weak direct correlation between serum lead and serum calcium ($r = 0.027$) in the patients (Table-4).

There were inverse correlations between serum calcium and serum iron levels ($r = -0.398$), a weak inverse correlation between serum lead and serum iron levels ($r = -0.069$), and a weak direct correlation between serum lead and serum calcium ($r = 0.027$) in the controls (Table-5).

Element	Corellation with Pb(Pmm)	Correlation with Ca (Pmm)	Correlation with Fe (Pmm)
Fe (Pmm)	-0.069	-0.398	-----
Pb (Pmm)	-----	0.027	-0.069
Ca (Pmm)	0.027	-----	-0.398

Table-4: The correlations between Pb, Ca, and Fe levels in the patients.

Element	Corellation with Pb (Pmm)	Correlation with Ca (Pmm)	Correlation with Fe (Pmm)
Fe (Pmm)	-0.028	-0.163	-----
Pb (Pmm)	-----	-0.162	-0.028
Ca (Pmm)	-0.162	-----	-0.163

Table-5: The correlations between Pb, Ca, and Fe levels in the controls

This study revealed a significant changes in serum Fe compared with serum Pb $p < 0.03$, ahightly significant changes in serum Fe compared with serum Ca $p < 0.0001$, and a non significant changes in serum Pb compared with serum Ca (table-6).

	Pb (Pmm) Pb	Ca(Pmm) Ca	Fe (Pmm) Fe
Pb(Pmm)	-----	0.117343052	0.036847942
Ca(Pmm)	0.117343052	-----	0.0001
Fe(Pmm)	0.036847942	0.0001	-----

Table-6: P value of the patients with their finding of Pb, ca, and Fe.

Discussion:

Iron interferes with insulin inhibition of glucose production by the liver, hepatic extraction and metabolism of insulin decrease with increase iron stores leading to peripheral hyperinsulinemia ^[24]. Mechanisms through which iron causes insulin resistance with ultimate impact on glucose homeostasis probably exist in the liver ^[25]. Insulin resistance may be the cause rather than the consequence of disturbances in iron metabolism ^[26]. Other workers suggest that hyperglycaemia may precedes the elevation of iron levels in diabetes ^[27], while other researchers have found that there is asignificant association between decrease in iron stores and neonatal hypoglycaemia ^[28].

In our study it was found that there is no significant changes in serum iron levels in the patients compared with the controls levels .Other studies found that anemia is a common finding in diabetic patients ^[29], anemia associated with micro and macrovascular complications in diabetic patients ^[30], and there is no correlation between plasma ferritin level and glycemic control or diabetic microangiopathic complications ^[31].

One prospective cohort study in the US showed that heme iron intake from non red meat sources were not associated with the risk of type 2 diabetes ^[32]. Other study found that an elevation in serum ferritin can be seen in pre-diabetes stage, before the occurrence of an overt diabetes mellitus ^[33].

In this study it was found that there is a strong inverse correlation between serum calcium and serum iron levels in the patients, which agreed with

Many studies showed that calcium decrease iron absorption and bioavailability and down regulating iron transport into the cell ^[34], also other study indicate that calcium reduce and delay the uptake of iron from (FeCl₂) solution introduced into isolated gastrointestinal loops in vivo in rats ^[35].

Other researchers found that Dietary calcium supplements are unlikely to have a biological significant impact on iron balance ^[36].

Lead has interactive connection with diabetes, therefore there is a positive correlation between fasting blood sugar and blood lead concentration, and one of the complications of diabetes is kidney damage which may be due to high blood lead level ^[37].

As a result of high calcium level in diabetes the absorption of lead is expected to be low, but lead from endogenous sources such as lead in bone and or from previous environmental exposure will remain in the circulation, this is probably responsible for the observed high blood lead level in diabetic patients ^[38]. Many other workers have linked decline in kidney function to bone or blood lead levels ^[39].

In this study calcium level in diabetic patients were significantly high compared with the normal subjects this finding agreed with other studies which found that subject with low calcium level had lowest concentration of glucose and least insulin resistance, and subjects with high calcium level had highest concentration of glucose and insulin resistance ^[40].

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