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The relationship of heavy metals-induce oxidative stress in type ll diabetic patients

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Abstract:

Diabetes mellitus is a metabolic disorder where the body is unable to produce insulin or being resistant to it, leading to high level of blood glucose, increasing the risk of cardiovascular and kidney diseases, also early death or disabilities. According to the high rates of diabetes prevalence in recent years and decreased age of affliction to the second and third decades of life, recognition the possible risk factor of diabetes is of the highest importance. Lead, Cadmium and Mercury are heavy metal, used in different alloys, have various functions in our life and industries. One of the suggested pathogenic mechanisms of heavy metal is interferences with the oxidative stress pathway in diabetic patients.

Keyword: Mellitus Diabetes, heavy metal, oxidative stress

Introduction

Diabetes mellitus (DM)

DM, which is often called diabetes, represents a set of the metabolic disorders where there are high levels of blood sugar over an extended period. High blood sugar signs include the increased thirst, frequent urination, and increased hunger. In the case where it is left untreated, diabetes may result in causing several complications(1). The acute complications may be including hyperosmolar hyperglycemic state, diabetic ketoacidosis, or death (2). Severe long-term problems may include the cardio-vascular disease, chronic kidney disease, stroke, foot ulcers, and damages to eyes(1) .

Types of diabetes

The classification and diagnostic criteria fulfill 2 key purposes, first, identifying and classifying

the individuals with diabetes and so provide appropriate treatment, and secondly providing tools for the epidemiological studies and determining diabetes prevalence and incidence as well as its risk factors(6) . Before the late 1970's, there was no consensus on the diagnostic criteria for the glycaemic responses and diabetes to various glucose challenges have been applied(7) .

Diabetes may be categorized to the general categories below (8) :

1-Type l diabetes mellitus (as a result of the destruction of the Beta-cells, typically resulting in absolute deficiency of the insulin).

2- Type II diabetes mellitus (T2DM) (as a result of the progressive insulin secretory defects on insulin resistance background).

3- Gestational diabetes mellitus, diabetes that has been diagnosed in 2nd or 3rd trimester of the pregnancy, which isn't explicitly overt diabetes.

4- Certain diabetes types that result from other reasons, for example, monogenic diabetes syndromes like the maturity onset diabetes of the young (MODY) and neonatal diabetes.

Heavy metals

Endocrine-disrupting chemicals, including the heavy metals or synthetic chemicals that are found in in the surroundings, food and consumer an industrial products, interfering with the synthesis, activity, secretion, and metabolism of the body hormones. Some of the metals bay result in causing injuries to endocrine pancreas. Several studies have suggested that being exposed to them may lead to diabetes mellitus and cause the disturbance of the homeostasis of the insulin (27). Also, mechanical evaluation strategies and develop of endocrine toxicity molecular markers of the heavy metals was proposed.

Mercury (Hg)

Mercury can be described as a persistent and widespread heavy metal in the environment. It became one of the important concerns in the modern time public health, due to the increasing addition of its presence in some of the human food chain components. For instance, fish consumption has been advantageous to preventing the Alzheimer and the cardio-vascular diseases; on the other hand, numerous reports showed that the consumption of fish has been the main mercury exposure source (31). Mercury can be found in 3 forms in environment, which includes metallic or elemental mercury, organic mercury and inorganic mercury. The compounds of mercury are utilized in general in the dry-cell batteries, arc-lamps, fluorescent bulbs, mirrors,

and in extracting silver and gold from the ores, dental amalgam filling, thermometers, and vaccine preserver (32). Numerous researches discussed the potential relationships between diabetes and mercury. Heavy metals like the mercury result in increasing the oxidative stress and induce mitochondrial dysfunction. Although, mercury does not have any known physiological functions, it is toxic to human body through increasing the oxidative stress that was considered as pathogenetic mechanism for a variety of the metabolic disorders, which include the diabetes(33).

Cadmium (Cd)

Cd can be defined as a common beneficial heavy metal all over the world. It's a soft, silver-white metal, naturally found in the air, soil and water. Cd is a very important notorious toxic heavy metal, widespread in the environmental and industrial pollution particularly in the Ni-Cd rechargeable batteries and electroplating. By cadmium release into the water, it's absorbed by the plant or is up taken by fish and some other animals (41). Cd isn't bio-chemically or physiologically essential to the organisms and long-term exposure to the cadmium leads to kidney dysfunctions that could result in inducing the proximal tubule damages and blockades.

Lead (Pb)

Different researches have shown the strong correlation between the blood lead levels with the oxidative stress in general populations and assumed that the oxidative stress has to be taken under consideration in developing lead-mediated illnesses, even amongst the individuals who have rather low environmental exposure to the Pb (in other words, less than 10μg/dL) (49, 50). Pb is a heavy metal which is toxic the majority of human body organs and it interferes with the cellular functions and body metabolism. Pb was researched in several of the pathological conditions and this metal level in the environment are greatly concerning (51). The correlation between the long-term environmental exposure to the Pb and T2DM remains unknown.

Patients and methods

Our case-control investigation has been done on 100 patients with diabetes mellitus in Wasit's hospital. The level of fasting blood sugar, HbA1c, lipid panel, urea, creatinine, lead, mercury, cadmium, SOD, GSH, GPx, MAD, FRAP, and their demographic information were assessed.

Collecting Blood Samples

A venous blood sample has been obtained by taking of a volume of 10ml from each patient. The samples of the serum have been isolated with centrifugation at 3000rpm for 10min. Then, the obtained serums were analyzed for biochemical parameters

Results:

One hundred patients (50 males and 50 females with the mean age of 42.48±6.92) were observed with an average BMI of 29.31±7.77. There has been a positive association between blood lead and GPX (r=0.222, p=0.026), blood Cadmium and cholesterol (r=0.239, p=0.017), blood cadmium and LDL (r=0.214, p=0.032), and blood mercury and urea (r=0.232, p=0.020), and blood Mercury and FRAP (r=0.3150, p=0.0010).

Blood Heavy Metals Levels

Table 3.2 shows the level of heavy metals in the studied diabetic patients**.**

Blood bio-chemical parameters and oxidative stress markers

Table 3.3 shows the level of bio-chemical parameters and oxidative stress markers in studied diabetic patients**.**

Discussion:

Heavy metals have a long half-life and the body does not have any mechanism for excreting them, so they are stored in the body tissues after absorption. Heavy metals like the cadmium, mercury, and lead have no physiological activity in the body, but cause metabolic disorders like diabetes mellitus and hypertension through a variety of factors, such as oxidative stress. Studies have shown that exposure to heavy metals like lead, mercury, and cadmium has been related to an increase in the risks of diabetes mellitus or may have an impact on the complications of diabetes. Lead can increase the risk of renal failure in diabetic patients. In addition, a dose-dependent association has been reported between lead, cadmium, mercury, and arsenic with gestational diabetes. Lead (Pb) is a heavy metal found in nature and can cause acute or chronic poisoning. Some studies show that the concentration of lead in biological samples (blood, serum and hair) of people with diabetes was significantly higher than healthy people. Cadmium is one of the most toxic environmental and industrial pollutants that is known as an important risk factor for diabetes. Oxidative stress had also been shown to be highly associated with diabetes

and its complications. Studies show that cadmium can accumulate in the pancreas and increase blood glucose by destroying beta cells in rodents.

Conclusion:

The findings of the present study demonstrated that lead, cadmium and mercury in measured levels can induce antioxidants expression in diabetic patients, so that these antioxidants are able to prevent free radical- induced lipid peroxidation. However, the effects of heavy metals induced-oxidative stress on oxidative damage to proteins and nucleic acids, immune and inflammatory responses, insulin resistance, trace elements and lipid hormones are not clear.

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Table3- 1. Demographic characteristics of studied diabetic patients.

Characteristic		
Gender	Female	50
	Male	50
Age (year)	Mean ± SD	Male:43.27±6.47 Female: 38.00± 7.92

	Min – Max	Male :(33-65) Female: (35-65)
BMI (kg/m^2)		29.31±7.77
Duration of DM, (year)		3.04±2.55

Table 3- 2. The mean ± SD of blood heavy metals levels in diabetic patients (n=100).

Heavy metal	
Lead (µmol/L)	0.11 ± 0.09
Cadmium (µmol/L)	4.77 ± 2.10
Mercury (ng/ml)	3.74 ± 2.24

Table 3- 3. The mean ± SD of blood heavy metals levels in diabetic patients (n=100).

Parameters	mean ± SD
FBS (mg/dl)	149.46 ± 38.70
HbA1C (%)	7.28 ± 1.28
Total cholesterol (mg/dl)	204.53 ± 47.94
HDL- cholesterol (mg/dl)	42 ± 12.05
LDL- cholesterol (mg/dl)	129.10 ± 52.20
ALT (IU/L)	25.58 ± 10.16
AST (IU/L)	24.53 ± 14.15
Urea (mg/dl)	26.72 ± 9.58
Creatinine (mg/dl)	1.03 ± 0.27
MDA (μmol/Lit)	38.56 ± 30.39
FRAP (mmol/L)	0.40 ± 0.28
GPX (U/mL)	0.005 ± 0.005
SOD (U/mL)	7.69 ± 6.04
GSH (U/mL)	6.03 ± 4.83