ISSN: 03875547
Volume 44, Issue 06, December, 2021

Study of the activity of the Meprin alpha hormone and lipid profile parameters in patients with diabetes in Kirkuk city

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Keywords:
Diabetic mellitus, Meprin alpha hormone, Lipid profile.

ABSTRACT

Diabetes mellitus is a collection of metabolic illnesses marked by hyperglycemia caused by insulin production, insulin sensitivity, or both. Diabetes-related chronic hyperglycemia is linked to lengthy deterioration, malfunction, and destruction of multiple organs, including the retina, renal, brain, hearts, and circulatory system. Investigation roles of Meprin alpha hormone and lipid profile parameters in pathogenesis of diabetes. Our study show high levels of glucose, cholesterol, TG, LDL, VLDL, and meprin alpha hormone in patients with DM compared to control with high significant different ($p<0.05$). in contrast, our results revealed decreased levels of HDL in patients than controls high significant different ($p<0.05$). We concluded the Meprin alpha hormone is play a major role in pathogenesis of diabetic mellitus and have raised sensitivity in screening patients with diabetes.

1. INTRODUCTION

Diabetes mellitus (DM) is a collection of metabolic illnesses characterized by high blood glucose levels caused by issues with insulin synthesis, insulin usage, or both. The World Health Organization has reported an increase in the prevalence of diabetes mellitus (DM) in many places around the world over last few years [17]. Hyperglycemia related to a relative or absolute insulin shortage characterizes this condition [1]. Insulin deficiency, wether absolute or partial, affects glucose, peptide, fat, fluid, and electrolyte metabolic. Insulin has a wide range of effects on human lipid accumulation. It increases fatty acid synthesis throughout the hepatic, adipose cells, and the gut. Insulin had been shown to boost cholesterol production [13]. By 2040, the number of individuals afflicted from diabetes worldwide is expected to increase between 415 million to 642 million [30]. Each region is seeing an increase in the number of patients with Type 2 Diabetes Mellitus (T2DM), with 75 percent of those affected residing in developing nations [35]. Roughly 61.3 percent of diabetic individuals have hypertension, while 74.3 percent of diabetic patients over 65 have increased blood pressure. Both diabetes and hypertension were independent predictors for heart failure, and their cohabitation increases the accumulated risk of HF [25]. Up to 75% of customers who attended diabetic clinics have serious gastrointestinal issues [2]. With a rising global prevalence, diabetes is expected to become a prominent cause of illness and death mostly in next. Dyslipidemia is a well-known potential risk for macro-vascular problems

in people with T2DM, and so it represents 10-73 percent of this group [21]. Increased low-density lipoprotein cholesterol (LDL-C), reduced high-density lipoprotein cholesterol (HDL-C), or enhanced triglyceride (TG) levels are all prevalent symptoms of DM dyslipidaemia [36]. Moreover, the U.k Retrospective Diabetes Analysis revealed that both low HDL-C and high LDL-C risk CVD in people with diabetes. In just this community, all domestic and international standards suggest rigorous lipid regulation [12]. Dyslipidemia is a leading cause of Coronary Heart Disease (CHD). Since of disturbances in lipoproteins, such as serum triglycerides (TC) 69 percent, serum cholesterol 56.6 percent, Low Density Lipoprotein cholesterol (LDL) 77 percent, and High Density Lipoprotein cholesterol (HDL) 71 percent, cvd is a cause of illness and death in dm patients [5].

Meprins were astacin-family zinc-dependent metalloproteinases which were first identified and described by brush-border coats of mice, rats renal, and people intestine [27]. It must have been identified as a protease that's been significantly abundant in renal brush boundary membrane as well as intestinal mucosa cells when it was first identified [37]. Meprin is made up of two homologous component domains, the meprin (MEP1A) region and the meprin (MEP1B) area, which have a 42 percent amino acid sequence similarity [39]. Meprins have indeed been linked to the pathogenesis of DN in both mouse and human versions of the disease [7]. Throughout the Pima Indians, a Native American ethnicity with extraordinarily high rates of type 2 diabetic as well as ESRD, single nucleotide variants (SNPs) in the Meprin gene revealed linked to DN and end stage renal disease (ESRD) [15]. Meprin gene and protein upregulation were reduced in the kidney of diabetic rats and db/db mice well before onset of overt renal disease. Meprin and meprin double depletion resulted in a much more extreme condition of kidney impairment in mouse with streptozotocin (STZ)-induced type 1 diabetes, showing that meprins defend towards DN [33]. In diabetics Black Men, renal meprins and two meprin objectives (nidogen-1 and MCP-1) were positively linked only with degree of renal damage [10]. Several of the recognized meprin receptors are also involved in the pathogenesis of DN (inflammatory condition and fibrosis, for example) [19].

The focus of this research is to determine the level of Meprin alpha hormone in DM patients' and role it in pathogenesis of diabetes.

2. Material and Methods

The study included healthy normal people as a comparison group (control) and their number (30 samples) were (15) males and (15) females. Their ages range from (11 to 85) years, and they were among the visitors to Kirkuk General Hospital for routine checkups. In this research, 60 blood samples were obtained in the period from 1/8/2021 until 1/10/2021, and their ages ranged between (11-85) years. It included (30) male samples and (30) female samples, Samples (samples) were collected from Kirkuk General Hospital after careful diagnosis by specialized doctors. And based on the clinical symptoms and questionnaire questions of the patient through a questionnaire form for each patient.

Blood samples of all patients have taken a Meprin α, total cholesterol, high density lipoprotein (HDL), low density lipoprotein (LDL), triglycerides (TG), glucose. Determination of Human Meprin α. Serum meprin α activity has been determined by using kit assayed according to the manufactured procedure (Bioassay technology Laboratory. Estimation of Glucose Concentration in serum Basic Principle: The level of glucose in the blood was estimated using the diagnostic kit provided by Randox England, according to the enzymatic method based on the Trinder reaction and as in the following equations. Estimation of Triglycerides Concentration in serum Basic Principle. The concentration of triglycerides in the blood serum was determined by using the enzymatic method. And by using the diagnostic kit equipped by the french company Biolabo. The principle of the detector is illustrated by the following equations. Estimation of High Density lipoprotein–

cholesterol (HDL-Ch) Concentration in serum Basic Principle The level of HDL-Ch was determined in the blood serum by using the diagnostic kit equipped by the French company Biolabo. The principle of the method depends on the enzymatic method in which the chylomicron and lipoproteins of LDL – Ch and –Ch VLDL are deposited with the addition of Phosphotungstic acid in the presence of magnesium ions. Only HDL-Ch remains in serum after centrifugation. Estimation of low Density lipoprotein–cholesterol (LDL-Ch) Concentration in serum Basic Principle: The concentration of LDL cholesterol was calculated according to the following relationship:

(HDL + VLDL) _ Total cholesterol = LDH

2.1 Statistical Analysis

The results were analyzed statistically using (SPSS) version 23 and the system (XLSTAT) and represent the values in the tables (Mean ± SD). The (test-t) test and (ANOVA test) were used to compare the groups, and at a probability level (P≤ 0.05) for the significant values and (P≤ 0.001) for the high.

3. RESULTS

Our study show high mean levels of glucose in patients (13.01±0.66) than control (4.15 ±0.68) with high significant different (p<0.05). Based on gender, glucose levels scored high levels in male and females patients (13.14±1.76, 12.78±0.70) respectively than male and female controls (4.30 ±0.76, 3.97 ±0.79) respectively with high significant different (p<0.05) (table 1).

Table 1; Glucose concentrations in the blood serum of type 1 diabetes patients associated with the control group

Variables		Control group	Patient group
Glucose mmol/L	Males	4.30n.s±0.76	13.14**±1.76
	Females	3.97n.s±0.79	12.78**±0.70
	Total	4.15n.s±0.68	13.01**±0.66

** The presence of moral superiority (P≤ 0.01) n.s There is no moral difference

Our study revealed there is significant different between patients and control (95.64±4.60 vs. 84.37±5.46) for Meprinα parameter (p<0.05). while, others parameters don't scored significant differences between study groups (p>0.05). respect to gender, our results appeared significant different between females of patients and controls for cholesterol (6.88±0.22 vs. 6.13 ±0.17), triglycerides (2.50±0.35 vs. 1.71 ±0.48), HDL (1.47±0.31 vs. 1.40 ±0.21), and VLDL (0.50±0.13 vs. 0.34 ±0.04). Meprinα parameter scored significant different in males and females for patients and controls (95.34 ±4.10 vs. 86.37±3.18, 95.30±4.50 vs. 81.37±2.54) (table 2).

Table 2; Fat concentrations (Ch, TG, HDL-Ch, LDL-Ch, and VLDL-Ch, Meprinα hormone) in the blood serum of patients with type 1 diabetes.

Variables		Control group	Patient group
Ch mmol/L	Males	4.64n.s±0.41	5.04n.s±0.24
	Females	6.13n.s±0.17	6.88*±0.22
	Total	5.25n.s±0.41	5.98n.s±0.56
TG mmol/L	Males	0.87±0.26	1.07n.s±0.36
	Females	1.71n.s±0.48	2.50*±0.35
	Total	1.30n.s±0.30	1.80n.s±0.32

HDL mmol/L	Males	1.02n.s±0.16	0.90n.s±0.29
	Females	1.40n.s±0.21	1.47**±0.31
	Total	1.23n.s±0.35	1.18n.s±0.40
LDL mmol/L	Males	2.84n.s±0.53	2.03n.s±0.44
	Females	2.03n.s±0.56	4.16n.s±0.56
	Total	2.61n.s±0.72	3.75n.s±0.54
VLDL mmol/L	Males	0.17n.s±0.06	0.21n.s±0.07
	Females	0.34n.s±0.04	0.50*±0.13
	Total	0.26n.s±0.11	0.36n.s±0.15
Meprinα ng⁄ml	Males	86.37±3.18	95.34** ±4.10
	Females	81.37±2.54	95.30**±4.50
	Total	84.37±5.46	95.64**±4.60

** The presence of moral superiority (P≤ 0.01)
n.s There is no moral difference

4. Discussion

Sugar is the primary fuel for cells. Glucose, on the other hand, cannot enter cells until insulin is present. A suitable amount of insulin is generated by a healthy pancreas to transport glucose into the cells. Very little insulin is created in a dysfunctional pancreas, and the bodily tissues don't really response to an insulin is released. As just an outcome, glucose builds up in the blood, its quantity rises, and diabetes mellitus develops [16]. When compared with control people, the results of this investigation revealed a considerable increase in glucose in T2DM patients. The causes of this condition, which commonly arises beyond the ages of 40, could include -cell weakening, hyperinsulinemia and/or activity modicums, and increased insulin resistant [30]. [38], [18] increased amounts of Cholestrols, TG, LDL, and low rates of HDL in patients compared to controls, and all these findings are consistent with our findings. [29] looked into the link between t2dm and lipid and lipoprotein irregularities, whereas [3] focused on high incidence of dyslipidemia (DD) in patients with type 2 diabetes. [9] found that metabolic syndrome combined with type 2 diabetes increases the risk of CVD, whereas [11] found that raised non-HDL-C values in type 2 diabetes patients increase the likelihood of CVD. [34] successfully proved that hypertriglyceridemia plays a role in the development of CVD-related mortality in diabetics. Several research studies have identified lipid panel and hypertension as key cardiovascular complications, with a stronger link to the disease than poorly regulated glucose in diabetics [38].

Researchers discovered a statistically meaningful big influence in FBS, HbAlc, TG, VLDL, HDL, and lipoprotein concentrations of patients compared to the control group, but no large impact in LDL and cholesterol levels. As a result, they came to the conclusion that lipoprotein might not be a reliable risk factor for cardiovascular disease [24]. When elevated concentrations of triglycerides were combined with low concentrations of HDL-C, the odds of having a heart attack increased by 7.36 times in diabetics compared to the control [38]. Insulin resistance is connected with metabolic disorders such as high triglyceride density and low HDL-C levels in the blood. As a result, hypertriglyceridemia can be used as a marker for the metabolism syndrome and type 2 diabetes. Furthermore, the triglyceride-to-HDL-C ratios can be used as a surrogate for quantifying the influence of hyperglycemia on CVD incidence by using it as a diagnostic biomarker for glucose intolerance [26]. Furthermore, past prospective triglyceride researchers have found a substantial link among CVD returns and lower HDL-C and LDL-C values in people with T2DM [32]. According to a meta-analysis, alterations in serum lipid profiles constitute one of the fundamental hallmarks of diabetic neuropathy (DN). Lipid concentrations must be investigated as a standard laboratory indicator for evaluating the risk of DN since they will assist doctors in selecting appropriate therapy and therefore maximizing use of resources

available [8].

Our findings suggest that diabetic patients have higher amounts of Meprin alpha hormone versus controls, which is consistent with [33]. In both mice and humans versions of diabetic nephropathy (DN), meprin metalloproteases have indeed been found to play a role in the pathophysiology of the disease [14]. Unfortunately, we only have a limited understanding of the underlying mechanics. Inflammation has been identified as an underlying factor in the evolution of diabetic kidney damage in several investigations. Meprin A possesses anti-inflammatory properties, but meprin B has both pro-inflammatory and anti-inflammatory properties [23]. In addition, in infected mice, the equilibrium of meprin A and meprin B promotes the course of inflammatory conditions [4]. As a result, it's possible that a lack of meprin B and heterodimeric meprin A (-) tip the balance toward anti-inflammatory actions mediated by homomeric meprin A (-) and so shields diabetic kidney disease patients from harm. In an animal model of type I diabetes, [6] found a considerable down-regulation of genes and protein level for the both meprin and meprin in an animal model of type I diabetes, which contradicts our findings. The identified metabolites show that meprin affects diabetes consequences including such diabetic kidney disease by affecting different metabolite patterns, according to [20]. The advantages of angiotensin-converting enzyme (ACE) blocker treatment on the course of diabetic nephropathy could be due, in part, towards its effect on renal Meprin production [31].

5. Conclusions

We conclude the Meprin α is play predict role in pathogenesis of diabetes and have high sensitivity in screening patients with DM. High levels of lipid profile in DM patients refer to occurance CVD in DM patients.

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