

Evaluation the Role of Amylin Hormone and some Biochemical Parameters in Type 2 Diabetic Patients with Cardiovascular disease

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Received: 20 January 2023

Accepted: 15 April 2023

Citation: Hussein RJA, Majid A (2023) Evaluation the Role of Amylin Hormone and some Biochemical Parameters in Type 2 Diabetic Patients with Cardiovascular disease. History of Medicine 9(1): 1100–1105. <https://doi.org/10.17720/2409-5834.v9.1.2023.130>

Abstract

Background: Type 2 diabetes mellitus (T2DM) and coronary artery disease (CAD) poses major threat worldwide contributing to excessive morbidity and mortality, these co-morbidities synergistically interact with inflammatory mechanisms. The study aimed to observe levels the Amylin, Creatine phospho kinase (CPK), Total cholesterol (TC), Triglycerides (TG), High density lipoprotein (HDL), low density lipoprotein (LDL) and very low density lipoprotein (VLDL). Also to evaluate correlation between (Amylin, CPK, TC, TG, HDL, LDL and VLDL). Methods: Serum Amylin, CPK, TC, TG, HDL, LDL and VLDL levels were determined in 50 patients with acute myocardial infraction, 50 patients with (type 2 diabetes with myocardial infraction) and 50 healthy subjects. Results: The results show a significant increase in the concentration of serum (amylin, CPK, TC, TG, LDL and VLDL) in (T2DM with AMI) group in comparison with the (AMI and controls) groups ($p \leq 0.05$). But it was found no significant deference in the concentration of serum amylin between (AMI and controls) groups ($p \leq 0.05$). Also it was found no significant deference in the concentration of serum CPK between (T2DM with AMI and AMI) groups ($p \leq 0.05$). While it was found a significant decrease in the concentration of serum HDL in (T2DM with AMI) group in comparison with the (AMI and controls) groups ($p \leq 0.05$). It was found a positive correlation between serum amylin and (CPK, TC, TG, LDL and VLDL) and a negative correlation between serum amylin and HDL. Conclusion: We finding a positive correlation between amylin and (CPK, TC, TG, LDL and VLDL). Also we finding negative correlation between amylin and HDL.

Keywords

Myocardial infraction, Type 2 diabetes, Amylin, Creatin phospho kinase, Lipid profile.

Diabetes mellitus (DM) has been known as a heterogeneous metabolic disorder characterized by the presence of hyperglycemia due to impairment of insulin secretion, defective insulin action or both. The chronic hyperglycemia of diabetes is associated with relatively specific long-term microvascular complications affecting the eyes, kidneys and nerves, as well as an

increased risk for cardiovascular disease (CVD) [Egan and Dinneen, 2019].

Elevation of blood glucose level for a long time causes serious complications is abnormality in eyes with complete loss of vision, renal failure and nerve damage causes abnormal functioning of gastrointestinal tract, urinary tract and also cardiovascular (CV) system [Ahmed et al., 2017]. Cardiovascular

diseases are commonly manifested by myocardial infarction and the World Health Organization (WHO) has recommended that MI rates can be used as a proxy for cardiovascular disease rates in epidemiological studies (Mendis et al., 2011, Al-Abbas, 2019). A myocardial infarction occurs when an atherosclerotic plaque slowly builds up in the inner lining of a coronary artery and then suddenly ruptures, causing catastrophic thrombus formation, totally occluding the artery and preventing blood flow downstream. Cardiac hypertrophy is a general term signifying an increased workload and is characterized with an increase in cardiac mass in response to applied stimulus [Majid and Sayer, 2018]. The use of a large number of cardiovascular biomarkers, meant to complement the use of the electrocardiogram, echocardiography cardiac imaging, and clinical symptom assessment. Myocardial infarction is diagnosed when blood levels of sensitive and specific biomarkers such as cardiac troponin or CKMB are increased in the clinical setting of acute myocardial ischemia [Wang et al., 2020]. The symptoms of MI include chest pain, which travels from left arm to neck, shortness of breath, vomiting, abnormal heart beating, weakness [Lu et al., 2015]. Important risk factors are earlier cardiovascular disease, old age, tobacco smoking, high blood levels of certain lipids (LDL and TG) and small levels of (HDL) cholesterol, diabetes, high blood pressure, lack of physical activity, obesity, chronic kidney disease, excessive alcohol consumption and the use of cocaine and amphetamines (Graham et al., 2007; Auda et al., 2018).

In general, the majority of amylin's actions on the cardiovascular system are believed to be mediated by activation of CGRP receptors, widely expressed within the vasculature (Hay et al., 2015). Amylin and insulin are released by pancreatic islets of β -cells in response to dietary food-stuffs including glucose and fats. Amylin has vital function in controlling glucose homeostasis and restraining food intake via "meal ending satiation", probably by the activation of its receptor in brain's postrema region [Lee et al., 2021]. The aim of this study is evaluated the amylin, CPK, TC, TG, HDL, LDL and VLDL in Type 2 diabetic patients with cardiovascular disease.

Materials and Methods

This study was conducted at AL- Nasiriyah Heart Center, and AL-Azher Privet hospital It included (150) subjects, control(50) and patients (100) diagnosed with (Acute Myocardial Infarction and Acute Myocardial Infarction with DM), an age rang(40-70). About(5mL)of blood samples of the patients with Acute Myocardial Infarction, acute myocardial infarction(AMI) with DM patients and controls were taken and allowed to clot at room temperature in empty disposable tubes centrifuge to separate it in the centrifuge at 3000 rotor per minute (rpm)for 10min, the serum samples were separated and stored at (-20°C) until analyzed for serum amylin was determined using ELISA technology by spectrophotometer, serum creatine phospho kinase, total cholesterol, triglycerides, high density lipoprotein, low density lipoprotein and very low density lipoprotein were purchased from Biolabo (France)

Statistical Analysis

Statistical analysis was done using the software spss version 15.0, The results were expressed as (mean \pm SD) with LSD. One way ANOVA test was used to compare parameters in different studied groups. P-values ($p \leq 0.05$) were considered statistically significant. person's correlation (r) was applied to determine the relationship among the present study parameters. P-values ($p \leq 0.05$) were considered statistically significant.

Results and Discussin

Amylin and Creatine Kinase

Table (1) show a significant increase in the concentration of serum amylin in (T2DM with AMI) group in comparison with the (AMI and controls) groups ($p \leq 0.05$). But it was found no significant deference in the concentration of serum amylin between (AMI and controls) groups ($p \leq 0.05$).

Table (1) show a significant increase in the concentration of serum CPK in (T2DM with AMI and AMI) groups in comparison with the controls group ($p \leq 0.05$). But it was found no

significant deference in the concentration of serum CPK between (T2DM with AMI and AMI) groups ($p \leq 0.05$).

Table (1): Serum Amylin and creatine kinase levels of control and patient's groups

Group	No.	Amyline (pg/ml)	CPK (IU/L)
AMI	50	9.52±2.28 ^b	639.50±60.89 ^a
T2DM with AMI	50	49.23±9.27 ^a	647.56±61.07 ^a
Controls	50	10.06±2.02 ^b	100.60±12.96 ^b
LSD		1.88	16.71

* Each value represents mean \pm SD values with non-identical superscript (a, b or c ...etc.) were considered significantly differences ($P \leq 0.05$).

AMI: Acute Myocardial Infarction

T2DM with AMI: Type 2 Diabetic and Acute Myocardial Infarction

In this cross sectional study, we enrolled total of 150 participants, of which 50 were healthy control, and the other 150 angiographically diagnosed cases of T2DM-CAD, aged 40 to 70 years were of both gender, they observed an elevated form of amylin, including an early phase of protein aggregation. [Reinehr et al.,2007]. Although, increased insulin secretion in obesity is consistent with the increased amylin concentration and hyperamylinemic phase due to longlasting exposure to hyperglycemia. The islets of pancreas facilitate selective amylin secretion and alter the secretory ratio of amylin to insulin [Reinehr et al.,2007]. These increased circulatory levels of amylin get accumulated and converts its soluble monomeric form into its non-soluble oligomeric fibrils, which has great potential to aggregates into toxic nanoparticles. These toxic amylin amyloid gets accumulated into the islets of pancreas and causes destruction and apoptosis of beta cell, and decreases the total beta cell volume. The

Table (2): Lipid Profile levels of control and patients group

Groups	No.	TC (mg/dl) mean±SD	TG (mg/dl) mean±SD	HDL (mg/dl) mean±SD	LDL (mg/dl) mean±SD	VLDL (mg/dl) mean±SD
AMI	50	217.80± 19.11 ^b	194.52±12.79 ^b	39.82±7.51 ^b	139.07±21.56 ^b	38.90±2.55 ^b
T2DM with AMI	50	238.42 ±30.04 ^a	220.68±21.84 ^a	28.82±5.17 ^c	165.46±31.13 ^a	44.14±4.36 ^a
Control	50	171.96±18.64 ^c	119.92±14.68 ^c	58.60±6.04 ^a	89.37±18.85 ^c	23.98±2.93 ^c
LSD		7.70	5.60	2.09	8.10	1.21

Legend as in table (1)

Diabetic is more vulnerable to coronary heart disease; thus rising obesity-related diabetic

accumulation of increased amylin concentration leads to toxic effect on the beta cell function in T2DM that alters cardiac function. Creatine kinase (CK), consisting of two cytosolic subunits either from brain (B) or muscle (M), appeared as three isoforms including CKBB, CK-MB and CKMM. Of these [Chang et al., 2015].

The CPK is found in the heart with large quantities which are needed for providing the heart muscles with a high energy that is enough for muscles contraction, The cardiac muscle contains huge amounts from the isoenzyme CK-MB of CK enzyme, [Karras and Kane,2001]. In AMI, ischemia in myocardium persists for prolonged time more than (4–6) hr. and finally causes death for ischemic myocytes converting to necrotic cells which release its contents and enzymes such as (CK), due to the destruction of cell membrane by three factors that are formed because of the lower oxygen in cells : (1) production of internal free radicals, (2) phospholipase activation and (3) releasing of lysosome enzymes [Puleo et al.,1994].

Lipid profile

Table (2) show a significant increase in the concentration of serum TC, TG, LDL and VLDL in (T2DM with AMI) group in comparison with the (AMI and controls) groups ($p \leq 0.05$). Also it was found a significant increase in the concentration of serum TC, TG, LDL and VLDL in AMI group in a comparison with the controls groups ($p \leq 0.05$). But was found in the same table(2) a significant decrease in the concentration of serum HDL in (T2DM with AMI) group in comparison with the (AMI and controls) groups ($p \leq 0.05$). Also it was found show a significant decrease in the concentration of serum HDL in AMI group in a comparison with the controls groups ($p \leq 0.05$).

dyslipidemia (DD) comprises elevated concentrations of triglycerides with preponderance of high LDL cholesterol and low HDL-cholesterol [Raj et al.,2001]. These significantly raised the

levels of Total Cholesterol, Triglyceride, LDL-C, VLDL-C, and decreased HDL-C ($p \leq 0.05$) in study subjects as compared with healthy control, and find their association with circulatory amylin concentration we performed Pearson's correlation and found positive association of circulatory amylin concentration with total cholesterol, TG, LDL-C, VLDL-C and negative association with HDL-C. Elevated levels of triglyceride are known to cause impairment in lipoprotein metabolism which leads to an increase in the risk of CVD. Our statistical analysis shows that triglyceride levels are significantly higher in DM thus linking them closely to T2DM (Table 2) [Mcbride,2008]. Table 3 and figures 1, 2, 3, 4, 5, and 6 Explain the correlation between amylin hormone and other parameters for this study .It was found a positive correlation between amylin hormone and (CPK, TC, TG, LDL and VLDL).Also it was found negative correlation between amylin hormone and HDL

Table (3) Correlation between amylin hormone and other parameters for this study

amylin with	r	Results
CPK	0.37	positive correlation
TC	0.38	positive correlation
TG	0.31	positive correlation
HDL	-0.42	negative correlation
LDL	0.39	positive correlation
VLDL	0.31	positive correlation

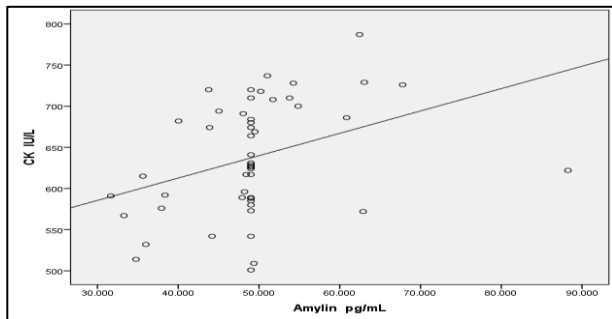


Figure 1. Show the positive correlation between Amylin and CPK

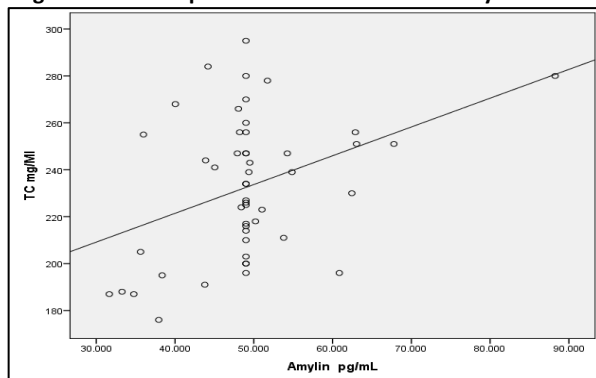


Figure 2. Show the positive correlation between Amylin and TC

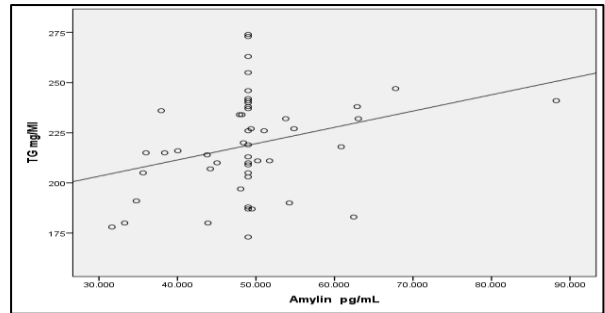


Figure 3. Show the positive correlation between Amylin and TG

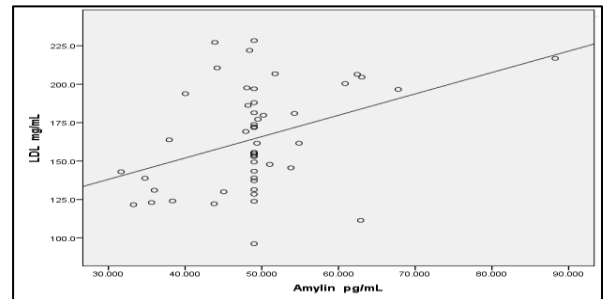


Figure 4. Show the positive correlation between Amylin and LDL

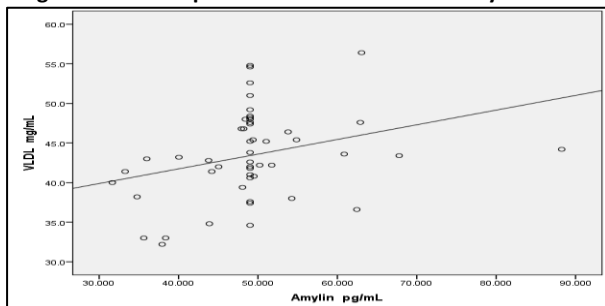


Figure 5. Show the positive correlation between Amylin and VLDL

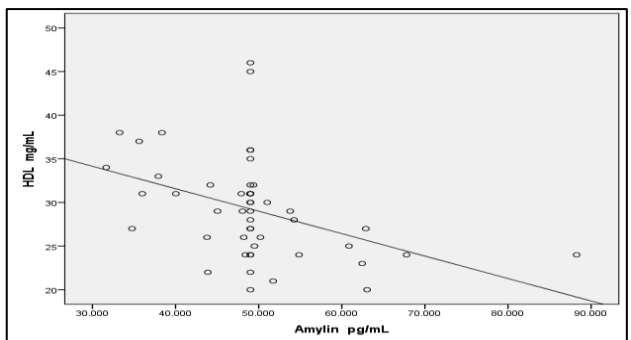


Figure 6. Show the negative correlation between Amylin and HDL

Conclusion

The information obtained in this analysis was used to arrive at the following conclusions: In patients with type 2 diabetic with cardiovascular disease , we discovered that the levels of Amylin, CPK, TC, TG, LDL, and VLDL e had risen dramatically. HDL levels, on the other hand, showed a significant decrease in patients with type2 diabetic with cardiovascular .

Via coefficient correlation (r), we discovered a positive correlation between amylin hormone and (CPK, TC, TG, LDL and VLDL) as well as a negative correlation between amylin hormone and HDL

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