Study the Physiological, Some Biochemical, Lipid Profile Status, and clinical Markers in type 2 Diabetes Mellitus Patients in Al-Najaf Al-Ashraf Governorate.

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Abstract

Diabetes care relies heavily on glucose monitoring, which is carried out by both patients and their healthcare providers. Fasting plasma glucose (FPG) measures alone do not provide an overall picture of illness prognosis and related consequences, as recent investigations have demonstrated. Post-prandial glucose excursion test was used in this study to see if oral hypoglycemic agent treatment could help patients with type 2 diabetes keep their blood sugar levels under control. A total of 24 individuals with type 2 diabetes mellitus were enrolled in this study, including 12 in the good glycemic control group and 12 in the poor glycemic control group. As a control group, 12 healthy individuals were chosen and compared to the study's parameters of interest. Blood glucose, lipid profile, C-peptide, renal function and microalbuminurea, glycated haemoglobin and post-prandial glucose excursion profile were measured at the beginning of the study. T2DM patients should have a post-prandial glucose excursion test instead of relying on fasting plasma glucose levels to anticipate proper acute and long-term control during pharmaceutical therapy for proper acute and long-term glycemic control.

Keywords: Physiological, Biochemical, Lipid Profile Status, Clinical Markers, and 2 Diabetes Mellitus.

1. Introduction

A metabolic condition called diabetes mellitus is characterized by chronic hyperglycemia. (Excess circulating glucose) is typically accompanied by signs of extreme thirst, weight loss, and increased urine production (1).

Type 2 diabetes mellitus the most common kind of diabetes, also known as non-insulin-dependent diabetic Mellitus (NIDDM) or adult-onset diabetes, can affect anyone at any age.

Insulin resistance is typically the first sign of this kind of diabetes, a condition where the response of the fat, muscle, and liver cells to insulin is impaired. Treatment includes using oral hypoglycemic agents, in addition to dietary restriction and regular exercise (2).

Particularly in the early stages of the disease, the progression of type 2 DM is frequently gradual and asymptomatic. The World Health Organization (WHO) criteria for clinical diagnosis are met by around half of persons, leaving the vast majority of diseases undiagnosed (3). The "Iceberg" conception of diabetes has been used to represent this concept since the majority of the illness is hidden below what may be considered the clinical level, as a result, people with early type 2 diabetes frequently go undiagnosed until their symptoms first manifest between the ages of 50 and 65. (4)

2. Materials and Methods

1- control groups and Patients

This study was carried out on 24 patients (11 males and 13females) with type 2 diabetes mellitus. The samples were taken from the Al Sadr Medical City/Najaf from Diabetes Mellitus and Endocrinology Center. Their age range was 41-73 years; they had been diagnosed previously and marked as diabetes mellitus type 2 patients and had a sickness history of at least 3 years. After careful clinical and biochemical evaluation, they are classified into two groups as follows.

Group A: this include 12 patients, who are previously maintained on oral hypoglycemic agents, but with poor glycemic control according to the results of fasting plasma glucose levels.

Group B: this include 12 patients, who are previously maintained on oral hypoglycemic agents, but with

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good glycemic control according to the results of fasting plasma glucose level.

2- obtaining blood samples

Five milliliters of venous blood were sucked using disposable syringes following an overnight fast (8–12 hours). Samples were collected from 9:30 to 10:00 am. By centrifuging the blood at 2000 x g for 10 minutes, the serum was separated from the blood and stored in unassuming plastic tubes that were kept frozen at -20 C until analysis in disposable serum tubes. At room temperature, the blood was allowed to coagulate in plain tubes for 30 to 45 minutes.

Biochemical measurement

1- Measuring the level of fasting blood glucose concentration

Bio Merieux in France provided the glucose kit for the quantitative assessment of glucose in human serum.

2- Glycated hemoglobin (HbA1c) determination

The kit for measuring glycated haemoglobin in human serum quantitatively was made available by Bio Merieux in France.

3- Total Cholesterol (TC) Measurement

Bio Merieux, based in France, supplied the Total Cholesterol kit for quantitative assessment of Total Cholesterol in human serum.

4-High Density Lipoprotein Cholesterol (HDL-C) Measurement

Bio Merieux in France created the HDL-C kit for quantitatively quantifying HDL-C in human serum.

5-Low Density Lipoprotein Cholesterol (LDL-C) Measurement

In order to quantitatively measure LDL-C in human serum Bio Merieux, France, provided the LDL-C Kit.

6- Measuring the levels of triglycerides (TG)

French company Bio Merieux supplied a kit for the quantitative detection of triglyceride in human serum.

7. The measurement of serum urea

An already assembled laboratory kit was used to measure the serum urea. The enzymatic hydrolysis of urea in accordance with the following reaction served as the foundation for the concept of determination (5).

8. Determination of Serum Creatinine

An already assembled lab kit was used to measure the serum creatinine. principle relies on the formation of a colorful complex by the interaction of picrate and creatinine in an alkaline solution.

9. Determination of Microalbuminuria

The determined of microalbuminuria was using a pre-made laboratory kit. The method of determination is based on the formation of a red complex as a result of a reaction between proteins and pyrogallol/molybdate. The color was directly proportional to the albumin concentration in the urine.

10. Determination of Serum C-peptide

The immunoradiometric assay of C-peptide is a "Sandwich" type assay. The same kit may be used to assay C-peptide in urine after dilution or directly in serum and plasma.

Biostatistical analysis

Analysis of the data was carried out using Minitab, Megastatistics, and SPSS for Excel on a home computer Mean standard deviation was utilised as a way to represent the findings. For a result to be considered significant, it had to meet the p-value of 0.05. (p-value).

3. Results and Discussion

3.1. Type 2 Diabetic Patients' FPG, HbA1c, and C-peptide levels:

The data presented in table (3-1) clearly demonstrated that in both, well controlled and poorly controlled, DM patients, FPG levels are significantly higher than in controls (97% and 206% respectively); however, when FPG levels in the two groups were compared, considerably higher values observed in poor glycemic control group (55%, P<0.001).

Table (3-1) also indicated that HbA1c quantities in both patient groups are higher than it would be for healthy controls (38% and 99% respectively, P<0.001). When HbA1c quantities in both patient groups were compared, the poor glycemic control group demonstrated significantly higher levels (45%, P<0.001) compared to the good glycemic control group.

When the levels of HbA1c in both groups are correlated with the extent of glycemic control in terms of FPG level, only the poor glycemic control group shows a significant correlation in this respect (r = 0.62, P<0.05), while the other group shows the lower and non-significant correlation in this respect.

To evaluate the stimulatory response of the oral hypoglycemic agent used in the treatment (glibnclamide), C-peptide levels were measured and found to be still significantly lower than control in both DM patients groups (36% and 54% respectively, P<0.001) in comparison to controls, when C-peptide levels (% change with respect to control) were compared, good glycemic control group showed significantly higher value (40%, P<0.001) in comparison to poor glycemic control group.

Table (3-1) Glucose, HbA1c, and C-peptide levels in type 2 diabetic patients are measured.

Parameter Group	FBG (mmol/L)	HbA1c %	C-Peptide (pmol/L)
Control	3.6 ± 0.27 [a]	4.37 ± 0.58 [a]	398.4 ± 34.4 [a]
Good glycemic	7.1 ± 0.61 [b]	6.02 ± 0.578 [b]	254.8 ± 38.7 [b]
Poor glycemic	11.02 ± 3.32 [c]	8.7 ± 0.94 [c]	182.5 ± 27.5 [c]
Results are represented as mean ± SD.			

Values with different superscripts (a, b, and c) are considered to be substantially different across groups (P < 0.001).

3.2. The Post-Patient Glucose Excursion in DM Patients with Poor and Excellent Glycemic Control

In an attempt to explore the effect of solid meal challenge given to fasted controls and DM patients groups on glucose spike post-prandially, PPGE test was performed, and the results in table (3-2) clearly demonstrated that glucose spike, measured as AUC during 4 hours, in both DM patients groups were significantly higher (79% and 192% respectively, P<0.001) with respect to controls; however, when AUC values in both DM groups were compared, good glycemic control group showed significantly lower PPGE value (79%, P<0.001). AUC which represents PPGe in both groups demonstrated good correlation with the glycemic control status in term of FPG with comparable r values and higher levels of significance (r = 0.88 and 0.95, P<0.001 respectively), indicating that this parameter is a good predictor of glycemic control as a result of treatment with oral hypoglycemic agents.

3.3. Lipid Profile Status in Good and Poor Glycemic Control DM patients

The data presented in tables (3-3) showed that total serum cholesterol levels in both DM patients' groups were significantly higher than those in controls (5% and 29% respectively, P<0.05). Meanwhile, total cholesterol levels in poor glycemic control were significantly higher than those observed for good glycemic control group (23%, P<0.05).

Table (3-2) Post-prandial glucose excursion spike (AUC0-4) in poor and good glycemic management in people with type 2 diabetes.

Group Parameter	Control	Good glycemic	Poor glycemic
AUC min. mmol/L	32.3 ± 1.6 a	57.9 ± 4.4 b	94.5 ± 22.2 c
AUC min. mgl/dl	504.9 ± 27.4 a	930.1 ± 79.4 b	1477.8 ± 339.8 c
Results are represented as mean ± SD.			

Values with non-identical superscripts (a, b, and c) are considered to be substantially different across groups (P < 0.001).

Table (3-3) Lipid profile status in good and poor glycemic management in people with type 2 diabetes.

Parameter Groups	TC (mmol/L)	TG (mmol/L)	HDL (mmol/L)	LDL (mmol/L)
Control	4.77 ± 0.283 a	1.51 ± 0.235 a	1.2 ± 0.11 a	2.96 ± 0.26 a
Good glycemic	5.03 ± 0.30 b	1.912 ± 0.294 b	1.03 ± 0.057 b	3.26 ± 0.37 b
Poor glycemic	6.165 ± 0.48 c	2.465 ± 0.768 c	0.87 ± 0.01 c	4.33 ± 0.51 c
Results are represented as mean ± SD.				

Values with non-identical superscripts (a, b, and c) are considered to be substantially different across groups (P<0.05).

3.4. Glycated Hemoglobin (HbA1c), C-peptide Levels in Type 2 DM Patients and Fasting Plasma Glucose (FPG)

According to reports, 90% of diabetes patients have type 2 conditions and often need therapeutic intervention with oral hypoglycemic medications for glucose management (6). Type 2 diabetes treatment choices and expectations have significantly evolved in recent years. While food and lifestyle modifications continue to be the primary methods of therapy for this condition, new substances are being developed expanding the toolbox of the doctor. When the objective of therapy has been predicated on reducing FPG and HbA1c, the administration of oral antidiabetic medications is typically essential within several months of any planned lifestyle modifications (7). The ability of a drug or regimen plan to lower plasma glucose without causing hypoglycemia is the basis for treatment success (8). However, new research indicates that this therapy paradigm may be inadequate and that aberrations in mealtime glucose control have a key role in the development and prognosis of the disease (9).

The results presented in table (3-1) indicated that FPG in both groups, good and poor glycemic control patients, was significantly higher compared to normal controls and FPG, when used as a parameter, may represent an indication for a certain limit of decrease in hyperglycemia, but still insufficient to prove successful treatment since FPG levels, even when they showed a significant decrease in good glycemic control compared to poor one, they are still higher than normal.

Abnormally high blood sugar levels following food intake (or glucose excursion-spikes after meals) develop extremely early in type 2 DM diabetes because early-phase insulin production is lost, and these (spikes) now a days have been shown to significantly contribute to disease pathophysiology, and more accurate predictors of long-term glycemic management than FPG levels and identified as a cardiovascular risk factor death (3, 4). Accordingly, this study was concerned about evaluation of the involvement of HbA1c and PPGE assessment in determining effectiveness of DM treatment. So, the data presented in table (3-1) indicated that HbA1c levels, in both DM patients' groups when these levels were compared with each other, they also showed significant differences. However, when HbA1c levels

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were correlated with FPG levels, only poor glycemic control patients demonstrate significantly positive correlation, while no such relationship was observed in the other group, which give an indication about the idea that FPG was a poor predictor for glycemic control. Accordingly, modern treatment of DM will more often focus on reducing HbA1c and addressing glucose spikes (10).

Stimulation of insulin production in a rhythm that corresponds to the physiological beginning of the insulin response to food (absent in all type 2 diabetics), prevent resistance to insulin action, and this event was found to be lost in DM patients, and regarded as the disease's major abnormality (11). Restoring a natural insulin production profile reduces glucose spikes during meals and may place less stress on the insulin producing pancreatic β-cells (12).

3.5. Post-prandial Glucose Excursion Test and AUC in Type 2 DM Patients

After having a meal, plasma glucose concentrations are referred to as post-prandial glucose levels (13). Many factors determine the post-prandial glucose profile, involving gastrointestinal absorption, glucagon release and insulin and their coordinated impacts on peripheral tissues and liver glucose metabolism (14). The results of PPGET observed in this study showed significant increase in PPG levels represented by AUC0-4, in both groups of DM patients included in this study, during the standard period of follow up recommended by the test (Table 3-2) compared to normal controls. However, AUC0-4 obtained for both DM groups showed significant differences, but as indicated later, both of the two values were significantly higher compared to controls, indicating poor glycemic control in both groups.

Several studies have shown that post-prandial hyperglycemia is a significant contributor to glucose control and may even play a role in the development of diabetes. Feinglos et al. found that insulin lispro treatment of post-prandial hyperglycemia in people with type 2 diabetes improved post-prandial glucose management and decreased fasting plasma HbA1c and glucose. (15). Researchers found that lowering post-prandial glucose levels rather than fasting glucose levels is more effective at lowering HbA1c levels, and the risk of developing diabetes was nearly twice that of HbA1c levels (16). The endothelium may be harmed by even mild post-prandial hyperglycemia (114-198 mg/dL), according to other recent studies that found it more predictive of atherosclerosis than fasting plasma glucose (FPG).

3.6. Type 2 Diabetic Patients' Lipid Profile

Patients with type 2 diabetes are more prone to dyslipidemia, and coronary heart disease (CHD) and macrovascular complications are the main causes of mortality and disability in these people (17).

It is widely recognized that diabetes mellitus causes hyperlipidemia as a result of altered lipoprotein metabolism brought on by an increase in synthesis, a reduction in clearance, and/or a change in lipoprotein composition brought on by changes in glucose and insulin levels (18).

The results demonstrated that type 2 diabetes patients' total cholesterol levels were significantly higher than those of controls (Table 3-3) that mean prevalence of hypercholesterolemia, where it was hypothesized that this discovery was caused by a rise in non-enzymatic LDL glycosylation, which refers to metabolic inhibition of LDLc-receptor activation (19). There's a Table There's (3-3), Type 2 diabetes patients have significantly higher levels of triglyceride compared to their healthy counterparts. This study's findings are in line with earlier research. Type 2 DM hypertriglyceridemia is caused by both reduced clearance of VLDL-TG and increased synthesis, according to studies by Abrams et al. and Kissebah et al (20). Dyslipidemia in people with type 2 diabetes is characterised by elevated triglyceride levels, notably in VLDL-cholesterol, which is high in triglycerides, and decreased HDL-c cholesterol. Dyslipidemia, according to Turner et al., is characterised by an elevated level of LDL-c (21). Type 2 diabetes patients may have low HDL because of insulin resistance, which alters hepatic function and increases the activity of the enzyme hepatic lipase, which aids in lowering HDL. (22).

This research discovered that type 2 DM lipoprotein abnormalities were significantly attributed to low HDL-c blood levels in diabetics (Table 3-3). Numerous studies have shown that individuals with type 2 diabetes and insulin resistance have a marked lipid imbalance with low HDL-c and high TG levels (23).

Patients with type 2 diabetes had significantly higher LDL levels than the control group in this study (Table 3-3). This finding jibed well with previous findings (24). Glycosylation of LDL and chronic insulin insufficiency may be responsible for the decreased elimination of LDL-c, which may be linked to the highly atherogenic particles (25).

4. Conclusion

1. Fasting plasma glucose is not an effective marker for determining glycemic control both in diagnosis and treatment follow up in type 2 diabetes mellitus.
2. post-prandial glucose excursion test and HbA1c levels can be considered as a reliable and sensitive marker both for treatment and diagnosis follow up in type 2 DM patients.
3. PPGE test was recommended to be implanted in the assessment protocol of the effectiveness of treatments recommended for type 2 DM patients.

Recommendations

Larger scale screening program include PPGE test is recommended at routine institutional level to provide widely applied, evidence-based criteria

for implementing this test in routine practice of diagnosis and monitoring of glycemic control.

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