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Estimating The Levels Of (Coenzyme Q10) In Patients With Type II Diabetes Mellitus

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Abstract
Type II Diabetes Mellitus (T2DM) and its precursor, pre-diabetes, are characterized by chronic oxidative stress and metabolic dysfunction. Nuclear Factor Erythroid 2–Related Factor 2 (Nrf2), a master regulator of antioxidant defenses, are crucial in cellular protection. This study aimed to estimate the levels of serum Nrf2 in T2DM patients, pre-diabetic individuals, and healthy controls, and to evaluate their diagnostic potential. In order to obtain the necessary ethical permits, the team of the ethical committee, the faculty of medicine, the university of Karbala, and the Karbala Health Directorates / Karbala-Iraq contributed their support.
This study's aim was to assess the CoenzymeQ10 levels in sera of (T2DM) patients ,pre diabetic and healthy control subjects
Methods: *A case-control study in Iraq, involving 46 type 2 diabetes patients, 30 control volunteers, and 12 prediabetic volunteers aged 20-75, was conducted from September 2024 to July 2025.*
Results*The study analyzed glycated hemoglobin (HbA1c) and lipid levels in diabetic and prediabetic groups, with diabetic and prediabetic groups showing typical glycemic and dyslipidemia patterns. Serum CoQ10 levels showed a significant decline from healthy controls (mean 1.6 U/L) to the prediabetic group (mean 0.89 U/L), with the lowest in diabetic patients(mean 0.38 U/L). ROC curve analysis showed excellent diagnostic accuracy of CoQ10, with an AUC of 0.9724 ($p<0.0001$) ,optimal lower limit of <1.275 U/L.for diabetic patients and 0.9013 ($p < 0.0001$), optimal lower limit of < 1.120 U/L.for prediabetes. A significant positive correlation was found between CoQ10 levels both diabetic ($r = 0.4$, $p = 0.05$) and prediabetic ($r = 0.65$, $p = 0.001$) .*
Conclusion: *Serum CoQ10 levels decrease with metabolic dysregulation, serving as an accurate biomarker for diagnosing pre-diabetes and Type II Diabetes Mellitus, highlighting its potential as a non-invasive tool for glucose metabolism monitoring.*

1.1. INTRODUCTION

Diabetes mellitus (DM) is a major metabolic disease characterized by elevated blood glucose levels due to a combination of genetic and environmental factors [1]. It is divided into three types: type 1 (T1DM), type 2 (T2DM), and gestational diabetes (GDM) [2]. Type 2 diabetes occurs when the pancreas produces insufficient amounts of insulin or cells display an inappropriate response to it [1]. Risk factors for type 2 diabetes include obesity, hypertension, lifestyle, age, nutrition, physical activity, and genetic factors [3]. Complications of diabetes can be acute or chronic, ranging from minor to major complications [4]. CoQ10, a vitamin-like antioxidant, is a popular nutritional supplement for treating a variety of health conditions, including cardiovascular disease, diabetes, neurological disorders, and metabolic disorders [5]. Patients with type 2 diabetes suffer from elevated blood lipid levels, which are targeted by reactive oxygen species, leading to decreased intracellular antioxidant levels. Antioxidant therapy is an effective approach for managing the progression of type 2 diabetes [6].

The term "prediabetes" refers to blood glucose levels above normal, but below the diagnostic threshold for diabetes, due to impaired glucose metabolism. Laboratory markers for prediabetes include fasting blood glucose, 2-hour blood glucose, or glycated hemoglobin (HbA1c). In 2003, the American Diabetes Association lowered the fasting plasma glucose threshold range to 100–125 mg/dL or 5.6–6.9 mmol/L (IFGADA)

1.2. Coenzyme Q10 (Co Q10)

2,3-Dimethoxy-5-methyl-6-polyprenyl-1,4-benzoquinone) is an essential biomolecule that functions in the electron transport chain within the mitochondria in the inner membrane. It is also characterized by being a lipid-soluble molecule

due to its non-polar structure, which allows it to move within the inner mitochondrial membrane and facilitates energy transfer in the form of ATP. Its importance also lies in its role as an antioxidant, as it significantly affects the redox state within the cell, in addition to regulating gene expression. Figure (1.1) shows the chemical structure of this important compound [7].

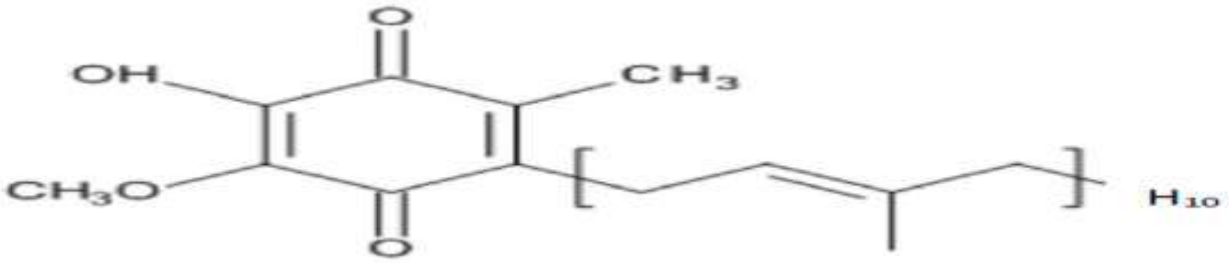

Figure (1.1) *The chemical structure of CoQ10*

The molecule is generated through several processes involving mevalonic acid, the formation of which is blocked by hydroxyl-methylglutaryl coenzyme A (HMG CoA) reductase inhibitors . Coenzyme Q10, in its reduced form ubiquinol, has demonstrated the capacity to block the oxidation of proteins, DNA, and lipids. Coenzyme Q10 in serum is predominantly associated with low-density lipoprotein (LDL) cholesterol transport and is not present in significant concentrations in its unbound form. Its reduced form in circulating lipoproteins and prevents LDL peroxidation. The suppression of LDL peroxidation may be crucial to its antiatherogenic properties [8]. Coenzyme Q10 (CoQ10) is a vitamin-like compound produced in various tissues throughout the human body. CoQ10 plays a crucial role in cellular energy production through oxidative phosphorylation in mitochondria, facilitating the transfer of electrons from complexes I and II to complex III of the mitochondrial respiratory chain by taking two electrons from NADH to form CoQ10H2. This occurs in complex I, while in complex II, it takes electrons from FADH2 and then donates the electrons received to complex III, which is oxidized to CoQ10 .In addition, CoQ10 acts as a potent lipid-soluble antioxidant, protecting cell membranes from oxidative damage caused by free radicals [9]. In addition to its function in mitochondrial activity, CoQ10 is found in numerous subcellular organelles, such as lysosomes, peroxisomes, the Golgi apparatus, and the endoplasmic reticulum. In addition to providing antioxidant protection to organelle membranes from oxidative stress, CoQ10 is involved in regulating intralysosomal pH [10]. CoQ10 has been shown to directly influence the expression of numerous genes, including those associated with the inflammatory process [11].

2. Study Design and Setting

A case-control study was conducted in the Department of Chemistry and Biochemistry, College of Medicine, University of Karbala. included 88 individuals aged 18–75 years. Data were collected from December 2024 to February 2025.

Patient Group All patients were diagnosed by a consultant physician with type 2 diabetes based on clinical symptoms and laboratory tests (FBS, HbA1c). Pre-diabetic group, non-diabetic group

Inclusion criteria: Type II Diabetes Mellitus, without insulin therapy, across all age groups and both genders, selected controls exhibiting normal fasting blood sugar and haemoglobin A1c (HbA1c) results.

Exclusion criteria: Diabetes Mellitus I (DM I),Gestational Diabetes Mellitus (GDM),Chronic Heart diseases, Chronic Joints diseases, Cancers, Auto-immunity patient.

2.1. Biochemical Analyses

Blood samples were collected after 12 hours of fasting for biochemical analyses in appropriate tubes for each biochemical test. Fasting blood glucose, HbA1c, total cholesterol, HDL-cholesterol, LDL, VLDL, AST, ALT and triglycerides were measured using standard enzymatic, Also the body mass index was calculated for each sample methods, with up to 5 ml each from the control, prediabetic, and diabetic groups. Each blood sample was then separated into two parts as follows:

A. A 1 ml sample was placed in an EDTA tube to determine glycated hemoglobin (HbA1c) using the latex turbidity method on a Lifotroni H8.

B. Blood samples containing 4 ml were placed in gelatin tubes and incubated at room temperature for 10 to 15 minutes. The serum was then centrifuged for 10 to 15 minutes at 3,000 × 3,000 g to enhance serum separation.

C. The samples were then examined in HPLC to detect and quantify CoQ10 levels.

2.2.Measurement of Serum Human CoQ10 Concentration

Preparation of CoQ10 standard

Stock solutions of 1mM CoQ10 were prepared in ethanol protected from light and stored at -20C° for two months. Before analysis the accurate concentration of CoQ10 in the working standard solution was obtained by spectrophotometry at 275 nm, e¼14020 L=mol. cm. CoQ10 calibration curve at concentration levels of 0.1, 0.35, 1.2, 3.5, 7.0, and 15.0 mM were prepared in the mobile phase from 1mM CoQ10 stock solutions. **Concentration of CoQ10 standard =** 20 ppm

Measurement of coenzyme Q10 in a group of patients and healthy individuals

Before the analysis, the samples were allowed to thaw at room temperature.600 uL of plasma were supplemented with 800 uL of cold1-propanol, stirred with vortex for 2 min, and centrifuged at 9000 g during10 min at 4C to spin down the protein precipitate and finally the organic layer was evaporated to dryness under a stream of nitrogen. Use a 0.45 HPLC syringe filter to filter the sample and transfer it to a 1.5 ml vial. The dry residue was dissolved in 400 uL of mobile phase and then 100 uL of the treated sample is injected into the equipment. Utilize the HPLC device to determine the absorbance of the sample. The subsequent findings were attained

HPLC analysis : A German HPLC model, SYKAMN (Germany).This model was used to determine and detect CoQ10 in human plasma using a column with a mobile phase of methanol and water at a ratio of 98:2 v/v, a flow rate of 0.7 mL/min, and a column temperature of 30°C. The column used was a C18-ODS-2, measuring 25 cm x 4.6 mm, and the detector was a UV-Vis (at a wavelength of 275 nm) detector for 15 minutes

3.RESULTS

3.1.Distribution of Past Medical History

The study revealed significant differences in medical history between diabetic and non-diabetic groups. 23.9% of the diabetic group had a family history of type 2 diabetes. 41.7% of the pre-diabetic group had a family history, compared to 13.33% of the healthy control group. 65.2% of the diabetic group had hyperlipidemia. The incidence of hyperlipidemia (in the pre-diabetic group) was 0.00%, while the non-diabetic group had hyperlipidemia (6.7%). 45.6% of the diabetic group were physically active. 66.6% of the pre-diabetic group were physically active, compared to 90.0% of the non-diabetic group. The study included 88% of diabetic patients who were treated with blood sugar-lowering medications. The study also found that 12% of the diabetic patients were not receiving treatment and were following a diet.

3.1. Hemoglobin (HbA1c)

The study found an increasing pattern of serum glycated hemoglobin (HbA1c) levels in three groups: control, prediabetic, and diabetic patients. The mean HbA1c values corresponded to clinical diagnostic criteria. The wide range in diabetic patients indicated significant variability in glycemic control, while the narrower ranges in the control and prediabetic groups indicated a more stable level (Table 3.1,Figure 3.1)

Table (3.1) Serum Levels of glycated Hemoglobin among study groups

	DM	Pre DM	Control
Hba1c Median (Mini-Max)	7.9 (5.2-13)	5.9 (5.7-6.1)	4.9 (4.7-5.6)

Figure (3.1) *Distribution of Serum Levels of HbA1c among study groups (Post Hoc ANOVA test was *: significant at p ≤ 0.05, **: significant at p ≤ 0.01, ***: significant at p ≤ 0.001), ****: significant at p ≤ 0.0001*

3.2.Lipid Profile

Lipid profile data show distinct patterns across three groups, indicating a progressive metabolic deterioration from a healthy state to prediabetes and the onset of diabetes. Triglycerides (TG), high-density lipoprotein (HDL), and total cholesterol correlated with the glycemic status of the groups. Triglyceride levels showed an upward trend from the control group to the prediabetic group, and then to diabetes. See the following table and figure

Table (3.2) Serum Levels of Lipid profile among study groups

		DM	*Pre DM*	*Control*
TG	*Median (Mini-Max)*	162 (60-617	131 (100-145)	99 (84-153)
HDL	*Median (Mini-Max)*	48 (33-68	62 (42-67)	65 (39-69)
LDL	*Median (Mini-Max)*	93 (21-150	90 (86-94)	68 (50-104)
CHOLESTROL	*Median (Mini-Max)*	188 (90-308	185 (168-193)	164 (124-199)

Figure (3.2) Distribution of Serum Levels of Lipid profile among study groups (Post Hoc ANOVA test was *: significant at p ≤ 0.05, **: significant at p ≤ 0.01, ***: significant at p ≤ 0.001), *: significant at p ≤ 0.0001***

3.3. Liver Function Enzymes

Table (3.3) presents the median and range for Alanine Aminotransferase (ALT) and Aspartate Aminotransferase (AST) in diabetic patients (DM), pre-DM group, and healthy controls. The median ALT levels showed a descending trend from healthy controls to DM patients, with the highest median ALT in healthy controls, followed by the Pre-DM group , and the lowest in DM Patients .

AST showed a descending trend across the groups, with Healthy Controls having the highest median , followed by the Pre-DM group , and DM patients . The Healthy Control group had the widest overall range for AST , possibly due to outliers or a broader spectrum of physiological conditions.

While the median values for both ALT and AST show a slightly decreasing trend from healthy controls to DM patients, the broad ranges indicate heterogeneity within each group, suggesting differences in liver health or metabolic compensatory mechanisms among these specific cohorts or a need for more nuanced statistical analysis beyond medians and ranges.

Table (3.3) Serum Levels of Liver function enzymes among study groups

		DM	*Pre DM*	*Control*
ALT	*Median (Mini-Max)*	20 (9.5-61	29 (10-36	31 (29-32
AST	*Median (Mini-Max)*	23 (15-42	26 (16-33	28 (16-83

Figure (3.3) Distribution of Serum Levels of Liver function enzymes among study groups (Post Hoc ANOVA test was *: significant at p ≤ 0.05, **: significant at p ≤ 0.01, ***: significant at p ≤ 0.001), *: significant at p ≤ 0.0001***

3.3. Comparison of CoQ10 Mean Values between The study Groups

Table (3.4) illustrated the median and range (Min-Max) for serum Co Q10 in DM Patients, Pre-DM Group, and Healthy Controls. there was a **clear and significant descending trend** in serum Co Q10 levels from Healthy Controls to the Pre-DM group, and further to DM Patients. **Healthy Controls exhibit the highest median Co Q10 (1.6)**, with a tight and high range (1.3-1.7), indicative of robust antioxidant status. The **Pre-DM group shows an intermediate median (0.89)**, with a broader range (0.22-1.6), indicating some individuals may have Co Q10 levels similar to healthy controls, while others are lower. **DM Patients have the lowest median Co Q10 (0.38)**, with a broad range (0.16-1.5), demonstrating a considerable reduction in this vital antioxidant. The lower median and often lower values in the range for diabetic patients are consistent with increased oxidative stress and mitochondrial dysfunction known to occur in diabetes. This trend strongly suggests that Co Q10 levels are progressively depleted as individuals move from a healthy metabolic state through pre-diabetes to overt diabetes, potentially reflecting increased oxidative burden or impaired Co Q10 synthesis/utilization in these conditions. **Co Q10 levels clearly demonstrate a progressive decline from healthy individuals to pre-diabetic and diabetic patients.** This reduction in Co Q10 in pre-diabetes and diabetes highlights its potential as a marker for oxidative stress and metabolic health deterioration, which is a significant finding given Co Q10's crucial role in cellular energy production and antioxidant defense.

Table (3.4) Serum Levels of Co Q10 among study groups

		DM Patients	Pre DM group	Healthy Control
Co Q10	Median (Mini-Max)	0.38 (0.16-1.5)	0.89 (0.22-1.6)	1.6 (1.3-1.7)

Figure (3.6) Distribution of Serum Levels of Co Q10 among study groups (Post Hoc ANOVA test was *: significant at p ≤ 0.05, **: significant at p ≤ 0.01, ***: significant at p ≤ 0.001), *: significant at p ≤ 0.0001***

3.4. Comparison of CoQ10 Mean Values According to Study groups

The Pearson correlation coefficient (r) and the corresponding p-value for various biomarker pairs within the DM patient group. A p-value less than 0.05 is considered statistically significant. There is a **positive and statistically significant correlation** between serum CoQ10 and (r = 0.4, p = 0.05). This indicates that in DM patients, as CoQ10 levels tend to decrease, suggesting a potential interplay or parallel regulation of this antioxidant-related molecule. CoQ10 shows a **positive weak and statistically significant correlation** with HDL (r = 0.332, p = 0.005). This is an important finding, suggesting that low levels of the antioxidant CoQ10 are associated with low levels of "good" cholesterol (HDL) in diabetic patients. **Cholesterol (Chol), Triglycerides (TG), LDL, HbA1c, ALT, and AST:** CoQ10 did **not show statistically significant correlations** with Cholesterol (r = -0.372, p = 0.172), TG (r = -0.131, p = 0.642), LDL (r = -0.184, p = 0.511), HbA1c (r = -0.154, p = 0.584), ALT (r = 0.094, p = 0.739), or AST (r = -0.179, p = 0.523).

The significant positive correlation between CoQ10 and HDL is clinically relevant. In diabetes, low HDL is a common feature of dyslipidemia and contributes significantly to increased cardiovascular risk. This finding suggests that low CoQ10 levels in diabetic patients might be protective or associated with a less unfavorable lipid profile, specifically concerning HDL.

The Pearson correlation coefficient (r) and the corresponding p-value for various biomarker pairs within the Pre-DM patient group. As per the table's definition, p-values less than 0.05 are considered statistically significant.

CoQ10 also shown a **negative correlation** with HbA1c (r = -0.920, p = 0.027). . This indicates that within the Pre-DM group, individuals with low CoQ10 levels tend to have higher HbA1c, which is consist finding given CoQ10's antioxidant role and its general depletion in diabetes progression.

CoQ10 shows a **weak negative and statistically significant correlation** with AST (r = -0.234, p = 0.05). This suggests that as CoQ10 levels increase, AST levels tend to slightly decrease.

The Pre-DM group exhibits a strong nehative correlation of CoQ10 with HbA1c is an interesting finding specific to this group that merits deeper investigation.

3.5. **Association of Serum Levels of CoQ10 among study groups**

This ability of CoQ10 to predict the likelihood of an individual belonging to the DM Patient group or the Pre-DM group, as opposed to the Healthy Control group. An Odds Ratio (OR) of 1 means no association, an OR greater than 1 means increased odds, and an OR less than 1 means decreased odds.

The Odds Ratio (OR) for CoQ10 in DM Patients was 1.097 (95% CI: 1.035-1.174), with a p-value of <0.001, indicating high statistical significance. An OR of 1.097 suggests that for every one-unit increase in serum CoQ10 levels, the odds of being a DM patient (compared to a healthy control) are 1.097 times higher (approximately 9.7% higher). The confidence interval does not include 1, reinforcing significance.

The Odds Ratio (OR) for CoQ10 in the Pre-DM group was 4.85 (95% CI: 3.01-4.90), with a p-value of <0.001, indicating high statistical significance. An OR of 4.85 implies that for every one-unit increase in serum CoQ10 levels, the odds of being in the Pre-DM group (compared to a healthy control) are 4.85 times higher. The very high OR and non-overlapping confidence interval indicate a strong predictive power.

3.6 Receiver Operating Characteristic (ROC) curve

The diagnostic performance of serum CoQ10 levels in identifying DM patients and Pre-DM individuals.

The Diagnostic Performance for DM, An AUC of 0.9724 is exceptionally high. This indicates excellent diagnostic accuracy for serum CoQ10 in differentiating DM patients from healthy individuals.

The optimal cut-off, can correctly identify 87.50% of individuals who truly have Diabetes Mellitus (true positives). An individual with a serum CoQ10 level below 1.275 is optimally classified as a DM patient. This aligns perfectly with the

descriptive statistics which showed DM patients having a median CoQ10 of 0.38 and healthy controls having a median of 1.6, confirming that lower CoQ10 is indicative of DM. while the diagnostic performance in Pre-DM, results were shown that An AUC of 0.9013 is also very high, indicating excellent diagnostic accuracy for serum CoQ10 in differentiating Pre-DM individuals from healthy controls. This means that CoQ10 levels can correctly identify 76.00% of individuals who are in the pre-diabetic stage. Also CoQ10 levels can correctly identify 93.55% of individuals who are not pre-diabetic (i.e., healthy controls), demonstrating a very good ability to rule out pre-diabetes.

An individual with a serum CoQ10 level below 1.120 is optimally classified as being in the Pre-DM group. This is consistent with the descriptive statistics where the Pre-DM group had a median CoQ10 of 0.89 and healthy controls had 1.6, showing lower CoQ10 in pre-diabetes. Serum CoQ10 levels demonstrate a good diagnostic utility for both Diabetes Mellitus and the Pre-DM state. The cut-off points (< 1.275 for DM and < 1.120 for Pre-DM) are intuitive, indicating that progressively lower levels of CoQ10 are associated with a higher likelihood of being in the diabetic state, which is consistent with the depletion of this antioxidant in metabolic disorders. The high sensitivity and specificity for both classifications suggest that CoQ10 could serve as a valuable non-invasive biomarker for screening and diagnosis in the context of impaired glucose metabolism.

Figure (3.7) Receiver operating characteristic curve of CoQ10 ***levels among patients groups***

4.DISCUSSION

This study examined various biomarkers related to diabetes, revealing a clear pattern of HbA1c levels across healthy controls, pre-diabetes, and Type II Diabetes Mellitus patients. The trend reflects the deterioration of glycemic control along the spectrum of glucose dysregulation. HbA1c measures average blood glucose levels over the preceding 2-3 months and is a widely accepted diagnostic criterion for diabetes and pre-diabetes. The median values observed in this study are in excellent agreement with diagnostic thresholds set by major health organizations (e.g., HbA1c <5.7% for non-diabetic, 5.7%-6.4% for pre-diabetes, and ≥6.5% for diabetes) [12].

The distinct separation in median HbA1c values between the groups emphasizes the utility of this biomarker in identifying individuals at different stages of glucose metabolism. The gradual increase from optimal glycemic control in healthy individuals to impaired glucose regulation in pre-diabetes illustrates the natural continuum of the disease [13]. Early detection of pre-diabetes is crucial as individuals in this stage are at significantly increased risk of progressing to type 2 diabetes and developing cardiovascular complications[14].

The wide range of HbA1c observed in DM patients (5.2% - 13%) is clinically pertinent, reflecting various factors such as the duration of the disease, treatment efficacy, patient adherence to medication and lifestyle interventions, and the presence of diabetes-related complications [15].

This variability underscores the need for individualized management strategies in diabetes care. Conversely, the tighter ranges for both Healthy Controls (4.7-5.6%) and the Pre-DM group (5.7-6.1%) suggest a more consistent metabolic state within these populations. In healthy individuals, glucose regulation mechanisms are generally robust, leading to stable HbA1c levels. In pre-diabetes, while glucose regulation is impaired, it has not yet deteriorated to the extent seen in overt diabetes, resulting in a narrower band of elevated but not severely high HbA1c values [12].

In conclusion, the HbA1c data from this study effectively differentiates the three glycemic states, providing clear biochemical evidence for the classification of groups [16]

4.1.lipid profile

The lipid profile data reveals patterns of metabolic dysregulation in pre-diabetes and overt diabetes, primarily driven by insulin resistance, a key factor in the pathophysiology of both conditions [17; 18]. The study groups showed an ascending trend in Triglyceride (TG) levelsfrom healthy controls (median 99 mg/dL) to the Pre-DM group (131 mg/dL) and significantly higher in DM Patients (162 mg/dL) is a classical feature. Elevated triglycerides in diabetic and pre-diabetic states result from increased hepatic very-low-density, which is a classical feature of diabetic dyslipidemia [17; 18].

High-Density Lipoprotein (HDL) showed a descending trend across the groups, with the highest median in healthy controls(65 mg/dL), moderately lower in the Pre-DM group(62 mg/dL), and significantly reduced in DM patients(48 mg/dL). This low HDL, particularly below the clinically desirable threshold(typically >50-60 mg/dL), is another characteristic of diabetic dyslipidemia [12]. Insulin resistance leads to increased catabolism of HDL particles and reduced synthesis of apolipoprotein A-I (apoA-I), a major component of HDL, thereby diminishing its anti-atherogenic functions,

such as reverse cholesterol transport [19; 20]. The increasing trend in Low-Density Lipoprotein (LDL) levels from healthy controls (median 68 mg/dL) to Pre-DM (90 mg/dL) and DM Patients (93 mg/dL) is another critical observation. The wide range in LDL among DM patients highlights the diverse metabolic profiles within the diabetic population [21; 22]. lipoprotein (VLDL) production and impaired catabolism of triglyceride-rich lipoproteins due to reduced lipoprotein lipase (LPL) activity, both consequences of insulin resistance [19; 23]. Total cholesterol levels also showed an ascending trend, mirroring the changes in LDL and reflecting the overall lipid burden. The close medians for total cholesterol between Pre-DM and DM groups further reinforce that significant lipid disturbances are present even before a full diagnosis of diabetes, placing these individuals at heightened cardiovascular risk [24; 12].

4.2.Liver function

The study reveals intriguing patterns in serum Alanine Aminotransferase (ALT) and Aspartate Aminotransferase (AST) levels, particularly in diabetic patients. These enzymes are biomarkers for liver function and cellular integrity, with elevated levels indicating hepatocellular injury. [25].

The study reveals a significant subset of diabetic patients with type 2 diabetes (DM) exhibit elevated ALT levels, possibly due to NAFLD/NASH, which affects 60-70% of patients [26].This variability suggests that despite a low median, a significant proportion of individuals are experiencing liver pathology. While ALT and AST are useful screening tools, their median values alone should not rule out liver pathology in high-risk populations. The liver enzyme data, particularly lower median ALT and AST, may reflect NAFLD progression, metabolic adaptations, and individual variability [27].

4.3. Coenzyme Q10 (CoQ10) levels

The study reveals contrasting patterns in serum and Coenzyme Q10 (CoQ10) levels, with CoQ10 emerging as a distinct indicator of metabolic health deterioration in pre-diabetes and diabetes. CoQ10 is an essential lipid-soluble antioxidant and crucial component of the mitochondrial electron transport chain, protecting lipids, proteins, and DNA from oxidative damage. The study found a significant descending trend in serum CoQ10 levels from Healthy Controls (median 1.6) to the Pre-DM group (0.89) and further to DM Patients (0.38) , attributed to increased oxidative stress in diabetes [28].

CoQ10 levels show a decline from healthy individuals to pre-diabetic and diabetic patients, highlighting its role as a biomarker for oxidative stress and metabolic health deterioration. Depletion of CoQ10 increases susceptibility to oxidative damage and mitochondrial dysfunction, central to diabetes pathogenesis and complications [29].

4.4.Association Odds Ratio (OR)

Binary logistic regression analysis evaluated the independent predictive ability of serum CoQ10 levels in classifying individuals into diabetic or prediabetic groups, compared to a healthy control group.

It indicated statistically significant higher odds ratios for CoQ10 in both diabetic patients (OR = 1.097, $p < 0.001$) and prediabetic patients (OR = 4.85, $p < 0.001$) compared to a healthy control group.

CoQ10 levels are already strong predictors of grouping. This is consistent with the excellent diagnostic performance of CoQ10, as low CoQ10 levels were correctly identified as ideal cutoff points for classifying diabetic and prediabetic patients. It is likely that the model accurately identified CoQ10 as a strong discriminator. CoQ10 is known to play a key role in mitochondrial function and antioxidant defense, and its depletion is closely linked to the development of insulin resistance and diabetes [28].

4.5.Receiver Operating Characteristic (ROC) Curve

Receiver operating characteristic (ROC) curve analysis accurately assesses the diagnostic performance of serum Coenzyme Q10 (CoQ10) levels in distinguishing between individuals with diabetes mellitus (DM) and pre-diabetes (pre-DM) from healthy individuals. Taken together, the results demonstrate that CoQ10 is a highly promising biomarker for assessing metabolic health.

The diagnostic measures of CoQ10 demonstrate its high efficacy in identifying various glycemic conditions. The report "Exceptional Diagnostic Accuracy for Diabetes" showed an area under the curve (AUC) of 0.9724, which is a very high value. An AUC value greater than 0.9 is generally considered excellent, indicating that CoQ10 can almost accurately distinguish between individuals with diabetes and healthy controls [30; 31].

The distinct cutoff points (<1.275 for diabetes and <1.120 for prediabetes) are intuitive and reflect the gradual decline in CoQ10 as individuals transition from a healthy metabolic state through prediabetes to overt diabetes. This decline is

attributed to increased oxidative stress and mitochondrial dysfunction, two key factors in the pathophysiology of these conditions [28; 32].

The high sensitivity and specificity of both classifications suggest that CoQ10 could serve as a valuable, non-invasive biomarker for early screening, diagnosis, and risk stratification in the context of impaired glucose metabolism. CoQ10's ability to accurately identify individuals at prediabetes is crucial, as early detection enables timely lifestyle measures or pharmacological strategies to prevent or delay the progression to type 2 diabetes and its associated complications [14]. Furthermore, given CoQ10's pivotal role in cellular energy production and antioxidant defense, its diagnostic utility highlights its pivotal role in the metabolic disturbances of diabetes, potentially guiding future therapeutic strategies involving CoQ10 supplementation.

5.CONCLUSIONS

The Study reveals that Coenzyme Q10 (CoQ10) depletes significantly as individuals transition from a healthy metabolic state to overt diabetes. This decline correlates with worsening glycemic control and an unfavorable lipid profile in established diabetes. CoQ10 plays a critical role in mitigating oxidative stress and supporting mitochondrial function. It demonstrated excellent diagnostic accuracy in distinguishing diabetic and pre-diabetic individuals, making it a promising non-invasive biomarker for early intervention and personalized management strategies.

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