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Assessment of Serum Apelin Level in Iraqi Type 2 Diabetic Nephropathy Patients

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Abstract

The present study is investigated the relationship between Apelin concentration and various biochemical parameters in patients with type 2 diabetic nephropathy. A total of 30 patients diagnosed with Diabetic Nephropathy at Al-Yarmouk and Al-Karama teaching hospitals were included in the study and compared to 40 healthy individuals forming the control group. The study was identified a significant increase in Apelin concentration among patients with type 2 diabetic nephropathy, compared to the control group. Additionally, various biochemical parameters were analyzed, and a strong correlation was found between their concentrations and Apelin levels. Considerable elevation of serum nitrogen compounds like urea and creatinine, as well as fasting blood glucose and glycated hemoglobin (HbA1c) were observed in the type 2 diabetic nephropathy patients. A positive correlation between Apelin and both creatinine and glycated hemoglobin levels was observed. Conversely, a negative correlation was observed between Apelin and the glomerular filtration rate (GFR), indicating potential implications for kidney function in these patients. These findings emphasize the significance of monitoring Apelin concentration along with other biochemical variables as essential indicators for the management and understanding of type 2 diabetic nephropathy. Further research in type 2 diabetic nephropathy could offer valuable insights into potential interventions and treatment strategies for improving patient outcomes.

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1. Introduction

Diabetes mellitus is a group of metabolic diseases which is characterized by hyperglycemia causes as a result of impairment in insulin secretion, insulin action, or both [1]. Diabetes-related chronic hyperglycemia is associated with long-term damage, dysfunction, and failure of various organs, particularly the eyes, kidneys, nerves, heart, and blood vessels [2]. Type2 Diabetes mellitus is the end stage of a chronic and progressive disease. It is characterized by various combination of insulin resistance and decreased pancreatic cell activity due to inherited and induced abnormalities. Microvascular complications, such as diabetic nephropathy, cause morbidity and mortality in type 2 diabetes patients. Therefore, it will be much easier to manage and screen microvascular complications if they are diagnosed early, and protect those macrovascular complications risk [3]. Recent research suggests that the incidence of Type 2 Diabetic Nephropathy increases significantly with the disease progression. About

30% of Type 2 Diabetes patients were affected by this complication [4]. Several factors, such as prolonged high blood sugar levels, hypertension, family history of kidney disease, smoking, and obesity, contribute to the progression of Type 2 Diabetic Nephropathy. The diagnosis involves urine and blood tests, and management typically involves the improvement of diabetes control by blood sugar levels, monitoring and control of blood pressure, dietary modifications, and smoking cessation [5]. Adipokines, are hormones released by adipose tissue, and play a crucial role in the progression of certain illnesses. Apelin, is a peptide hormone which is secreted by white adipose tissue and expressed in multiple organs, including the heart, lung, kidney, liver, and adrenal glands. There are various forms of apelin, including apelin 36, 19, 17, 15, 13, and 12, Figure (1). Certain cell types, which include islet cells of the pancreas, express APLN as an endogenous ligand for the G protein-coupled APJ receptor. Numerous clinical investigations have evaluated apelin concentrations in the body fluids of healthy individuals and patients with a wide range of diseases, including diabetes and cardiovascular disease [6], [7]. Recent research has established apelin as a biomarker of diabetic nephropathy. Studies have shown the significance of apelin as an adipokine in diabetes. It has a potential therapeutic target and a biomarker. The increasing prevalence of diabetes and obesity has emerged the need for development treatments, apelin is one of the most promising candidates for diabetes [8]. In an experimental study, the administration of apelin to diabetic mice resulted a several positive effects. It was shown that apelin led to a decrease in kidney and glomerular hypertrophy, effectively reducing their enlargement, demonstrated a beneficial impact on kidney inflammation and oxidative stress, and partially alleviated the condition of albuminuria in these mice [9].

Despite these promising findings, there is limited and conflicting data available regarding serum apelin concentrations in type 2 diabetes mellitus with severity of diabetic nephropathy's stages.

This study aims to determine whether this adipokine correlate with the severity of type 2 diabetic nephropathy patients.

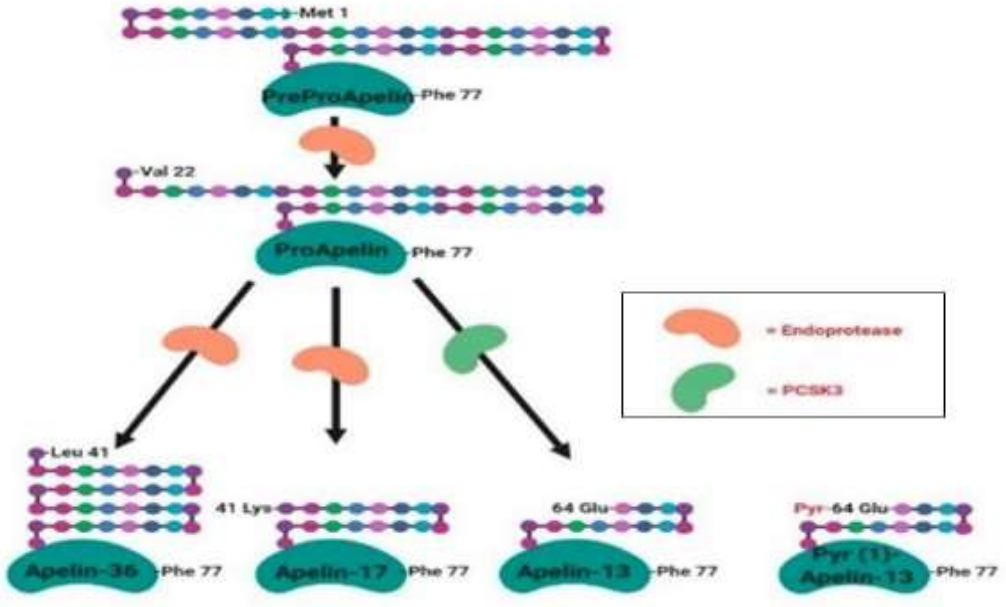

Figure 1. The structure and different forms of human apelin are characterized as follows. Initially, human apelin exists in a preproapelin form consisting of 77 amino acids. This precursor is subjected to cleavage by endopeptidases that target regions rich in basic amino acids. As a result, it is transformed into proapelin, comprising 55 amino acids. Subsequently, tissue-specific active isoforms are produced, varying in length with 36, 17, 13, and Pyr-13 amino acids.
The cleavage of proapelin to yield apelin-13 is facilitated by PCSK3 (proprotein convertase subtilisin/kexin 3).[10]

2. Materials and Methods

This study comprised 70 individuals with ages ranging from 35 to 65 years. They were divided into two groups: GI of 30 patients with diabetic nephropathy (DN) and GII of 40 healthy individuals (controls). They were collected from Al-Yarmouk and Al-Karama Teaching Hospitals in Baghdad, Iraq.

2.1. Exclusion criteria

Individuals with type1 diabetes, gestational diabetes, patients with kidney disease other than diabetic kidney disease and thyroid gland disorders were excluded.

2.2. Blood sample collection

Blood samples were collected from the study participants, and were processed according to established protocols. In brief, 8 milliliters of venous blood were drawn from each individual, with 2 milliliters collected in EDTA tubes for HbA1c testing and 6 milliliters collected in Gel tubes for other tests. The Gel tubes were centrifuged at 3500 rpm for 10 minutes in order to separate the serum from the clot, and the resulting serum was then transferred to Eppendorf tubes. All tubes were stored at -20°C until hormonal assays were conducted, in order to maintain sample integrity. The procedures performed were in accordance with established ethical guidelines and regulatory requirements.

2.3. Hormone and Analytical assessment

Apelin was measured using enzyme linked immunosorbent assay (My biosource, USA). Glucose, HbA1c, Urea and Creatinine were estimated by colorimetric methods (Cobas, Germany). All participants were subjected to the following history; symptoms, family history, treatment history, age, Body Mass Index (BMI).

2.4. Statistical analysis

Using Graphpad Prism version 8.0, statistical analyses were conducted. Descriptive statistics, such as the mean and standard deviation (sd), and analytical statistics, such as the student t-test, were calculated. P value<0.05 was regarded as statistically significant.

3. Results and Discussion

According to the study findings, there were no statistically significant differences ($p>0.05$) in age and BMI between diabetic nephropathy group (DN) and healthy individuals (control). Fasting blood glucose (FBG) and HbA1c levels were found to be significantly higher ($p<0.05$) in type 2 diabetic nephropathy patients compared to healthy controls [(276.3 ±83.22), (94.23 ± 8.492)], [(10.18 ± 1.150), (5.636 ± 0.5037)] respectively (figure 2 and 3). The main challenge in diabetic nephropathy is blood glucose management. Several recent studies have shown a direct impact of blood glucose levels and glycated hemoglobin (HbA1c) on the development of type 2 diabetic nephropathy. In agreement with a study showed that blood glucose levels and HbA1c were significantly higher in the diabetic nephropathy group compared to the healthy controls [9],[10]. Therefore, regular monitoring of blood glucose levels and HbA1c is recommended to prevent the progression of diabetic nephropathy.

The exact mechanism underlying the increase in blood glucose levels and HbA1c in patients with diabetic nephropathy is not fully understood. However, several factors may contribute to this phenomenon. One possible explanation is insulin resistance, which is a common feature of type 2 diabetes. Insulin resistance reduces the ability of cells to respond to insulin, leading to elevated blood glucose levels. In addition, impaired insulin secretion by the pancreas may also contribute to hyperglycemia in diabetic nephropathy.

The results indicate that blood urea levels are significantly higher (p-value <0.05) in type 2 diabetic nephropathy patients compared to healthy controls [(988.43 ± 31.95), (33.59 ± 5.973)] respectively, These findings agreed with a study revealed that blood urea level in diabetic nephropathy patients was higher than healthy control [11]. (Figure 4). This suggests that elevated blood urea levels may be help in evaluation kidney function in type 2 diabetic nephropathy. The increase in blood urea levels in type 2 diabetic nephropathy patients is thought to be due to impaired kidney function. Diabetic nephropathy is a complication of diabetes that affects the kidneys and can lead to kidney damage and impaired kidney function. As the kidneys become damaged, they become less efficient at filtering waste products from the blood, resulting in the accumulation of nitrogenous waste products such as urea.

The results showed that the mean creatinine level in diabetic nephropathy patients was significantly ($p<0.01$) higher than that of healthy controls [(1.593±0.5466), (0.7210±0.1307)] respectively, (figure 5). This finding suggests that diabetic nephropathy patients have impaired kidney function, due to the elevated levels of creatinine. The elevation of creatinine levels in diabetic nephropathy patients can be attributed to the progressive damage to the kidneys caused by chronic hyperglycemia. High blood glucose levels can contribute to diabetic nephropathy by causing damage to the kidneys' small blood vessels. A similar findings was reported by other study that agreed with present data showed that serum creatinine level significantly increase in diabetic nephropathy subjects compared to healthy individuals [12]. The results showed that the mean eGFR level in diabetic nephropathy patients was significantly lower than that of healthy controls ($p < 0.01$) (figure 6). The decrease in glomerular filtration rate (GFR) observed in type 2 diabetic nephropathy patients is because the glomeruli become damaged, the GFR decreases, impairing the kidneys' ability to filter waste products from the blood.

This results of waste products accumulation in the bloodstream, causing further damage to the kidneys and other organs. These findings agreed with a study reported that the progression of diabetic nephropathy is associated with a decline of glomerular filtration rate (GFR) [13]. Apelin level was significantly higher in diabetic nephropathy patients (378.6 ± 73.96) compared to healthy controls (101.6 ± 14.64), ($p < 0.01$), (figure 7). In addition to the important role of apelin in the regulation of glucose metabolism, Apelin is expressed in the glomeruli, tubules, and collecting ducts of the kidneys. It is thought to play a role in the regulation of renal blood flow and glomerular filtration rate, which are crucial for maintaining kidney function. A similar finding was demonstrated that apelin level was significantly increased in type2 diabetes complication as well as diabetic nephropathy [14], [15].

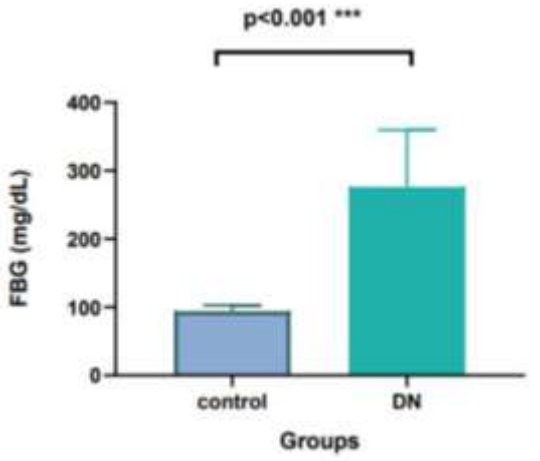

Figure 2. Blood glucose level in two studied groups.

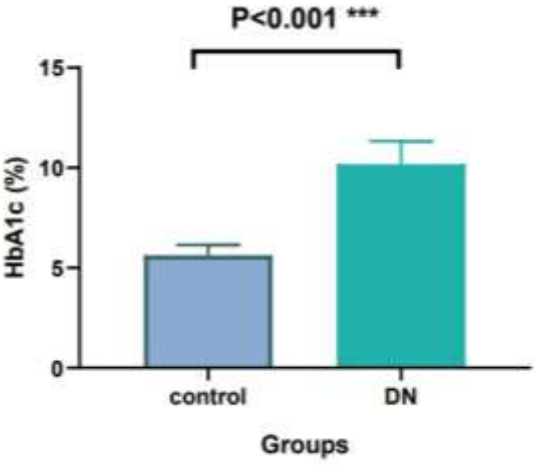

Figure 3. HbA1c level in two studied groups.

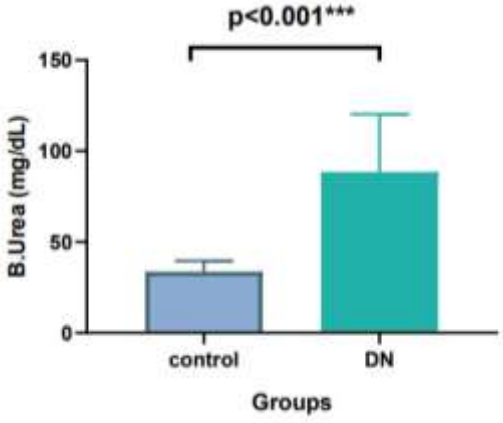

Figure 4. B.Urea level in two studied groups.

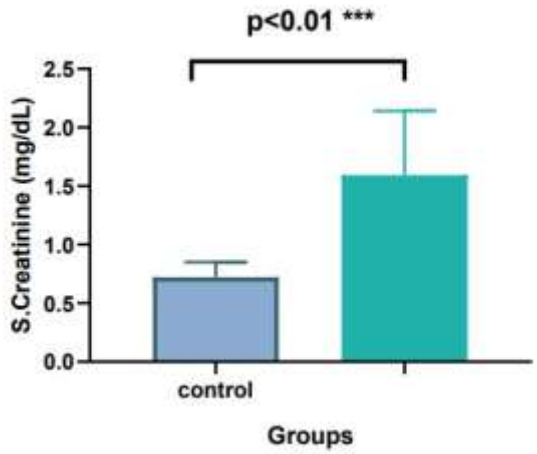

Figure 5. S.Creatinine level in two studied groups.

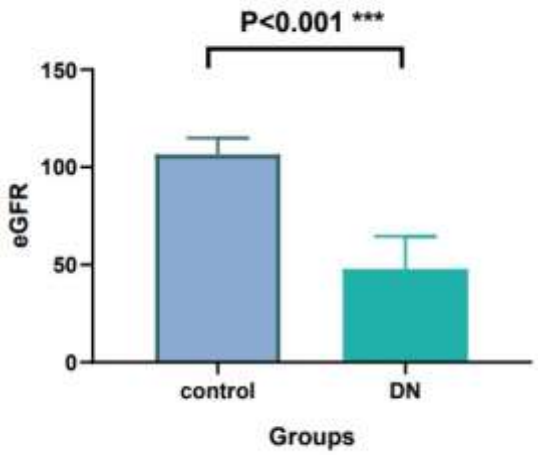

Figure 6. eGFR level in two studied groups.

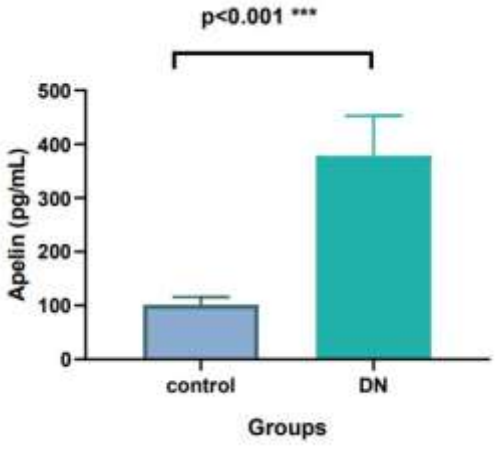

Figure 7. Apelin level in two studied groups.

4. Conclusions

The findings of this study suggest that Apelin may play a role in the progression of diabetic nephropathy. As the Apelin levels were significantly higher in diabetic nephropathy patients compared to healthy individuals. Further studies are required to comprehensively understand the mechanism of Apelin and to clarify its precise role in the pathology of the disease.

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Conflicts of Interest: The authors confirm that there are no conflicts of interest.

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