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Original Article

Biochemical Parameters in Patients with Diabetic Nephropathy versus Individuals with Diabetes Alone, Non-diabetic Nephropathy, and Healthy Controls: A Case-control Study

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Abstract

Background and objectives: Chronic diabetes mellitus is marked by hyperglycemia and metabolic dysfunction, increasing the risk of complications such as nephropathy. This study aimed to evaluate key biochemical parameters among participants with diabetic nephropathy (DNp), diabetes control (DC), nephropathy control (NC), and healthy control groups.

Methods: A prospective case-control study was conducted with 200 participants categorized into four groups: DNp, NC, DC, and healthy controls. Biochemical parameters, including glucose, glycated hemoglobin, waste metabolites, proteins, enzymes, electrolytes, and lipids, were analyzed using an Advia 1800 chemical system analyzer (Siemens, Germany) with standard kits.

Results: Among the four investigated groups, the DNp group exhibited augmented fasting glucose (178.75 ± 61 mg/dL), glycated hemoglobin (8.13 ± 1.7%), creatinine (5.67 ± 1.8 mg/dL), and blood urea nitrogen (72.02 ± 22.8 mg/dL), indicating poor glycemic control and impaired kidney function. In contrast, the DC group showed elevated random glucose levels (280 ± 3.1 mg/dL). Elevated inflammatory markers (C-reactive protein, 6.35 ± 6.3 mg/L; lactate dehydrogenase, 1,216.43 ± 634 U/L) were observed in the NC group. Compared to the other groups, the DC group demonstrated augmented lipid profiles, including elevated triglycerides (230.67 ± 59 mg/dL), very low-density lipoprotein (48.5 ± 16.5 mg/dL), low-density lipoprotein (107.41 ± 16 mg/dL), and cholesterol (169 ± 19 mg/dL). Statistical analysis was performed using one-way analysis of variance followed by a t-test to investigate differences among groups at $P < 0.05$.

Conclusions: Altered biochemical variations were noted among groups. The DNp group showed renal dysfunction and poor glycemic control, the DC group had dyslipidemia and hyperglycemia, and the NC group showed elevated inflammatory markers. Early testing is indispensable for the timely diagnosis and management of diabetic complications.

Keywords: Diabetes mellitus; Diabetic nephropathy; Biochemical parameter; Lipid profile; Serum electrolyte; Creatinine.

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Introduction

Diabetes mellitus is a chronic metabolic disorder characterized by persistent hyperglycemia. This may be due to impaired insulin secretion or resistance to the peripheral actions of insulin, which cause alterations in energy metabolism. The characteristic feature of all kinds of diabetes mellitus is hyperglycemia, but each type has a different etiology, pathogenic processes, natural history, and treatment. Diabetes mellitus is categorized into two classes based on specific features and etiology: type 1 diabetes

mellitus and type 2 diabetes mellitus.[1] Hyperglycemia detected during pregnancy is known as gestational diabetes mellitus.[1] If diabetes mellitus is not treated, increased glucose significantly impairs health and leads to early death.[2] Although the exact cause of diabetes is still unknown, the majority of patients have evidence of a response mechanism involving autoantibodies that destroy beta islet cells. Low levels of C-peptide in the blood or urine indicate little to no insulin production in type 1 diabetes mellitus patients.[1] The main characteristic of all types of diabetes is chronic hyperglycemia. The hyperglycemic state is managed by coordinating fluid resuscitation, insulin therapy, and electrolyte replacement, and the patient's routine test results are monitored.[3] Chronic hyperglycemia can lead to the development of many diabetes-specific complications that are generally categorized as macrovascular or microvascular.[4]

Type 2 diabetes mellitus is a polygenic disease known as non-insulin-dependent diabetes mellitus and ketosis-resistant diabetes mellitus that occurs in 90–95% of individuals. Type 2 diabetes mellitus is a disease characterized by tissue insulin resistance, a poor compensatory insulin secretory response, and insufficient insulin production by pancreatic islet cells. Insulin secretion is unable to maintain glucose levels in balance, leading to hyperglycemia. The main cause of type 2 diabetes mellitus is obesity or an increased body fat percentage, primarily in the abdominal area. Adipokine dysregulation and increased release of free fatty acids are two inflammatory mechanisms utilized by adipose tissue to enhance insulin resistance in this disease. Blood vessel, kidney, eye, and nerve complications occur in diabetes mellitus patients and are the major causes of morbidity and death from polygenic disorders.[5]

According to the World Health Organization, 108 million individuals worldwide were diagnosed with diabetes in 1980, and the prevalence of diabetes continues to rise yearly.[6] The burden of non-communicable diseases, a significant health issue, is steadily increasing. It is expected that the prevalence of diabetes mellitus will increase, resulting in a global public health burden of approximately 200 million people by 2040.[7] Approximately 33 million people have diabetes, indicating that Pakistan currently has the third-highest number of people with diabetes worldwide after China and India. Additionally, the prevalence of diabetes was substantially greater in urban regions (15.1%) than in rural areas (1.6%).[8]

Diabetic nephropathy (DNp) is a chronic consequence of both type 1 and type 2 diabetes. It is characterized by a decreased kidney glomerular filtration rate (GFR) or increased urine albumin excretion. DNp is the primary cause of end-stage renal disease worldwide.[9] In individuals with chronic diabetes, inadequate blood glucose regulation leads to structural alterations in the kidney. Thickened basement membranes, increased extracellular matrix, multicellular damage, and fibrosis are the most frequent pathological alterations in the glomerulus.[10] Long-term exposure to a glucose-rich environment damages kidney cells more severely by activating the polyol pathway, increasing the hexosamine biosynthesis pathway, activating protein kinase C, and encouraging the synthesis of advanced glycation end products that are responsible for DNp.

The present study was performed to compare the demographic, anthropometric, and biochemical profiles of DNp patients with those of diabetic patients, non-diabetic nephropathy patients, and healthy controls (HC), seeking to identify distinctive patterns and relationships that help in the early detection and management of DNp.

Materials and methods

Study design and execution

A case–control study was conducted to determine detailed history and risk factors (questionnaire) and to perform biochemical analysis at Gambat Institute of Medical Sciences, Gambat, Khairpur, from March 2023 to December 2023. This study was conducted in accordance with the ethical standards outlined in the Declaration of Helsinki (as revised in 2024) and was approved by the Ethics Committee of the Gambat Institute of Medical Sciences (P.PAQJIMS/MC/ORIC/ERC-80), Gambat, Khairpur. All participants were informed about the study project, and consent was subsequently obtained from all participants. Written or verbal consent was obtained.

All groups were initially interviewed using a standard questionnaire composed of different subsections, as follows:

- The first section included demographic factors and detailed patient information.
- The second section included information on dietary habits (breakfasts, evening snacks, types of oil, sweets, fast foods, meat, vegetables, fruits, dairy products, etc.).
- The third part of the questionnaire included anthropometric measurements (weight, height, and body mass index (BMI)).

Initially, 290 participants were assessed for eligibility, and 200 were included in the present study, as given below (Fig. 1).

Each group comprised 50 participants. Blood samples were collected from all participants, and different biochemical and other tests were analyzed.

Inclusion and exclusion criteria

Participants aged 18–60 years of both genders who provided informed consent and fulfilled the group-specific clinical inclusion criteria were enrolled in the study. The DNp group comprised patients with clinically confirmed DNp associated with type 1 or type 2 diabetes mellitus. The NC group included non-diabetic individuals diagnosed with nephropathy. The DC group consisted of participants with type 1 or type 2 diabetes mellitus but without evidence of kidney disease, whereas the HC group included healthy controls without any chronic conditions such as diabetes or renal disorders.

Participants with acute infections at the time of sampling, a history of major surgery within the previous three months, lactation or pregnancy, or severe comorbid conditions such as cardiomyopathy, neuropathy, retinopathy, cancer, endocrine disorders, or liver disease were excluded from the study.

Questionnaire and interviews

A standard questionnaire was designed to conduct the study. The questionnaire was divided into three parts. The first section included demographic factors and detailed patient information. The second section included information on dietary habits (breakfasts, evening snacks, types of oil, sweets, fast foods, meat, vegetables, fruits, dairy products, etc.). The third part of the questionnaire included anthropometric measurements.

Determination of BMI

The height of the patients was measured using a calibrated measuring device. The calculation formula for BMI was as follows:

$$\text{BMI} = \frac{\text{Weight (kg)}}{\text{Height (m)}^2}$$

Blood sampling and processing

Intravenous blood samples (12 h after fasting) and random blood

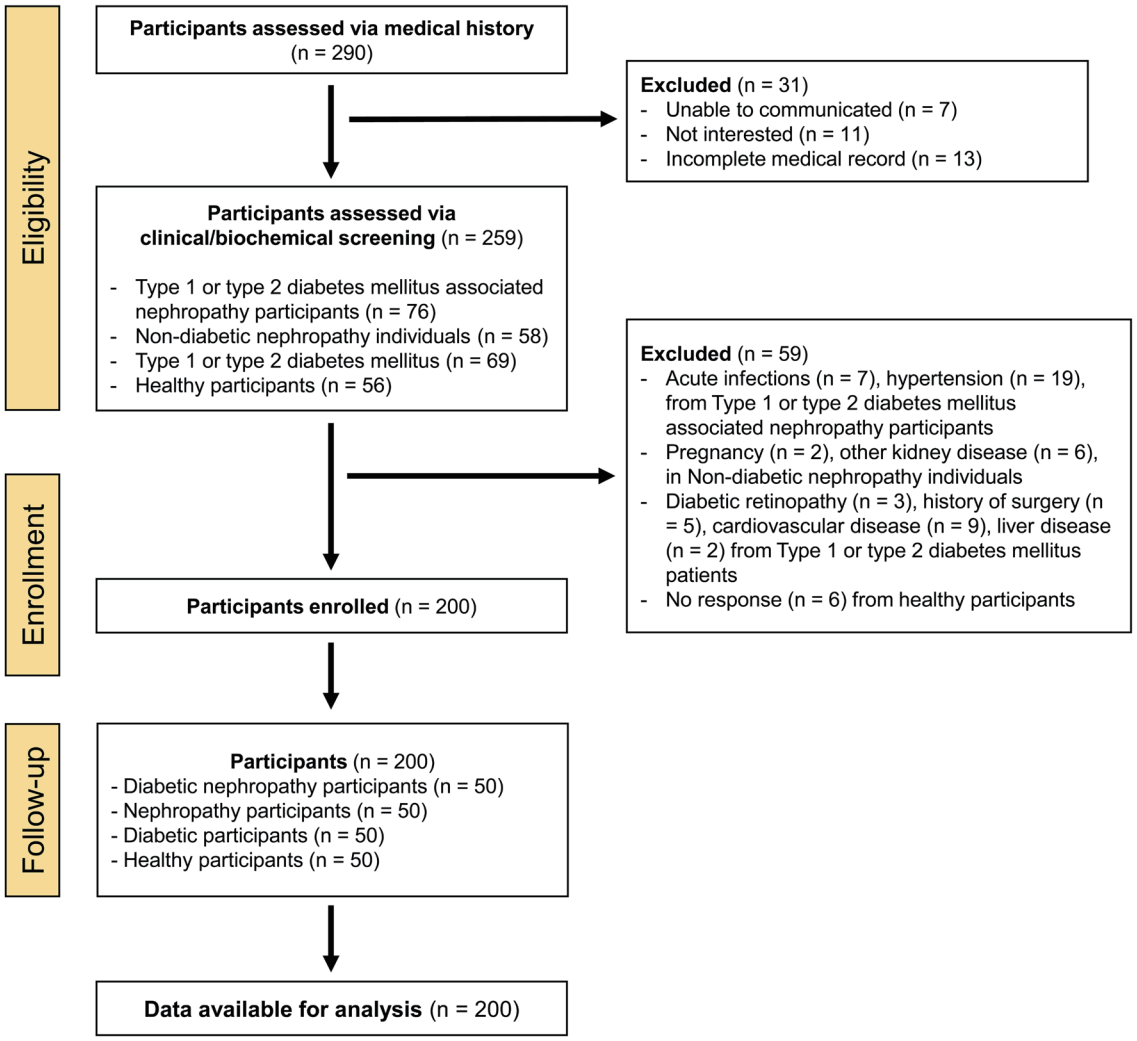

Fig. 1. Flow chart of study participants. The study participants were divided into four different groups as follows: I. DNp; II. Nephropathy control (NC); III. Diabetic control (DC); IV. HC.

samples (2 h after a meal) were drawn from DNp, HC, DC, and NC participants. Intravenous blood samples (5 mL) were drawn from all patients and controls.

For biochemical examinations, venous blood samples were collected in tubes specifically designed for each test. For the HbA1c test, ethylene diaminetetra acetic acid-containing tubes were used to prevent clotting. Glucose measurements, including fasting blood sugar and random blood sugar, were performed using tubes containing sodium fluoride and potassium oxalate, which inhibit glycolysis and prevent coagulation, respectively. Serum samples for lipid profiling, C-reactive protein (CRP), lactate dehydrogenase (LDH), bone chemistry, creatinine (Crt), and electrolyte analysis were obtained using gel separator tubes after centrifugation, which provided a clear serum fraction for accurate analysis.

Biochemical analysis

The biochemical parameters—fasting and random blood sugar, HbA1c, lipid profile (cholesterol, low-density lipoprotein (LDL), high-density lipoprotein (HDL) and triglycerides (TG), very low-density lipoprotein (VLDL)), LDH, CRP, urea, creatinine, and electrolytes (sodium, chloride, bicarbonate, calcium, potassium, and phosphate)—were analyzed using a chemical system analyzer (Advia 1800, Siemens, Germany) with appropriate kits.

Statistical analysis

The results were expressed as the mean ± standard deviation. For comparisons between groups (patients vs. healthy and diseased controls), one-way analysis of variance was performed using SPSS version 15 (SPSS Inc., Chicago, IL). A *P*-value of less than 0.05 was considered statistically significant.

Results

Anthropometric and demographic results

The current study results demonstrated that the BMI of the HC group belonged to the ideal weight category, while in the DNp group, 40% were of ideal weight and 36% were underweight individuals. In contrast, the DC group prevalence belonged to obese (36%) and overweight (32%) participants. Detailed results are pre-

Table 1. Anthropometric measurements

	Groups			
	DNp (%)	DN (%)	DC (%)	HC (%)
Ideal weight	40	56	32	100
Under weight	36	30	–	–
Over weight	14	–	36	–
Obese	10	14	32	–

DC, diabetic control; DNp, diabetic nephropathy; HC, healthy control; NC, nephropathy control.

sented in Table 1. Reported BMI values were as follows: underweight below 18, ideal weight 18 to 25, overweight 25 to 30, and above 30 as obese.[11]

Demographic characteristics are shown in Table 2. Participants in the DNp and NC groups were 66% male, whereas 50% of participants in the DC and HC groups were male. The maximum number of participants among all groups belonged to the middle class and had a sedentary lifestyle.

Glucose and glycated hemoglobin levels

A measure of the surge in blood glucose level induced by the intake of carbohydrates compared with a standard quantity of glucose is the glycemic index. The results of this study revealed increased fasting glucose concentrations, random glucose levels, and glycated hemoglobin levels in the DC and DNp groups among the four investigated groups. The results are shown in Table 3.

Inflammatory markers and waste metabolites

Proteins, as body components, are macromolecules that play various important roles in the human body as messengers. Enzymes are proteins that act as biological catalysts by accelerating chemical reactions. Among all investigated groups, the concentrations of CRP and LDH were greater in the NC group than in the DNp group. The results are presented in Table 4.

Urea and creatinine are waste products produced during protein metabolism. Both of these waste products are carried to the kidneys and filtered into the urine. The assessment of these parameters and their concentrations is useful for evaluating kidney function. The concentrations of Crt and BUN decreased in the order of DNp > NC > HC > DC (Table 4).

Serum electrolytes

Electrolytes are essential for basic life functions, such as maintaining electrical neutrality in cells and generating and conducting action potentials in nerves and muscles. Important electrolytes, such as sodium (Na^+), chloride (Cl^-), potassium (K^+), calcium (Ca^{2+}), phosphate (HPO_4^-), and bicarbonate (HCO_3^-), were investigated in all groups. The results are shown in Table 5.

Table 2. Demographic characteristics

	Groups			
	DNp (%)	NC (%)	DC (%)	HC (%)
Gender				
Male	66	66	50	50
Female	34	34	50	50
Marital status				
Married	100	86	88	76
Unmarried	–	14	12	24
No. of children				
0–2	25	61.4	22.7	26.3
3–5	32	24.3	#	42.1
6–8	18	14.3	40.9	31.6
≥9	25	#	36.4	#
Life style				
Physically active	33	29	84	34
Sedentary	67	71	16	66
Wealth Index				
Richer	10	–	18	12
Middle	70	86	64	88
Poorer	20	14	18	–

#, no child; –, no observed data. DC, diabetic control; DNp, diabetic nephropathy; HC, healthy control; NC, nephropathy control.

Lipid profile

Lipid profile patterns are associated with different lipid-related diseases in the blood. A lipid profile usually includes LDL, HDL, VLDL, TG, and cholesterol. Among all groups, low concentrations of LDL, HDL, and cholesterol were observed in the DNp group. The results are given in Table 6.

Discussion

DNp is a severe global health concern and a devastating complication associated with both type 1 and type 2 diabetes. It is a promi-

Table 3. Assessment of blood glucose and glycated hemoglobin levels in diabetic nephropathy patients and control individuals

Parameter	Groups			
	DNp	NC	DC	HC
FBS (mg/dL)	178.75 ± 61.4^c	98.29 ± 3.5^a	150.17 ± 45.5^b	92.0 ± 7.5^a
RBS (mg/dL)	163.20 ± 37.3^c	88.14 ± 19.8^a	280 ± 3.1^b	155.34^a
HbA1c (%)	8.13 ± 1.7^b	4.27 ± 0.7^a	8.73 ± 1.0^b	4.92 ± 0.3^a

All results are presented as mean ± standard deviation. Statistical analysis was performed using one-way analysis of variance followed by a post hoc Tukey's multiple comparison test at the 95% confidence level ($P < 0.05$). Different superscript letters (a, b, c) denote statistically significant differences between groups; values sharing the same letter are not significantly different. DC, diabetic control; DNp, diabetic nephropathy; FBS, fasting blood sugar; HbA1c, glycated hemoglobin; HC, healthy control; NC, nephropathy control; RBS, random blood sugar.

Table 4. Assessment of inflammatory markers and waste metabolites in diabetic nephropathy patients and other control groups

	Groups			
	DNp	**NC**	**DC**	**HC**
Inflammatory markers				
CRP	5.44 ± 4.1[b]	6.35 ±6.3[b]	0.48 ± 0.2[a]	0.14 ± 0.09[a]
LDH	492.54 ± 126.6[b]	1,216.43 ± 634.1[c]	488.17 ± 59.6[b]	337.78 ± 40.8[a]
Waste metabolites				
Crt (mg/dL)	5.67 ± 1.8[b]	4.86 ± 1.3[b]	0.67 ± 0.1[a]	0.71 ± 0.1[a]
BUN (mg/dL)	72.02 ± 22.8[c]	44.14 ± 10.8[b]	10.33 ± 2.1[a]	12.11 ± 2.0[a]

All results are presented as mean ± standard deviation. Statistical analysis was performed using one-way analysis of variance followed by a post hoc Tukey's multiple comparison test at the 95% confidence level ($P < 0.05$). Different superscript letters (a, b, c) denote statistically significant differences between groups; values sharing the same letter are not significantly different. BUN, blood urea nitrogen; CRP, C-reactive protein; Crt, creatinine; DC, diabetic control; DNp, diabetic nephropathy; HC, healthy control; LDH, lactate dehydrogenase; NC, nephropathy control.

Table 5. Assessment of electrolytes in diabetic nephropathy patients and other control groups

Electrolytes	Groups			
	DNp	**NC**	**DC**	**HC**
Na^+	134.91 ± 6.3[a]	130.86 ± 4.9[b]	131.33 ± 1.6[b]	137.44 ± 4.0[a]
Cl^-	99.65 ± 8.8[b]	96.86 ± 6.7[b]	94.67 ± 2.8[b]	104.44 ± 3.5[a]
K^+	4.74 ± 0.8[a]	3.78 ± 0.8[a]	3.97 ± 0.3[a]	4.23 ± 0.3[a]
HCO_3^-	17.78 ± 3.9[b]	20.5±0.6 [b]	15.38 ± 2.1[b]	29.6 ± 2.8[a]
Ca^{++}	7.78± 0.8[b]	8.60 ± 0.8[b]	10.45 ± 2.2[a]	9.42 ± 0.3[a]
HPO_4^-	5.03 ± 2.1[b]	3.31 ± 1.1[a]	5.93 ± 1.8[b]	4.28 ± 0.4[a]

Statistical analysis was performed using one-way analysis of variance followed by a post hoc Tukey's multiple comparison test at the 95% confidence level ($P < 0.05$). All results are presented as mean ± standard deviation. Different superscript letters (a, b, c) denote statistically significant differences between groups; values sharing the same letter are not significantly different. Cl^-, chloride; Ca^{++}, calcium; DC, diabetic control; DNp, diabetic nephropathy; HC, healthy control; HCO_3^-, bicarbonate; HPO_4^-, phosphate; K^+, potassium; Na^+, sodium; NC, nephropathy control.

nent driver of renal disease, and the number of diabetes cases is increasing globally.[12] The current study aimed to investigate various biochemicals, such as proteins, enzymes, waste metabolites, serum electrolytes, and lipid profiles, as predictive biomarkers and to compare them among DNp patients and other controls, such as diabetic patients, nephropathy patients, and healthy controls, for timely intervention and improved disease management.

Various anthropometric and demographic parameters, including low income, marital status, and higher BMI, have been reported to be associated with a lower quality of life and mental health scores. Recently, D'Souza *et al*.[13] reported that general health, emotional well-being, and poor physical functioning were contributing factors to quality of life and played a significant role in increasing the risk of DNp. BMI was used as an essential parameter to evaluate the weight status of study participants. The empirical formula was used to calculate BMI (BMI = weight (kg) / height^2 (m^2)).[14] Gender-specific differences have been reported in the literature, with genetic and hormonal factors playing a significant role in DNp, specifically the protective roles of progesterone and estrogen in females. Furthermore, estrogen replacement therapy has provided

Table 6. Lipid profile assessment in diabetic nephropathy patients and other control groups

	Groups			
	DNp	**NC**	**DC**	**HC**
LDL	75.42 ± 29.5[c]	67.58 ± 24.2[c]	107.41 ± 16.6[b]	88.15 ± 11.2[a]
HDL	27.59 ± 14.6[c]	36.54 ± 16.6[b]	44.55 ± 11.3[a]	46.47 ± 3.2[a]
Ch	131.28 ± 31.4[c]	142.57 ± 34.1[b]	169 ± 19.67[a]	150 ± 12.7[a]
VLDL	29.46 ± 7.2[d]	36.00 ± 17.9[c]	48.50 ± 16.5[b]	12.22 ± 3.4[a]
TG	163.32 ± 58.2[c]	178.28 ± 73.0[c]	230.67 ± 59.1[b]	57.78 ± 13.0[a]

All results are presented as mean ± standard deviation. Statistical analysis was performed using one-way analysis of variance followed by a post hoc Tukey's multiple comparison test at the 95% confidence level ($P < 0.05$). Different superscript letters (a, b, c) denote statistically significant differences between groups; values sharing the same letter are not significantly different. Ch, cholesterol; DC, diabetic control; DNp, diabetic nephropathy; HC, healthy control; HDL, high-density lipoprotein; LDL, low-density lipoprotein; NC, nephropathy control; TG, triglycerides; VLDL, very low-density lipoprotein.

protective effects on renal outcomes in menopausal women.[15]

Glucose is a main and important molecule that provides energy for the body. However, consistently increased blood glucose concentrations are associated with the triggering or progression of different diseases, such as diabetes mellitus and its related complications. DNp is also a prominently connected disorder.[16] An abnormal increase in diabetes occurs due to insufficient insulin synthesis or altered cellular sensitivity. This causes enduring disturbances in the metabolism of key biomolecules such as lipids, carbohydrates, and proteins, subsequently leading to long-term complications.[17] Furthermore, increased glucose also causes glycation, which is a process involving the nonenzymatic attachment of glucose to major molecules such as proteins. HbA1c characterizes the level of glycated hemoglobin in red blood cells and is presented as a percentage. Glycation is an important indicator of the typical glucose concentration over a specific duration, usually two to three months. HbA1c is a key biomarker that provides a comprehensive depiction of glucose metabolism for monitoring glycemic levels in diabetes management.[18] In this study, elevated blood glucose and glycated hemoglobin levels were also observed in DNp patients.

High blood sugar levels result in irreparable injury to nephrons, which are delicate functional units of the kidneys. This causes the progressive loss of kidney function, including imbalanced electrolytes, altered essential fluids, and ultimately disrupted homeostasis, possibly contributing to DNp. It is estimated that approximately 20–30% of diabetic patients develop DNp.[19]

Creatinine and blood urea nitrogen are waste metabolites in humans and are end products of nitrogen metabolism. Moreover, these fragments are easily filtered from nephrons because of their small size, which makes them suitable biomarkers for evaluating kidney function and detecting possible kidney disease.[20,21] Creatinine is effectively filtered by the glomerulus and is considered a reliable indirect indicator of the GFR. An altered GFR results in increased creatinine and urea levels, indicating impaired renal function. Compared with healthy individuals, type 1 and type 2 diabetic patients exhibit increased concentrations of renal biomarkers, such as creatinine and blood urea nitrogen, indicating the need for attentive monitoring and management of DNp.[19,22] In this study, the concentrations of BUN and Crt were greater in the DNp group than in the NC group.

Various vital biomolecules, such as proteins, have a number of critical functions in the body, including roles as messengers, body components, and biological catalysts. Previously, it has been reported that CRP is an important independent risk factor, and its concentration is positively correlated with the progression and pathogenesis of type 2 DNp.[23–25] A significant association between augmented CRP levels and heart disease in DNp patients has also been confirmed.[25,26] Microalbuminuria is a precursor of nephropathy in both type 1 and type 2 DNp patients. Higher CRP levels have been connected to the development of microalbuminuria and early-stage kidney impairment in diabetic patients.[25,27] The present study demonstrated that the concentrations of CRP and LDH were greater in the NC group than in the DNp group. The association between LDH and kidney disease–related mortality has also been documented. These findings suggest the importance of LDH as a valuable biomarker for predicting disease severity and overall kidney disease. Previously, it has been reported that hemodialysis patients with LDH levels > 280 U/L are at increased risk of cardiovascular mortality and all-cause mortality, whereas those with LDH levels < 240 U/L have improved survival outcomes, exhibiting a positive correlation between LDH levels and mortality risk.[28] Another study reported a positive association between augmented LDH levels and increased risk of cardiovascular mortality in patients with DNp.[29] A previously published study demonstrated that elevated LDH levels are correlated with poorer overall survival in patients with renal cell carcinoma, indicating that LDH may serve as a suitable prognostic marker for disease.[30] Increased CRP levels, which represent low-grade inflammation, are important markers of DNp, indicating that chronic inflammation is a critical factor in the progression of this complication.[31]

Electrolytes are essential for fundamental life functions, such as the maintenance of electrical neutrality in cells and the generation and conduction of action potentials in nerves and muscles.[32] Important electrolytes, such as sodium, potassium, chloride, calcium, phosphate, and bicarbonate, were investigated in all groups. Increased or normal plasma sodium levels with higher blood glucose demonstrate a considerable reduction in total body water, indicating a critical necessity for fluid replacement to address the underlying dehydration.[33] The progression of hyperkalemia is a common complication in patients with type 2 diabetes mellitus and can limit the effective use of renin–angiotensin–aldosterone system inhibitors, particularly in patients with diabetes and kidney disease.[34] One recent study showed that sodium–glucose cotransporter-2 inhibitors preserve and even increase serum chloride levels in patients with type 2 diabetes mellitus without heart failure. The use of chloride concentrations via deliberate diuretics can reestablish body fluid distribution, providing a potential therapeutic approach for the management of related complications.[35] An increased serum calcium concentration has been connected to an increased risk of type 2 diabetes.[36] An increase in serum phosphate concentration in elderly patients with type 2 diabetes and renal disease can result in metabolic and vascular dysfunction, aggravating the risk of complications and highlighting the significance of phosphate management in this disease.[37] An investigation of healthy individuals revealed an increased serum bicarbonate concentration and its association with a decreased risk of prediabetes and subclinical inflammation in males. This finding suggests a probable sex-specific association between bicarbonate and metabolic health.[38]

Lipid profile patterns are associated with different diseases and usually include LDL, HDL, VLDL, TG, and cholesterol. Among all groups under observation, low concentrations of LDL, HDL, and cholesterol were observed in the DNp group. The maintenance of glucose and lipid metabolism plays an important role in different diseases, such as diabetes, metabolic syndrome, and others.[39,40]

There are various limitations to the present study, including a small sample size and a short study duration. Participants from a single institute may not be representative of the larger population. Moreover, some probable confounding variables, such as medication adherence and lifestyle factors, were not fully accounted for. Future studies with larger sample sizes and longer durations are suggested to validate these results and explore the association of biochemicals with disease, along with underlying mechanisms.

Future directions

There are several promising research avenues, such as exploring effective biomarkers for the early detection and prediction of diabetes-related problems. Future studies should explore the correlations between disease progression and specific biochemical parameters and conduct longitudinal studies to track time-dependent variations in biochemical parameters in individuals with diabetes and associated complications. Additionally, future research should aim to reveal the fundamental biochemically regulated mechanisms driving this disease, thereby uncovering new avenues for

therapeutic development and improved patient care. The present project is likely to reveal unique biochemical profiles in patients with DNp, distinguishing them from diabetic patients, nephropathy patients, and healthy individuals in specific regions. These findings will highlight the critical necessity for consistent monitoring of biochemical parameters in individuals with diabetes and diabetes-related complications, such as DNp, to improve disease management.

Conclusions

This study demonstrated that patients with DNp exhibited the most severe biochemical disturbances when compared with DC and HC. DNp exhibited markedly elevated glycemic indices and significantly impaired renal function. Inflammatory and enzymatic markers varied across groups, with CRP elevated in DNp and NC, and LDH highest in NC. Lipid profiles displayed distinct patterns among groups, as DC exhibited prominent dyslipidemia with the highest lipid levels, while DNp presented the lowest concentrations.

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Conflict of interest

ARP has been an editorial board member of *Exploratory Research and Hypothesis in Medicine*. since December 2018. The authors declare that they have no conflicts of interest.

Author contributions

Sample collection (HM), initial drafting of the manuscript (HM, FR), study design (SQA, ARP), data analysis (SQA, MS, SB), writing of the manuscript (SQA), critical analysis of the manuscript (SQA), project supervision, and preparation of the manuscript (ARP). All authors have made substantial contributions, read and approved the manuscript for submission.

Ethical statement

This study was conducted in accordance with the ethical standards outlined in the Declaration of Helsinki (as revised in 2024) and was approved by the Ethics Committee of the Gambat Institute of Medical Sciences (P.PAQJIMS/MC/ORIC/ERC-80), Gambat, Khairpur. All participants were informed about the study project, and consent was subsequently obtained from all participants. Written or verbal consent was obtained.

Data sharing statement

All data generated and analyzed in the study are available in the manuscript.

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