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Clinical and biochemical of Foot temperature in diabetic patients

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Abstract

Elevated foot temperature is a frequently observed symptom among individuals with diabetes, commonly attributed to peripheral neuropathy. In contrast, impaired kidney function represents a major chronic complication associated with diabetes. This study focuses on evaluating the influence of diabetes on renal function and its potential link to increased foot temperature. Participants included individuals diagnosed with either type 1 or type 2 diabetes, ranging from 25 to 75 years of age. Blood samples were collected and processed using gel tubes for serum isolation through centrifugation at 4000 rpm to facilitate biochemical analysis. Additional blood samples were preserved in EDTA tubes for the assessment of glycated hemoglobin (HbA1C). The study involved a total of 100 participants, comprising 75 diabetic patients and 25 healthy individuals serving as the control group. Investigations included quantifying accumulated blood glucose and assessing renal function parameters. The results showed a relationship between HbA1c levels and kidney function, with values of urea p value 0.02, creatinine p0.018, and blood glucose p0.001. Age also played a role in kidney function, with values of urea p value0.021 and creatinine p value0.049. Regarding gender, the results showed that the prevalence of diabetes was higher in men than women, at 57.1% compared to 42.9% in women. Conclusion declining kidney function is a significant chronic complication of diabetes. The relationship between the two is evident in that chronic disruption of blood sugar control leads to microvascular damage.

Keywords: Diabetes; Heat; Urea; Insulin; HbA1C

1. Introduction

Diabetes is a widespread and rapidly growing global health concern, posing serious challenges in most countries. This condition arises when the body fails to produce adequate insulin, the hormone responsible for regulating blood sugar levels. Consequently, diabetes can lead to severe complications such as heart disease, kidney failure, blindness, nerve damage, and blood vessel disorders. the disease is broadly categorized into two types. type 1 diabetes, which affects approximately (5–10%) of individuals with diabetes, occurs when the pancreas produces insufficient insulin. type 2 diabetes develops when the body's cells become resistant to insulin's effects, even though adequate amounts may be produced, Insulin plays a crucial role in enabling glucose absorption by cells, particularly (muscle and fat cells). sufficient insuli n or proper cell response, glucose remains unutilized, leading to elevated blood sugar levels, diabetes is one of the leading causes of mortality worldwide, highlighting the importance of early detection and diagnosis, timely identification and analysis of diabetes-related data are pivotal for effective management and prevention, making advancements in classification methods a critical need for addressing this health crisis (2).

The release and function of insulin must precisely align with the body's metabolic needs, demanding meticulous control of the molecular mechanisms governing its synthesis, secretion, and action in target tissues. Any disruptions within these processes can upset metabolic balance, potentially precipitating the onset of type 2 diabetes mellitus (T2DM). The risk factors for T2DM involve a complex interplay of genetic, metabolic, and environmental influences, each contributing to the likelihood of developing the condition. Non-modifiable factors, such as ethnicity, family history, and genetic

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predisposition, are strongly determined by one's genetic makeup. However, epidemiological evidence highlights that addressing modifiable risk factors can prevent many cases of T2DM. These factors include reducing obesity rates, increasing physical activity levels, and embracing healthier dietary habits. Notably, type 2 diabetes often exhibits a hereditary pattern within families. Siblings in families with a history of T2DM face a relative risk roughly 2 to 3 times higher than those in families without such a history, with this risk surging to 30 times if two siblings are already affected. Additionally, the risk is greater when the mother has diabetes compared to cases where the father is affected. Other contributing factors include a body mass index (BMI) of 30 or higher and abnormal fasting glucose levels exceeding 5.5 mmol/L. In comparison, the relative risk of developing type 1 diabetes is around 15, while the risk for maturity-onset diabetes in young adults is significantly higher, at about 50. Despite efforts to pinpoint the genetic factors behind complex polygenic conditions like type 2 diabetes, progress has been challenging. However, genome-wide association studies (GWASs) achieved a breakthrough in 2007, identifying common genetic variants linked to type 2 diabetes. Among these, a single nucleotide polymorphism (SNP) in the TCF7L2 gene demonstrated the strongest association with the disease, building on earlier findings from genetic association analyses. Other SNPs linked to type 2 diabetes have been identified in genes such as SLC30A8, FTO, CDKAL1, CDKN2A, CDKN2B, HHEX, IGF2BP2, and GCKR.(4)

Insulin resistance in skeletal muscle and the liver, alongside impaired insulin secretion from pancreatic β-cells, represents the central dysfunctions in type 2 diabetes mellitus (T2DM). Resistance of β-cells to glucagon-like peptide 1 (GLP1) accelerates their progressive functional decline, while elevated glucagon levels and heightened hepatic sensitivity to glucagon drive excessive glucose production by the liver. Insulin resistance within adipocytes leads to increased lipolysis and elevated plasma free fatty acid (FFA) concentrations, which further exacerbate insulin resistance in both muscle and liver tissues and contribute to β-cell dysfunction. Additionally, enhanced renal glucose reabsorption through the sodium/glucose co-transporter 2 (SGLT2) and a higher threshold for urinary glucose excretion underlie persistent hyperglycemia. Resistance to insulin, leptin, GLP1, amylin, and peptide YY's appetite-suppressing effects, coupled with lower brain dopamine levels and higher serotonin levels, promotes weight gain, which intensifies existing insulin resistance. While the "ominous octet" model encapsulates these mechanisms, the inclusion of vascular insulin resistance and systemic inflammation expands this framework into the "decadent decoplet." Key molecular players include AMPK (AMP-activated protein kinase), DPP4 (dipeptidyl peptidase 4), IκB (inhibitor of NF-κB), MAPK (mitogen-activated protein kinase), NF-κB (nuclear factor-κB), receptor agonists (RA), reactive oxygen species (ROS), TLR4 (Toll-like receptor 4), TNF (Tumor Necrosis factor), and TZDs (Thiazolidinediones). Figure (1) (5).

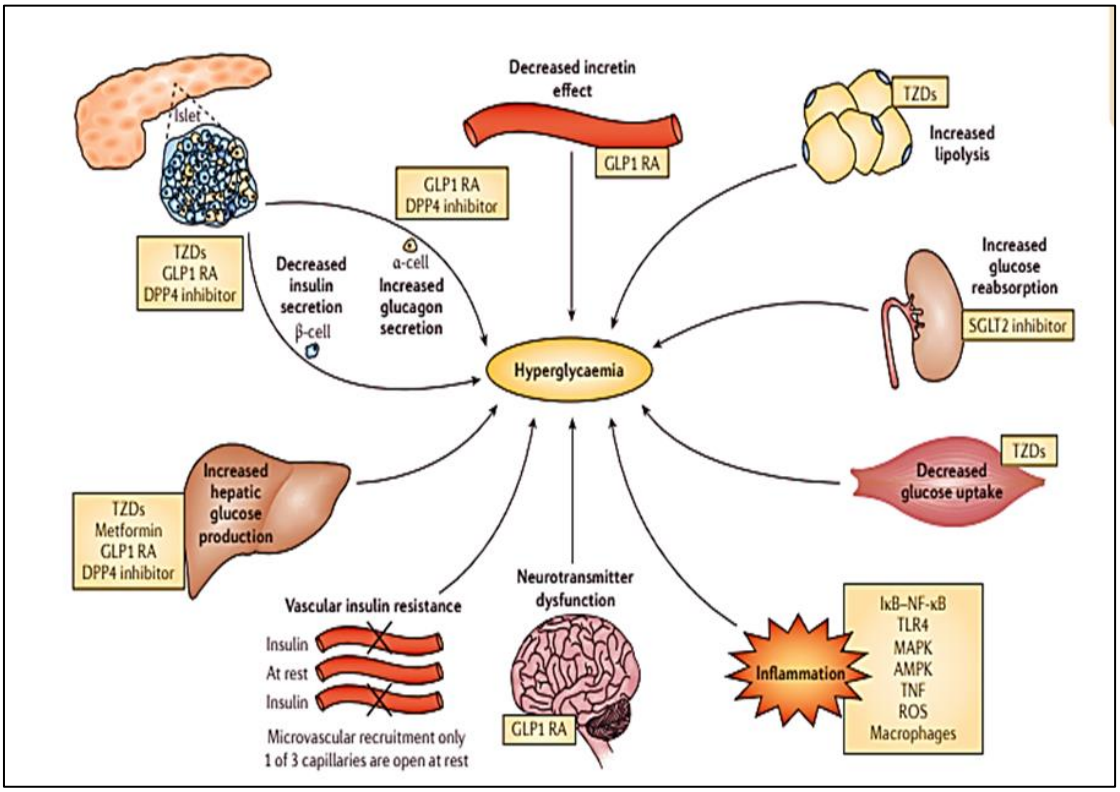

Figure 1 Hyperglycemia

Diabetic kidney disease (DKD) is linked to the rapid deterioration of renal function and has become the leading cause of chronic kidney disease (CKD) and end-stage renal disease worldwide. The advancement of DKD is not solely due to diabetic nephropathy but also stems from various diabetes-related complications, including neurologic bladder, recurring urinary tract infections, macrovascular angiopathy, and the side effects of medications. Patients with advanced DKD face an elevated risk of kidney failure and mortality. Recent research has identified that an estimated glomerular filtration rate (eGFR) of less than 45 mL/min/1.73 m^2 (CKD stage 3b) at the point of nephrologist referral serves as a crucial risk indicator for adverse outcomes in diabetes patients. This underscores the importance of timely identification and enhanced implementation of nephroprotective strategies for patients vulnerable to advanced DKD. Evidence from prior studies has highlighted a strong association between DKD and diabetic peripheral neuropathy (DPN). Patients with DPN tend to experience a higher incidence of albuminuria along with lower eGFR levels compared to those without DPN. Sheen and colleagues noted that abnormalities in thermal perception in the lower limbs, as assessed by quantitative sensory testing (QST), are significantly correlated with reduced eGFR and elevated albuminuria among type 2 diabetes patients. While the timeline regarding the onset of DPN and DKD in individuals with type 2 diabetes mellitus (T2DM) remains ambiguous, it is hypothesized that assessing the severity of thermal perception dysfunction in all four limbs via QST could serve as a valuable tool in identifying patients at heightened risk of kidney failure.(6)

Foot ulcers are a prevalent and significant complication among individuals with diabetes, carrying an estimated lifetime incidence ranging from 19% to 34%. Such ulcers predominantly result from plantar tissue stress associated with ambulation in diabetic individuals who lack protective sensation. This process is posited to be preceded by a localized elevation in skin temperature, which is indicative of inflammation in the underlying tissues—a phenomenon often summarized as "skin heating up before tissue breakdown." The concept that an increase in skin temperature precedes the deterioration of insensitive diabetic feet was first introduced by Bergholt and Brand in 1975. Subsequent histological investigations have provided further validation, demonstrating that repeated mechanical stress applied to the denervated footpads of rats leads to progressive inflammation, elevated skin temperature, necrosis of the underlying tissues through autolysis, and eventual tissue degradation. Comparable findings were observed in human studies, wherein repeated applications of mechanical stress to the fingertips resulted in progressively escalating skin temperature responses over successive days, with temperatures rising more quickly and persisting for longer durations. These results suggest that similar pathogenic mechanisms may be operative in human tissue.(7)

2. Material and Method

Study design: The study included individuals with both type 1 and type 2 diabetes, aged 25-75 years. Blood samples were placed in gel tubes for centrifugation at 4000 rpm to separate the serum and conduct biochemical tests. The other blood group was placed in EDTA tubes for glycated hemoglobin (HbA1C). Total samples were 100 (75 diabetic patients and 25 healthy individuals (control group).

Biochemical tests: Tests were performed, including (B.Sugar, s.creatinin, (Uric acid, B.Urea) using the Mindray device, and HbA1C concentration using the ichroma Π device.

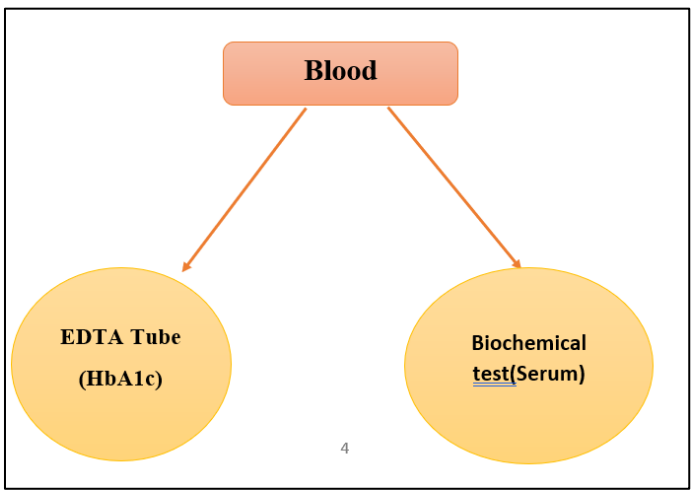

Figure 2 A diagram illustrating blood distribution

3. Result

Table 1 Comparison of Mean Biochemical Parameters Between Healthy and Diabetic Groups

Parameter	Healthy (Mean ± Range)	Diabetic (Mean ± Range)	p-value
Age (years)	55.0 (29–68)	56.7 (28–75)	0.481 (NS)
HbA1C (%)	5.37 (4.8–6.1)	8.64 (4.5–12.4)	0.001*
Blood Urea (mg/dL)	27.15 (19.6–32.0)	39.69 (24.3–58.0)	0.015*
Serum Uric Acid (mg/dL)	6.17 (4.7–7.9)	6.46 (4.2–8.4)	0.238 (NS)
Serum Creatinine (mg/dL)	0.80 (0.6–0.9)	0.95 (0.7–1.3)	0.044*
Blood Sugar (mg/dL)	95.08 (89–105)	217.94 (89–379)	0.001*

Table 2 Mean and Range of Parameters Within Each Group

Case Type	Age (Mean ± Range)	HbA1C (Mean ± Range)	B. Urea (Mean ± Range)	S. Uric Acid (Mean ± Range)	S. Creatinine (Mean ± Range)	B. Sugar (Mean ± Range)
Healthy	55.0 (29–68)	5.37 (4.8–6.1)	27.15 (19.6–32.0)	6.17 (4.7–7.9)	0.80 (0.6–0.9)	95.08 (89–105)
Diabetic	56.7 (28–75)	8.64 (4.5–12.4)	39.69 (24.3–58.0)	6.46 (4.2–8.4)	0.95 (0.7–1.3)	217.94 (89–379)

Table 3 Gender Distribution Among Study Groups

Gender	Healthy n (%)	Diabetic n (%)	Total n (%)	p-value
Male	6 (50.0%)	12 (57.1%)	18 (54.5%)	0.742 (NS)
Female	6 (50.0%)	9 (42.9%)	15 (45.5%)	
Total	12 (100%)	21 (100%)	33 (100%)	

Table 4 Correlation Between HbA1C and Other Biochemical Parameters in Diabetic Patients

Parameter	Pearson's r	Strength	p-value
Blood Urea	0.61	Moderate Positive	0.002*
Serum Uric Acid	0.29	Weak Positive	0.131 (NS)
Serum Creatinine	0.47	Moderate Positive	0.018*
Blood Sugar	0.83	Strong Positive	0.001*

Table 5 Relationship Between Age and Biochemical Parameters (All Participants)

Parameter	Correlation with Age (r)	Interpretation	p-value
HbA1C	0.32	Weak positive correlation	0.102 (NS)
Blood Urea	0.48	Moderate positive correlation	0.021*
Serum Uric Acid	0.26	Weak positive correlation	0.181 (NS)
Serum Creatinine	0.39	Moderate correlation	0.049*
Blood Sugar	0.34	Weak correlation	0.088 (NS)

Table 6 Comparison of Mean Values Between Male and Female Diabetic Patients

Parameter	Male (Mean ± SD)	Female (Mean ± SD)	p-value
Age (years)	54.3 ± 13.2	61.4 ± 10.5	0.146 (NS)
HbA1C (%)	8.45 ± 1.9	9.65 ± 2.1	0.042*
Blood Urea (mg/dL)	40.1 ± 8.9	37.4 ± 9.2	0.271 (NS)
Serum Uric Acid (mg/dL)	6.59 ± 1.1	6.32 ± 1.0	0.398 (NS)
Serum Creatinine (mg/dL)	0.97 ± 0.17	0.91 ± 0.14	0.222 (NS)
Blood Sugar (mg/dL)	225.8 ± 72.6	209.4 ± 69.3	0.319 (NS)

Table 7 Classification of HbA1C Levels in Diabetic Patients

HbA1C Category	Range (%)	Number of Patients	Percentage (%)
Controlled	< 7.0	4	19.0
Moderately Controlled	7.0–8.9	7	33.3
Poorly Controlled	≥ 9.0	10	47.7
Total		21	100.0

Table 8 Summary of Key Significant Findings

Variable	Significantly Higher in	Statistical Test	p-value	Significance
HbA1C	Diabetic group	t-test	0.001*	Significant
Blood Urea	Diabetic group	t-test	0.015*	Significant
Serum Creatinine	Diabetic group	t-test	0.044*	Significant
Blood Sugar	Diabetic group	t-test	0.001*	Highly Significant
Gender	No significant difference	Chi-square	0.742	NS

4. Discussion

This study investigated differences between diabetic and non-diabetic subjects in several clinical and biochemical parameters. The results revealed higher levels of HbA1C and daily blood glucose compared to statistically significant levels. These findings are consistent with the role of HbA1C as an indicator of long-term glycemic control and blood glucose as an acute indicator of glucose metabolism, as both parameters are essential for the diagnosis and monitoring

of diabetes. He et al. (2021) highlight that metabolic disturbances caused by diabetes mellitus can result in a range of complications, including male reproductive dysfunction. In individuals with diabetes, prolonged hyperglycemia can trigger (diabetic neuropathy, oxidative stress, disrupted zinc metabolism, and insulin resistance). Furthermore, insulin deficiency and resistance may harm key components of the endocrine and reproductive systems, such as (the hypothalamus, pituitary gland, gonads, and adjacent glands). These disruptions can lead to reduced secretion of essential sex hormones, including (gonadotropin-releasing hormone, follicle-stimulating hormone, luteinizing hormone, and testosterone). Consequently, structural damage may occur in the male reproductive organs, including testicular atrophy, stromal cell degeneration, seminiferous tubule injury, and sperm cell impairment.

Balasubramanian et al. (2021) Circulation plays a critical role in maintaining internal balance and defending against tissue injury and infection, supporting the development of comprehensive assessment strategies for diabetic foot complications. Galicia et al. (2020) highlighted the central factors contributing to the persistence of type 2 diabetes, including(nutritional determinants, physical inactivity, bacterial dysbiosis, and metabolic syndrome), noting its association with accelerated atherosclerosis. Uerena further elucidates that hypertension and diabetes rank among the most prevalent etiologies of kidney disease. Similarly, Ibrahim observed that diabetes triggers substantial disruptions in vital biomarkers, such as total lipid concentration, triglycerides, fasting and random blood glucose levels, low-density lipoprotein (LDL), and very low-density lipoprotein (VLDL). He et al. (2021) identified four major conditions through which diabetes mellitus (DM) exerts its impact on male reproductive health: erectile dysfunction, ejaculatory disorders, structural alterations in reproductive organs, and changes in semen quality. Empirical evidence indicates that 59% of men with diabetes experience erectile dysfunction (ED), with most cases of diabetic impotence (DMED) characterized by penile nerve thickening or neuropathy exhibiting a beaded morphology. The decline in serum testosterone (T) induced by diabetes mellitus (DM) significantly impairs vascular endothelial function. Nitric oxide (NO), a critical neurotransmitter in the physiological mechanism of penile erection, plays a central role in the relaxation of smooth muscle cells in both the corpus cavernosum and the penile microvasculature. Penile erection fundamentally relies on these processes mediated by NO. Hyperglycemia exacerbates the condition through the augmentation of reactive oxygen species (ROS), the accumulation of advanced glycation end products (AGEs), to inhibition of endothelial nitric oxide synthase (eNOS) activity. This, in turn, diminishes the endothelial synthesis and subsequent availability of NO, contributing to the pathogenesis of erectile dysfunction (ED). Additionally, diabetic neuropathy results in reduced NO production alongside elevated levels of the vasoconstrictor endothelin, which have been directly associated with impaired erectile function. Diabetes mellitus also induces several metabolic perturbations, including (alterations in the sorbitol metabolic pathway, arteriosclerosis, and disruptions in neurotrophic support). These changes manifest as glycogen accumulation, thickening of the basal membrane surrounding somatic nerve sheath cells, and axonal disintegration, which collectively result in sensory and motor nerve damage. Furthermore, demyelination of sympathetic nerves within the pelvic region inhibits autonomic nerve function, contributing to erectile dysfunction. Research by Iqbal et al. (2025) underscores the potential of novel Schiff base derivatives containing strategically fused imidazole–triazole cores to serve as effective agents in alpha-amylase and alpha-glucosidase inhibition. These compounds exhibit superior enzymatic inhibitory activity when compared to the standard therapeutic agent acarbose, demonstrating IC50 values of 7.30 ± 0.20 μM and 7.80 ± 0.10 μM against alpha-amylase and alpha-glucosidase, respectively. This highlights their potential as promising candidates for advancing therapeutic approaches in diabetes management.

The presence of foot heat can be considered an indirect indicator of extensive vascular damage, possibly involving the kidneys, which is reflected in kidney function indicators such as elevated creatinine or decreased glomerular filtration rate (GFR). Therefore, linking neurological symptoms with laboratory tests of kidney function contributes to early diagnosis and reducing complications.

5. Conclusion

Hot feet are a common symptom in diabetics due to peripheral neuropathy. On the other hand, declining kidney function is a significant chronic complication of diabetes. The relationship between the two is evident in that chronic disruption of blood sugar control leads to microvascular damage, causing both:

- Peripheral neuropathy (causing a sensation of heat or burning in the feet).
- Diabetic nephropathy (measured by changes in kidney function parameters such as creatinine and GFR).

Therefore, the presence of hot feet may be an indirect indicator of the likelihood of the presence or development of broader systemic complications, including the kidneys. Studies confirm that diabetics with peripheral neuropathy are more susceptible to nephropathy due to a combined mechanism of vascular damage and chronic inflammation.

Compliance with ethical standards

Disclosure of conflict of interest

No conflict of interest to be disclosed.

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