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Immediate Glycemic Impact of Caffeine Consumption: A Prospective Analytical Observational Study Comparing Type 2 Diabetic Patients on Metformin with Healthy Individuals

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ABSTRACT

Background: Caffeine, widely consumed through beverages like coffee, may influence glucose metabolism. While habitual coffee consumption has been linked to reduced Type 2 Diabetes Mellitus (T2DM) risk, acute caffeine intake can impair glucose tolerance, especially in diabetic individuals.

Objective: To evaluate and compare the immediate glycemic response to caffeine consumption in T2DM patients on metformin therapy versus healthy individuals.

Methods: A prospective analytical observational study was conducted with 100 participants (50 T2DM patients on metformin 500 mg twice daily and 50 healthy adults), all habitual coffee consumers. Fasting capillary blood glucose (CBG) was measured, followed by ingestion of standardized black coffee (200 mg instant coffee powder containing ~21.25 mg caffeine in 75 mL water). A second CBG was recorded 45 minutes post-consumption. Statistical analysis was performed using paired and independent t-tests.

Results: Both groups showed significant increases in CBG post-caffeine (T2DM: +16.8 mg/dL, $p<0.001$; Healthy: +7.5 mg/dL, $p<0.001$). The rise in glucose was significantly greater in the T2DM group compared to healthy individuals ($p<0.001$).

Conclusion: Caffeine consumption induces a significant acute rise in blood glucose, more pronounced in T2DM patients despite metformin therapy. These findings highlight the need for personalized dietary guidance in diabetes management regarding caffeine intake.

Keywords: *Caffeine, Type 2 Diabetes Mellitus, Metformin, Blood Glucose, Acute Glycemic Response*

1. INTRODUCTION

Caffeine, a naturally occurring methyl xanthine alkaloid, is the most widely consumed psychoactive substance globally, predominantly through beverages like coffee and tea.[1,2] Its effects on the central nervous system such as enhanced alertness and reduced fatigue are well known. However, the metabolic implications of caffeine, especially its influence on glucose homeostasis, remain an area of ongoing investigation and debate. While some studies suggest that chronic coffee consumption may confer protective effects against the development of Type 2 Diabetes Mellitus (T2DM), acute ingestion of caffeine has been associated with impaired glucose tolerance and reduced insulin sensitivity.[3-6]

Type 2 Diabetes Mellitus is a metabolic disorder characterized by chronic hyperglycemia resulting from insulin resistance and progressive pancreatic beta-cell dysfunction. Pharmacological interventions, including metformin, remain the cornerstone of therapy for glycemic control in T2DM. Metformin enhances insulin sensitivity and suppresses hepatic gluconeogenesis, thus lowering blood glucose levels. However, lifestyle and dietary factors, including caffeine intake, may influence glycemic control and potentially interfere with the therapeutic efficacy of anti-diabetic medications.[7-10]

In clinical practice, many diabetic patients regularly consume coffee, often unaware of its potential to acutely elevate blood glucose levels.[11,12] Although observational data have linked habitual coffee consumption with a lower risk of T2DM development, the acute glycemic response to caffeine in patients with established diabetes remains inconsistent across various studies. Furthermore, limited data exist comparing the postprandial glycemic response to caffeine between diabetic individuals on pharmacotherapy and healthy, normoglycemic individuals.[13-17]

This study was conducted to fill this knowledge gap by evaluating and comparing the immediate glycemic effect of caffeine ingestion in individuals with T2DM on metformin therapy versus healthy controls. By employing a prospective analytical observational approach, the study aimed to simulate real-life conditions wherein habitual coffee consumption occurs without dietary or pharmacological modifications. The findings are expected to guide patients and healthcare providers in making informed decisions regarding caffeine intake as part of diabetes management.

2. METHODOLOGY

Study Design

This study was conducted as a prospective, analytical, observational study utilizing a pre-post (within-subject) design. The objective was to evaluate the immediate glycemic effects of caffeine consumption in two defined populations: individuals diagnosed with Type 2 Diabetes Mellitus (T2DM) who were on stable oral metformin therapy (500 mg twice daily), and healthy adults with no known metabolic disorders. The investigation aimed to assess the real-world impact of a single caffeine dose, consumed as black coffee, on capillary blood glucose levels without any additional pharmacological or dietary interventions. Importantly, data for each participant was collected on a single day to capture the acute glycemic response to caffeine in a controlled, fasting state. Participants were enrolled based on specific eligibility criteria. Inclusion criteria included adults aged 20 to 50 years, with a stable body weight between 50 and 70 kg, and a habitual intake of at least one cup of coffee per day for the past three consecutive months. Diabetic participants were required to have a confirmed diagnosis of T2DM with stable glycemic control and have been on metformin monotherapy for at least two years. Healthy controls were selected based on the absence of any metabolic, endocrine, or chronic medical conditions. Exclusion criteria for both groups included pregnancy, lactation, psychiatric illness, cardiovascular or neurological disease, insulin use, other antidiabetic agents besides metformin, tobacco or alcohol use, caffeine allergy, and participation in another clinical study within the past three months.

Study Procedure

Eligible participants were recruited from outpatient clinics and through community outreach following screening and informed consent. Each participant underwent the study protocol on **a** single designated day. All participants were instructed to fast for at least eight hours before arriving at the study site, with only water permitted during the fasting period. Upon arrival, baseline capillary blood glucose (CBG) was measured using a validated glucometer to establish fasting glucose levels. Immediately afterward, each participant consumed a standardized serving of black coffee consisting of 200 mg of instant coffee powder dissolved in 75 ml of hot water, delivering approximately 21.25 mg of caffeine. The coffee was consumed within five minutes under direct supervision. After caffeine intake, participants remained seated and were not permitted to consume any food or beverages for the next 45 minutes. A second CBG measurement was recorded exactly 45 minutes post-consumption to assess the immediate effect of caffeine on glucose levels. Each participant, therefore, underwent two blood glucose **tests** on the same day one before coffee consumption (fasting) and one 45 minutes after. During the visit, a structured questionnaire was administered to collect demographic details, medical history, and coffee consumption habits.

Statistical Analysis

Data were compiled and analyzed using SPSS Version 26.0. Descriptive statistics were used to summarize demographic variables and glucose levels. Paired t-tests were used to evaluate within-group differences between pre- and post-caffeine blood glucose levels. Independent t-tests were employed for between-group comparisons of mean glucose change. A p-value of less than 0.05 was considered statistically significant. Graphs and tables were generated to illustrate glycemic changes across the two study populations.

3. RESULTS

Participant Characteristics

A total of 100 participants were enrolled in the study and were equally divided into two groups:

- **Group A (n = 50)**: Type 2 Diabetes Mellitus (T2DM) patients receiving a stable dose of metformin 500 mg twice daily for at least 2 years.
- **Group B (n = 50)**: Healthy individuals without diabetes or other chronic metabolic conditions.

All participants were regular coffee consumers (≥1 cup/day for the last 3 months) and met the inclusion criteria of being aged 20–50 years and weighing between 50–70 kg.

Table 1: Socio-demographic Characteristics of Study Participants

Variables	Total (n = 100)	T2DM Group (n = 50)	Healthy Group (n = 50)
Age Group (years)			

21–30	10 (10%)	2 (4%)	8 (16%)
31–40	44 (44%)	20 (40%)	24 (48%)
41–50	46 (46%)	28 (56%)	18 (36%)
Gender			
Male	54 (54%)	26 (52%)	28 (56%)
Female	46 (46%)	24 (48%)	22 (44%)
Weight (kg)			
50–59	50 (50%)	24 (48%)	26 (52%)
60–70	50 (50%)	26 (52%)	24 (48%)
Education Level			
Illiterate	24 (24%)	14 (28%)	10 (20%)
Literate	58 (58%)	30 (60%)	28 (56%)
Reading Proficient	18 (18%)	6 (12%)	12 (24%)

The table 1 majority of participants were aged 31–50 years, with a nearly equal gender distribution. Weight was evenly distributed between the two specified weight ranges. Literacy was higher among healthy individuals, while a slightly higher proportion of illiterate participants were observed in the diabetic group.

Immediate Glycemic Response to Caffeine

Capillary blood glucose levels were measured before and 45 minutes after ingestion of 200 mg of instant black coffee powder (containing approximately 21.25 mg caffeine in 75 ml hot water). The data showed significant changes in glycemic response both within and between the two groups.

Table 2: Comparison of Pre- and Post-Caffeine Blood Glucose Levels

Group	Pre-Caffeine (mg/dl)	Post-Caffeine (mg/dl)	Mean Difference (mg/dl)	p-value
T2DM (n=50)	148.60 ± 16.75	165.40 ± 17.90	+16.80 ± 4.21	< 0.001
Healthy (n=50)	94.30 ± 8.50	101.80 ± 9.25	+7.50 ± 2.80	< 0.001

The table 2 both groups demonstrated a statistically significant increase in capillary blood glucose following caffeine ingestion. The T2DM group exhibited a greater rise in glucose levels (+16.8 mg/dl) compared to the healthy group (+7.5 mg/dl). The difference was statistically significant in both within-group (paired t-test) and between-group comparisons (independent t-test).

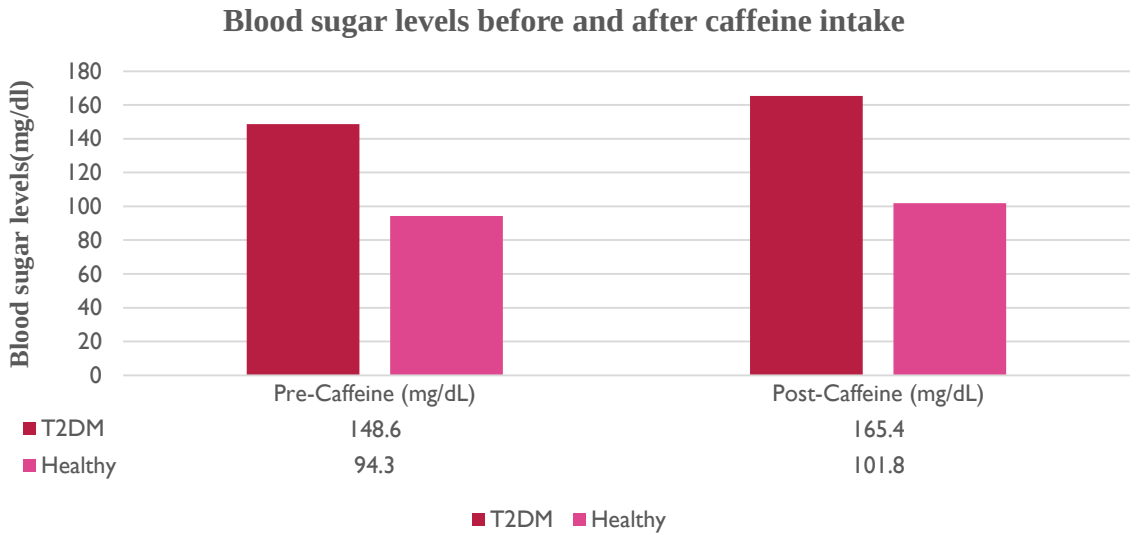

Figure 1: Comparison of Pre- and Post-Caffeine Blood Glucose Levels

Between-Group Comparison of Glycemic Shift

To compare the magnitude of change in glycemic levels between T2DM and healthy individuals, independent t-test analysis was performed.

Table 3: Between-Group Comparison of Glycemic Change

Group	Mean Change (mg/dl)	Standard Deviation	p-value
T2DM	16.80	4.21	> 0.001
Healthy	7.50	2.80	< 0.001

The table 3 average increase in blood glucose post-caffeine intake was significantly higher in the T2DM group compared to the healthy group ($p < 0.001$), indicating an amplified glycemic response in patients with type 2 diabetes, despite ongoing metformin therapy.

4. DISCUSSION

The present study aimed to investigate the acute glycemic response to caffeine ingestion among two cohorts: T2DM patients on metformin therapy and healthy adults. The findings indicate a statistically significant increase in capillary blood glucose levels following caffeine intake in both groups, with a markedly higher glycemic elevation observed in the T2DM group.

The rise in post-caffeine glucose levels in diabetic individuals (+16.8 mg/dl) was nearly twice that observed in healthy participants (+7.5 mg/dl). This suggests that caffeine has a more pronounced hyperglycemic effect in individuals with impaired glucose regulation, potentially due to a combination of reduced insulin sensitivity and altered hormonal counter-regulatory responses. Caffeine is known to increase circulating catecholamines such as epinephrine, which can promote hepatic glucose output and temporarily inhibit insulin-mediated glucose uptake. In healthy individuals, this effect is usually buffered by an intact insulin response; however, in T2DM patients, this compensation may be inadequate, resulting in a more substantial glucose spike.

Additionally, caffeine has been shown to antagonize adenosine receptors, particularly the A1 and A2A subtypes, which are involved in regulating glucose metabolism and insulin action. The adenosine blockade may further impair insulin sensitivity, especially in insulin-resistant individuals. While metformin is known to enhance peripheral glucose uptake and inhibit gluconeogenesis, the acute effect of caffeine may transiently override the drug's pharmacodynamic action, leading to increased post-consumption glucose levels.[18,14]

The statistically significant increase observed in healthy individuals, though modest, also highlights that caffeine has a physiological impact on glucose homeostasis even in the absence of underlying metabolic disease. This finding aligns with previous studies reporting acute impairment in glucose tolerance among healthy adults following caffeine consumption.

The uniformity in demographic characteristics, body weight, and habitual coffee consumption patterns across both groups

strengthens the internal validity of this study.[19,20] Moreover, the use of a standardized coffee preparation ensures consistency in caffeine exposure. However, it is essential to consider that the study evaluated the immediate effects of a single caffeine dose; chronic consumption patterns and their long-term metabolic outcomes were not addressed. Additionally, individual variations in caffeine metabolism, genetic polymorphisms affecting adenosine receptor sensitivity, and gut micro biota profiles may contribute to differential glycemic responses, warranting further investigation.

The findings underscore the need for personalized dietary recommendations in diabetic care, particularly concerning caffeine intake. Clinicians should consider advising patients to monitor their post-consumption glucose levels when consuming caffeinated beverages and possibly adjust dietary habits or medication schedules accordingly.

5. CONCLUSION

This prospective observational study demonstrates that caffeine consumption leads to an immediate and statistically significant elevation in blood glucose levels, with a more pronounced effect observed in individuals with Type 2 Diabetes Mellitus who are on metformin therapy. The study reinforces the notion that while caffeine may offer certain metabolic benefits when consumed chronically, its acute effects on glycemic control are complex and potentially detrimental, particularly in individuals with existing insulin resistance.

The observed differential glycemic response between diabetic and healthy individuals highlights the importance of individualized dietary counseling and glucose monitoring in diabetes management. Diabetic patients, especially those relying on oral hypoglycemic agents like metformin, should be made aware of the possible short-term hyperglycemic impact of caffeine. Further research is warranted to explore the interaction between caffeine metabolism, pharmacotherapy, and glycemic variability, with larger sample sizes and longer observation periods.

These insights may contribute to refining dietary guidelines for diabetic populations and enhancing overall glycemic control strategies through evidence-based lifestyle modifications.

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Authors' contribution -Kingston Samraj Kirubakaran J, Vinothini M, Srinivas K conceived and designed the study; Kingston Samraj Kirubakaran J, Vinothini M conducted the study; Srinivas K supervised the study; Kingston Samraj Kirubakaran J, Vinothini M analyzed the data and wrote the manuscript and had primary responsibility for the content; Srinivas K reviewed the manuscript. All authors have read and agreed to the published version of the manuscript.

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Conflict of interest statement – The authors declare that there is no conflict of interest regarding the publication of this article.

Informed consent - We have obtained informed consent from all individuals included in this study.

Availability of data and materials – The datasets generated and analyzed during the current study are available from the corresponding author, Dr. Srinivas k., Assistant professor at J.K.K.Nattraja college of pharmacy, on reasonable request. However, the data are not publicly available because they contain information that could compromise the privacy of research participants.

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