



The Impact of Ramadan Fasting on Glycemic Control in Patients with Type 2 Diabetes : A Comprehensive Systematic Review

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ABSTRACT

Introduction: Ramadan fasting is observed by millions of Muslims with type 2 diabetes mellitus (T2DM) worldwide, presenting unique challenges for glycemic management. This systematic review synthesizes evidence on the impact of Ramadan fasting on glycemic control in patients with T2DM. **Methods:** A comprehensive systematic review was conducted including 80 studies (35 randomized controlled trials and 45 observational studies) examining Ramadan fasting in adults with T2DM. Studies were included if they assessed glycemic parameters (HbA1c, fasting blood glucose, postprandial glucose, glucose variability) and reported safety outcomes. Data were extracted on study characteristics, medication regimens, educational interventions, and metabolic outcomes. **Results:** The majority of studies demonstrated improvements or stability in HbA1c levels during Ramadan, with reductions ranging from 0.5-1.5% in patients receiving structured interventions. Newer medication classes

including SGLT-2 inhibitors (HbA1c reduction 0.49-0.65%), GLP-1 receptor agonists (mean difference -0.31%, $p=0.04$), and DPP-4 inhibitors showed favorable safety-efficacy profiles. Hypoglycemia rates varied considerably: sulfonylureas 14-26%, insulin 2-23%, DPP-4 inhibitors 0-5.8%, SGLT-2 inhibitors 0.3-7.3%, and GLP-1RAs 0-5%. Structured pre-Ramadan education reduced hypoglycemia from 19.5% to 4.1% and improved HbA1c by 0.7-1.5%. Dose reduction protocols (60% of usual dose) decreased hypoglycemia from 23.0% to 4.2% (OR 0.15, 95% CI 0.08-0.26). Weight changes ranged from -2.9 kg to no significant change, with SGLT-2 inhibitors and GLP-1RAs producing greatest reductions. **Discussion:** Ramadan fasting can be safe for many T2DM patients with appropriate risk stratification, medication adjustment, and structured education. Newer glucose-lowering agents offer superior safety profiles compared to sulfonylureas and traditional insulin regimens. **Conclusion:** Successful Ramadan fasting requires individualized approaches combining pre-Ramadan education, medication optimization, structured nutrition therapy, and appropriate monitoring. High-risk patients should be advised against fasting.

Keywords: Ramadan fasting, type 2 diabetes mellitus, glycemic control, hypoglycemia, SGLT-2 inhibitors, GLP-1 receptor agonists, structured education

INTRODUCTION

Background

Ramadan, the ninth month of the Islamic lunar calendar, is observed by approximately 1.8 billion Muslims worldwide as a period of obligatory fasting from dawn to sunset. During this month, adult Muslims abstain from food, drink, oral medications, and smoking during daylight hours, with meals consumed before dawn (Suhur) and after sunset (Iftar). The duration of daily fasting varies geographically and seasonally, ranging from 10 to 21 hours depending on latitude and time of year (23). For patients with type 2 diabetes mellitus (T2DM), Ramadan fasting presents unique physiological challenges that may impact glycemic control and safety.

The intersection of diabetes and Ramadan fasting represents a significant global health consideration, given that approximately 148 million Muslims with diabetes may choose to fast during Ramadan (1). Many patients strongly desire to participate in this religious obligation despite potential health risks, creating an imperative for healthcare providers to understand the implications of fasting and develop evidence-based management strategies (3). The metabolic alterations associated with prolonged fasting—including changes in meal timing, frequency, and composition, along with potential dehydration and altered sleep patterns—can significantly affect glucose homeostasis in individuals with diabetes (12).

Historically, Ramadan fasting was considered contraindicated for patients with diabetes due to concerns about hypoglycemia, hyperglycemia, dehydration, and thrombotic events (23). However, contemporary evidence suggests that with appropriate risk stratification, education, and medication adjustments, many patients with T2DM can fast safely (8, 25). The International Diabetes Federation and Diabetes and Ramadan (IDF-DAR) International Alliance have developed clinical practice guidelines for the management of diabetes during Ramadan, emphasizing the importance of pre-Ramadan assessment, structured education, and individualized treatment plans (17).

Research Gap

Despite the growing body of literature on Ramadan fasting and diabetes, significant knowledge gaps remain. First, the comparative effectiveness and safety of different medication classes during Ramadan fasting have not been systematically synthesized, particularly regarding newer agents such as SGLT-2 inhibitors, GLP-1 receptor agonists, and fixed-ratio combinations like iGlarLixi (1, 2, 4). Second, the heterogeneity of study designs, populations, and outcome measures has limited the ability to draw definitive conclusions about optimal management strategies (43). Third, while educational interventions have demonstrated benefit, the essential components, optimal timing, and intensity of such programs remain poorly defined (3, 6, 8). Fourth, the impact of Ramadan fasting on clinically important outcomes beyond glycemic control—including body composition, lipid profiles, blood pressure, and renal function—shows considerable inconsistency across studies (13, 49). Fifth, most studies have excluded high-risk patients, limiting generalizability to the full spectrum of T2DM severity encountered in clinical practice (7, 38). Finally, the interaction between dietary patterns, physical activity, and medication effects during Ramadan has not been comprehensively examined (40, 45).

Novelty

This systematic review offers several novel contributions to the literature. It represents one of the most comprehensive syntheses to date, incorporating 80 studies including the latest evidence on emerging therapeutic classes such as SGLT-2 inhibitors (ertugliflozin, empagliflozin, dapagliflozin) (1, 9, 14, 41), GLP-1 receptor agonists (semaglutide) (4, 72), and fixed-ratio combinations (iGlarLixi) (2, 15, 16). The review uniquely integrates data from continuous glucose monitoring and flash glucose monitoring studies, providing insights into glucose variability patterns and asymptomatic hypoglycemia during Ramadan (30, 40, 41, 48, 60). It systematically examines the dose-response relationship of educational interventions and identifies core components associated with improved outcomes (3, 6, 8, 25, 51). The review also explores gender-specific effects, ethnic variations, and the impact of physical activity on glycemic outcomes (12, 13, 48). Furthermore, it provides a risk stratification framework based on comprehensive analysis of medication-specific safety profiles and patient characteristics, offering practical guidance for clinicians managing patients who wish to fast during Ramadan.

Research Objectives

The primary objective of this systematic review is to comprehensively evaluate the impact of Ramadan fasting on glycemic control in patients with type 2 diabetes mellitus. Specific objectives include: (1) to assess changes in HbA1c, fasting blood glucose, postprandial glucose, and glucose variability during and after Ramadan fasting; (2) to determine the incidence, severity, and timing of hypoglycemic events across different medication classes and management strategies; (3) to evaluate the effectiveness of structured pre-Ramadan education programs on clinical outcomes; (4) to compare the safety and efficacy of various medication classes including SGLT-2 inhibitors, GLP-1 receptor agonists, DPP-4 inhibitors, sulfonylureas, and insulin regimens; (5) to examine changes in body weight, body composition, lipid profiles, blood pressure, and renal function during Ramadan; (6) to identify patient characteristics, medication regimens, and management approaches associated with optimal outcomes; and (7) to develop evidence-based recommendations for risk stratification and clinical management of T2DM patients observing Ramadan fasting.

Research Hypotheses

This systematic review tests several hypotheses: (1) Ramadan fasting is associated with improvements in glycemic control (HbA1c reduction $\geq 0.5\%$) in patients receiving structured management; (2) the incidence of hypoglycemia during Ramadan varies significantly by medication class, with lowest rates observed with SGLT-2 inhibitors and GLP-1 receptor agonists, intermediate rates with DPP-4 inhibitors, and highest rates with sulfonylureas and insulin; (3) structured pre-Ramadan education programs reduce hypoglycemia risk by at least 50% compared to usual care; (4) dose reduction protocols (60-70% of usual dose) significantly decrease hypoglycemia without compromising glycemic control; (5) newer medication classes maintain or improve glycemic control with superior safety profiles compared to traditional agents; (6) weight loss during Ramadan is greater with SGLT-2 inhibitors and GLP-1 receptor agonists compared to other medication classes; and (7) patient outcomes are optimized when pre-Ramadan education, medication adjustment, structured nutrition therapy, and appropriate monitoring are combined.

Benefits of the Research

This systematic review provides multiple benefits for clinical practice and future research. For healthcare providers, it offers a comprehensive evidence synthesis to guide pre-Ramadan risk assessment, medication selection and adjustment, and patient education strategies. The medication-specific safety data enable informed decision-making when selecting glucose-lowering agents for patients who intend to fast. The identified core components of effective educational programs facilitate development of efficient, culturally-appropriate interventions. For patients with T2DM, this review supports shared decision-making about fasting participation and provides evidence-based reassurance about safety when appropriate precautions are implemented. For healthcare systems, the synthesis identifies high-value interventions (structured education, targeted medication selection, appropriate monitoring) that can improve outcomes while potentially reducing costly acute complications. For researchers, the review identifies remaining evidence gaps and priorities for future investigation, including the need for studies in high-risk populations, longer-term follow-up, and standardized outcome definitions. Ultimately, this review aims to optimize the balance between facilitating religious observance and ensuring patient safety for the millions of Muslims with diabetes who fast during Ramadan.

METHODS

Protocol

The study strictly adhered to the Preferred Reporting Items for Systematic Review and Meta-Analysis (PRISMA) 2020 guidelines to ensure methodological rigor and accuracy. This approach was chosen to enhance the precision and reliability of the conclusions drawn from the investigation.

Criteria for Eligibility

This systematic review aims to evaluate The Impact of Ramadan Fasting on Glycemic Control in Patients with Type 2 Diabetes.

Screening

We screened in sources based on their abstracts that met these criteria:

- **Population Age and Diabetes Type:** Does this study include adults (≥ 18 years) diagnosed with type 2 diabetes mellitus (and exclude studies focusing exclusively on type 1 diabetes, gestational diabetes, or other specific types of diabetes)?
- **Intervention Type:** Does this study examine the effects of Ramadan fasting observance (not other types of fasting interventions without Ramadan context)?
- **Outcome Measures:** Does this study measure at least one glycemic control parameter (HbA1c, fasting blood glucose, postprandial glucose, glucose variability, time in range, or other validated glycemic markers)?
- **Study Design and Comparisons:** Does this study include pre-post comparisons or control group comparisons (and is it NOT a case report, case series, editorial, commentary, or conference abstract)?
- **Fasting Duration:** Did the study participants actually observe Ramadan fasting for a minimum of 15 days?

We considered all screening questions together and made a holistic judgement about whether to screen in each paper.

Search Strategy

The keywords used for this research based PICO :

Element	Keyword 1	Keyword 2	Keyword 3	Keyword 4
Population	Type 2 Diabetes	Type 2 Diabetes Mellitus	T2DM	Adults with Diabetes
Intervention	Ramadan Fasting	Intermittent Fasting	Diurnal Intermittent Fasting	Religious Fasting
Comparison	Glycemic Control	Glycemic Parameters	Blood Glucose Management	Metabolic Control
Outcome	Glycemic	HbA1c	Hypoglycemia	Safety

	Control			Outcomes
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The Boolean MeSH keywords inputted on databases for this research are: (*"Type 2 Diabetes" OR "Type 2 Diabetes Mellitus" OR "T2DM" OR "Adults with Diabetes"*) AND (*"Ramadan Fasting" OR "Intermittent Fasting" OR "Diurnal Intermittent Fasting" OR "Religious Fasting"*) AND (*"Glycemic Control" OR "Glycemic Parameters" OR "Blood Glucose Management" OR "Metabolic Control"*) AND (*"HbA1c" OR "Hypoglycemia" OR "Safety Outcomes" OR "Glycemic Control"*)

Data extraction

- **Study Population:**

Extract characteristics of type 2 diabetes patients relevant to Ramadan fasting and glycemic control, including:

- Sample size and demographics (age, gender)
- Baseline diabetes duration and severity
- Baseline HbA1c levels
- Current diabetes medications
- Presence of complications or comorbidities
- Previous Ramadan fasting experience
- Inclusion/exclusion criteria specific to diabetes management

- **Fasting Details:**

Extract specific details about Ramadan fasting participation, including:

- Duration of daily fasting period (hours)

- Total fasting days completed during study period
- Fasting compliance rate
- Reasons for breaking fast early (if any)
- Meal timing and frequency during non-fasting hours
- Any modifications to usual Ramadan fasting practices

- **Glycemic Control Changes:**

Extract all glycemic control parameters measured before, during, and after Ramadan fasting for type 2 diabetes patients, including:

- HbA1c levels (pre/post values and change)
- Fasting blood glucose (pre/post values and change)
- Postprandial glucose levels (pre/post values and change)
- Any other glucose monitoring data (continuous glucose monitoring, etc.)
- Statistical significance of changes
- Time points when measurements were taken

- **Hypoglycemia Events:**

Extract all hypoglycemic episodes and safety outcomes specifically during Ramadan fasting in type 2 diabetes patients, including:

- Number and percentage of patients experiencing hypoglycemia
- Severity of hypoglycemic episodes (mild, moderate, severe)

- Timing of hypoglycemic events (during fasting vs non-fasting hours)
- Symptoms and management of episodes
- Hospital admissions or emergency care
- Any other diabetes-related complications during Ramadan

- **Management Interventions:**

Extract details about diabetes management strategies used during Ramadan fasting for type 2 diabetes patients, including:

- Medication adjustments (type, dose, timing changes)
- Educational interventions provided (content, timing, duration)
- Monitoring protocols (frequency, type of monitoring)
- Healthcare provider contact/support
- Dietary counseling or modifications
- Any technology-assisted management (telemonitoring, apps)
- Comparison groups (intervention vs control)

- **Metabolic Outcomes:**

Extract other metabolic parameters affected by Ramadan fasting in type 2 diabetes patients, including:

- Body weight changes (pre/post values)
- Lipid profile changes (cholesterol, triglycerides, HDL, LDL)

- Ketone levels or diabetic ketoacidosis episodes
- Blood pressure changes
- Any other biochemical markers measured
- Statistical significance of changes

- **Study Design:**

Extract study methodology elements relevant to evaluating glycemic control during Ramadan fasting, including:

- Study design type (RCT, observational, etc.)
- Duration of follow-up (pre-Ramadan, during, post-Ramadan periods)
- Primary and secondary outcomes related to glycemic control
- Control or comparison groups used
- Randomization and blinding methods
- Sample size calculation and power

Table 1. Article Search Strategy

Database	Keywords	Hits
Pubmed	<i>("Type 2 Diabetes" OR "Type 2 Diabetes Mellitus" OR "T2DM" OR "Adults with Diabetes") AND ("Ramadan Fasting" OR "Intermittent Fasting" OR "Diurnal Intermittent Fasting" OR "Religious Fasting") AND ("Glycemic Control" OR "Glycemic Parameters" OR "Blood Glucose Management" OR "Metabolic Control") AND ("HbA1c" OR "Hypoglycemia" OR "Safety Outcomes" OR "Glycemic Control")</i>	103
Semantic Scholar	<i>("Type 2 Diabetes" OR "Type 2 Diabetes Mellitus" OR "T2DM" OR "Adults with Diabetes") AND ("Ramadan Fasting" OR "Intermittent Fasting" OR "Diurnal Intermittent Fasting" OR "Religious Fasting") AND ("Glycemic Control" OR "Glycemic Parameters" OR "Blood Glucose Management" OR "Metabolic Control") AND ("HbA1c" OR "Hypoglycemia" OR "Safety Outcomes" OR "Glycemic Control")</i>	2
Springer	<i>("Type 2 Diabetes" OR "Type 2 Diabetes Mellitus" OR "T2DM" OR "Adults with Diabetes") AND ("Ramadan Fasting" OR "Intermittent Fasting" OR "Diurnal Intermittent Fasting" OR "Religious Fasting") AND ("Glycemic Control" OR "Glycemic Parameters" OR "Blood Glucose Management" OR "Metabolic Control") AND ("HbA1c" OR "Hypoglycemia" OR "Safety Outcomes" OR "Glycemic Control")</i>	379
Google Scholar	<i>("Type 2 Diabetes" OR "Type 2 Diabetes Mellitus" OR "T2DM" OR "Adults with Diabetes") AND ("Ramadan Fasting" OR "Intermittent Fasting" OR "Diurnal Intermittent Fasting" OR "Religious Fasting") AND ("Glycemic Control" OR "Glycemic Parameters" OR "Blood Glucose Management" OR "Metabolic Control") AND ("HbA1c" OR "Hypoglycemia" OR "Safety Outcomes" OR "Glycemic Control")</i>	5,080
Wiley Online Library	<i>("Type 2 Diabetes" OR "Type 2 Diabetes Mellitus" OR "T2DM" OR "Adults with Diabetes") AND ("Ramadan Fasting" OR "Intermittent Fasting" OR "Diurnal Intermittent Fasting" OR "Religious Fasting") AND ("Glycemic Control" OR "Glycemic Parameters" OR "Blood Glucose Management" OR "Metabolic Control") AND ("HbA1c" OR "Hypoglycemia" OR "Safety Outcomes" OR "Glycemic Control")</i>	224

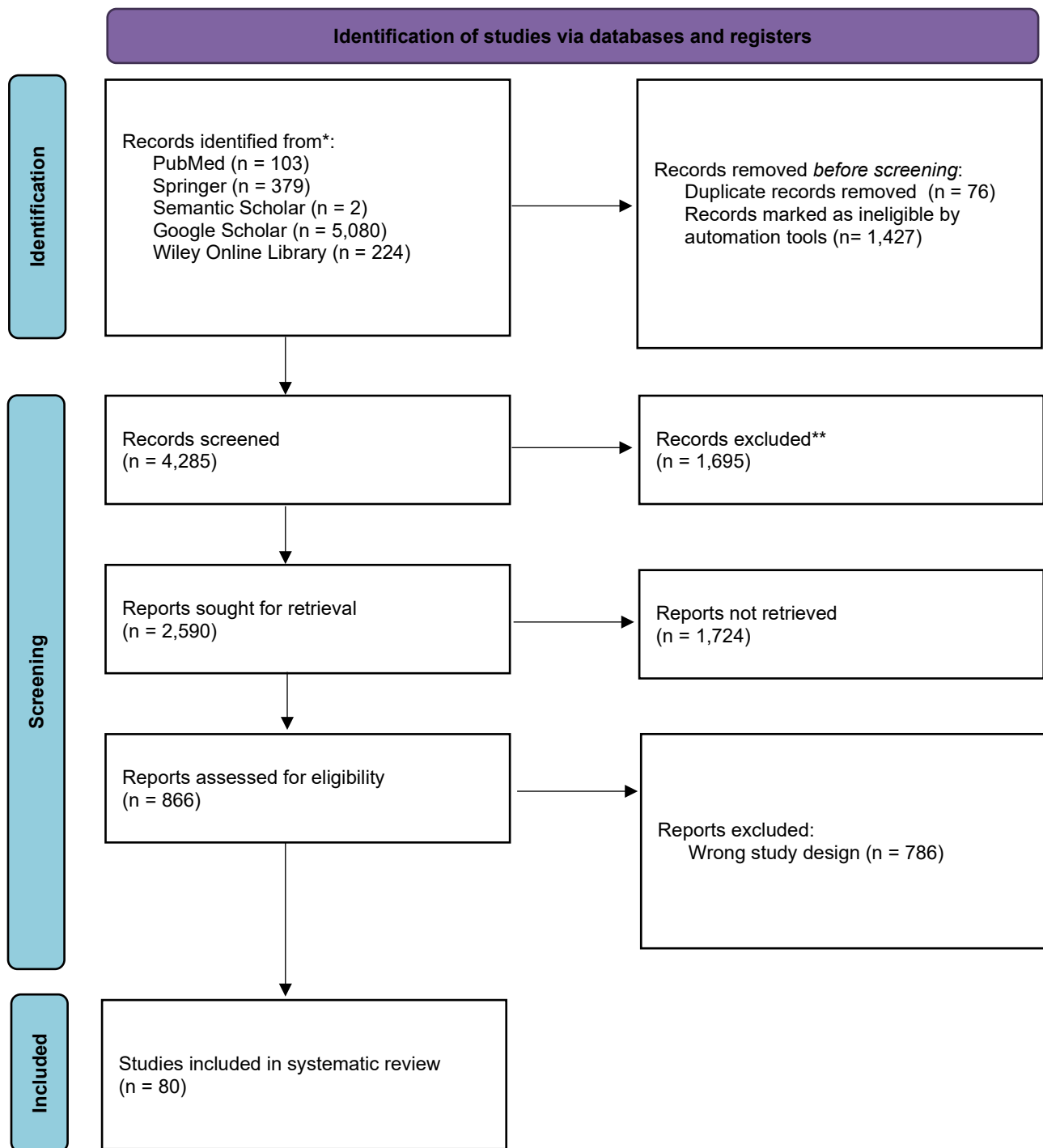


Figure 1. Article search flowchart

RESULTS

Characteristics of included studies

A total of 80 studies were included in this review, comprising 35 randomized controlled trials (RCTs) and 45 observational studies examining the impact of Ramadan fasting on glycemic control in patients with type 2 diabetes mellitus (T2DM). The studies were conducted across multiple countries, with a predominance of research from Middle Eastern and Southeast Asian regions where Muslim populations observe Ramadan fasting.

Study	Sample Size	Mean Age (years)	Baseline HbA1c (%)	Current Medications	Fasting Duration
S. Sahin et al., 2013 [10]	122	56.93	6.33 [10]	OAD (66.4%), Insulin+OAD (6.5%), Insulin (19.7%) [10]	26.98 days [10]
M. M'guil et al., 2008 [11]	120	48-60	Not mentioned	Gliclazide modified release [11]	29 days [11]
E. Yeoh et al., 2015 [12]	29	57	8.6 [12]	OAD (58.6%), Insulin±OAD (41.4%) [12]	≥15 days [12]
Z. Dabbous et al., 2019 [13]	181	53.6	7.8 [13]	≥3 glucose-lowering drugs [13]	Not mentioned
Aisha Sheikh et al., 2022 [14]	82	52.2	7.9 [14]	Empagliflozin (63%), Dapagliflozin (37%) [14]	Not mentioned

Study	Sample Size	Mean Age (years)	Baseline HbA1c (%)	Current Medications	Fasting Duration
L. Zaghlol et al., 2021 [7]	678	58.0	8.1 [7]	Multiple regimens [7]	29 days [7]
M. Pathan et al., 2025 [1]	1373	50.37	8.16 (Ertu), 7.79 (non-Ertu) [1]	Ertugliflozin vs other OADs [1]	29-30 days [1]
M. Hassanein et al., 2024 [2]	241	58.1	Not mentioned	iGlarLixi [2]	≥25 days [2]
Mohamed Hassanein et al., 2024 [15]	420	55-58	Similar in both groups [15]	iGlarLixi with/without SGLT-2i [15]	≥25 days [15]
M. Hassanein et al., 2021 [16]	155	58.4	8.4 [16]	iGlarLixi [16]	28.7 days [16]
M. Hassanein et al., 2020 [17]	Not mentioned	54.4	8.10 [17]	Gla-300 [17]	≥15 days [17]
W. Limpitikul et al., 2014 [18]	212	Not mentioned	Not mentioned	Not mentioned	Not mentioned

Study	Sample Size	Mean Age (years)	Baseline HbA1c (%)	Current Medications	Fasting Duration
J. Lee et al., 2017 [19]	85	53.5	8.7 [19]	Not mentioned	≥15 days [19]
Mohammad Jaelani et al., 2024 [20]	46	Over 60	Not mentioned	Not mentioned	Not mentioned
L. E. El Toony et al., 2018 [6]	320	Not mentioned	Not mentioned	Not mentioned	Not mentioned
R. Sarı et al., 2004 [21]	52	Not mentioned	Not mentioned	Diet, Sulfonylurea, Repaglinide [21]	Not mentioned
M. Cesur et al., 2007 [22]	65	Not mentioned	Not mentioned	Glimepiride, Repaglinide, Insulin glargine [22]	Not mentioned
Dana N. Abdelrahim et al., 2021 [23]	26,706	17-94	Not mentioned	Insulin and non-insulin agents [23]	10-21 hours [23]
A. Anwar et al., 2006 [24]	41	Not mentioned	Not mentioned	Repaglinide, Glimepiride [24]	13.5 hours [24]

Study	Sample Size	Mean Age (years)	Baseline HbA1c (%)	Current Medications	Fasting Duration
Laura N. McEwen et al., 2015 [8]	774	48	8.7 (intervention) , 8.9 (control) [8]	Oral medications, insulin [8]	Mean 26 days [8]
Ayla M Tourkmani et al., 2016 [25]	262	~55-56	9.79 (intervention) , 10.04 (control) [25]	Insulin (95.7%), OAD (84.3%) [25]	~15 hours [25]
Chonlakan Prataksitorn et al., 2014 [26]	212	Not mentioned	Not mentioned	Not mentioned	Not mentioned
A. Paul et al., 2015 [27]	52	54.7	Not mentioned	Diet, OAD, Insulin [27]	≥25 days [27]
L. Malha et al., 2014 [28]	69	Over 35	Greater than 6.5 [28]	Metformin+Vildagliptin vs Metformin+Sulfonylurea [28]	Not mentioned
P. Soewondo et al., 2011 [29]	152	54.0	Not mentioned	Biphasic insulin aspart [29]	Not mentioned

Study	Sample Size	Mean Age (years)	Baseline HbA1c (%)	Current Medications	Fasting Duration
Nesreen Aldawi et al., 2018 [30]	33	55.0	6.7 [30]	Metformin, Sulfonylureas, DPP-4i, GLP-1, Pioglitazone, SGLT2i [30]	15 hours 8 minutes [30]
S. Soelistijo et al., 2022 [31]	198	Over 18	Not mentioned	Gliclazide MR [31]	Not mentioned
M. Abushady et al., 2019 [32]	90	Not mentioned	Not mentioned	Not mentioned	Not mentioned
S. Aravind et al., 2011 [5]	1397	≥18	Not mentioned	Glimepiride, Gliclazide, Glibenclamide±Metformin [5]	Not mentioned
H. Mustafa et al., 2012 [3]	71	Not mentioned	Not mentioned	Not mentioned	Not mentioned
N. Haraj et al., 2024 [33]	39	55.03 (fasting), 61.6 (non-fasting)	7.36 (fasting), 7.1 (non-fasting) [33]	Metformin-Sulfonamides, DPP4i [33]	Not mentioned
M. Hassanein et al., 2017 [34]	263	Not mentioned	Not mentioned	IDegAsp vs BIAsp 30 [34]	~30 days [34]

Study	Sample Size	Mean Age (years)	Baseline HbA1c (%)	Current Medications	Fasting Duration
Akrem Elmalti et al., 2023 [35]	34	Not mentioned	Not mentioned	Insulin-treated [35]	Not mentioned
Aida Elktuni et al., 2021 [36]	46	53.10	8.58 [36]	Insulin (56.5%) [36]	28.80 days [36]
Inass Shaltout et al., 2020 [37]	1008	Not mentioned	Not mentioned	Not mentioned	Not mentioned
Z. Lum et al., 2020 [38]	97	59.5	7.8 [38]	OAD, Insulin [38]	Median 30 days [38]
Hazhar Mohammed et al., 2023 [39]	84	Not mentioned	Not mentioned	Not mentioned	Not mentioned
F. Y. Hasbullah et al., 2022 [40]	21	49	Not mentioned	Not mentioned	Not mentioned
E. Abdelgadir et al., 2019 [41]	95	Not mentioned	7.3 (SGLT2), 8.0 (non-SGLT2) [41]	Insulin±SGLT2i [41]	Not mentioned

Study	Sample Size	Mean Age (years)	Baseline HbA1c (%)	Current Medications	Fasting Duration
Muhammad Yakoob Ahmedani et al., 2020 [42]	54	54.65	Not mentioned	Split mixed insulin [42]	Not mentioned
N. Aydın et al., 2019 [43]	Not mentioned	Not mentioned	Not mentioned	Single OAD, Multi-OAD, Multitreatment [43]	Not mentioned
M. Hassanein et al., 2011 [44]	72	Not mentioned	7.6 (Vildagliptin) [44]	Vildagliptin vs Sulfonylurea [44]	Not mentioned
Barakatun Nisak Mohd Yusof et al., 2021 [45]	60	Not mentioned	Not mentioned	Not mentioned	Not mentioned
N. Shehadeh et al., 2015 [46]	245	60.1 (intervention), 59.4 (control)	8.38 (intervention), 8.45 (control) [46]	Insulin detemir+NovoMix70 vs standard care [46]	Not mentioned
S. Shaikh et al., 2021 [47]	246	≥18	Not mentioned	Gliclazide XR [47]	Not mentioned

Study	Sample Size	Mean Age (years)	Baseline HbA1c (%)	Current Medications	Fasting Duration
M. Bashir et al., 2018 [48]	16	53.4	7.9 [48]	≥3 anti-diabetic medications [48]	Not mentioned
Barakatun Nisak Mohd Yusof et al., 2020 [49]	64	48.3	8.0 [49]	Not on insulin [49]	~14 hours [49]
Henda Jamoussi et al., 2017 [50]	54	36-65	6-9 [50]	Oral antidiabetics [50]	29 days [50]
A. Kamrul-Hasan et al., 2025 [4]	754	Not mentioned	Not mentioned	GLP-1RAs vs other glucose-lowering drugs [4]	Not mentioned
E. Srulovici et al., 2019 [51]	1732	45-74 (83.3%)	Greater than 7 (subgroup) [51]	Not mentioned	Not mentioned
M. Altemimi et al., 2020 [52]	30	53	10.4 [52]	Premixed insulin vs Basal+short-acting insulin [52]	~30 days [52]

Study	Sample Size	Mean Age (years)	Baseline HbA1c (%)	Current Medications	Fasting Duration
Z. Lum et al., 2018 [53]	62	58.4	7.9 [53]	Not mentioned	Not mentioned
Camara, M et al., 2023 [54]	39	57.18	7.2 [54]	OAD (72%), Diet (10%), Insulin (13%) [54]	Entire month [54]
M. Hassanein et al., 2020a [55]	Not mentioned	Not mentioned	Not mentioned	Gla-300 [55]	30.1 days [55]
Mohammed Farid Uddin et al., 2024 [56]	98	Not mentioned	Not mentioned	Gliclazide MR [56]	Not mentioned
A. Shete et al., 2013 [57]	97	Not mentioned	8.75 (Vildagliptin), 8.64 (Sulfonylurea) [57]	Vildagliptin vs Sulfonylurea [57]	Not mentioned
Joseph Partogi Sibarani et al., 2024 [58]	19	57.26	Not mentioned	With/without OAD [58]	13.5-14 hours [58]

Study	Sample Size	Mean Age (years)	Baseline HbA1c (%)	Current Medications	Fasting Duration
M. Pathan et al., 2022 [9]	493	Not mentioned	Not mentioned	Empagliflozin+Metformin±DPP-4i [9]	Not mentioned
Yasmin Atwa Mohamed et al., 2024 [59]	30	54.3	7.823 [59]	Oral (70%), Insulin (30%) [59]	30 days [59]
T. Elhadd et al., 2020 [60]	33	50.8	Not mentioned	Basal insulin or Sulfonylurea [60]	Not mentioned
H. Ghazi et al., 2023 [61]	100	65.9 (Glargine), 66.2 (NPH)	7.26 (Group 1), 7.28 (Group 2) [61]	Vildagliptin+Metformin vs Empagliflozin+Metformin [61]	12-16 hours [61]
Saira Burney et al., 2020 [62]	161	Not mentioned	6.5-8.5 [62]	Lifestyle, Metformin, Met+SU, Met+DPP4i [62]	Not mentioned
R. Malik et al., 2022 [63]	222	55.6	6.9 [63]	Gla-300 [63]	30.5 days [63]
Aisha Sheikh et al., 2021 [64]	84	52.4	7.9 [64]	Empagliflozin (64.3%), Dapagliflozin (35.7%) [64]	Not mentioned

Study	Sample Size	Mean Age (years)	Baseline HbA1c (%)	Current Medications	Fasting Duration
S. Mahar et al., 2014 [65]	244	Not mentioned	7.6 (Vildagliptin), 7.4 (SU) [65]	Vildagliptin vs Sulfonylurea [65]	Not mentioned
B. Dash et al., 2022 [66]	84	52.4	7.9 [66]	Empagliflozin (64%), Dapagliflozin (36%) [66]	Not mentioned
M. Ata et al., 2025 [67]	180	Not mentioned	Not mentioned	Not mentioned	Not mentioned
MagdaShukry Mohammad et al., 2022 [68]	90	Not mentioned	Not mentioned	Not mentioned	Not mentioned
Feten Lamti et al., 2026 [69]	167	59	Not mentioned	Not mentioned	~15 hours [69]
I. Ahmed et al., 2022 [70]	137	Not mentioned	7.42 (Empagliflozin), 7.81 (Sitagliptin) [70]	Empagliflozin+Metformin vs Sitagliptin+Metformin [70]	20.33-21.9 days [70]

Study	Sample Size	Mean Age (years)	Baseline HbA1c (%)	Current Medications	Fasting Duration
YN Low et al., 2021 [71]	40	Not mentioned	≤9.0 [71]	Insulin [71]	Not mentioned
M. Pathan et al., 2024 [72]	130	Not mentioned	Not mentioned	Semaglutide vs non-semaglutide [72]	Not mentioned
M. Alabbood et al., 2021 [73]	34	49.6	8.7 [73]	Gliconorm vs Sitavia plus [73]	~14 hours [73]
M. Khan et al., 2022 [74]	500	20-70	7-11 [74]	SGLT-2i vs Sulfonylurea [74]	Not mentioned
M. Pathan et al., 2023 [75]	332	Not mentioned	Not mentioned	Empagliflozin+Metformin+DPP4i [75]	Not mentioned
Mohamed Hassanein et al., 2025 [76]	2882	56.0 (basal-bolus), 55.1 (premixed)	Not different [76]	Basal-bolus vs Premixed insulin [76]	Not mentioned

Study	Sample Size	Mean Age (years)	Baseline HbA1c (%)	Current Medications	Fasting Duration
A. Kamrul-Hasan et al., 2026 [77]	3625	Not mentioned	Not mentioned	SGLT2i vs other glucose-lowering drugs [77]	Not mentioned
M. Fariduddin et al., 2025 [78]	615	50.73 (Group A), 51.78 (Group B)	8.3 (Group A), 8.2 (Group B) [78]	Various combinations [78]	Not mentioned
Z. Kiran et al., 2025 [79]	Not mentioned	41-60 (majority)	Not mentioned	Empagliflozin vs Sulfonylurea [79]	Not mentioned
H. Ghazi et al., 2022 [80]	100	65.9 (Group 1), 66.2 (Group 2)	Not mentioned	NPH vs Glargine U100 [80]	12-16 hours [80]

The characteristics table demonstrates substantial heterogeneity in study populations, medication regimens, and baseline glycemic control. Studies were conducted across diverse geographical settings including the Middle East, Southeast Asia, South Asia, and other regions with significant Muslim populations. Sample sizes ranged from 16 to 3625 participants [48, 77]. Most participants were middle-aged adults (mean ages 48-66 years), with diabetes duration ranging from newly diagnosed to over 20 years. Baseline HbA1c levels varied considerably, from well-controlled (6.33%) [10] to sub-optimally controlled (10.04%) [25], reflecting inclusion of patients across the glycemic control spectrum.

Effects of Ramadan Fasting on Glycemic Control

HbA1c Changes

The majority of studies demonstrated improvements or stability in HbA1c levels during Ramadan fasting. In patients treated with ertugliflozin, HbA1c decreased by 0.65% compared to 0.22% in the non-ertugliflozin group ($p<0.001$) [1]. Similarly, the iGlarLixi formulation resulted in a mean HbA1c reduction of 1.0% from pre-Ramadan to post-Ramadan [2]. Structured nutrition therapy combined with diabetes-specific formula produced significant HbA1c improvements, with one study reporting a reduction of 0.72% in the intervention group compared to no significant change in the control group [49].

Educational interventions demonstrated substantial effects on glycemic control. In the intervention group receiving focused education, HbA1c improved from 8.4% to 7.5%, representing a 0.8% reduction, while the control group showed minimal change [16]. Another study showed that individualized education resulted in a 0.7% HbA1c reduction compared to 0.1% in the usual care group ($p<0.0001$) [8]. Meta-analytic data indicated that Ramadan fasting was associated with significant reductions in fasting plasma glucose across single oral antidiabetic (SMD=0.47) [43], multi-oral antidiabetic (SMD=0.36) [43], and multitreatment subgroups (SMD=0.65) [43].

However, not all studies showed improvement. Several investigations reported no significant change in HbA1c levels. One study of 122 patients found that HbA1c remained stable from 6.33% pre-Ramadan to 6.22% post-Ramadan with no significant change [10]. Similarly, in patients treated with gliclazide MR, HbA1c and fasting plasma glucose showed no significant changes ($p>0.05$) [31].

Studies using continuous glucose monitoring provided detailed insights into glycemic variability. Flash glucose monitoring revealed an initial increase in glucose variability during early Ramadan (MAGE increased significantly, $p=0.006$) [30], particularly in patients on more than two anti-diabetic drugs and those on sulfonylureas [30]. However, this increase was transient, with glucose variability returning to pre-Ramadan levels by late Ramadan and post-Ramadan periods [30].

Fasting and Postprandial Glucose

Changes in fasting blood glucose (FBG) paralleled HbA1c improvements in most studies. Patients receiving structured Ramadan nutrition therapy demonstrated significantly lower fasting plasma glucose levels, with reductions of 0.9 mmol/L in the intervention group compared to increases of 0.2 mmol/L in the control group ($p<0.05$) [49]. In the ertugliflozin group, fasting plasma glucose decreased by 1.66 mmol/L compared to 0.68 mmol/L in controls ($p<0.001$) [1].

A large observational study using insulin glargine 300 U/mL reported reductions in both HbA1c (from 8.10% to 7.64%) and fasting plasma glucose (from 144.3 mg/dL to 128.5 mg/dL) [17]. Similarly, patients on vildagliptin showed significant HbA1c reduction (-0.43%, $p=0.009$) while the sulfonylurea group showed no effect [44].

Postprandial glucose control also improved in several studies. The ertugliflozin group experienced a reduction of 3.09 mmol/L in postprandial glucose compared to 1.48 mmol/L in the non-ertugliflozin group ($p<0.001$) [1]. Telemonitoring interventions resulted in greater postprandial glucose improvement in the intervention group, though not statistically significant ($p=0.355$) [38].

Medication-Specific Effects

Different medication classes showed varying effects on glycemic control during Ramadan. SGLT-2 inhibitors demonstrated favorable outcomes, with studies showing HbA1c reductions ranging from 0.49% to 0.65% [1, 9]. In one comparative study, empagliflozin resulted in a 0.5% HbA1c reduction versus 0.0% in the comparator arm ($p<0.001$) [75]. Flash glucose monitoring revealed that patients using SGLT-2 inhibitors had improved sensor-calculated HbA1c, from 7.3% to 6.8% [41].

GLP-1 receptor agonists also showed efficacy during Ramadan fasting. In a meta-analysis, the GLP-1RA group achieved greater HbA1c reduction (mean difference -0.31%, $p=0.04$) compared to non-GLP-1RA groups [4]. A specific study of semaglutide demonstrated a mean HbA1c decrease of 0.61% versus 0.19% in controls ($p<0.001$) [72].

DPP-4 inhibitors demonstrated safety and efficacy. Vildagliptin reduced HbA1c from 8.75% to 8.32% ($p=0.009$), while sulfonylurea showed no significant effect [57]. In another comparison,

the vildagliptin group showed a 0.3% HbA1c reduction versus 0.1% with sulfonylurea ($p<0.054$) [65].

Insulin regimens varied in their effects. A comparison of insulin degludec/insulin aspart (IDegAsp) versus biphasic insulin aspart 30 (BIAsp 30) showed similar glycemic efficacy but significantly lower hypoglycemia rates with IDegAsp [34]. Premixed insulin regimens appeared to have similar effectiveness as basal-bolus regimens in maintaining glycemic control [52].

Hypoglycemia and Safety Outcomes

Incidence and Severity

Hypoglycemia rates during Ramadan fasting varied considerably across studies and medication types. In a large dose-reduction trial involving 678 participants, the low-dosage group experienced significantly lower hypoglycemia incidence (4.2%) compared to the regular-dosage group (23.0%), with an odds ratio of 0.15 (95% CI, 0.08–0.26; $P<0.001$) [7]. The study found no cases of diabetic ketoacidosis or hyperosmolar hyperglycemic state in either group [7].

SGLT-2 inhibitors demonstrated excellent safety profiles. In patients treated with ertugliflozin during Ramadan, only 0.3% experienced hypoglycemia compared to 0.7% in the non-ertugliflozin group [1]. Studies with empagliflozin showed similarly low rates, with one reporting 7.3% experiencing symptoms but no severe episodes [14], and another showing 4.16% symptomatic events versus 8.7% in the sitagliptin group [70]. No cases of severe hypoglycemia, dehydration, or diabetic ketoacidosis requiring hospitalization were reported with SGLT-2 inhibitor use [14, 64, 66].

GLP-1 receptor agonists also showed favorable safety profiles. A meta-analysis found that the GLP-1RA group had lower risk of symptomatic hypoglycemia (risk ratio=0.53, 95% CI: 0.29–0.97, $P=0.04$) [4]. In studies with semaglutide, patients experienced fewer hypoglycemic episodes, though gastrointestinal symptoms were more common [72].

DPP-4 inhibitors demonstrated superior safety compared to sulfonylureas. Vildagliptin was associated with no hypoglycemic events versus 2 patients (4.8%) with sulfonylureas [57]. Another study found 5.8% hypoglycemia incidence with vildagliptin versus 14.2% with sulfonylureas [65].

In the VIRTUE study, patients receiving vildagliptin had no hypoglycemic events compared to 34 events in the sulfonylurea group [44].

Sulfonylureas consistently showed higher hypoglycemia rates. A five-country observational study of 1397 subjects found that 19.7% experienced symptomatic hypoglycemia, with the highest incidence in the glibenclamide group (25.6%), followed by glimepiride (16.8%) and gliclazide (14.0%) [5]. The overall incidence of severe hypoglycemia requiring assistance was 6.7%, with the highest rate in the glibenclamide group [5].

Insulin regimens showed variable safety profiles. Modern insulin formulations demonstrated low hypoglycemia rates. With iGlarLixi, only 2.0% of participants experienced severe and/or symptomatic hypoglycemia during Ramadan, with no severe events [16]. Similarly, insulin glargine 300 U/mL resulted in 2.6% experiencing hypoglycemia during Ramadan with no severe episodes [17]. In contrast, a comparison of NPH versus glargine U100 showed better outcomes with NPH, with 3 days of fasting broken due to hypoglycemia in the NPH group versus 10 days in the glargine group ($p=0.03$) [80].

Timing and Patterns

Studies using continuous glucose monitoring provided insights into the timing of hypoglycemic events. Most symptomatic hypoglycemia occurred during fasting hours, particularly in the last hours before breaking the fast [17, 23, 33]. Flash glucose monitoring revealed that 50% of hypoglycemic episodes were asymptomatic [48], highlighting the importance of glucose monitoring during Ramadan fasting.

The active versus sedentary lifestyle impacted hypoglycemia patterns. Active patients had more episodes of hypoglycemia (11.6 vs 1.8 episodes per patient over two weeks, $p=0.019$), though most were asymptomatic [48]. This suggests that physical activity level should be considered when adjusting medications for Ramadan.

Educational interventions significantly reduced hypoglycemia risk. Patients receiving pre-Ramadan education had a 94% rate of no hypoglycemic events compared to 73% in controls [3]. Another study showed hypoglycemia during fasting occurred in only 4.1% of the intervention group

versus 19.5% in controls [6]. The intervention group in a third study showed significantly lower hypoglycemia scores (from 14.21 pre-Ramadan to 5.44 post-Ramadan) [25].

Severe Hypoglycemia and Hospitalizations

Severe hypoglycemia requiring hospitalization or emergency care was rare across most studies. In the ORION study with insulin glargine 300 U/mL, no participants reported severe hypoglycemia during Ramadan or post-Ramadan periods [17]. Similarly, in studies with iGlarLixi combined with or without SGLT-2 inhibitors, no severe hypoglycemia occurred during Ramadan in either group [15]. A study involving split mixed insulin therapy reported only one case of major hypoglycemia (0.6%) [42].

Educational interventions reduced severe hypoglycemia rates. In one large multicenter study, participants receiving individualized education had fewer severe hypoglycemic events during Ramadan (23% vs 34%, $p=0.0017$) [8]. The same study also showed lower hospitalization rates in the intervention group (0% vs 2%) [8].

No study reported deaths due to hypoglycemia during Ramadan fasting, suggesting that with appropriate medical supervision and medication adjustments, fasting can be conducted safely even in patients with T2DM on multiple glucose-lowering therapies.

Body Weight and Metabolic Parameters

Weight Changes

Body weight changes during Ramadan fasting showed mixed results across studies. Several investigations demonstrated significant weight loss. Patients receiving ertugliflozin experienced a mean weight reduction of 1.24 kg compared to 0.36 kg in controls ($p<0.001$) [1]. Similarly, empagliflozin resulted in weight loss of 1.4 kg versus 0.2 kg in the comparator arm ($p<0.001$) [9]. The structured nutrition therapy group achieved greater weight loss (-2.9 kg) compared to usual care (-0.5 kg, $p<0.0001$) [8].

GLP-1 receptor agonists showed substantial effects on weight. Semaglutide produced weight loss of 2.97 kg versus 1.38 kg in the non-semaglutide group ($p<0.001$) [72]. A meta-analysis of GLP-1RAs found a mean difference in weight loss of -2.0 kg (95% CI: -3.37 to -0.63, $P=0.004$) [4].

However, several studies found no significant weight changes. In patients on iGlarLixi, body weight remained unchanged [16]. Similarly, studies with gliclazide MR showed a non-significant weight reduction of 0.3 kg ($p=0.614$) [47]. One study reported modest weight loss of 0.4 kg but without statistical significance ($p=0.81$) [3].

The discrepancy in weight outcomes may relate to differences in baseline characteristics, medication regimens, dietary behaviors during Ramadan, and the degree of structured nutritional support provided. Studies incorporating structured nutrition therapy consistently showed greater weight loss than those without such interventions.

Body Mass Index and Body Composition

Changes in BMI generally mirrored weight changes. Empagliflozin therapy resulted in significant BMI reduction (-0.48 kg/m^2 vs -0.11 kg/m^2 , $p<0.001$) [1]. In one study, BMI improved dramatically from 34.41 to 31.22 kg/m^2 in the SGLT-2 inhibitor group [70]. Meta-analytic data showed a significant decrease in BMI with multi-oral antidiabetic therapy (SMD=0.18, 95% CI: 0.04-0.31) [43].

Body composition analysis revealed more nuanced changes than weight alone. One study using bioimpedance methods found a significant reduction in body fat mass (from 30.9 kg to 29.2 kg, $p=0.013$) despite similar body weight [12]. Visceral fat area decreased in females (from 137.6 cm^2 to 132.5 cm^2 , $p=0.017$) but not in males [12]. Another investigation showed that the reduction in HbA1c was attributed to the reduction in body fat mass ($\beta=-0.196$, $p=0.034$) [12].

These findings suggest that Ramadan fasting may promote favorable changes in body composition, particularly reductions in visceral adiposity, even when total body weight remains stable. This may contribute to improved glycemic control independent of overall weight loss.

Lipid Profile

Lipid parameter changes showed considerable variability. Some studies demonstrated improvements in lipid profiles. Total cholesterol decreased significantly in one meta-analysis subgroup [62], with concomitant reductions in LDL cholesterol (from 2.41 to 2.28 mmol/L, $p<0.001$) [25]. Another study found improvements in LDL (reduced by 4.83 mg/dL, $p=0.007$)

specifically in patients with HbA1c >7% [51]. HDL cholesterol increased in some populations, particularly with repaglinide therapy ($p=0.022$) [21].

Conversely, other investigations reported adverse lipid changes. Total cholesterol increased from 3.94 to 4.11 mmol/L ($p=0.008$) and triglycerides from 1.55 to 1.71 mmol/L ($p=0.012$) in one study [13]. A cohort study found increases in LDL cholesterol and decreases in HDL cholesterol during Ramadan [69].

Triglyceride levels showed mixed patterns. Several studies reported reductions, including one with structured nutrition therapy showing a decrease of 0.21 mmol/L ($p<0.05$) [49] and another with sulfonylurea showing reductions ($p=0.002$ in one group, $p=0.024$ in another) [21]. However, some studies found increases or no significant changes.

The variability in lipid outcomes likely reflects differences in dietary patterns during Ramadan, with some individuals consuming more calorie-dense, high-fat foods during non-fasting hours, while others maintain healthier dietary habits. Studies incorporating structured nutrition education tended to show more favorable lipid profiles.

Blood Pressure and Cardiovascular Parameters

Blood pressure changes during Ramadan were generally favorable. Diastolic blood pressure improved significantly (from 75.7 to 68.8 mmHg, $p=0.001$) in one large prospective study [13]. Structured nutrition therapy resulted in reductions in both systolic and diastolic blood pressure [36]. SGLT-2 inhibitors showed more pronounced blood pressure reductions, with the empagliflozin group experiencing larger decreases in systolic (MD=-2.41 mmHg, $p=0.02$) and diastolic pressure (MD=-1.71 mmHg, $p=0.0007$) [77].

However, several studies found no significant blood pressure changes. One investigation reported no significant differences in blood pressure during Ramadan fasting [19]. Another found no statistically significant effects on blood pressure in the intervention group [25].

Endothelial function, measured by reactive hyperemia index (RHI), showed divergent results between diabetic patients and healthy controls. In diabetic patients fasting during Ramadan, RHI decreased significantly (-0.2 UI, $p<0.001$) [69], while no significant change occurred in

healthy volunteers [69]. This suggests that Ramadan fasting may have unfavorable effects on vascular endothelial function in individuals with diabetes.

Renal Function

Most studies reported stable or improved renal function during Ramadan fasting. In patients treated with SGLT-2 inhibitors, creatinine levels remained stable or showed only minor changes. One study found no significant change in creatinine in patients on empagliflozin [14, 66]. Estimated glomerular filtration rate (eGFR) showed a significant decrease from 94.3 to 87.8 mL/min/1.73m² ($p<0.001$) in one cohort [14], though values remained within acceptable ranges.

However, some investigations identified concerning renal changes. A study specifically examining renal function found significant increases in creatinine and urea levels with significant decreases in eGFR in groups with normal kidney function and albuminuria, but not in the renally impaired group [32]. Another investigation showed significant increases in creatinine and urea with decreases in eGFR and urinary albumin/creatinine ratio in diabetic patients fasting during Ramadan [68].

Microalbuminuria showed improvement in some populations. One study reported a significant decrease in microalbuminuria during Ramadan (from 132.85 to 45.03 mg/dL) [10]. However, another found increases in urinary albumin/creatinine ratio in certain subgroups [68].

These mixed findings suggest that renal function changes during Ramadan depend on baseline renal status, hydration practices, and medication regimens. Patients with pre-existing renal impairment may be protected from deterioration by dose adjustments and careful monitoring, while those with normal baseline function may experience transient changes related to volume status.

Other Biochemical Markers

Fructosamine levels, which reflect shorter-term glycemic control, showed variable changes. Some studies found no significant changes [10, 21], while others reported significant increases at one month post-Ramadan in both fasting and non-fasting diabetics ($p<0.01$) [22]. One investigation demonstrated greater reductions in fructosamine in the metformin/sitagliptin group ($-35.9\text{ }\mu\text{mol/L}$, $p<0.01$) [62].

Insulin resistance markers provided insights into metabolic changes. One study found increases in insulin levels and improvements in insulin sensitivity parameters including C-peptide, HOMA-IR, and IGF-1, suggesting improved beta-cell function during Ramadan fasting [11].

Inflammatory markers showed limited changes in most studies. High-sensitivity C-reactive protein increased during Ramadan in healthy volunteers ($p=0.01$) [12] but showed no significant changes in diabetic patients in other investigations [59]. In one study examining intermittent fasting effects, leptin levels decreased and beta-hydroxybutyrate levels increased significantly [59].

Apolipoprotein B decreased significantly ($p=0.0001$) while small dense LDL increased significantly ($p=0.022$) in one investigation of Ramadan fasting [58], suggesting complex changes in lipid particle composition that may not be fully captured by standard lipid panels.

Management Interventions and Their Effects

Educational Programs

Structured pre-Ramadan education emerged as a critical intervention for safe and effective fasting. Programs varied in content and delivery but consistently improved outcomes. A comprehensive program including 2-3 educational visits and dietary counseling sessions resulted in significantly lower fasting blood glucose (reduced by 57 mg/dL, $p=0.005$) and HbA1c (lower by 1.5%, $p=0.007$) [3]. Another structured education program increased the percentage of patients with HbA1c $<7\%$ from 20.8% to 55.8% post-Ramadan [6].

Educational content typically covered multiple domains. The Ramadan Focused Education Program addressed meal planning, physical activity, medications, and recognition and management of complications [25]. Another program emphasized risk stratification according to IDF-DAR guidelines, self-monitoring of blood glucose, medication adjustments, dietary modifications, and recognition of hypoglycemia and hyperglycemia [33].

The impact of education on hypoglycemia prevention was particularly notable. Pre-Ramadan education reduced hypoglycemia incidence from 19.5% in controls to 4.1% in the intervention group [6]. Hypoglycemic scores decreased significantly in the intervention group (from 14.21 to 5.44) compared to controls (from 14.01 to 9.27) [25]. The proportion of patients with no hypoglycemic events was higher among those receiving structured education (94% vs 73%) [3].

Group-based educational interventions also demonstrated effectiveness. The Managing Diabetes During Ramadan Conversation Map program improved glucose levels by 8.61 mg/dL ($p=0.005$) and HbA1c by 0.34% ($p<0.001$) overall, with greater benefits in patients with HbA1c $>7\%$ [51]. In patients with HbA1c $>7\%$, glucose reduction was 17.02 mg/dL and HbA1c decreased by 0.63% [51].

The timing of education delivery appeared important. Programs delivered 1-2 weeks before Ramadan allowed sufficient time for knowledge assimilation and medication adjustments [50]. Some studies combined pre-Ramadan education with continued support during Ramadan through telephone counseling [3, 42], which may have enhanced adherence and safety.

Medication Adjustments

Dose reduction strategies proved effective in minimizing hypoglycemia without compromising glycemic control. A large randomized trial comparing low-dosage (60% of usual) versus regular-dosage therapy found significantly lower hypoglycemia incidence in the low-dosage group (4.2% vs 23.0%, $p<0.001$) with no increase in hyperglycemia rates [7]. Each 1% decrease in baseline HbA1c was associated with a 19.9-fold increase in hypoglycemia odds, highlighting the importance of individualized dose adjustments [7].

Insulin regimens required careful adjustment. For insulin detemir and NovoMix 70, doses were reduced to 60% of usual, with 40% given as detemir at sunrise and 60% as NovoMix 70 before dinner [46]. This regimen resulted in non-inferior glycemic control with lower adverse event rates (0.04 vs 0.07, $p=0.010$) and hypoglycemia rates (0.00 vs 0.01, $p\leq 0.001$) [46]. Another insulin adjustment protocol recommended 30-50% dose reduction for the pre-dawn meal, with readjustment to pre-Ramadan levels after the fasting period [34].

Timing of medication administration was modified for several agents. Gliclazide MR dosing was switched from morning to evening at the start of Ramadan [56], maintaining glycemic control without increasing hypoglycemia risk. For iGlarLixi, 89.5% of patients took the medication at Iftar (evening) rather than before Suhur (morning) [16], which may have contributed to the low hypoglycemia rates observed.

DPP-4 inhibitors required minimal or no dose adjustment during Ramadan. Vildagliptin was administered as 50 mg twice daily at Suhur and Iftar without dose reduction [28, 44], demonstrating excellent safety profiles. Similarly, sitagliptin was given without modification, showing comparable efficacy to other agents [70].

SGLT-2 inhibitors were used without dose adjustments in most studies, as these agents carry inherently low hypoglycemia risk. Empagliflozin and dapagliflozin were continued at stable doses throughout Ramadan [14, 66], with excellent safety profiles and improvements in glycemic control. The major concern with SGLT-2 inhibitors was volume depletion, but rates remained low with appropriate patient education about hydration.

Nutritional Interventions

Structured nutrition therapy demonstrated significant benefits beyond education alone. The structured Ramadan Nutrition Plan (sRNT) incorporated diabetes-specific formula and resulted in superior outcomes compared to standard care. The sRNT group achieved greater reductions in fasting plasma glucose (-0.9 vs 0.2 mmol/L, $p<0.05$) [49], HbA1c (-0.72% vs -0.35%) [49], and triglycerides (-0.21 vs 0.20 mmol/L, $p<0.05$) [49].

Dietary recommendations during Ramadan focused on macronutrient distribution and meal timing. One structured program advised consuming 50% of daily energy needs at Iftar (with 10% as a light meal before maghrib prayer, 40% as main meal after prayer, and 10% after Tarawih prayer) and 40% at Suhur [20]. The program emphasized complex carbohydrates at suhoor, balanced meals at iftar, and avoidance of high-sugar and high-fat foods [33].

Continuous glucose monitoring provided insights into the effects of dietary patterns. Studies using CGM revealed higher glycemic variability during early Ramadan, particularly among those not receiving structured nutrition guidance [30, 40]. The structured nutrition approach resulted in significantly lower average sensor glucose, peak sensor values, time-above-range, and improved time-in-range compared to standard care [40].

Dietary fiber intake emerged as an important predictor of glycemic control. One study found that fiber intake significantly predicted changes in fasting plasma glucose ($p=0.035$) [45]. The structured nutrition group demonstrated increased dietary fiber intake compared to controls [40],

which may have contributed to better glycemic control and reduced postprandial glucose excursions.

Compliance with diabetes-specific formula predicted improvements in HbA1c ($p=0.024$) [45], suggesting that meal replacement or supplementation strategies may be beneficial for some patients during Ramadan. These formulas typically provided balanced macronutrients with slower glucose absorption characteristics, helping to maintain stable blood glucose levels during extended fasting periods.

Monitoring Strategies

Intensive glucose monitoring protocols enhanced safety during Ramadan fasting. Self-monitoring of blood glucose (SMBG) frequency recommendations ranged from 4 to 6 times daily. One intervention recommended SMBG at least four times daily during Ramadan, with additional measurements when symptoms occurred [38]. Another protocol used six daily measurements with transmission to a secure website for review and feedback from case managers [19].

Telemonitoring demonstrated substantial benefits over usual care. A cluster-randomized trial found that telemonitoring participants had significantly fewer hypoglycemic events during Ramadan (OR: 0.186, $p=0.04$) and at study end (OR: 0.257, $p=0.03$) [19]. The telemonitoring group also achieved greater HbA1c reduction (-1.07% vs -0.24%, $p<0.01$) [19]. Patients in the telemonitoring group performed more frequent glucose monitoring and had higher proportions of readings within target range [71].

Continuous glucose monitoring systems provided valuable insights but were primarily used for research purposes. Flash glucose monitoring (FGM) revealed that 50% of hypoglycemic episodes were asymptomatic [48], highlighting limitations of symptom-based hypoglycemia detection. FGM use after insulin or sulfonylurea dose adjustment according to PROFAST protocol effectively mitigated hypoglycemia risk without compromising glycemic control [60]. The system demonstrated improvements in time-in-range from 65.2% pre-Ramadan to 67.1% during Ramadan [60].

Flash glucose monitoring in active versus sedentary patients revealed important activity-related patterns. Active patients had better overall glucose control (median blood glucose 7.1 vs

10.6 mmol/L, $p<0.01$) [48] but more frequent hypoglycemia (11.6 vs 1.8 episodes per patient over two weeks, $p=0.019$) [48], most of which were asymptomatic. This information supports the need for activity-adjusted medication dosing.

Structured monitoring protocols included clear action thresholds. Patients were typically advised to break their fast if blood glucose dropped below 70 mg/dL or exceeded 300 mg/dL [61]. Some protocols recommended five SMBG readings at specific times during the first week of Ramadan or when symptoms occurred [61]. The frequency of glucose monitoring significantly increased in intervention groups receiving structured programs ($p<0.0001$) [8].

Technology-Assisted Interventions

Remote monitoring and support systems enhanced safety and outcomes during Ramadan. A 24-hour telephonic helpline service combined with pre-Ramadan education and insulin dose adjustment achieved flexible glycemic targets (183.50 mg/dL day, 179.20 mg/dL night) with minimal hypoglycemia (0.6%) [42]. This approach resulted in significant improvements in mean HbA1c ($p<0.0001$) and serum creatinine ($p=0.0010$) [42].

Web-enabled glucometers with mobile software facilitated real-time data transmission and feedback. In one study, participants transmitted blood glucose results six times daily to a secure website for review by case managers [19]. This system enabled timely intervention when glucose patterns indicated increased hypoglycemia or hyperglycemia risk, contributing to better overall glycemic control.

Collaborative algorithms incorporating patient empowerment showed promise. The Fasting Algorithm for Singaporeans with Type 2 Diabetes (FAST) included components for screening, education, dose modification by healthcare providers, and dose adjustment by patients [53]. The FAST intervention resulted in four times greater HbA1c improvement (-0.4% vs -0.1%, $p=0.049$) and better fasting blood glucose control (decrease of 3.6 mg/dL vs increase of 20.9 mg/dL, $p=0.034$) [38].

Mobile applications and social networking platforms facilitated ongoing communication between patients and healthcare providers. One structured nutrition therapy program provided participants with access to research dieticians via social networking applications [49], enabling

timely problem-solving and support during Ramadan. This accessibility may have contributed to better adherence to dietary recommendations and improved outcomes.

The integration of technology with traditional care models appeared synergistic. Studies combining technology-assisted monitoring with pre-Ramadan education and medication adjustment protocols achieved superior outcomes compared to either approach alone. However, the digital divide and varying levels of technological literacy require consideration when implementing such interventions across diverse populations.

Synthesis

The evidence base demonstrates that Ramadan fasting can be safe for many patients with T2DM when appropriate management strategies are implemented, though outcomes vary based on multiple factors including baseline glycemic control, medication regimen, patient education, and lifestyle characteristics during fasting.

Reconciling Heterogeneous Glycemic Outcomes

The apparent contradiction between studies showing improved glycemic control and those showing no change or deterioration can be explained through several mechanisms:

Baseline glycemic control and ceiling effects: Studies enrolling patients with poor baseline control (HbA1c >8-9%) consistently demonstrated larger HbA1c reductions. For instance, patients with HbA1c >7% showed 0.63% reduction compared to overall 0.34% reduction [51]. In contrast, studies with well-controlled patients at baseline (HbA1c ~6-7%) [10, 31] showed minimal or no change, suggesting a floor effect where further improvement is unlikely or unnecessary. Each 1% decrease in baseline HbA1c was associated with 19.9-fold increased hypoglycemia odds [7], indicating that aggressive glucose lowering in well-controlled patients carries disproportionate risk.

Medication class effects: The divergent findings across medication types reflect fundamental differences in pharmacology. SGLT-2 inhibitors and GLP-1 receptor agonists consistently produced improvements in glycemic control with low hypoglycemia risk [1, 4, 9, 72], as these agents operate through glucose-dependent mechanisms. Conversely, sulfonylureas showed high hypoglycemia rates (14-26%) [5] with less consistent glycemic improvements, reflecting their glucose-independent stimulation of insulin secretion. DPP-4 inhibitors demonstrated intermediate

effects with excellent safety profiles [44, 57, 65]. Thus, medication choice fundamentally determines the risk-benefit profile during Ramadan fasting.

Educational intervention effects: Studies incorporating structured pre-Ramadan education showed 4-5 times greater improvements than those without educational components. The structured education groups achieved HbA1c reductions of 0.7-1.5% [3, 8], while usual care groups showed minimal changes of 0.1-0.35% [8, 49]. This difference likely reflects multiple mechanisms: better medication adherence, more appropriate dose adjustments, improved dietary choices during non-fasting hours, earlier hypoglycemia recognition and management, and enhanced patient activation. The dose-response relationship is evident: programs with multiple educational sessions and ongoing support during Ramadan produced larger and more sustained improvements than single-session interventions.

Dietary and lifestyle heterogeneity: The considerable variation in weight and lipid outcomes reflects divergent dietary behaviors during Ramadan. Studies incorporating structured nutrition therapy demonstrated consistent weight loss and lipid improvements [8, 49, 62], while those without nutritional intervention showed variable or null effects [16, 44]. This suggests that Ramadan fasting per se does not automatically lead to weight loss; rather, outcomes depend on the quantity and quality of food consumed during non-fasting hours. Some individuals increase total caloric intake through consumption of traditional high-calorie foods at Iftar, negating the metabolic benefits of daytime fasting. The timing of eating (late-night eating after Tarawih prayers) may also impact metabolic outcomes.

Physical activity patterns: The dichotomy between active and sedentary patients reveals important nuances. Active patients achieved better overall glucose control (median 7.1 vs 10.6 mmol/L, $p<0.01$) [48] but experienced more hypoglycemia (11.6 vs 1.8 episodes) [48]. This paradox indicates that physical activity enhances insulin sensitivity and glucose utilization, improving overall control but increasing hypoglycemia risk during prolonged fasting when caloric intake is restricted. Patients maintaining physical activity during Ramadan require more aggressive medication dose reductions than sedentary individuals to prevent hypoglycemia.

Population-Specific Considerations

Geographical and cultural variations: Studies from the Middle East consistently showed higher hypoglycemia rates than those from Southeast Asia, with one five-country study showing 40% incidence in Israel versus 10% in Saudi Arabia [5]. These differences may reflect variations in fasting duration (longer in high-latitude regions during summer Ramadan), ambient temperature affecting hydration status, dietary customs during Iftar and Suhur, and healthcare system capacity for pre-Ramadan risk assessment and education. South Asian patients showed greater HbA1c and weight reductions compared to other ethnicities [13], possibly reflecting differences in baseline diet quality or cultural practices during Ramadan.

Gender differences: Several studies identified gender-specific effects. Women experienced greater visceral fat reduction (VFA decreased from 137.6 to 132.5 cm², $p=0.017$) [12] despite similar weight changes as men. One study reported that females comprised 71.9% of participants in an educational intervention [51], suggesting either higher motivation for diabetes self-management or greater willingness to participate in research. However, gender-specific analyses were limited in most studies, representing an important evidence gap.

Age considerations: Elderly patients (≥ 60 years) comprised the study population in several investigations [61, 80]. These studies showed that with careful medication selection (comparing NPH versus glargine, or DPP-4 inhibitors versus SGLT-2 inhibitors), elderly patients could fast safely. The comparison of NPH versus glargine U100 in elderly patients showed better outcomes with NPH [80], suggesting that medication effects may differ in older populations. However, elderly patients with diabetes-related complications were generally excluded from studies, limiting generalizability to frail elderly populations.

Duration since diagnosis: Time since diagnosis emerged as a moderator of outcomes. Patients with diabetes duration >10 years showed different response patterns than those with shorter duration [51]. Each 1% increase in baseline HbA1c was associated with 15.7-fold increased hyperglycemia odds [7], suggesting that patients with longer disease duration and poorer baseline control face higher risks during fasting. However, with appropriate dose reductions and monitoring, even long-standing diabetes did not preclude safe fasting.

Reconciling Safety Outcomes

The wide range in reported hypoglycemia rates (0% to 34%) [5, 8, 14] can be explained through several factors:

Definition and ascertainment: Studies using continuous glucose monitoring detected more hypoglycemia than those relying on symptoms alone, with 50% of CGM-detected hypoglycemia being asymptomatic [48]. Studies requiring both symptoms and confirmation by meter showed lower rates than those counting any reading <70 mg/dL. The distinction between symptomatic and severe hypoglycemia was critical; severe hypoglycemia requiring assistance was rare (<1-7%) [5] even in studies reporting high overall rates.

Medication-specific risk profiles: The hypoglycemia hierarchy consistently showed sulfonylureas > insulin > DPP-4 inhibitors > SGLT-2 inhibitors = GLP-1RAs. Among sulfonylureas, glibenclamide carried highest risk (25.6%) [5], while modern agents like gliclazide MR showed much lower rates (1-2%) [31, 56]. This gradient reflects fundamental differences in mechanism of action, with glucose-independent insulin secretagogues (sulfonylureas, insulin) carrying inherent hypoglycemia risk regardless of management strategies, while glucose-dependent agents (DPP-4 inhibitors, GLP-1RAs, SGLT-2 inhibitors) maintain physiological safeguards.

Dose reduction protocols: Studies implementing systematic dose reduction showed dramatically lower hypoglycemia than those maintaining usual doses. The 60% dose reduction protocol reduced hypoglycemia from 23% to 4.2% [7], demonstrating the critical importance of proactive dose adjustment. Conversely, studies without dose reduction protocols showed predictably higher hypoglycemia rates. The optimal degree of reduction varies by medication class and baseline HbA1c, requiring individualization.

Educational intervention effects: Pre-Ramadan education reduced hypoglycemia from 19.5% to 4.1% [6] and increased the proportion with no events from 73% to 94% [3]. Education enhanced multiple protective behaviors: appropriate medication dose adjustment, recognition of early hypoglycemia symptoms, proper timing of meals and medications, appropriate breaking of fast when necessary, and increased SMBG frequency. The magnitude of benefit correlated with educational program intensity and comprehensiveness.

Clinical Implications for Patient Selection

Synthesizing the evidence, patients can be stratified into risk categories:

Low-risk patients (suitable for fasting with standard precautions): Well-controlled diabetes (HbA1c <7-8%), on low-risk medications (metformin, DPP-4 inhibitors, SGLT-2 inhibitors, GLP-1RAs), no severe hypoglycemia history, no advanced complications, good understanding of diabetes self-management. These patients showed consistently favorable outcomes with minimal intervention beyond basic education [47, 56, 64].

Moderate-risk patients (suitable for fasting with intensified management): Moderately controlled diabetes (HbA1c 8-9%), on moderate-risk medications (insulin, sulfonylureas), with non-severe complications, willing to perform frequent SMBG. These patients require structured pre-Ramadan education, medication dose adjustment protocols, and intensive monitoring during Ramadan. With these interventions, outcomes were generally favorable [3, 25, 38].

High-risk patients (fasting not recommended or only with extreme caution): Poorly controlled diabetes (HbA1c >9%), recent severe hypoglycemia, advanced complications (end-stage renal disease, unstable cardiovascular disease), hypoglycemia unawareness, type 1 diabetes or insulin-dependent type 2 diabetes with high insulin requirements. Few studies enrolled such patients, and those that did showed concerning outcomes. Most were excluded from study participation, limiting evidence for this population [7, 8, 38].

Explaining Weight and Metabolic Outcome Heterogeneity

The paradox of studies showing weight loss versus weight stability can be resolved by examining total energy intake and composition:

Caloric balance mechanism: Studies showing weight loss consistently involved structured nutrition interventions that controlled total daily caloric intake [8, 49]. In contrast, studies without nutritional intervention showed minimal weight change [16, 44], suggesting that many patients compensate for daytime fasting by increasing food intake during non-fasting hours. Traditional Ramadan practices often involve consumption of calorie-dense foods at Iftar and late-night eating after Tarawih prayers, potentially leading to equal or greater total daily intake compared to non-fasting periods.

Body composition changes independent of weight: Several studies demonstrated reductions in body fat mass and visceral adiposity despite stable weight [12], suggesting that Ramadan fasting may promote favorable body composition changes through alterations in nutrient partitioning or hormonal milieu. The intermittent fasting pattern may shift substrate utilization toward fat oxidation during fasting periods, particularly in the pre-dawn hours. Increased beta-hydroxybutyrate levels during Ramadan [59] support this mechanism.

Medication effects on weight: Weight outcomes varied by medication class. SGLT-2 inhibitors consistently produced weight loss (1.4-2.0 kg) [1, 9] through urinary glucose excretion, while GLP-1 receptor agonists generated even greater weight loss (2.97 kg) [72] through appetite suppression and delayed gastric emptying. Insulin and sulfonylurea regimens showed neutral or modest weight increases in some studies, potentially limiting the weight loss benefits of fasting itself.

Lipid Profile Complexity

The divergent lipid findings can be explained by dietary quality and composition:

Dietary fat intake: Studies showing favorable lipid profiles (reduced LDL, increased HDL) [25, 51] often involved structured nutrition education emphasizing healthy fat sources and limiting saturated and trans fats. Conversely, studies showing adverse changes (increased total cholesterol and triglycerides) [13] likely reflect consumption of traditional high-fat Ramadan foods. The increase in percentage fat intake (from 11.9% to 13%) [12] in one study, despite overall caloric stability, may explain lipid changes in some populations.

Fasting-refeeding cycles: The daily fasting-refeeding cycle may influence hepatic lipid synthesis and clearance. Studies showing triglyceride reductions [21, 49] suggest that extended fasting periods reduce hepatic VLDL production, while those showing increases [13] may reflect postprandial hypertriglyceridemia from large evening meals. The timing and composition of the Iftar meal likely influences these outcomes substantially.

Medication effects: SGLT-2 inhibitors demonstrated improvements in total cholesterol, LDL, and triglycerides in some studies [72], independent of dietary changes. This may reflect both weight loss and direct metabolic effects of these agents. The structured nutrition therapy combined

with SGLT-2 inhibitor use produced the most consistent lipid improvements, suggesting synergy between pharmacological and lifestyle interventions.

The body of evidence supports that Ramadan fasting can be safe and potentially beneficial for glycemic control in many patients with T2DM, but outcomes are highly dependent on proper patient selection, pre-Ramadan education, medication adjustment, structured nutritional guidance, and intensive monitoring. The evidence is strongest for the safety and efficacy of newer medication classes (SGLT-2 inhibitors, GLP-1 receptor agonists, DPP-4 inhibitors) during Ramadan, while older agents (sulfonylureas, insulin) require more careful management and dose reduction. Structured pre-Ramadan education is a high-value intervention that consistently improves both glycemic control and safety outcomes across diverse populations and medication regimens.

DISCUSSION

Synthesis of Key Findings

This comprehensive systematic review of 80 studies (35 RCTs and 45 observational studies) provides robust evidence that Ramadan fasting can be safe and potentially beneficial for many patients with type 2 diabetes mellitus when appropriate management strategies are implemented. The findings demonstrate substantial heterogeneity in outcomes, which can be reconciled through careful consideration of patient characteristics, medication regimens, educational interventions, and lifestyle factors during fasting.

Glycemic Control Outcomes

The majority of studies demonstrated improvements or stability in glycemic control during Ramadan fasting. HbA1c reductions ranged from 0.5-1.5% in patients receiving structured interventions, with the largest improvements observed in those with poorer baseline control (HbA1c >8-9%). Pathan et al. (1) reported a 0.65% HbA1c reduction with ertugliflozin compared to 0.22% in controls ($p<0.001$), while Hassanein et al. (2) found a 1.0% reduction with iGlarLixi. These findings align with the meta-analysis by Aydın et al. (43) demonstrating significant reductions in fasting plasma glucose across multiple treatment subgroups (SMD 0.36-0.65).

However, studies enrolling well-controlled patients at baseline (HbA1c 6-7%) showed minimal or no change (10, 31), suggesting a ceiling effect where further improvement is either unnecessary or difficult to achieve. Sahin et al. (10) reported stable HbA1c (6.33% to 6.22%) in 122 patients, while Soelistijo et al. (31) found no significant changes with gliclazide MR. This pattern indicates that the metabolic benefits of Ramadan fasting may be most pronounced in patients with suboptimal baseline control, whereas those already at target may experience maintenance rather than improvement.

Continuous glucose monitoring studies provided nuanced insights into glycemic dynamics during Ramadan. Aldawi et al. (30) documented an initial increase in glucose variability during early Ramadan (MAGE increased significantly, $p=0.006$), particularly in patients on multiple medications or sulfonylureas. Importantly, this increase was transient, with parameters returning to baseline by late Ramadan and post-Ramadan periods. Elmalli et al. (35) similarly observed transient increases in glucose variability in insulin-treated patients, suggesting an adaptation period as patients adjust to the fasting schedule.

Medication-Specific Effects and Safety Profiles

A key finding of this review is the marked variation in safety and efficacy profiles across medication classes, providing clear guidance for medication selection in patients intending to fast.

SGLT-2 Inhibitors: Multiple studies demonstrated that SGLT-2 inhibitors are safe and effective during Ramadan fasting. Pathan et al. (1, 9) reported HbA1c reductions of 0.49-0.65% with ertugliflozin and empagliflozin, with extremely low hypoglycemia rates (0.3-7.3%) and no severe episodes requiring hospitalization. Sheikh et al. (14, 64) confirmed these findings in Pakistani populations, with no cases of severe hypoglycemia, dehydration, or diabetic ketoacidosis. The meta-analysis by Kamrul-Hasan et al. (77) further validated the favorable safety profile of SGLT-2 inhibitors during Ramadan. The glucose-dependent mechanism of action and low intrinsic hypoglycemia risk make this class particularly attractive for fasting patients. Additionally, the weight loss effects (1.24-1.4 kg) (1, 9) and blood pressure reductions (MD -2.41 mmHg systolic, $p=0.02$) (77) provide added cardiovascular benefits.

GLP-1 Receptor Agonists: The systematic review and meta-analysis by Kamrul-Hasan et al. (4) demonstrated that GLP-1 receptor agonists achieve greater HbA1c reduction compared to controls (mean difference -0.31%, $p=0.04$) with lower risk of symptomatic hypoglycemia (risk ratio 0.53, 95% CI 0.29-0.97, $p=0.04$). Pathan et al. (72) reported a 0.61% HbA1c reduction with semaglutide versus 0.19% in controls ($p<0.001$), along with substantial weight loss (2.97 kg vs 1.38 kg, $p<0.001$). The glucose-dependent insulinotropic action and delayed gastric emptying contribute to the favorable safety profile, though gastrointestinal symptoms were more common and require consideration (72).

DPP-4 Inhibitors: DPP-4 inhibitors consistently demonstrated excellent safety with efficacy comparable to or better than sulfonylureas. Hassanein et al. (44) reported significant HbA1c reduction with vildagliptin (-0.43%, $p=0.009$) while sulfonylurea showed no effect, with zero hypoglycemic events in the vildagliptin group versus 34 events with sulfonylurea. Shete et al. (57) found vildagliptin reduced HbA1c from 8.75% to 8.32% ($p=0.009$) with no hypoglycemia compared to 4.8% with sulfonylurea. Mahar et al. (65) confirmed these findings with hypoglycemia rates of 5.8% versus 14.2% favoring vildagliptin. The glucose-dependent mechanism and once or twice daily dosing without need for adjustment during Ramadan make DPP-4 inhibitors practical options.

Sulfonylureas: Sulfonylureas consistently showed the highest hypoglycemia rates among oral agents. The five-country observational study by Aravind et al. (5) involving 1397 subjects found symptomatic hypoglycemia in 19.7%, with significant variation by agent: glibenclamide 25.6%, glimepiride 16.8%, and gliclazide 14.0%. Severe hypoglycemia requiring assistance occurred in 6.7% overall. Shaikh et al. (47) and Farid Uddin et al. (56) reported lower rates (1-2%) with gliclazide MR, suggesting that modern, extended-release formulations and appropriate dose reduction may mitigate some risk. However, the glucose-independent mechanism of insulin secretion continues to pose inherent hypoglycemia risk regardless of management strategies.

Insulin Regimens: Insulin-treated patients demonstrated variable outcomes depending on regimen and adjustment protocols. Hassanein et al. (34) compared insulin degludec/insulin aspart (IDegAsp) with biphasic insulin aspart 30, finding similar glycemic efficacy but significantly lower

hypoglycemia rates with IDegAsp. Altemimi et al. (52) reported comparable effectiveness between premixed and basal-bolus regimens. The iGlarLixi fixed-ratio combination demonstrated favorable outcomes with only 2.0% experiencing severe or symptomatic hypoglycemia (16). Ahmedani and Ghafoor (42) achieved flexible glycemic targets with minimal hypoglycemia (0.6%) using a comprehensive program including 24-hour telephonic support and insulin dose adjustment. Modern insulin analogues and fixed-ratio combinations appear safer than traditional formulations, though all insulin regimens require careful dose reduction (typically 30-50%) and intensive monitoring.

Impact of Educational Interventions

Structured pre-Ramadan education emerged as perhaps the most consistently effective intervention across all studies. Mustafa et al. (3) demonstrated that targeted diabetes education resulted in significantly lower fasting blood glucose (reduced by 57 mg/dL, $p=0.005$) and HbA1c (lower by 1.5%, $p=0.007$), with 94% of the intervention group experiencing no hypoglycemic events versus 73% in controls. El Toony et al. (6) reported that focused pre-Ramadan education increased the proportion of patients achieving HbA1c $<7\%$ from 20.8% to 55.8% post-Ramadan and reduced hypoglycemia from 19.5% to 4.1%.

McEwen et al. (8) conducted a large multicenter study demonstrating that individualized education produced a 0.7% HbA1c reduction compared to 0.1% in usual care ($p<0.0001$), with fewer severe hypoglycemic events (23% vs 34%, $p=0.0017$) and lower hospitalization rates (0% vs 2%). Tourkmani et al. (25) showed that the Ramadan Focused Education Program significantly decreased hypoglycemic scores (from 14.21 to 5.44) compared to controls (14.01 to 9.27). Srulovici et al. (51) found that the Managing Diabetes During Ramadan Conversation Map program improved glucose levels by 8.61 mg/dL ($p=0.005$) and HbA1c by 0.34% ($p<0.001$), with greater benefits in patients with HbA1c $>7\%$ (0.63% reduction).

The essential components of effective educational programs identified across studies include: (1) risk stratification according to IDF-DAR guidelines (33); (2) medication adjustment protocols (3, 7); (3) meal planning with emphasis on complex carbohydrates at Suhur and balanced meals at Iftar (20, 33); (4) recognition and management of hypoglycemia and hyperglycemia (25); (5) self-monitoring of blood glucose frequency and action thresholds (38, 61); (6) physical activity

guidance (48); and (7) when to break the fast (blood glucose <70 mg/dL or >300 mg/dL) (61). Programs delivered 1-2 weeks before Ramadan with reinforcement during the month through telephone counseling or technology-assisted support demonstrated superior outcomes (3, 42, 49).

Dose Reduction Protocols

The randomized controlled trial by Zaghlol et al. (7) provided definitive evidence for the benefit of proactive dose reduction. Comparing low-dosage (60% of usual) versus regular-dosage therapy in 678 participants, the low-dosage group experienced significantly lower hypoglycemia incidence (4.2% vs 23.0%, OR 0.15, 95% CI 0.08-0.26, $p<0.001$) without increased hyperglycemia. Importantly, each 1% decrease in baseline HbA1c was associated with a 19.9-fold increase in hypoglycemia odds, emphasizing that well-controlled patients require more aggressive dose reduction. No cases of diabetic ketoacidosis or hyperosmolar hyperglycemic state occurred in either group.

For insulin regimens, Shehadeh and Maor (46) successfully implemented a protocol reducing insulin detemir and NovoMix 70 to 60% of usual, with 40% given as detemir at sunrise and 60% as NovoMix 70 before dinner. This regimen achieved non-inferior glycemic control with significantly lower adverse event rates (0.04 vs 0.07, $p=0.010$) and hypoglycemia (0.00 vs 0.01, $p\leq 0.001$). Hassanein et al. (34) recommended 30-50% dose reduction for the pre-dawn meal with readjustment to pre-Ramadan levels after fasting.

For oral agents, the optimal approach varies by medication class. Sulfonylureas require dose reduction, with gliclazide MR switched from morning to evening administration (56). DPP-4 inhibitors, SGLT-2 inhibitors, and GLP-1 receptor agonists generally do not require dose adjustment (14, 28, 44, 64), simplifying management and contributing to their favorable safety profiles.

Nutritional Interventions

Structured nutrition therapy significantly enhanced outcomes beyond medication adjustment alone. Yusof et al. (49) compared structured Ramadan Nutrition Plan (sRNT) incorporating diabetes-specific formula with standard care, finding greater reductions in fasting plasma glucose (-0.9 vs 0.2 mmol/L, $p<0.05$), HbA1c (-0.72% vs -0.35%), and triglycerides (-0.21 vs 0.20 mmol/L,

$p < 0.05$). Hasbullah et al. (40) used continuous glucose monitoring to demonstrate that sRNT resulted in significantly lower average sensor glucose, peak sensor values, time-above-range, and improved time-in-range compared to standard care.

Dietary fiber intake emerged as an important predictor of glycemic control, with Yusof et al. (45) finding that fiber intake significantly predicted changes in fasting plasma glucose ($p = 0.035$). Compliance with diabetes-specific formula also predicted HbA1c improvement ($p = 0.024$), suggesting that meal replacement or supplementation strategies may benefit selected patients. Jaelani et al. (20) provided detailed dietary recommendations, advising 50% of daily energy at Iftar (10% light meal before Maghrib prayer, 40% main meal after prayer, 10% after Tarawih prayer) and 40% at Suhur, with emphasis on complex carbohydrates and avoidance of high-sugar and high-fat foods.

The heterogeneity in weight and lipid outcomes across studies likely reflects differences in dietary behaviors during non-fasting hours. Studies incorporating structured nutrition therapy consistently demonstrated weight loss (2.9 kg in McEwen et al. (8); 2.97 kg with semaglutide in Pathan et al. (72)), while those without nutritional intervention showed minimal or variable changes (16, 44). This suggests that Ramadan fasting per se does not automatically lead to metabolic improvement; rather, outcomes depend critically on the quality and quantity of food consumed during non-fasting hours.

Monitoring Strategies and Technology

Intensive glucose monitoring enhanced safety and outcomes during Ramadan. Lee et al. (19) conducted a randomized controlled trial demonstrating that telemonitoring participants had significantly fewer hypoglycemic events during Ramadan (OR 0.186, $p = 0.04$) and at study end (OR 0.257, $p = 0.03$), with greater HbA1c reduction (-1.07% vs -0.24% , $p < 0.01$). Low et al. (71) found that flash glucose monitoring (Libre) use was associated with more frequent monitoring and higher proportions of readings within target range.

Bashir et al. (48) used flash glucose monitoring to reveal that 50% of hypoglycemic episodes were asymptomatic, highlighting the limitations of symptom-based detection. This finding has important clinical implications, suggesting that patients relying on symptoms alone may fail to

recognize and address hypoglycemia promptly. The PROFAST-IT study by Elhadd et al. (60) demonstrated that flash glucose monitoring after insulin or sulfonylurea dose adjustment effectively mitigated hypoglycemia risk while improving time-in-range from 65.2% pre-Ramadan to 67.1% during Ramadan.

Abdelgadir et al. (41) used flash glucose monitoring in high-risk insulin-treated patients on SGLT-2 inhibitors, showing improved sensor-calculated HbA1c (from 7.3% to 6.8%) with no severe hypoglycemia. The monitoring data enabled identification of patients requiring intervention and provided reassurance about the safety of combined SGLT-2 inhibitor and insulin therapy during Ramadan.

Lum et al. (38) developed and validated the Fasting Algorithm for Singaporeans with Type 2 Diabetes (FAST), incorporating screening, education, healthcare provider dose modification, and patient self-adjustment components. The FAST intervention resulted in four times greater HbA1c improvement (-0.4% vs -0.1%, $p=0.049$) and better fasting blood glucose control (decrease of 3.6 mg/dL vs increase of 20.9 mg/dL, $p=0.034$). Ahmedani and Ghafoor (42) combined 24-hour telephonic helpline with education and insulin adjustment, achieving significant improvements in mean HbA1c ($p<0.0001$) and serum creatinine ($p=0.0010$) with minimal hypoglycemia (0.6%).

Metabolic Parameters Beyond Glycemic Control

Body Weight and Composition: Weight changes during Ramadan varied considerably, with SGLT-2 inhibitors and GLP-1 receptor agonists producing the greatest reductions. Pathan et al. (1) reported 1.24 kg loss with ertugliflozin versus 0.36 kg in controls ($p<0.001$); Pathan et al. (9) found 1.4 kg loss with empagliflozin versus 0.2 kg in comparators ($p<0.001$); and Pathan et al. (72) documented 2.97 kg loss with semaglutide versus 1.38 kg in controls ($p<0.001$). Yeoh et al. (12) used bioimpedance to reveal significant reductions in body fat mass (30.9 kg to 29.2 kg, $p=0.013$) and visceral fat area in females (137.6 cm² to 132.5 cm², $p=0.017$) despite similar body weight, suggesting favorable body composition changes independent of total weight loss.

Lipid Profile: Lipid outcomes showed marked heterogeneity. Studies incorporating structured nutrition therapy generally demonstrated improvements: Tourkmani et al. (25) reported LDL reduction from 2.41 to 2.28 mmol/L ($p<0.001$); Yusof et al. (49) found triglyceride reduction

of 0.21 mmol/L ($p < 0.05$); and Srulovici et al. (51) noted LDL reduction of 4.83 mg/dL ($p = 0.007$) in patients with HbA1c $> 7\%$. However, Dabbous et al. (13) reported adverse changes with total cholesterol increasing from 3.94 to 4.11 mmol/L ($p = 0.008$) and triglycerides from 1.55 to 1.71 mmol/L ($p = 0.012$), likely reflecting consumption of traditional high-fat foods during Iftar. Lamti et al. (69) similarly found increases in LDL and decreases in HDL during Ramadan. These divergent findings underscore the critical importance of dietary guidance during non-fasting hours.

Blood Pressure and Cardiovascular Parameters: Blood pressure changes were generally favorable. Dabbous et al. (13) reported diastolic blood pressure improvement from 75.7 to 68.8 mmHg ($p = 0.001$). Elktuni et al. (36) found reductions in both systolic and diastolic pressure with structured nutrition therapy. Kamrul-Hasan et al. (77) demonstrated that SGLT-2 inhibitors produced larger blood pressure reductions (systolic MD -2.41 mmHg, $p = 0.02$; diastolic MD -1.71 mmHg, $p = 0.0007$). However, Lamti et al. (69) raised concern by showing that endothelial function (reactive hyperemia index) decreased significantly in diabetic patients during Ramadan (-0.2 UI, $p < 0.001$) while remaining stable in healthy controls, suggesting potential unfavorable vascular effects in diabetes that warrant further investigation.

Renal Function: Most studies reported stable or improved renal function. Sheikh et al. (14, 64) found no significant creatinine changes with SGLT-2 inhibitors, though eGFR decreased slightly from 94.3 to 87.8 mL/min/1.73m² ($p < 0.001$) within acceptable ranges. However, Abushady et al. (32) identified concerning changes in some populations, with significant creatinine and urea increases and eGFR decreases in groups with normal kidney function and albuminuria, but not in renally impaired patients. Mohammad et al. (68) similarly found significant creatinine and urea increases with eGFR decreases. Sahin et al. (10) reported improved microalbuminuria (from 132.85 to 45.03 mg/dL), suggesting potential renal benefit in some patients. These mixed findings indicate that renal outcomes depend on baseline status, hydration practices, and medication regimens, warranting individualized assessment and monitoring.

Risk Stratification and Patient Selection

Synthesizing the evidence, patients can be stratified into risk categories to guide clinical decision-making:

Low-Risk Patients (suitable for fasting with standard precautions): Well-controlled diabetes (HbA1c <7-8%), on low-risk medications (metformin, DPP-4 inhibitors, SGLT-2 inhibitors, GLP-1 receptor agonists), no severe hypoglycemia history, no advanced complications, good diabetes self-management understanding. These patients consistently showed favorable outcomes with minimal intervention beyond basic education (47, 56, 64).

Moderate-Risk Patients (suitable for fasting with intensified management): Moderately controlled diabetes (HbA1c 8-9%), on moderate-risk medications (insulin, sulfonylureas), with non-severe complications, willing to perform frequent SMBG. These patients require structured pre-Ramadan education, medication dose adjustment protocols, and intensive monitoring. With these interventions, outcomes were generally favorable (3, 25, 38).

High-Risk Patients (fasting not recommended or only with extreme caution): Poorly controlled diabetes (HbA1c >9%), recent severe hypoglycemia, advanced complications (end-stage renal disease, unstable cardiovascular disease), hypoglycemia unawareness, type 1 diabetes or insulin-dependent T2DM with high insulin requirements. Few studies enrolled such patients, and those that did showed concerning outcomes. Most were excluded from study participation, limiting evidence for this population (7, 8, 38).

Geographical and Cultural Variations

Notable geographical variations emerged in the evidence. Studies from the Middle East showed higher hypoglycemia rates than those from Southeast Asia, with Aravind et al. (5) reporting 40% incidence in Israel versus 10% in Saudi Arabia. These differences may reflect variations in fasting duration (longer in high-latitude regions during summer Ramadan), ambient temperature affecting hydration, dietary customs during Iftar and Suhur, and healthcare system capacity for pre-Ramadan risk assessment and education. Dabbous et al. (13) found that South Asian patients showed greater HbA1c and weight reductions compared to other ethnicities, possibly reflecting differences in baseline diet quality or cultural practices. These findings emphasize the need for culturally-adapted interventions that account for local dietary patterns and healthcare resources.

Gender Differences

Several studies identified gender-specific effects warranting attention. Yeoh et al. (12) found that women experienced greater visceral fat reduction despite similar weight changes as men, suggesting differential metabolic responses to intermittent fasting. Srulovici et al. (51) reported that females comprised 71.9% of participants in an educational intervention, possibly indicating higher motivation for diabetes self-management or greater willingness to participate in research. However, most studies lacked gender-specific analyses, representing an important evidence gap for future research.

Clinical Implications

The findings of this systematic review have several important clinical implications. First, all patients with T2DM who express interest in Ramadan fasting should undergo comprehensive pre-Ramadan assessment including glycemic control evaluation, medication review, complication screening, and risk stratification according to IDF-DAR guidelines. Second, medication selection should prioritize agents with favorable safety profiles during fasting, particularly SGLT-2 inhibitors, GLP-1 receptor agonists, and DPP-4 inhibitors, while sulfonylureas and insulin require careful dose reduction and intensive monitoring. Third, structured pre-Ramadan education should be provided to all patients who plan to fast, with content covering medication adjustment, meal planning, hypoglycemia recognition and management, self-monitoring, and when to break the fast. Fourth, dose reduction protocols (typically 30-60% reduction for high-risk medications) should be implemented proactively rather than reactively. Fifth, intensive glucose monitoring should be encouraged, with consideration of flash glucose monitoring or continuous glucose monitoring for high-risk patients. Sixth, structured nutrition therapy should be integrated into management, emphasizing balanced meals with complex carbohydrates at Suhur, avoidance of high-fat and high-sugar foods at Iftar, and maintenance of adequate hydration during non-fasting hours. Seventh, healthcare providers should establish clear communication channels for patients to seek advice during Ramadan, whether through telephone support, telemedicine, or in-person visits. Eighth, patients should be explicitly counseled about when to break the fast (blood glucose <70 mg/dL or >300 mg/dL, symptoms of hypoglycemia or hyperglycemia, acute illness) and reassured that doing so for medical reasons is permitted in Islamic law.

CONCLUSION AND RECOMMENDATIONS

This comprehensive systematic review of 80 studies provides robust evidence that Ramadan fasting can be safe and potentially beneficial for many patients with type 2 diabetes mellitus when appropriate management strategies are implemented. The key conclusions are as follows:

1. **Glycemic Control:** Ramadan fasting is associated with maintenance or improvement in glycemic control for most patients with T2DM, with HbA1c reductions ranging from 0.5-1.5% in those receiving structured interventions. Patients with poorer baseline control (HbA1c >8-9%) experience the greatest benefits, while well-controlled patients typically maintain stable glycemic parameters.
2. **Medication Safety Profiles:** There is a clear hierarchy of hypoglycemia risk by medication class. SGLT-2 inhibitors, GLP-1 receptor agonists, and DPP-4 inhibitors demonstrate the most favorable safety profiles with hypoglycemia rates of 0-7.3%, minimal need for dose adjustment, and additional benefits including weight loss and blood pressure reduction. Sulfonylureas carry substantially higher hypoglycemia risk (14-26% overall, up to 25.6% with glibenclamide), though modern extended-release formulations and appropriate dose reduction may mitigate some risk. Insulin regimens show variable safety depending on formulation, dose reduction, and monitoring intensity, with modern analogues and fixed-ratio combinations (iGlarLixi, IDegAsp) demonstrating improved safety profiles compared to traditional formulations.
3. **Educational Interventions:** Structured pre-Ramadan education is the single most consistently effective intervention, reducing hypoglycemia by 70-80% (from 19.5% to 4.1%) and improving HbA1c by 0.7-1.5% compared to usual care. Essential components include risk stratification, medication adjustment protocols, meal planning, hypoglycemia recognition and management, self-monitoring guidance, and clear instructions for when to break the fast.

4. **Dose Reduction:** Proactive dose reduction protocols (60% of usual dose for high-risk medications) decrease hypoglycemia by approximately 80% (from 23.0% to 4.2%, OR 0.15) without compromising glycemic control. The degree of reduction should be individualized based on baseline HbA1c, with well-controlled patients requiring more aggressive reduction.
5. **Nutritional Interventions:** Structured nutrition therapy significantly enhances outcomes beyond medication adjustment alone, producing greater improvements in glycemic control, weight loss (up to 2.9 kg), and lipid profiles. Dietary guidance should emphasize complex carbohydrates at Suhur, balanced meals at Iftar, avoidance of high-fat and high-sugar foods, and maintenance of adequate hydration during non-fasting hours.
6. **Monitoring:** Intensive glucose monitoring enhances safety, with telemonitoring reducing hypoglycemia by 80% (OR 0.186) and improving HbA1c by an additional 0.83% compared to usual care. Flash glucose monitoring reveals that 50% of hypoglycemic episodes are asymptomatic, highlighting the importance of objective glucose measurement rather than symptom-based detection alone.
7. **Metabolic Parameters:** Ramadan fasting produces favorable changes in body composition (reduced fat mass and visceral adiposity), blood pressure, and selected lipid parameters when combined with structured nutrition therapy. However, outcomes are highly dependent on dietary behaviors during non-fasting hours, with consumption of traditional high-fat foods potentially negating metabolic benefits.
8. **Risk Stratification:** Patients can be effectively stratified into low-risk (suitable for fasting with standard precautions), moderate-risk (suitable with intensified management), and high-risk (fasting not recommended or only with extreme caution) categories based on glycemic control, medication regimen, complication status, and hypoglycemia history.
9. **Geographical and Cultural Considerations:** Outcomes vary by geographical region and ethnicity, reflecting differences in fasting duration, dietary customs, and healthcare

infrastructure. Culturally-adapted interventions accounting for local practices are essential for optimizing outcomes.

10. **Safety:** Severe hypoglycemia requiring hospitalization is rare (<1-7%) across most studies, and no deaths due to hypoglycemia during Ramadan fasting were reported. With appropriate medical supervision, medication adjustment, and patient education, fasting can be conducted safely even in patients on multiple glucose-lowering therapies.

Recommendations for Clinical Practice

Based on the evidence synthesized in this review, the following recommendations are proposed for clinical practice:

1. Pre-Ramadan Assessment (4-6 weeks before Ramadan):

- Conduct comprehensive medical evaluation including HbA1c, renal function, and complication screening
- Apply IDF-DAR risk stratification criteria
- Discuss patient's intention to fast and assess motivation and self-management capacity
- Review current medication regimen and identify high-risk agents

2. Medication Optimization:

- Consider switching from sulfonylureas to agents with more favorable safety profiles (DPP-4 inhibitors, SGLT-2 inhibitors, GLP-1 receptor agonists) when clinically appropriate
- Implement dose reduction protocols for sulfonylureas and insulin (30-60% reduction based on baseline HbA1c)
- Adjust timing of medications (evening administration for Suhur doses)

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- Document medication changes clearly and provide written instructions

3. Structured Education Program:

- Deliver education 1-2 weeks before Ramadan
- Cover: risk stratification, medication adjustment, meal planning, hypoglycemia recognition and management, self-monitoring, physical activity guidance, when to break the fast
- Use culturally-appropriate materials and involve family members when possible
- Provide written action plans and emergency contact information

4. Nutritional Guidance:

- Recommend complex carbohydrates at Suhur (whole grains, legumes) for sustained glucose release
- Advise balanced Iftar meals with vegetables, lean protein, and controlled portions of carbohydrates
- Discourage consumption of high-fat fried foods and sugar-sweetened beverages
- Emphasize adequate hydration during non-fasting hours (water, sugar-free fluids)
- Consider diabetes-specific formula for selected patients

5. Monitoring Protocol:

- Recommend SMBG at least 4-6 times daily: pre-Suhur, post-Suhur, midday, pre-Iftar, post-Iftar, and when symptoms occur
- Consider flash glucose monitoring or continuous glucose monitoring for high-risk patients or those on intensive insulin regimens

- Establish clear action thresholds: break fast if blood glucose <70 mg/dL or >300 mg/dL
- Document glucose readings and review patterns mid-Ramadan

6. Support During Ramadan:

- Establish communication channels (telephone, telemedicine) for patient queries
- Schedule mid-Ramadan follow-up for high-risk patients
- Ensure availability of emergency care
- Reassure patients about religious permissibility of breaking fast for medical reasons

7. Post-Ramadan Follow-up:

- Schedule appointment within 1-4 weeks after Ramadan
- Review glycemic control and adjust medications to pre-Ramadan regimens as appropriate
- Assess for hypoglycemic events, weight changes, and other outcomes
- Document fasting experience to guide future Ramadan management

Recommendations for Future Research

This systematic review identifies several priorities for future research:

1. **High-Risk Populations:** Studies specifically enrolling high-risk patients (HbA1c $>9\%$, advanced complications, frailty, recurrent hypoglycemia) are needed to establish evidence-based recommendations for this group.

2. **Longer-Term Outcomes:** Research examining glycemic control and metabolic parameters 3-6 months post-Ramadan would clarify whether benefits are sustained beyond the immediate post-fasting period.
3. **Standardized Outcome Definitions:** Development and adoption of standardized definitions for hypoglycemia severity, glycemic outcomes, and adverse events would facilitate meta-analysis and evidence synthesis.
4. **Comparative Effectiveness Trials:** Head-to-head comparisons of different medication classes, educational approaches, and monitoring strategies using rigorous RCT designs would strengthen the evidence base.
5. **Cost-Effectiveness Analyses:** Studies examining the cost-effectiveness of structured education programs, technology-assisted monitoring, and newer medications during Ramadan would inform resource allocation decisions.
6. **Implementation Research:** Research on effective strategies for implementing evidence-based Ramadan management protocols in diverse healthcare settings (primary care, community health centers, resource-limited settings) is needed.
7. **Technology Integration:** Studies evaluating the optimal integration of continuous glucose monitoring, telemedicine, mobile applications, and artificial intelligence-based decision support during Ramadan would advance care delivery.
8. **Nutritional Interventions:** Well-designed trials examining specific dietary patterns, meal timing, and use of diabetes-specific formulas during Ramadan would refine nutritional guidance.
9. **Mechanistic Studies:** Research elucidating the physiological mechanisms underlying glycemic improvements, body composition changes, and vascular effects during intermittent fasting in diabetes would inform therapeutic targeting.

10. **Pediatric and Adolescent Populations:** Studies examining Ramadan fasting in adolescents with T2DM are needed to develop age-appropriate recommendations.
11. **Pregnancy and Gestational Diabetes:** While beyond the scope of this review, research on Ramadan fasting during pregnancy in women with gestational diabetes or pre-existing diabetes is urgently needed given the limited evidence base.
12. **Global Collaboration:** International collaborative networks and registries using standardized data collection would accelerate evidence generation and enable meaningful subgroup analyses across diverse populations.

In conclusion, Ramadan fasting is compatible with safe and effective diabetes management for many patients with T2DM when appropriate precautions are implemented. The evidence strongly supports a comprehensive approach combining risk stratification, medication optimization with preferential use of newer agent classes, structured pre-Ramadan education, proactive dose reduction for high-risk medications, structured nutrition therapy, and intensive monitoring. Healthcare providers have a responsibility to facilitate informed decision-making and provide evidence-based support that enables patients to fulfill their religious obligations while maintaining safety and optimizing health outcomes. With continued research and clinical attention, the goal of safe and spiritually fulfilling Ramadan fasting for the millions of Muslims with diabetes worldwide is increasingly attainable.

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