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The Triple Threat in Diabetes: Interconnection of Multidrug Resistance and Systemic Complications

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ABSTRACT

Diabetes mellitus represents a major global health challenge, predisposing individuals to chronic metabolic dysfunction, vascular complications, and increased susceptibility to infections. The rising prevalence of multidrug-resistant (MDR) organisms adds a critical layer of complexity, forming a "triple threat" where diabetes, antimicrobial resistance, and systemic complications reinforce each other. Impaired immunity in diabetic patients facilitates recurrent or persistent MDR infections, while prolonged infection and inflammation accelerate both macrovascular and microvascular damage. This interplay drives the progression of atherosclerosis, cardiovascular events, nephropathy, retinopathy, and neuropathy, worsening clinical outcomes and elevating healthcare costs. The convergence of these conditions establishes a self-perpetuating cycle of hyperglycemia, infection, and organ injury. Breaking this cycle demands integrated strategies that go beyond routine glycemic control, including antimicrobial stewardship, infection-prevention measures, and multidisciplinary approaches to patient management. Recognizing the interconnection between diabetes and MDR pathogens is essential for reducing disease burden and improving long-term outcomes.

KEYWORDS: Diabetes Mellitus; Drug Resistance, Multiple, Bacterial; Infections; Vascular Complications; Public Health.

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INTRODUCTION

Diabetes mellitus is a chronic metabolic disorder characterized by elevated fasting blood glucose levels, resulting from either inadequate insulin production by the pancreas or the body's inability to utilize insulin effectively (1,2). Insulin, a key regulatory hormone, facilitates cellular glucose uptake and energy production (3). Persistent hyperglycemia—commonly observed in uncontrolled diabetes—can lead to progressive damage to multiple organ systems, particularly the nerves and blood vessels (4). As a result, diabetes and its complications impose a substantial socioeconomic burden on both individuals and healthcare systems (5). Recent findings highlight an emerging triad of interconnected threats: diabetes, multidrug-resistant (MDR) infections (6,7), and systemic complications (8,9). This triad, often referred to as a vicious triad, significantly aggravates the clinical course and outcomes in diabetic patients (10). Chronic hyperglycemia compromises both innate and adaptive immune responses (11,12) by impairing neutrophil function (13), disrupting cytokine signaling (14), and altering T-cell activity (12), thereby increasing susceptibility to infections (15). Diabetic individuals are frequently exposed to antibiotic therapies, especially for recurrent urinary tract infections (16), foot ulcers (17), or skin infections (18)—conditions which promote the selection and propagation of MDR pathogens (19). These resistant infections are more difficult to manage, often requiring prolonged hospital stays and contributing to elevated morbidity and healthcare costs (20). Moreover, unresolved infections and poor glycemic control synergistically accelerate the onset and progression of systemic complications, including diabetic nephropathy, cardiovascular disease, and neuropathy (21). The interaction among these three elements is not merely cumulative but synergistic, with each factor exacerbating the other. This vicious triad presents a growing public health challenge (22), necessitating a comprehensive clinical approach that integrates optimal glycemic control (23), antimicrobial stewardship (24), and early identification and management of complications to improve outcomes in diabetic populations (25).

DIABETES

Definition (as per American Diabetes Associations 2024)

"Diabetes mellitus is a group of metabolic diseases characterized by hyperglycemia resulting from defects in insulin secretion, insulin action, or both. Chronic hyperglycemia in diabetes is associated with long-term damage, dysfunction, and failure of various organs, especially the eyes, kidneys, nerves, heart, and blood vessels" (26).

Epidemiology of DM

DM represents a significant global health challenge, affecting 589 million adults aged 20-79 years worldwide in 2024, equivalent to 1 in 9 adults. This burden is projected to escalate to 853 million by 2050, or 1 in 8 adults, driven by rising rates of type 2 diabetes. Notably, 81% of adults with diabetes reside in low- and middle-income countries, where healthcare access is often limited. In 2024, diabetes contributed to 3.4 million deaths globally, occurring at a rate of one death every 9 seconds, and accounted for USD 1.015 trillion in health expenditure, a 338% increase over the past 17 years. An alarming 43% of cases (252 million people) remain undiagnosed, with nearly 90% of these in low- and middle-income countries. Additionally, 635 million adults have impaired glucose tolerance and 488 million have impaired fasting glucose, placing them at high risk of developing type 2 diabetes. Hyperglycemia in pregnancy affects 1 in 5 live births, further compounding the global burden. In India, a high-prevalence region, 89.8 million adults have diabetes (10.5% age-standardized prevalence), with 43% undiagnosed and 334,922 diabetes-related deaths in 2024, alongside an estimated 940,840 individuals with type 1 diabetes across all ages (27).

Types of Diabetes Mellitus

DM is classified by the ADA based on etiology into four main categories: Type 1, Type 2, gestational diabetes mellitus, and other specific types (28), as illustrated in **Table 1**.

Table 1: ADA Classification of Diabetes Mellitus by Etiology

Type	Alternative Names	Definition/Etiology
Type 1 DM	Insulin-dependent diabetes, juvenile diabetes	Autoimmune destruction of pancreatic β-cells, leading to absolute insulin deficiency.
Type 2 DM	Non-insulin-dependent diabetes, adult-onset diabetes	Insulin resistance with relative insulin deficiency, often linked to obesity and genetics.
GDM DM	Pregnancy-induced diabetes	Insulin resistance during pregnancy due to placental hormones, usually resolves post- delivery.
Other Specific Types	Monogenic diabetes, Secondary diabetes	Includes monogenic forms (e.g., MODY), diabetes due to pancreatic disease, or drug-induced causes.

Table 1 : Show etiological classification of different types of diabetes mellitus (DM) with alternative name. Type 1 DM; Type 1 Diabetes Mellitus, Type 2 DM; Type 2 Diabetes Mellitus, GDM DM; Gestational Diabetes Mellitus, MODY; maturity-onset diabetes of the young.

Etiology of DM

The etiology of Diabetes Mellitus is illustrated in **Figure 1**, highlighting key contributing factors such as genetic predisposition, autoimmune mechanisms, insulin resistance, β-cell dysfunction, and environmental influences.

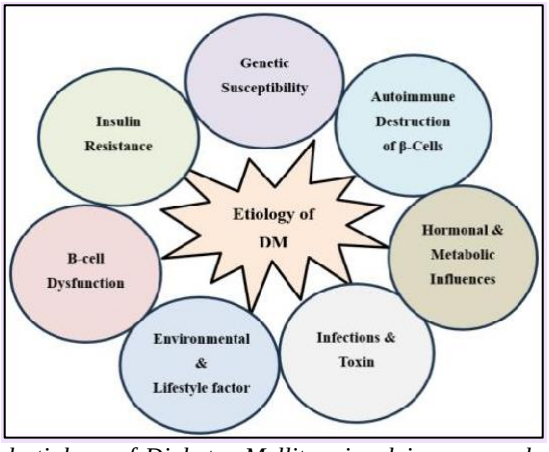


Figure 1 illustrates the multifactorial etiology of Diabetes Mellitus, involving a complex interplay of genetic, environmental, immunological, and metabolic factors. Genetic predisposition plays a significant role in both Type 1 and Type 2 diabetes, where specific gene mutations increase the risk of disease development. In Type 1 diabetes, autoimmune destruction of pancreatic β-cells leads to absolute insulin deficiency. In contrast, Type 2 diabetes is primarily driven by insulin resistance in peripheral tissues such

as muscle and adipose tissue, accompanied by progressive β-cell dysfunction and impaired insulin secretion. Environmental and lifestyle factors, including obesity, physical inactivity, high-calorie diets, and chronic stress, significantly contribute to the increasing global prevalence of Type 2 diabetes. Hormonal influences, such as those occurring during pregnancy (gestational diabetes) or in endocrine disorders like Cushing's syndrome and acromegaly, can also impair glucose metabolism. Additionally, viral infections and exposure to toxins are recognized as potential triggers, especially in autoimmune Type 1 diabetes. The figure illustrates these contributing factors, emphasizing how their combined effects disrupt normal glucose regulation and lead to the onset of diabetes.

Pathophysiology of DM

The molecular pathophysiology of DM varies by type but converges on hyperglycemia, increasing susceptibility to MDR infections and systemic complications, as illustrated in **Figure 2**. Type 1 DM results from autoimmune destruction of pancreatic β-cells, driven by T-cell-mediated responses and autoantibodies (e.g., GAD65, IAA), leading to caspase-mediated β-cell apoptosis and absolute insulin deficiency. This causes hyperglycemia via reduced GLUT4 translocation, impairing glucose uptake, and promotes immune dysfunction (e.g., reduced neutrophil phagocytosis, elevated IL-1β), increasing MDR pathogen susceptibility. Type 2 DM is characterized by insulin resistance, stemming from impaired IRS-1/PI3K/Akt signaling and elevated free fatty acids (FFAs), followed by β-cell dysfunction due to endoplasmic reticulum (ER) stress. Hyperglycemia ensues, accompanied by chronic inflammation (e.g., upregulated TNF-α, IL-6, NF-κB activation), which fosters MDR infections through biofilm formation. GDM arises from placental hormone-induced insulin resistance (e.g., cortisol, human placental lactogen, progesterone), reducing insulin sensitivity and GLUT4 activity, causing temporary hyperglycemia. This increases infection risk (e.g., MDR urinary tract infections) and future Type 2 DM risk due to β-cell stress. Other specific types include monogenic forms (e.g., HNF1A, GCK mutations in MODY) and secondary causes (e.g., pancreatitis, glucocorticoid use), leading to variable insulin production or signaling defects and hyperglycemia. All DM types enhance MDR susceptibility through immune impairment and biofilm formation, contributing to systemic complications, including macrovascular (atherosclerosis, cardiovascular disease) and microvascular (nephropathy, retinopathy, neuropathy) outcomes.

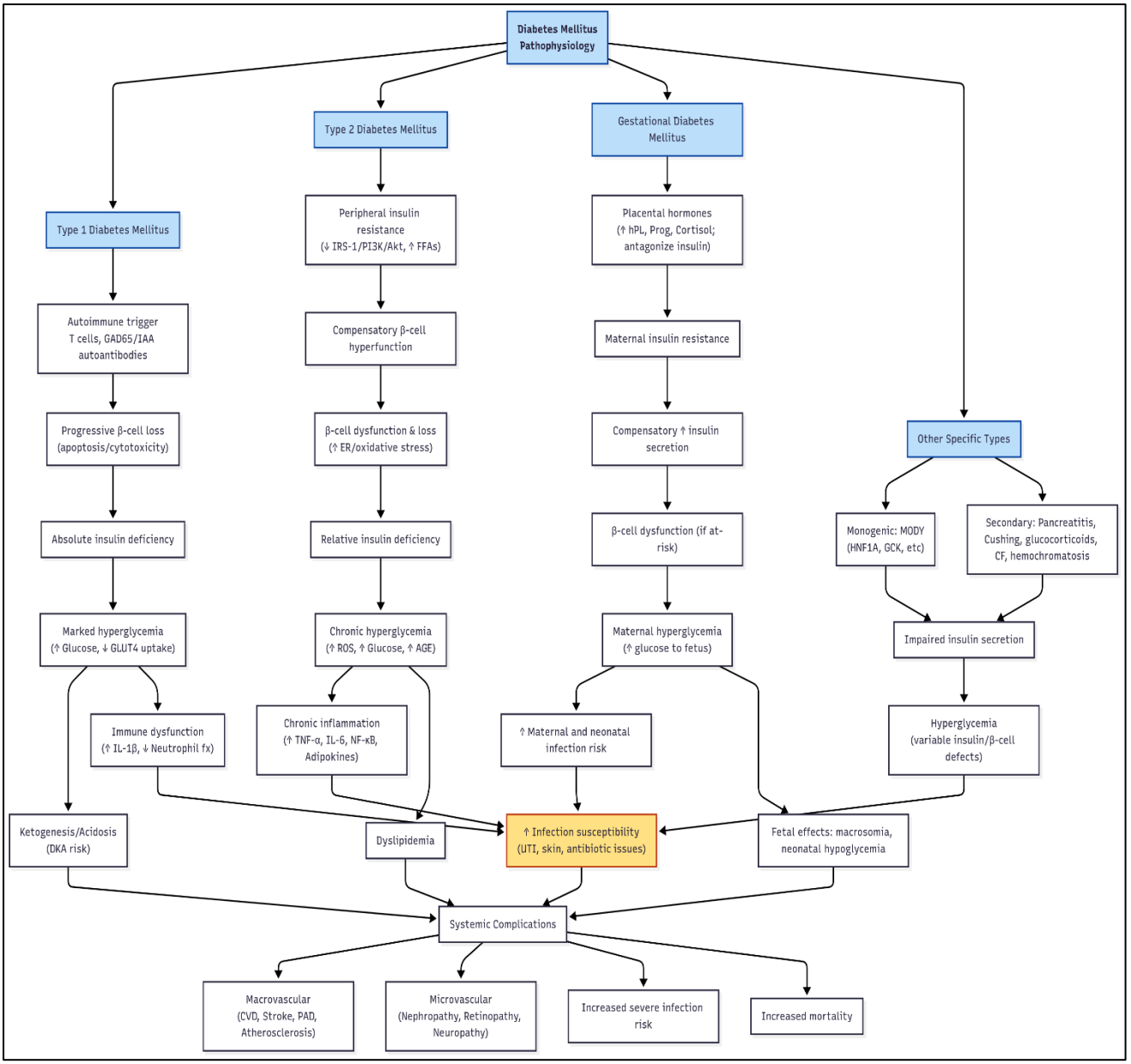


Figure 2: Illustrates the molecular pathophysiology of DM types, including Type 1 DM (autoimmune beta-cell destruction via

Glutamic Acid Decarboxylase 65 and Insulin Autoantibody-mediated responses, leading to caspase-mediated beta-cell apoptosis and absolute insulin deficiency), Type 2 DM (insulin resistance via impaired Insulin Receptor Substrate-1/Phosphoinositide 3-Kinase/Akt signaling, beta-cell dysfunction with endoplasmic reticulum stress, and chronic inflammation via Tumor Necrosis Factor-alpha/Interleukin-6), Gestational DM (placental hormone-induced insulin resistance with cortisol/Human Placental Lactogen/progesterone, causing temporary hyperglycemia), and other specific types (monogenic mutations like Hepatocyte Nuclear Factor 1 Alpha or Glucokinase in Maturity-Onset Diabetes of the Young or secondary causes like pancreatitis, impairing insulin secretion). Hyperglycemia drives immune dysfunction (e.g., reduced neutrophil activity, elevated Interleukin-1 beta) and biofilm formation, increasing susceptibility to multidrug-resistant pathogens. This contributes to systemic complications, including macrovascular (atherosclerosis, cardiovascular disease) and microvascular (nephropathy, retinopathy) damage.

Diagnosis Criteria of DM

Diagnosis of DM relies on standardized plasma glucose criteria or A1C levels, as recommended by the ADA 2024 Standards of Care. Diagnosis is confirmed with an A1C ≥6.5% (≥48 mmol/mol) using a National Glycohemoglobin Standardization Program (NGSP)-certified method, fasting plasma glucose (FPG) ≥126 mg/dL (≥7.0 mmol/L) after an 8-h fast, 2-h plasma glucose (2-h PG) ≥200 mg/dL (≥11.1 mmol/L) during a 75-g oral glucose tolerance test (OGTT), or random plasma glucose ≥200 mg/dL (≥11.1 mmol/L) with classic symptoms (e.g., polyuria, polydipsia) or hyperglycemic crises. In the absence of unequivocal hyperglycemia, two abnormal results are required for confirmation. Prediabetes is identified with A1C 5.7–6.4%, FPG 100–125 mg/dL, or 2-h PG 140–199 mg/dL, aiding prevention efforts. Recommendations emphasize NGSP-certified A1C assays, restricted point-of-care testing in Clinical Laboratory Improvement Amendments (CLIA)-certified labs, and plasma glucose use in conditions altering A1C (e.g., pregnancy, hemoglobin variants). This diagnostic framework, detailed in **Figure 3**, guides early detection and management of DM.

Current Prospective

Advancements in diabetes management have transformed care delivery, with continuous glucose monitoring (CGM) enhancing glycemic control by providing real-time data, now recommended for adults on non-insulin therapies and supported in hospital settings with appropriate protocols. New therapeutics, including sodium-glucose co-transporter 2 (SGLT2) inhibitors and glucagon-like peptide 1 (GLP-1) receptor agonists, offer cardiovascular and renal benefits, particularly for type 2 diabetes patients with heart failure or chronic kidney disease, and are prioritized in glycemic treatment plans. Obesity management has progressed with GLP-1 agonists and metabolic surgery, improving glycemia and comorbidities in eligible candidates. However, challenges persist: rising prevalence strains healthcare systems, access to care is limited by cost and medication shortages, and disparities affect older adults, children, and pregnant women. Hospital management faces complexities with hypoglycemia prevention, while socioeconomic barriers hinder adoption of positive health behaviors and technology, necessitating personalized, equitable approaches.

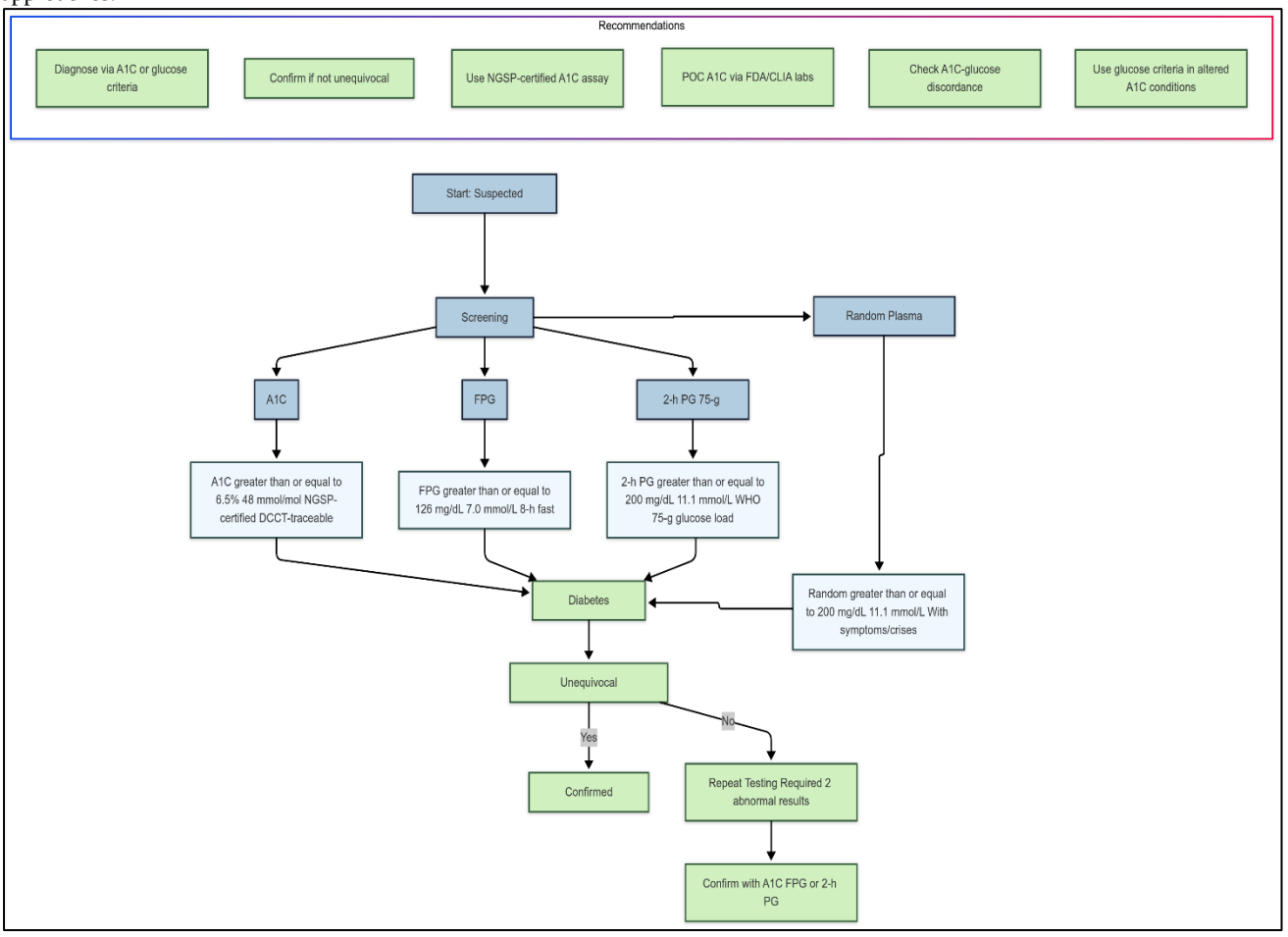


Figure 3: This flowchart outlines the diagnostic process for diabetes mellitus, incorporating A1C (≥6.5%), fasting plasma glucose (FPG ≥126 mg/dL), 2-h plasma glucose (2-h PG ≥200 mg/dL) during a 75-g oral glucose tolerance test (OGTT), and random plasma glucose (≥200 mg/dL with symptoms) per ADA 2024 criteria. Confirmation requires two abnormal results if hyperglycemia is not unequivocal. Prediabetes thresholds (A1C 5.7–6.4%, FPG 100–125 mg/dL, 2-h PG 140–199 mg/dL) are included for risk stratification. Recommendations (e.g., NGSP-certified A1C, CLIA-certified labs) ensure accuracy, with plasma glucose preferred in conditions like pregnancy or hemoglobin variants. (Source- ADA Standards of Care in Diabetes—2024).

Multidrug Resistance

MDR is the acquired ability of microorganisms, primarily bacteria, and cancer cells to resist multiple chemotherapeutic or antibiotic agents (29) from at least three distinct chemical classes with different mechanisms of action (30). This resistance results from the overexpression of efflux pumps (31) or other proteins that reduce intracellular drug concentrations below therapeutic levels (32). In diabetic patients, MDR exacerbates infection severity due to impaired immunity, contributing to systemic complications (33). MDR in diabetes mellitus, particularly T2DM, poses significant clinical challenges, especially in the context of infections such as diabetic foot ulcers (DFUs) (34) and tuberculosis (TB) (35). The mechanism of MDR in diabetes mellitus is multifaceted, driven by metabolic dysregulation (33,36), immune dysfunction (33), and alterations in gut microbiota (37,38), which collectively enhance infection persistence and the emergence of resistant bacterial strains, complicating treatment strategies (39).

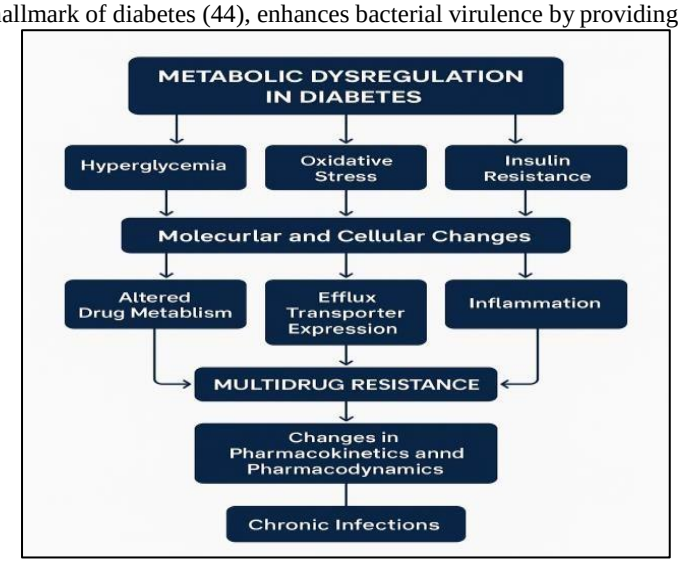
Prevalence of MDR in Diabetic Populations

The prevalence of MDR infections in diabetic populations is notably high, particularly in DFUs and urinary tract infections (UTIs), driven by compromised immune systems and frequent hospitalizations. In DFUs, approximately 50.86% of cases are infected with MDR bacteria, with a higher prevalence of gram-negative bacteria (32.84%) compared to gram-positive (19.81%), including common pathogens like Staphylococcus aureus and Escherichia coli (40). Among diabetic patients with UTIs, 82.5% of isolates are MDR, predominantly Escherichia coli resistant to penicillins and cephalosporins, with higher rates in females and the 41-60 age group (16). Risk factors such as previous hospitalizations, peripheral vascular disease, and nephropathy further elevate MDR risk, leading to prolonged hospital stays and increased healthcare costs (40,41). Addressing this challenge requires judicious antibiotic use, targeted treatment strategies, and effective diabetes management to mitigate complications and curb resistance.

Metabolic Dysregulation-Induced Multidrug Resistance in Diabetic Population

Metabolic dysregulation in diabetic populations profoundly drives through intricate molecular and cellular pathways, amplifying chronic infections and undermining antibiotic efficacy, as illustrated in **Figure 4** (42,43).

Figure 4 Hyperglycemia, a hallmark of diabetes (44), enhances bacterial virulence by providing a nutrient-rich environment and



activates the PI3K/Akt signaling pathway (45), promoting cell survival and fibronectin expression that fosters chronic infection persistence (46), while also altering drug metabolism by upregulating cytochrome P450 enzymes (47), leading to subtherapeutic antibiotic levels (e.g., isoniazid, rifampicin) against pathogens like Mycobacterium tuberculosis (36,48,49). Insulin resistance disrupts glucose uptake and insulin signaling, exacerbating oxidative stress and mitochondrial dysfunction, which further impair pharmacokinetics by reducing drug bioavailability and activate the mTOR pathway, dysregulating lipid and glucose metabolism and contributing to resistance, with mTOR inhibitors inducing hyperglycemia in 13–50% of cases (50,51). The nuclear factor-kappa B (NF-κB) pathway, triggered by chronic inflammation, amplifies pro-inflammatory cytokines (e.g., interleukin-1 beta (IL-1β) and tumor necrosis factor-alpha (TNF-α), compromising immune responses and reducing phagocytic activity of neutrophils and macrophages, thus enabling MDR pathogen survival (52). Efflux transporter expression, particularly ATP- binding cassette (ABC) transporters like MRP1, is upregulated by metabolic stress, enhancing drug efflux and diminishing therapeutic efficacy (53). Epigenetic modifications, including DNA methylation and microRNA dysregulation induced by oxidative stress, modulate gene expression, sustaining resistance (54–56). This inflammatory milieu, coupled with advanced glycation end products and trace element imbalances, alters pharmacodynamics, promoting resistant strains (57,58). Collectively, these mechanisms heighten MDR in diabetic patients, though targeted interventions like efflux pump inhibitors and glycemic control optimization show promise, necessitating further research (36).

Biofilm formation and bacterial virulence in diabetic microenvironments

Biofilm formation and bacterial virulence in diabetic microenvironments unfold as a highly coordinated molecular and cellular process, intricately linked to the pathogenesis of MDR within the hyperglycemic and inflamed diabetic wound bed, particularly in diabetic foot ulcers where chronic non-healing creates an ideal niche (59,60). At the molecular level, elevated glucose concentrations activate the icaADBC operon in Staphylococcus aureus (61), driving the synthesis of polysaccharide intercellular adhesin (PIA) (62) that forms the structural backbone of the biofilm matrix (63), while the intracellular second messenger cyclic diguanylate (c-di-GMP), generated by the DgcA enzyme, enhances matrix rigidity and impedes antibiotic diffusion, fostering resistance to agents like vancomycin (64). This process is amplified by quorum-sensing systems, where the luxS gene in Escherichia coli produces autoinducer-2 (AI-2), engaging the LsrR transcription factor to upregulate type 1 fimbriae and hemolysin genes, promoting bacterial adhesion to ulcerated tissue and toxin-mediated damage, a mechanism further intensified by the lasR and rhlR genes in Pseudomonas aeruginosa that boost pyocyanin production, enhancing virulence and survival under oxidative stress (65–67). At the cellular level, the diabetic microenvironment triggers macrophage polarization toward a pro-inflammatory M1 phenotype via toll-like receptor 4 (TLR4) and NF-κB signaling, releasing IL-1 and TNF-α that sustain inflammation, impair phagocytic clearance, and create a nutrient-rich haven for biofilm maturation, while oxidative stress from advanced glycation end products and trace element imbalances further compromises host defenses (57,68,69). Nutrient availability, particularly glucose, fuels bacterial proliferation and extracellular DNA (eDNA) release through cidA-mediated autolysis, reinforcing the biofilm scaffold and shielding pathogens from antibiotics, a critical factor in the 39% clindamycin resistance observed in diabetic foot infections (70–75). Bacterial virulence factors, such as P-fimbriae and hemolysins, enhance adhesion and tissue invasion, while quorum sensing orchestrates matrix exopolysaccharide synthesis via the pel locus, solidifying biofilm structure and contributing to antimicrobial resistance through lateral gene transfer of resistance-mediating proteins (76–79). The complex microbial community structure, dominated by diverse species like Staphylococcus and Pseudomonas, facilitates biofilm dispersal, enabling infection spread to secondary sites, a process exacerbated by impaired diabetic wound healing where biofilms delay closure and heighten infection risk, collectively driving MDR through a relentless cycle of molecular adaptation and cellular evasion that demands targeted therapeutic interventions to disrupt quorum sensing or dismantle biofilm matrices (80–82).

Frequent antibiotic exposure in diabetic patients driving resistance

Biofilm formation and bacterial virulence in diabetic microenvironments drive MDR and systemic complications, particularly in chronic diabetic foot ulcers, where hyperglycemia and inflammation create a niche for microbial persistence (59,60). Elevated glucose levels in the diabetic wound bed activate the *icaADBC* operon in *Staphylococcus aureus*, triggering the synthesis of polysaccharide intercellular adhesin (PIA), which forms the structural backbone of the biofilm matrix (61,62,63). Concurrently, the second messenger cyclic diguanylate (c-di-GMP), produced by the DgcA enzyme, strengthens matrix rigidity, limiting antibiotic diffusion and contributing to resistance against agents like vancomycin (64). Quorum-sensing systems amplify these effects, with the *luxS* gene in *Escherichia coli* producing autoinducer-2 (AI-2), engaging the LsrR transcription factor to upregulate type 1 fimbriae and hemolysin genes, promoting adhesion and toxin-mediated tissue damage (65). In *Pseudomonas aeruginosa*, *lasR* and *rhlR* genes enhance pyocyanin production, boosting virulence and survival under oxidative stress (66,67). These molecular adaptations are fueled by nutrient-rich conditions, particularly glucose, which supports bacterial proliferation and extracellular DNA (eDNA) release via *cidA*-mediated autolysis, reinforcing the biofilm scaffold and shielding pathogens, a key factor in the 39% clindamycin resistance observed in diabetic foot infections (70–75). Simultaneously, hyperglycemia and advanced glycation end products (AGEs) induce oxidative stress and trace element imbalances, compromising host defenses (57,68). This triggers macrophage polarization toward a pro-inflammatory M1 phenotype via toll-like receptor 4 (TLR4) and NF-κB signaling, releasing IL-1 and TNF-α, which sustain chronic inflammation and impair phagocytic clearance, creating a nutrient-rich haven for biofilm maturation (69). Bacterial virulence factors, such as P-fimbriae and hemolysins, enhance adhesion and tissue invasion, while quorum sensing orchestrates matrix exopolysaccharide synthesis via the *pel* locus, solidifying biofilm structure and facilitating lateral gene transfer of resistance-mediating proteins, driving MDR (76–79). The diverse microbial community, dominated by *Staphylococcus* and *Pseudomonas*, promotes biofilm dispersal, enabling infection spread to secondary sites and delaying wound closure, thus heightening systemic complication risks (80–82). This integrated cascade of molecular adaptations and cellular dysfunctions creates a self-reinforcing cycle of infection, resistance, and impaired healing. Targeted interventions, such as disrupting quorum sensing or dismantling biofilm matrices, are essential to break this cycle and improve outcomes in diabetic infections.

SYSTEMIC CONSEQUENCES OF THE DIABETES–MDR INTERPLAY

Macrovascular Complications

Macrovascular disease is one of the leading causes of morbidity and mortality in individuals with diabetes. Chronic hyperglycemia, dyslipidemia, and endothelial dysfunction create a pro-atherogenic environment, predisposing patients to coronary artery disease, peripheral arterial disease, and stroke. The coexistence of MDR infections further amplifies this risk. Persistent infections maintain a state of systemic inflammation, with sustained release of cytokines and reactive oxygen species, which accelerates atherosclerosis and destabilizes vascular plaques. In addition, infection-driven oxidative stress reduces nitric oxide bioavailability, impairing vasodilation and worsening vascular stiffness (7). Diabetic patients, who already suffer from impaired vascular repair mechanisms, are particularly vulnerable to this dual burden. MDR infections prolong inflammatory injury due to delayed or ineffective treatment, leading to earlier onset and greater severity of cardiovascular complications (83). Consequently, the risk of acute coronary syndromes, cerebrovascular accidents, and heart failure is significantly heightened in this population (7).

Microvascular Complications

Microvascular complications such as nephropathy, retinopathy, and neuropathy are central to the long-term burden of diabetes. These conditions are primarily driven by hyperglycemia-induced endothelial dysfunction, basement membrane thickening, and ischemic injury. MDR infections act as a catalyst in worsening these processes (68).In diabetic nephropathy, recurrent MDR

urinary tract infections cause repeated renal inflammation, scarring, and tubular damage, thereby accelerating the decline in renal function and hastening progression to end-stage kidney disease (4). In the retina, chronic systemic infection and inflammation aggravate capillary dropout and ischemic injury, intensifying the progression of diabetic retinopathy. Similarly, diabetic neuropathy is exacerbated by infection-induced vascular insufficiency and neuroinflammation, which amplify nerve ischemia and degeneration (84).

CONCLUSION

The coexistence of diabetes and MDR infections forms a vicious triad of metabolic dysfunction, impaired immunity, and persistent infection. This interplay not only worsens the risk of recurrent infections but also accelerates the progression of both macrovascular and microvascular complications. The combined impact results in higher morbidity, premature mortality, and escalating healthcare costs, underscoring the urgent need for targeted interventions. Addressing this challenge requires integrated and holistic strategies. Optimal glycemic control, antimicrobial stewardship, and infection-prevention programs must be implemented in parallel to reduce the mutual reinforcement between diabetes and MDR pathogens. Furthermore, coordinated efforts involving clinicians, microbiologists, public health experts, and policy-makers are essential to design and deliver comprehensive care models. Recognizing diabetes and MDR infections as interconnected public health threats rather than isolated entities will be critical in mitigating their combined burden and improving long-term patient outcomes.

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