JHWCR JOURNAL OF HEALTH, WELLNESS AND COMMUNITY RESEARCH 3007-0570

https://doi.org/10.61919/06h22489

Review Article

Impact of Anti-Allergic Drug Therapy on the Incidence of Diabetes Mellitus: A Narrative Review

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"Cite this Article" Received: 04 April 2026; **Accepted**: 02 May 2026; **Published**: 16 May 2026

Author Contributions: Concept: MHA and ME; Design: SI and HDM; Data Collection: AM and IA; Analysis: MHA, ME, and SI; Drafting: HDM, AM, and IA. **Ethical Approval**: Superior University, Lahore, Pakistan. **Informed Consent**: Written informed consent was obtained from all participants; **Conflict of Interest**: The authors declare no conflict of interest. **Funding**: No external funding; **Data Availability**: Available from the corresponding author on reasonable request; **Acknowledgments**: N/A.

ABSTRACT

Background: Anti-allergic medications are widely used for allergic rhinitis, asthma, urticaria, atopic dermatitis, and other hypersensitivity-related disorders. Because many patients require repeated or long-term therapy, potential metabolic consequences are clinically important, particularly in individuals with obesity, prediabetes, established diabetes, advanced age, or polypharmacy. Corticosteroids are well recognized to disturb glucose regulation, whereas the metabolic implications of antihistamines, leukotriene receptor antagonists, and mast cell stabilizers remain less clearly synthesized. **Objective:** This narrative review aimed to synthesize current pharmacological, mechanistic, and clinical evidence on the relationship between major anti-allergic drug classes and the risk of hyperglycemia, insulin resistance, and diabetes mellitus. **Methods:** A narrative synthesis was conducted using biomedical and pharmacological literature related to anti-allergic drugs, glucose metabolism, drug-induced hyperglycemia, insulin resistance, and diabetes mellitus. Evidence was organized thematically by drug class, including systemic and inhaled corticosteroids, first- and second-generation antihistamines, leukotriene receptor antagonists, and mast cell stabilizers. Emphasis was placed on biological mechanisms, relative diabetogenic potential, patient-level susceptibility, and clinical implications for prescribing and monitoring. **Results:** Systemic corticosteroids showed the strongest association with dysglycemia through increased hepatic gluconeogenesis, reduced peripheral glucose uptake, insulin resistance, adipose tissue effects, and β-cell stress. Inhaled and intranasal corticosteroids appeared lower risk but may be relevant with high cumulative exposure. Antihistamines were generally low risk, with first-generation agents carrying possible indirect metabolic concern through sedation, reduced activity, appetite change, and weight gain. Leukotriene receptor antagonists and mast cell stabilizers appeared metabolically neutral in routine use. **Conclusion:** Anti-allergic therapy has drug-class–specific metabolic implications. Corticosteroid exposure requires the greatest caution, while non-corticosteroid agents are generally metabolically safer. Individualized prescribing, dose minimization, and targeted glucose monitoring are most important for patients with existing metabolic risk. **Keywords:** Diabetes Mellitus; Anti-Allergic Agents; Corticosteroids; Antihistamines; Insulin Resistance; Hyperglycemia; Leukotriene Receptor Antagonists; Drug-Induced Diabetes.

INTRODUCTION

Allergic diseases represent a substantial and increasing clinical burden worldwide, affecting respiratory, dermatologic, ocular, and systemic health across diverse age groups. These conditions are typically driven by immune hypersensitivity reactions, most commonly involving immunoglobulin E–mediated activation of mast cells and basophils after exposure to allergens such as pollen, dust mites, food proteins, drugs, or environmental triggers (1). The resulting release of histamine, leukotrienes, prostaglandins, cytokines, and other inflammatory mediators produces the characteristic clinical manifestations of allergic disease, including pruritus, rhinorrhea, bronchoconstriction, edema, urticaria,

and, in severe cases, anaphylaxis. Because allergic disorders are often recurrent or chronic, many patients require repeated or long-term pharmacological therapy, making the safety profile of anti-allergic drugs an important consideration beyond immediate symptom control (2).

Anti-allergic medications include several pharmacological classes with distinct mechanisms of action and different levels of systemic exposure. H1-antihistamines reduce histamine-mediated symptoms by blocking H1 receptors and are widely used for allergic rhinitis, urticaria, and pruritic disorders, with first-generation agents producing greater central nervous system effects and second-generation agents offering more selective peripheral activity (3). Corticosteroids, administered orally, parenterally, inhalationally, intranasally, or topically, exert broader anti-inflammatory effects through genomic regulation of inflammatory pathways and remain essential in asthma, allergic rhinitis, atopic dermatitis, and severe allergic reactions (4). Leukotriene receptor antagonists, such as montelukast and zafirlukast, suppress leukotriene-mediated bronchoconstriction and inflammation, while mast cell stabilizers prevent mediator release and are generally associated with limited systemic metabolic effects (5). Although these agents are central to allergy management, their long-term metabolic consequences remain unevenly characterized across drug classes.

Diabetes mellitus is a chronic metabolic disorder defined by persistent hyperglycemia resulting from impaired insulin secretion, reduced insulin action, or both. Its major clinical importance lies not only in abnormal glucose homeostasis but also in its association with cardiovascular disease, nephropathy, neuropathy, retinopathy, infection risk, and increased healthcare burden (6). Type 1 diabetes mellitus is primarily caused by autoimmune destruction of pancreatic β-cells, whereas type 2 diabetes mellitus is driven by insulin resistance, progressive β-cell dysfunction, obesity, sedentary behavior, inflammation, and genetic susceptibility (7). Because the prevalence of type 2 diabetes and prediabetes continues to rise globally, even modest drug-related worsening of insulin sensitivity or glycemic control may have clinically meaningful implications, particularly in patients who already possess metabolic risk factors.

Drug-induced dysglycemia is increasingly recognized as an important contributor to new-onset diabetes and worsening glycemic control. Several medication classes, including glucocorticoids, atypical antipsychotics, thiazide diuretics, β-blockers, and calcineurin inhibitors, have been associated with impaired insulin secretion, increased hepatic glucose production, reduced peripheral glucose uptake, or direct β-cell dysfunction (8). Among anti-allergic therapies, corticosteroids have the clearest biological and clinical link with hyperglycemia because they increase hepatic gluconeogenesis, antagonize insulin action in skeletal muscle and adipose tissue, promote lipolysis, and may impair pancreatic β-cell compensation during prolonged exposure (9). The diabetogenic risk appears to be influenced by route of administration, cumulative dose, treatment duration, baseline body mass index, age, family history, and pre-existing impaired glucose tolerance (10).

In contrast, the metabolic effects of non-corticosteroid anti-allergic agents are less clearly defined. Second-generation antihistamines are generally regarded as metabolically neutral because of their receptor selectivity and limited central penetration; however, some observational and mechanistic evidence suggests that prolonged antihistamine exposure may indirectly influence body weight, appetite regulation, or insulin sensitivity in susceptible individuals (11). Leukotriene receptor antagonists have been investigated not only for respiratory and allergic indications but also for their potential effects on inflammatory pathways relevant to insulin resistance, although current evidence remains limited and should be interpreted cautiously (12). Mast cell stabilizers are considered to have minimal systemic metabolic activity, but the absence of strong adverse metabolic signals does not eliminate the need for clearer comparative synthesis across anti-allergic drug classes.

Despite the clinical relevance of this topic, the available literature remains fragmented. Corticosteroid-induced hyperglycemia has been widely discussed, but evidence concerning antihistamines, leukotriene receptor antagonists, mast cell stabilizers, and combination anti-allergic therapy is less consistently integrated. Existing discussions often focus on individual drug classes rather than presenting a clinically

oriented comparison of mechanisms, relative diabetogenic potential, patient-level risk factors, and monitoring implications. This creates an important knowledge gap for clinicians who must balance effective allergy control against the risk of metabolic harm, especially in patients with obesity, prediabetes, established diabetes, advanced age, polypharmacy, or chronic inflammatory disease.

Therefore, this narrative review aims to synthesize current pharmacological, clinical, and mechanistic evidence on the relationship between anti-allergic drug therapy and diabetes mellitus risk. Specifically, it evaluates how major anti-allergic drug classes influence glucose metabolism, identifies patient and treatment factors that increase susceptibility to drug-induced dysglycemia, and outlines practical implications for safer prescribing and glycemic monitoring. The central review question is: how do commonly used anti-allergic medications differ in their potential to disturb glucose homeostasis and contribute to diabetes risk, and which patients require the greatest metabolic caution during therapy?

MATERIALS AND METHODS

This narrative review was designed to synthesize pharmacological, mechanistic, and clinical evidence on the potential relationship between anti-allergic drug therapy and disturbances in glucose metabolism, including insulin resistance, hyperglycemia, and diabetes mellitus. A narrative approach was selected because the available evidence spans heterogeneous drug classes, study designs, populations, exposure routes, and outcome definitions, making a conceptually organized synthesis more appropriate than statistical pooling. The review focused on commonly used anti-allergic drug categories, including H1-antihistamines, corticosteroids, leukotriene receptor antagonists, mast cell stabilizers, and selected adjunctive agents used in allergic and inflammatory disorders.

A structured literature search was conducted using major biomedical and academic databases, including PubMed/MEDLINE, Google Scholar, ScienceDirect, and Scopus. The search covered literature relevant to allergy pharmacotherapy, glucose metabolism, drug-induced hyperglycemia, insulin resistance, and diabetes mellitus. Search terms were combined using Boolean operators and included “anti-allergic drugs,” “antihistamines,” “H1 receptor antagonists,” “corticosteroids,” “glucocorticoid-induced diabetes,” “steroid-induced hyperglycemia,” “leukotriene receptor antagonists,” “montelukast,” “mast cell stabilizers,” “cromolyn sodium,” “insulin resistance,” “blood glucose,” “type 2 diabetes mellitus,” and “drug-induced diabetes.” Additional relevant sources were identified through citation tracking of key articles, pharmacology texts, and clinical reviews addressing drug-induced metabolic effects.

Studies and scholarly sources were considered eligible when they discussed the pharmacological action of anti-allergic medications, their direct or indirect effects on glucose homeostasis, or their association with hyperglycemia, insulin resistance, weight gain, metabolic syndrome, or diabetes mellitus. Priority was given to clinical studies, observational cohort studies, randomized or controlled trials where available, meta-analyses, mechanistic studies, pharmacological reviews, and authoritative textbooks relevant to immunology, pharmacology, endocrinology, and metabolic disease. Articles were considered particularly relevant when they addressed dose, duration, route of administration, patient susceptibility, or comparative metabolic risk across drug classes. Sources were excluded when they focused exclusively on allergic disease without pharmacological treatment, diabetes without drug-related metabolic effects, non-human mechanisms with limited clinical relevance, or therapeutic agents outside the scope of allergy management.

The literature was synthesized thematically according to drug class and biological mechanism. Corticosteroids were evaluated separately because of their established effects on hepatic gluconeogenesis, peripheral insulin resistance, adipose tissue metabolism, and pancreatic β-cell function (13). Antihistamines were assessed with attention to first- and second-generation differences, central nervous system penetration, appetite regulation, sedation-related lifestyle effects, and possible associations with body weight or insulin sensitivity (14). Leukotriene receptor antagonists were reviewed in relation to inflammatory pathways, cytokine modulation, and potential effects on insulin resistance,

while mast cell stabilizers were evaluated according to systemic absorption and reported metabolic neutrality (15). Where evidence was limited or indirect, interpretation was framed according to biological plausibility and consistency across available studies.

Data were extracted narratively from included sources by identifying the drug class, representative agents, proposed mechanism of metabolic effect, direction of glycemic influence, patient risk factors, and clinical implications. Particular attention was given to whether reported effects were dose-dependent, duration-dependent, reversible after drug withdrawal, or more pronounced in patients with obesity, prediabetes, advanced age, family history of diabetes, sedentary lifestyle, or concurrent use of other diabetogenic medications. Evidence was then organized into clinically meaningful domains: mechanisms of dysglycemia, relative risk by anti-allergic drug class, patient-level susceptibility, implications for monitoring, and safer prescribing considerations.

Because this review used a narrative synthesis framework, formal statistical pooling, meta-analysis, and quantitative assessment of heterogeneity were not performed. The strength of evidence was interpreted qualitatively by considering study design, biological plausibility, consistency of findings, clinical relevance, and alignment with established pharmacological mechanisms. Corticosteroid-related evidence was interpreted as comparatively stronger because of consistent mechanistic and clinical support, whereas evidence for antihistamines, leukotriene receptor antagonists, and mast cell stabilizers was interpreted more cautiously due to fewer direct studies and greater reliance on indirect metabolic outcomes.

Potential selection bias was addressed by using broad search terms, including multiple drug classes, and incorporating both clinical and mechanistic literature. However, as is typical of narrative reviews, the synthesis was intended to provide an integrative clinical interpretation rather than a formally exhaustive or reproducible systematic review. The review therefore emphasizes conceptual clarity, drug-class comparison, mechanistic explanation, and practical relevance for clinicians managing allergic disease in patients with existing or emerging metabolic risk.

RESULTS

The synthesis showed a clear drug-class gradient in metabolic risk among anti-allergic therapies. Corticosteroids represented the highest-risk category because their effects directly intersect with core pathways of glucose regulation, including hepatic glucose output, peripheral insulin sensitivity, adipose tissue metabolism, and β-cell compensation. Systemic corticosteroids were consistently associated with the greatest diabetogenic potential, particularly when prescribed at high doses, for prolonged durations, or in repeated courses. Their metabolic effects are clinically relevant because they can produce both fasting and postprandial hyperglycemia and may precipitate new-onset diabetes in susceptible individuals. In comparison, inhaled and intranasal corticosteroids appear to have lower systemic metabolic impact, although prolonged high-dose exposure may still be relevant in patients with prediabetes, established diabetes, obesity, or other metabolic risk factors.

Antihistamines showed a weaker and more indirect relationship with glucose dysregulation. First-generation antihistamines may contribute to metabolic risk through sedation, reduced physical activity, appetite changes, and possible weight gain rather than through a direct effect on insulin signaling. This makes their metabolic relevance most important in patients already predisposed to obesity, sedentary behavior, or insulin resistance. Second-generation antihistamines were generally interpreted as metabolically safer because of their greater peripheral selectivity and reduced central nervous system penetration. However, prolonged use in metabolically vulnerable individuals may still warrant attention to weight change and lifestyle-related risk, particularly when antihistamines are used chronically rather than intermittently.

Leukotriene receptor antagonists and mast cell stabilizers appeared to occupy the lowest-risk categories. Leukotriene receptor antagonists did not show a consistent diabetogenic signal and may have biologically plausible neutral or favorable effects through suppression of inflammatory pathways involved in insulin resistance. However, the strength of this evidence remains limited, and these agents should be interpreted primarily as metabolically neutral rather than definitively protective. Mast cell stabilizers showed the least concern because their limited systemic absorption and localized mechanism of action make clinically significant effects on glucose metabolism unlikely.

Table 1. Evidence linking major anti-allergic drug classes with glucose metabolism and diabetes risk

Drug class	Representative agents	Principal anti-allergic mechanism	Main metabolic concern	Direction of effect on glucose metabolism	Relative evidence strength
Systemic corticosteroids	Prednisone, prednisolone, dexamethasone	Broad suppression of inflammatory gene transcription and cytokine activity	Hyperglycemia, insulin resistance, impaired β-cell compensation	Clearly adverse, especially with high-dose or prolonged therapy	Strong
Inhaled / intranasal corticosteroids	Budesonide, fluticasone	Local airway or nasal anti-inflammatory activity	Possible dysglycemia at high cumulative exposure or in susceptible patients	Usually lower risk than systemic therapy, but not metabolically negligible	Moderate
First-generation antihistamines	Diphenhydramine, chlorpheniramine	H1 receptor blockade with central nervous system penetration	Sedation, reduced activity, appetite or weight-related effects	Indirect and inconsistent adverse association	Low to moderate
Second-generation antihistamines	Cetirizine, loratadine, fexofenadine	Peripheral H1 receptor blockade with limited central effects	Possible weight gain or appetite-related metabolic effects in selected populations	Mostly neutral; indirect risk possible in susceptible patients	Low
Leukotriene receptor antagonists	Montelukast, zafirlukast	Blockade of leukotriene-mediated bronchoconstriction and inflammation	No consistent diabetogenic signal; possible anti-inflammatory metabolic benefit	Neutral to potentially favorable	Low to moderate
Mast cell stabilizers	Cromolyn sodium, nedocromil	Prevention of mast-cell mediator release	Minimal systemic metabolic effect	Neutral	Low
Combination anti-allergic therapy	Corticosteroid plus antihistamine or leukotriene antagonist	Multi-pathway allergic inflammation control	Risk mainly driven by corticosteroid exposure and patient susceptibility	Variable; adverse when systemic corticosteroid burden is high	Moderate

Table 2. Mechanistic pathways through which anti-allergic therapies may influence glucose homeostasis

Mechanistic pathway	Drug class most implicated	Biological effect	Expected clinical consequence
Increased hepatic gluconeogenesis	Corticosteroids	Enhanced hepatic glucose production through glucocorticoid receptor signaling	Fasting and postprandial hyperglycemia
Reduced peripheral glucose uptake	Corticosteroids	Impaired insulin-mediated glucose disposal in skeletal muscle and adipose tissue	Increased insulin resistance
β-cell functional stress	Corticosteroids	Increased insulin demand with possible inadequate pancreatic compensation	Worsening glucose tolerance or new-onset diabetes
Adipose tissue redistribution and lipolysis	Corticosteroids	Increased free fatty acid flux and visceral adiposity	Metabolic syndrome and insulin resistance
Sedation-related reduction in activity	First-generation antihistamines	Lower energy expenditure through central sedative effects	Indirect weight gain and worsening insulin sensitivity
Appetite or body-weight modulation	Some antihistamines	Possible changes in appetite regulation or body mass	Indirect dysglycemia in predisposed patients
Reduction of inflammatory signaling	Leukotriene receptor antagonists	Suppression of leukotriene-mediated inflammatory pathways	Potential improvement in insulin sensitivity, though evidence remains limited
Minimal systemic absorption	Mast cell stabilizers	Limited systemic pharmacological exposure	Negligible effect on glucose regulation

Across drug classes, patient susceptibility emerged as a major determinant of clinical risk. Obesity, prediabetes, established diabetes, advanced age, family history of diabetes, sedentary lifestyle, and polypharmacy increased the likelihood that anti-allergic therapy—especially corticosteroid therapy—

would disturb glucose regulation. The same medication exposure may therefore have different metabolic consequences depending on baseline insulin sensitivity, β-cell reserve, cumulative dose, and concurrent use of other diabetogenic drugs. This interaction between drug-related and patient-related factors supports a risk-stratified approach rather than a uniform interpretation of anti-allergic therapy as either safe or harmful.

Table 3. Drug-class comparison according to diabetogenic potential, modifying factors, and monitoring need

Drug class	Diabetogenic potential	Key modifying factors	Patients requiring closer monitoring	Practical monitoring implication
Systemic corticosteroids	High	Dose, duration, repeated courses, baseline glycemic status	Prediabetes, diabetes, obesity, elderly patients, family history of diabetes	Baseline and follow-up fasting or random glucose; consider postprandial monitoring
Inhaled / intranasal corticosteroids	Low to moderate	High dose, prolonged use, cumulative exposure	Patients with diabetes, metabolic syndrome, or prolonged high-dose exposure	Periodic glucose review in high-risk groups
First-generation antihistamines	Low to moderate	Sedation, appetite, reduced physical activity, long-term use	Obese patients, sedentary individuals, children or adults with weight gain	Monitor weight and metabolic risk rather than glucose alone
Second-generation antihistamines	Low	Long-term exposure, baseline obesity, appetite or weight changes	Patients with pre-existing metabolic risk	Routine glucose monitoring usually unnecessary unless other risks are present
Leukotriene receptor antagonists	Low	Chronic inflammatory burden, obesity, asthma severity	Patients with asthma and metabolic syndrome may benefit from broader metabolic assessment	No specific glucose monitoring required solely due to this class
Mast cell stabilizers	Very low	Limited systemic exposure	Routine high-risk metabolic groups only	No additional glucose monitoring required solely due to this class

Table 4. Patient-related risk factors that increase susceptibility to drug-induced dysglycemia during anti-allergic therapy

Risk factor	Mechanistic relevance	Drug class interaction	Clinical implication
Obesity	Promotes insulin resistance through adipose inflammation and free fatty acids	Amplifies corticosteroid-induced dysglycemia and possible antihistamine-associated weight effects	Prefer steroid-sparing strategies when feasible
Prediabetes or impaired fasting glucose	Reduced glycemic reserve and β-cell compensation	Strongly increases risk during systemic corticosteroid exposure	Baseline glucose and early follow-up monitoring are important
Established diabetes mellitus	Existing insulin secretory or action defect	Corticosteroids may worsen glycemic control rapidly	Anticipate medication adjustment during steroid courses
Advanced age	Declining β-cell function and reduced insulin sensitivity	Increases vulnerability to steroid-induced hyperglycemia	Use lowest effective dose and shorter duration where possible
Family history of diabetes	Genetic susceptibility to β-cell dysfunction and insulin resistance	Raises risk when exposed to diabetogenic drugs	Counsel and monitor during prolonged therapy
Sedentary lifestyle	Reduces insulin sensitivity and energy expenditure	May worsen indirect metabolic effects of sedating antihistamines	Encourage activity and weight control
Polypharmacy	Additive metabolic burden from multiple diabetogenic agents	Particularly relevant with corticosteroids plus thiazides, β-blockers, or antipsychotics	Conduct medication review before long-term therapy

Table 5. Clinical synthesis of evidence strength and prescribing implications by anti-allergic drug class

Drug class	Evidence interpretation	Main clinical message	Strength of clinical concern
Systemic corticosteroids	Consistent pharmacological and clinical evidence supports increased risk of hyperglycemia and diabetes, especially with prolonged or high-dose exposure	Use the lowest effective dose for the shortest feasible duration and monitor glucose in high-risk patients	High
Inhaled / intranasal corticosteroids	Lower systemic exposure reduces risk, but high cumulative dose and long-term use may still be relevant in susceptible patients	Consider metabolic risk when prescribing prolonged high-dose therapy	Moderate
First-generation antihistamines	Direct glycemic effects are not well established, but sedation and weight-related pathways may indirectly worsen insulin sensitivity	Avoid unnecessary long-term sedating antihistamine use in patients with obesity or metabolic risk	Low to moderate
Second-generation antihistamines	Generally metabolically safe, with limited evidence for direct glucose disruption	Appropriate first-line options when antihistamine therapy is needed in metabolically vulnerable patients	Low
Leukotriene receptor antagonists	No consistent evidence of diabetogenicity; anti-inflammatory effects may theoretically support metabolic neutrality or benefit	Can be considered metabolically safer adjuncts when clinically indicated	Low
Mast cell stabilizers	Minimal systemic absorption and negligible metabolic effect	Favorable option where suitable for allergic disease control	Very low

Overall, the synthesis indicates that the relationship between anti-allergic therapy and diabetes risk is not uniform across medications. The strongest and most clinically actionable evidence concerns corticosteroid-induced dysglycemia, particularly with systemic exposure. Antihistamines may have

indirect metabolic relevance, especially through weight- and activity-related mechanisms, but evidence for direct diabetogenicity remains limited. Leukotriene receptor antagonists and mast cell stabilizers appear metabolically neutral in routine clinical use. These findings support individualized prescribing decisions that consider drug class, dose, duration, route of administration, and patient-level metabolic vulnerability.

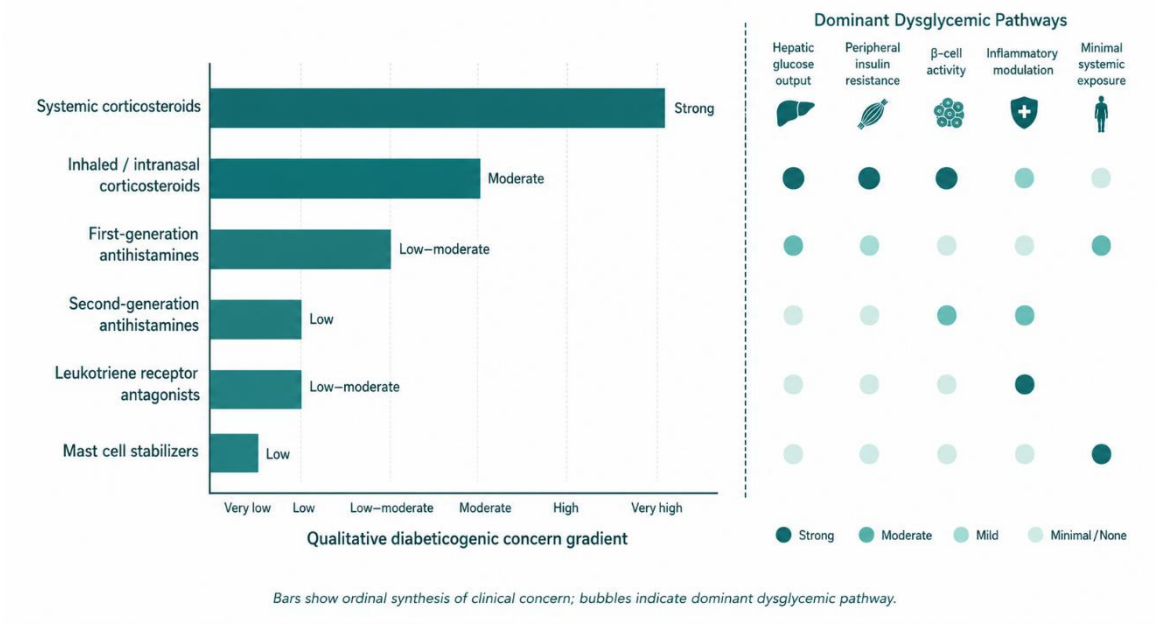

Figure 1. Drug-Class Gradient of Metabolic Concern and Dominant Dysglycemic Pathways

This figure presents a qualitative evidence-gradient synthesis of anti-allergic drug classes according to their relative metabolic concern and dominant dysglycemic pathways. Systemic corticosteroids occupy the highest concern category because they directly affect hepatic glucose production, peripheral insulin resistance, adipose tissue metabolism, and β-cell compensation. Inhaled and intranasal corticosteroids show a lower but still clinically relevant concern level, mainly under conditions of prolonged or high cumulative exposure. First-generation antihistamines demonstrate low-to-moderate concern driven primarily by indirect sedation-, activity-, and weight-related pathways, whereas second-generation antihistamines are largely metabolically neutral. Leukotriene receptor antagonists cluster toward the low-concern range, with their main relevance linked to inflammatory modulation rather than diabetogenicity, while mast cell stabilizers show the lowest concern because of minimal systemic exposure. This synthesis supports a drug-class–specific interpretation of diabetes risk, with corticosteroid burden and patient metabolic susceptibility serving as the most clinically important determinants.

DISCUSSION

This narrative review synthesized pharmacological, mechanistic, and clinical evidence on the relationship between anti-allergic drug therapy and disturbances in glucose metabolism. The principal finding is that diabetes risk is not uniform across anti-allergic medications but is strongly drug-class dependent. Corticosteroids, particularly systemic agents such as prednisone, prednisolone, and dexamethasone, represent the most clinically important class associated with hyperglycemia and diabetes risk. Their diabetogenic effect is biologically plausible and clinically well recognized because they increase hepatic glucose production, reduce peripheral insulin sensitivity, promote lipolysis and visceral adiposity, and increase the insulin secretory demand placed on pancreatic β-cells. In contrast, antihistamines appear to have weaker and mostly indirect metabolic effects, while leukotriene receptor antagonists and mast cell stabilizers generally show neutral or low-risk metabolic profiles. These findings support a risk-stratified interpretation in which the metabolic safety of anti-allergic therapy depends on drug class, dose, duration, route of administration, and patient susceptibility (16,17).

The strongest evidence concerns corticosteroid-induced dysglycemia. Glucocorticoids disrupt glucose regulation through multiple converging pathways, including stimulation of hepatic gluconeogenesis, inhibition of insulin-mediated glucose uptake in skeletal muscle and adipose tissue, and worsening of insulin resistance. These effects are especially relevant during high-dose, prolonged, or repeated systemic therapy. In clinical practice, corticosteroid-related hyperglycemia may present as new-onset diabetes, worsening of pre-existing diabetes, or transient but clinically significant postprandial hyperglycemia. The risk is amplified in individuals with obesity, impaired fasting glucose, prediabetes, older age, family history of diabetes, sedentary lifestyle, and concurrent use of other diabetogenic medications (18). Therefore, the clinical concern is not merely whether corticosteroids can raise blood glucose, but how cumulative exposure interacts with baseline metabolic reserve and β-cell compensatory capacity.

Route of corticosteroid administration is also important. Systemic corticosteroids carry the clearest metabolic risk because they produce widespread glucocorticoid receptor activation. Inhaled, intranasal, and topical corticosteroids generally produce lower systemic exposure and therefore lower metabolic concern, but they should not be considered completely irrelevant to glucose regulation, especially when used at high doses, over long durations, or in patients with existing metabolic disease. This distinction is clinically meaningful because many allergic and inflammatory disorders require recurrent or chronic corticosteroid exposure. A practical approach is to minimize systemic steroid use where appropriate, prescribe the lowest effective dose for the shortest clinically feasible duration, and consider steroid-sparing alternatives when symptom control can be achieved without compromising disease management (19,20).

The evidence for antihistamines is less definitive and should be interpreted more cautiously. H1-antihistamines do not appear to have a strong direct effect on glucose metabolism comparable to corticosteroids. However, first-generation antihistamines may contribute indirectly to metabolic risk through sedation, reduced activity, appetite modulation, and weight gain. These pathways are particularly relevant for patients who already have obesity, low physical activity, metabolic syndrome, or other insulin-resistance states. Second-generation antihistamines are generally more metabolically favorable because of their peripheral selectivity and reduced central nervous system penetration. Nevertheless, prolonged antihistamine use in susceptible individuals may still warrant attention to weight trajectory and lifestyle factors rather than routine glucose monitoring in all patients. This interpretation distinguishes established evidence from biologically plausible but less certain metabolic associations (21,22).

Leukotriene receptor antagonists and mast cell stabilizers appear to have the lowest diabetogenic potential among the major anti-allergic drug classes discussed. Leukotriene receptor antagonists, including montelukast and zafirlukast, act on inflammatory pathways that may intersect with insulin resistance, but current evidence is insufficient to classify them as metabolically protective. Their most defensible interpretation is metabolic neutrality, with possible benefit in selected inflammatory or obesity-related contexts requiring further investigation. Mast cell stabilizers, such as cromolyn sodium and nedocromil, have limited systemic absorption and no consistent signal for clinically meaningful glucose disruption. These agents may therefore be preferable from a metabolic-safety perspective when they are clinically suitable for the allergic condition being treated (23).

The findings of this review align with the broader concept of drug-induced diabetes as a multifactorial condition rather than a uniform pharmacological event. Medication exposure interacts with genetic predisposition, adiposity, inflammation, aging, β-cell reserve, and concurrent pharmacotherapy (24). This is especially important in patients receiving multiple medications with potential metabolic effects, such as corticosteroids combined with thiazide diuretics, β-blockers, atypical antipsychotics, or other agents associated with insulin resistance or impaired insulin secretion. Polypharmacy may increase the likelihood that a modest glycemic effect becomes clinically significant. Consequently, anti-allergic

therapy should be evaluated within the patient's total metabolic and medication profile rather than considered in isolation.

From a clinical perspective, these findings support individualized prescribing and monitoring. Patients receiving systemic corticosteroids, especially those with diabetes or prediabetes, should undergo baseline and follow-up glycemic assessment (25). Postprandial glucose monitoring may be particularly useful because glucocorticoid-induced hyperglycemia can be more pronounced after meals than in fasting measurements. Patients receiving repeated steroid bursts or prolonged therapy may require closer monitoring and, in some cases, temporary adjustment of glucose-lowering therapy. For non-corticosteroid anti-allergic drugs, routine intensive glucose monitoring is generally not necessary solely because of drug exposure, but weight gain, sedation, reduced activity, and baseline metabolic risk should guide clinical judgment.

The implications for practice are therefore practical and risk-based. Corticosteroids should remain available when clinically indicated because their anti-inflammatory effects can be essential and sometimes life-saving (26). However, their use should be accompanied by dose discipline, duration control, and metabolic surveillance in vulnerable patients. Second-generation antihistamines may be preferred over sedating first-generation agents when long-term symptom control is needed in patients with obesity or diabetes risk. Leukotriene receptor antagonists and mast cell stabilizers may be considered metabolically safer options when appropriate for the allergic phenotype, although therapeutic selection should still be driven by efficacy, indication, safety profile, and patient-specific factors.

This review has several limitations inherent to its narrative design. The evidence base includes heterogeneous study types, drug exposures, populations, outcome definitions, and follow-up durations. Formal risk-of-bias assessment, quantitative pooling, and certainty grading were not performed, so conclusions should be interpreted as an integrative clinical synthesis rather than a statistical estimate of risk. Evidence is also unevenly distributed across drug classes: corticosteroids are supported by stronger mechanistic and clinical literature, whereas antihistamines, leukotriene receptor antagonists, and mast cell stabilizers have fewer direct studies evaluating diabetes outcomes. As a result, the review can identify plausible risk gradients and clinical considerations but cannot provide pooled incidence estimates or definitive comparative risk rankings.

Future research should focus on prospective studies that directly compare anti-allergic drug classes using standardized glycemic outcomes, including fasting glucose, postprandial glucose, HbA1c, insulin resistance indices, and incident diabetes. Studies should stratify participants by baseline metabolic risk, obesity status, age, corticosteroid dose and duration, route of administration, and concurrent diabetogenic medications. Longitudinal research is also needed to determine whether antihistamine-associated weight changes translate into measurable alterations in insulin sensitivity or diabetes incidence. For leukotriene receptor antagonists, future trials should clarify whether anti-inflammatory effects produce clinically meaningful metabolic benefits or merely reflect theoretical biological plausibility. Such evidence would help clinicians better balance allergic disease control with long-term metabolic safety.

Overall, the evidence supports a clinically important hierarchy of metabolic concern among anti-allergic therapies. Systemic corticosteroids require the greatest caution because their effects on glucose metabolism are direct, multifactorial, and clinically consequential. Inhaled or intranasal corticosteroids carry lower but not negligible concern in high-risk patients. Antihistamines are largely low-risk, with first-generation agents carrying more indirect metabolic concern than second-generation agents. Leukotriene receptor antagonists and mast cell stabilizers appear metabolically neutral in routine use. A personalized approach that considers drug class, exposure burden, and baseline metabolic vulnerability is most appropriate for reducing the risk of therapy-associated dysglycemia while maintaining effective allergy control.

CONCLUSION

Anti-allergic drug therapy has drug-class–specific implications for glucose metabolism, with systemic corticosteroids carrying the clearest and most clinically important risk of hyperglycemia, insulin resistance, and possible diabetes onset, particularly when used at high doses, for prolonged periods, or in patients with pre-existing metabolic vulnerability. Inhaled and intranasal corticosteroids generally have lower systemic metabolic impact but may still require caution during long-term or high-dose exposure in high-risk individuals. Antihistamines appear largely metabolically safe, although first-generation agents may indirectly contribute to weight gain, reduced activity, and worsening insulin sensitivity in susceptible patients. Leukotriene receptor antagonists and mast cell stabilizers show minimal evidence of diabetogenicity and are best interpreted as metabolically neutral within routine clinical use. Overall, the most important implication is that clinicians should balance allergic disease control with individualized metabolic risk assessment, careful corticosteroid dosing, and targeted glucose monitoring for patients with obesity, prediabetes, established diabetes, advanced age, polypharmacy, or other risk factors for impaired glucose regulation.

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