



Evaluating the Evidence for a Link Between Glycemic Control and Keratosis Pilaris in Type 2 Diabetes: A Systematic Review

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ABSTRACT

Introduction: Type 2 Diabetes Mellitus (T2DM) is a systemic metabolic disorder frequently associated with a wide spectrum of cutaneous manifestations, which often reflect the underlying degree of glycemic control. Keratosis pilaris (KP), a common benign disorder of follicular keratinization, has been anecdotally linked to metabolic disturbances such as obesity and insulin resistance. However, a direct, evidence-based correlation between glycemic control, measured by glycated hemoglobin (HbA1c), and the severity of KP in the T2DM population has not been systematically evaluated, representing a significant gap in the literature.

Methods: A systematic review was conducted following PRISMA guidelines. PubMed, Google Scholar, Semanthic Scholar, Springer, Wiley Online Library databases were searched for observational studies published up to October 2024. The primary

search sought studies directly correlating HbA1c levels with KP severity in adult T2DM patients. Due to the absence of such studies, the search was broadened to include studies assessing KP in populations with related metabolic conditions (obesity, metabolic syndrome, insulin resistance). The Risk of Bias in Non-randomized Studies of Interventions (ROBINS-I) tool was used for quality assessment.

Results: The systematic search yielded no studies that directly investigated the correlation between HbA1c levels and KP severity in patients with T2DM. The review of broadened search results included 16 observational studies. These studies demonstrated a high prevalence of KP in populations with metabolic dysregulation, with rates of 42% to 64.7% reported in obese cohorts. Crucially, one study identified a statistically significant association between KP and the Homeostatic Model Assessment for Insulin Resistance (HOMA-IR) score in obese adolescents (). Other studies, however, did not find a significant link between KP and insulin levels, highlighting inconsistencies in the existing indirect evidence.

Discussion: The principal finding of this review is the definitive lack of direct evidence on the topic, which constitutes a critical research gap. Despite this, a strong biological rationale for a positive correlation is proposed, synthesized from indirect clinical and basic science evidence. Pathophysiological pathways involving hyperglycemia-induced Advanced Glycation End Products (AGEs) are known to impair keratinocyte differentiation and skin barrier function. Concurrently, compensatory hyperinsulinemia in T2DM can activate Insulin-like Growth

Factor-1 (IGF-1) receptors on follicular keratinocytes, promoting hyperproliferation—a key pathological feature of KP. This dual mechanism suggests that poor glycemic control could both initiate and exacerbate the follicular hyperkeratosis characteristic of KP.

Conclusion: While direct clinical evidence is currently absent, a compelling, mechanistically plausible link exists between poor glycemic control in T2DM and the severity of Keratosis Pilaris. This review highlights the urgent need for well-designed observational studies to investigate this association. If confirmed, KP could serve as a readily observable cutaneous marker for underlying insulin resistance or deteriorating glycemic control, prompting earlier clinical intervention.

Keywords: Keratosis Pilaris; Type 2 Diabetes Mellitus; Glycemic Control; HbA1c; Insulin Resistance; Systematic Review; Follicular Hyperkeratosis

INTRODUCTION

The Systemic Impact of Type 2 Diabetes Mellitus on Cutaneous Health

Type 2 Diabetes Mellitus (T2DM) is a chronic metabolic disease of escalating global prevalence, characterized by insulin resistance and relative insulin deficiency, leading to persistent hyperglycemia. While its systemic complications affecting the cardiovascular, renal, and nervous systems are well-documented, the skin is also a primary target organ, frequently reflecting the patient's underlying metabolic state. It is estimated that between 30% and 70% of all individuals with diabetes will develop a cutaneous complication at some point during their lifetime (Sasmaz and Buyukbese, 2015; Szymańska et al., 2023; Rader and St. Surin-Lord, 2021). These dermatoses are diverse, ranging from relatively benign conditions such as diabetic dermopathy and xerosis to severe, potentially life-threatening problems including recalcitrant infections and non-healing foot ulcers (Sasmaz and Buyukbese, 2015; Szymańska et al., 2023; Haveri, Inabnet, and Singh, 2023).

The high prevalence of skin disorders in T2DM is not a coincidental aggregation of unrelated conditions; rather, it represents a systemic failure of cutaneous homeostasis driven by metabolic derangement. The skin is not merely a passive barrier but an active participant in metabolic and endocrine processes, and its health serves as a crucial, visible indicator of systemic glycemic control (Basić-Jukić et al., 2019; Gowri, Chandravathi, and Sindhu, 2015). Consequently, the appearance or worsening of certain skin conditions can be the first clinical sign of undiagnosed diabetes or an alert to deteriorating metabolic control in a known diabetic patient (Sasmaz and Buyukbese, 2015). Poor glycemic control, quantified by elevated levels of glycated hemoglobin (HbA1c), is a well-established risk factor for the development and severity of numerous diabetic dermatoses, particularly cutaneous infections, where hyperglycemia impairs neutrophil function and creates a favorable environment for microbial growth (Basić-Jukić et al., 2019; Ali et al., 2020; Ahmed, Muhammad, and Qayum, 2014).

Keratosis Pilaris: A Disorder of Follicular Keratinization

Keratosis pilaris (KP) is an exceedingly common, benign genetic disorder of the hair follicle, characterized by the formation of small, rough, folliculocentric keratotic papules (Schwartz, 2021). The condition, often colloquially described as "chicken skin" or "goose bumps," typically affects the extensor surfaces of the upper arms, thighs, and buttocks (Haveri, Inabnet, and Singh, 2023). Its prevalence is highest in adolescents, affecting an estimated 50-80% of this demographic, and persists in approximately 40% of adults, making it one of the most common dermatological conditions encountered in clinical practice (Haveri, Inabnet, and Singh, 2023).

The underlying pathology of KP is a disorder of follicular keratinization (Schwartz, 2021). The process involves the abnormal accumulation of keratin, a structural protein of the skin, which forms a horny plug that obstructs the follicular orifice (Haveri, Inabnet, and Singh, 2023). This blockage prevents the hair shaft from emerging, leading to the characteristic bumpy texture and, in some cases, a coiled hair trapped beneath the papule. Perifollicular erythema may also be present, indicating a mild inflammatory component (Haveri, Inabnet, and Singh, 2023). While the precise etiology remains incompletely understood, a strong genetic predisposition with an autosomal dominant inheritance pattern is well-established (Haveri, Inabnet, and Singh, 2023). Furthermore, KP is frequently associated with other conditions characterized by impaired skin barrier function, such as atopic dermatitis and ichthyosis vulgaris, and has been linked to mutations in the filaggrin () gene, which is critical for epidermal integrity (Gruber et al., 2015). This classification of KP as a primary disorder of keratinization is fundamental, as it places the condition within a category of diseases directly influenced by biological processes that regulate keratinocyte proliferation, differentiation, and desquamation.

The Biological Plausibility of a Link: Metabolic Pathways Affecting the Pilosebaceous Unit

The association between KP and systemic metabolic disease is not a new concept, though it has been historically under-investigated. Clinical observations have noted an acquired increase in

KP-like lesions in states of metabolic flux, including obesity, pregnancy, and diabetes (Gruber et al., 2015). More specifically, KP is listed as a cutaneous manifestation associated with insulin resistance, obesity, and other endocrine disorders like Cushing's syndrome (Ansell, 2023; Pavlović et al., 2022). This clinical association has been substantiated by quantitative evidence. A notable cross-sectional study of 103 obese children and adolescents by Yılmaz et al. (2023) found a statistically significant association between the presence of KP and a higher Homeostatic Model Assessment for Insulin Resistance (HOMA-IR) score (), providing a direct link between KP and a key marker of the metabolic dysregulation central to T2DM (Yılmaz et al., 2023).

The link between KP and insulin resistance may represent the central, unifying mechanism. T2DM is fundamentally a state of progressive insulin resistance followed by compensatory hyperinsulinemia and eventual hyperglycemia. The finding that KP is associated with insulin resistance markers in non-diabetic obese populations suggests that the follicular pathology could be an early cutaneous sign of the metabolic cascade that culminates in T2DM. Therefore, KP may not simply be a complication of established, long-standing diabetes, but rather a clinical marker of the underlying insulin-resistant state itself. This re-contextualizes the investigation, suggesting that the primary driver may be hyperinsulinemia's effect on cellular growth, with hyperglycemia acting as a secondary, exacerbating factor.

Rationale, Research Gap, and Novelty of the Current Review

Despite the high prevalence of both T2DM and KP, and the strong biological plausibility of an association, a significant and perplexing gap exists in the medical literature. A preliminary review reveals that large cross-sectional studies cataloging the cutaneous manifestations in T2DM patients frequently fail to report KP among the observed conditions (Basić-Jukić et al., 2019; Hosseini et al., 2008; Niaz, Bashir, and Khan, 2019; Memon et al., 2017). Furthermore, systematic reviews on the broader topic of skin manifestations in metabolic syndrome often classify the association with KP as "moderate" or anecdotal, lacking the robust quantitative backing seen for

conditions like acanthosis nigricans (de Oliveira et al., 2024; Szymańska et al., 2023).

This absence of KP in major diabetic dermatoses studies is a critical finding in itself and warrants exploration. It suggests several possibilities: (1) the association is not clinically significant, and KP is no more prevalent or severe in T2DM patients than in the general population; (2) KP is so common and medically benign that it is systematically overlooked and underreported by clinicians and researchers who are focused on more morbid complications such as infections and ulcers; or (3) the association is real but has simply never been investigated with rigorous, targeted methodology. This systematic review is designed to formally establish and explore this research gap.

The novelty of this review lies not in identifying a definitive correlation from existing primary studies, but in being the first to systematically collate the extensive indirect evidence from metabolic, clinical, and basic science research to construct a comprehensive pathophysiological model specifically for the T2DM-KP association. Its primary contribution is to define the current void in the literature and present a compelling, multi-faceted biological rationale for why this void must be filled by future research.

Research Objectives and Formulated Hypothesis

Based on the identified research gap and the strong biological plausibility, this systematic review was undertaken with the following objectives:

1. To systematically search and review the literature for primary research studies that quantitatively evaluate the correlation between HbA1c levels and the severity of Keratosis Pilaris in patients with Type 2 Diabetes Mellitus.
2. To synthesize the available evidence on the prevalence and clinical associations of Keratosis Pilaris in populations with T2DM and related metabolic disorders, including obesity and metabolic syndrome.
3. To construct a detailed, evidence-based pathophysiological model of the potential T2DM-KP link, based on the known effects of hyperglycemia and hyperinsulinemia on cutaneous and

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follicular biology.

The central hypothesis of this review is that **a positive correlation exists between higher HbA1c levels, indicative of poorer glycemic control, and increased severity of Keratosis Pilaris in patients with Type 2 Diabetes Mellitus.** This relationship is proposed to be mediated by two synergistic pathways: (1) hyperglycemia-induced epidermal dysfunction and impaired keratinocyte differentiation, and (2) hyperinsulinemia-driven mitogenic signaling leading to follicular keratinocyte hyperproliferation.

METHODS

Protocol and Registration

This systematic review was conducted and reported in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines. The protocol for this review was not registered in a public repository.

Eligibility Criteria

Studies were selected based on a Population, Intervention/Exposure, Comparison, and Outcomes (PICO) framework.

- **Population:** The primary population of interest was adults (age ≥ 18 years) with a confirmed diagnosis of Type 2 Diabetes Mellitus. Due to the anticipated scarcity of literature for the primary question, the search was systematically broadened to include studies on populations with related metabolic conditions, such as obesity (Body Mass Index ≥ 30 kg/m²), metabolic syndrome (as defined by study authors), or diagnosed insulin resistance.
- **Intervention/Exposure:** The primary exposure of interest was poor glycemic control, as quantitatively measured by HbA1c levels. Secondary exposures included markers of insulin resistance (e.g., HOMA-IR) and degree of obesity (e.g., BMI).
- **Comparison:** The implicit comparison group was T2DM patients with good glycemic control

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(lower HbA1c levels) or, in broader studies, non-diabetic or non-obese control populations.

- **Outcomes:** The primary outcome sought was the severity of Keratosis Pilaris, assessed using a validated or described clinical scoring system. A comprehensive list of at least 15 potential outcomes was predefined for data extraction, including:
 1. Keratosis Pilaris Severity Score (e.g., Keratosis Pilaris Investigator Global Assessment [KP-IGA], Keratosis Pilaris Area Index [KPAI]) (Wong et al., 2024).
 2. Investigator Global Assessment (IGA) of KP (Wong et al., 2023).
 3. Objective skin roughness measurements (Wong et al., 2023).
 4. Objective erythema measurements (Wong et al., 2023).
 5. Prevalence of KP in the study cohort.
 6. Mean HbA1c level in patients with KP versus those without KP.
 7. Correlation coefficient (e.g., Pearson's r, Spearman's) between HbA1c and KP severity.
 8. Odds Ratio (OR) or Risk Ratio (RR) of having severe KP with poor glycemic control.
 9. Mean HOMA-IR score in patients with KP.
 10. Prevalence of KP stratified by BMI category.
 11. Presence or absence of perifollicular erythema.
 12. Patient-reported outcomes (e.g., pruritus, cosmetic impact).
 13. Body surface area (BSA) affected by KP.
 14. Density of keratotic papules (lesion count per unit area).
 15. Dermoscopic findings, such as the presence of coiled hairs (Haveri, Inabnet, and Singh, 2023).
- **Study Design:** Eligible study designs included observational studies, such as cross-sectional, cohort, and case-control studies. There were no restrictions on publication language or date.

Information Sources and Search Strategy

A comprehensive literature search was performed across three electronic databases: PubMed, Google Scholar, Semanthic Scholar, Springer, Wiley Online Library, from their inception

to October 2024. The search strategy combined Medical Subject Headings (MeSH) terms and keywords related to the condition, the population, and the exposure.

Study Selection Process

Two reviewers independently screened the titles and abstracts of all identified records against the predefined eligibility criteria. The full texts of potentially relevant articles were then retrieved and assessed for final inclusion. Any disagreements between the two reviewers at either stage were resolved through discussion and consensus, with arbitration by a third reviewer if necessary. A PRISMA flow diagram was used to document the entire study selection process.

Data Collection Process

A standardized data extraction form was developed and piloted. For each included study, two reviewers independently extracted the following information: first author and year of publication, study design, country of origin, participant characteristics (diagnosis, age, sex, sample size), methods of KP and metabolic parameter assessment, and all relevant quantitative outcome data.

Risk of Bias Assessment in Individual Studies

The methodological quality and risk of bias of each included observational study were independently assessed by two reviewers using the "Risk Of Bias In Non-randomized Studies – of Interventions" (ROBINS-I) tool (Sterne et al., 2016). This tool evaluates bias across seven domains: (1) bias due to confounding, (2) bias in selection of participants into the study, (3) bias in classification of interventions (exposures), (4) bias due to deviations from intended interventions, (5) bias due to missing data, (6) bias in measurement of outcomes, and (7) bias in selection of the reported result (Sterne et al., 2016).¹ Based on signaling questions within each domain, an overall risk of bias judgment—Low, Moderate, Serious, or Critical—was assigned to each study. Discrepancies were resolved by consensus.

Synthesis of Results

Given the anticipated heterogeneity in study populations, methodologies, and outcome reporting, a formal meta-analysis was not planned for the primary research question. Instead, a narrative synthesis of the findings was performed. The results were structured thematically, focusing on the direct evidence (or lack thereof) for the primary question, followed by a synthesis of indirect evidence from studies on related metabolic conditions. Key quantitative findings, such as prevalence rates and measures of association (e.g., p-values, odds ratios), were extracted and tabulated to facilitate comparison and interpretation.

Search Strategy

The keywords used for this research based PICO :

Element	Keyword 1	Keyword 2	Keyword 3	Keyword 4
Population (P)	Type 2 Diabetes Mellitus Patients	Adults with T2DM	Insulin Resistance	Hyperglycemic Individuals
Intervention (I)	Glycemic Control	HbA1c Levels	Poor Glycemic Control	Hyperglycemia
Comparison (C)	Good Glycemic Control	Lower HbA1c Levels	Non-Diabetic Controls	Normoglycemia
Outcome (O)	Keratosis Pilaris Severity	Follicular Hyperkeratosis	Cutaneous Manifestations	Skin Barrier Dysfunction

The Boolean MeSH keywords inputted on databases for this research are: (*"Type 2 Diabetes Mellitus Patients" OR "Adults with T2DM" OR "Insulin Resistance" OR "Hyperglycemic Individuals"*) AND (*"Glycemic Control" OR "HbA1c Levels" OR "Poor Glycemic Control" OR "Hyperglycemia"*) AND (*"Good Glycemic Control" OR "Lower HbA1c Levels" OR "Non-Diabetic Controls" OR "Normoglycemia"*) AND (*"Keratosis Pilaris Severity" OR "Follicular Hyperkeratosis" OR "Cutaneous Manifestations" OR "Skin Barrier Dysfunction"*).

Table 1. Article Search Strategy

Database	Keywords	Hits
Pubmed	("Type 2 Diabetes Mellitus Patients" OR "Adults with T2DM" OR "Insulin Resistance" OR "Hyperglycemic Individuals" AND "Glycemic Control" OR "HbA1c Levels" OR "Poor Glycemic Control" OR "Hyperglycemia" AND "Good Glycemic Control" OR "Lower HbA1c Levels" OR "Non-Diabetic Controls" OR "Normoglycemia" AND "Keratosis Pilaris Severity" OR "Follicular Hyperkeratosis" OR "Cutaneous Manifestations" OR "Skin Barrier Dysfunction")	25
Semantic Scholar	("Type 2 Diabetes Mellitus Patients" OR "Adults with T2DM" OR "Insulin Resistance" OR "Hyperglycemic Individuals") AND ("Glycemic Control" OR "HbA1c Levels" OR "Poor Glycemic Control" OR "Hyperglycemia") AND ("Good Glycemic Control" OR "Lower HbA1c Levels" OR "Non-Diabetic Controls" OR "Normoglycemia") AND ("Keratosis Pilaris Severity" OR "Follicular Hyperkeratosis" OR "Cutaneous Manifestations" OR "Skin Barrier Dysfunction")	250
Springer	("Type 2 Diabetes Mellitus Patients" OR "Adults with T2DM" OR "Insulin Resistance" OR "Hyperglycemic Individuals") AND ("Glycemic Control" OR "HbA1c Levels" OR "Poor Glycemic Control" OR "Hyperglycemia") AND ("Good Glycemic Control" OR "Lower HbA1c Levels" OR "Non-Diabetic Controls" OR "Normoglycemia") AND ("Keratosis Pilaris Severity" OR "Follicular Hyperkeratosis" OR "Cutaneous Manifestations" OR "Skin Barrier Dysfunction")	40
Google Scholar	("Type 2 Diabetes Mellitus Patients" OR "Adults with T2DM" OR "Insulin Resistance" OR "Hyperglycemic Individuals") AND ("Glycemic Control" OR "HbA1c Levels" OR "Poor Glycemic Control" OR "Hyperglycemia") AND ("Good Glycemic Control" OR "Lower HbA1c Levels" OR "Non-Diabetic Controls" OR "Normoglycemia") AND ("Keratosis Pilaris Severity" OR "Follicular Hyperkeratosis" OR "Cutaneous Manifestations" OR "Skin Barrier Dysfunction")	2
Wiley Online Library	("Type 2 Diabetes Mellitus Patients" OR "Adults with T2DM" OR "Insulin Resistance" OR "Hyperglycemic Individuals") AND ("Glycemic Control" OR "HbA1c Levels" OR "Poor Glycemic Control" OR "Hyperglycemia") AND ("Good Glycemic Control" OR "Lower HbA1c Levels" OR "Non-Diabetic Controls" OR "Normoglycemia") AND ("Keratosis Pilaris Severity" OR "Follicular Hyperkeratosis" OR "Cutaneous Manifestations" OR "Skin Barrier Dysfunction")	997

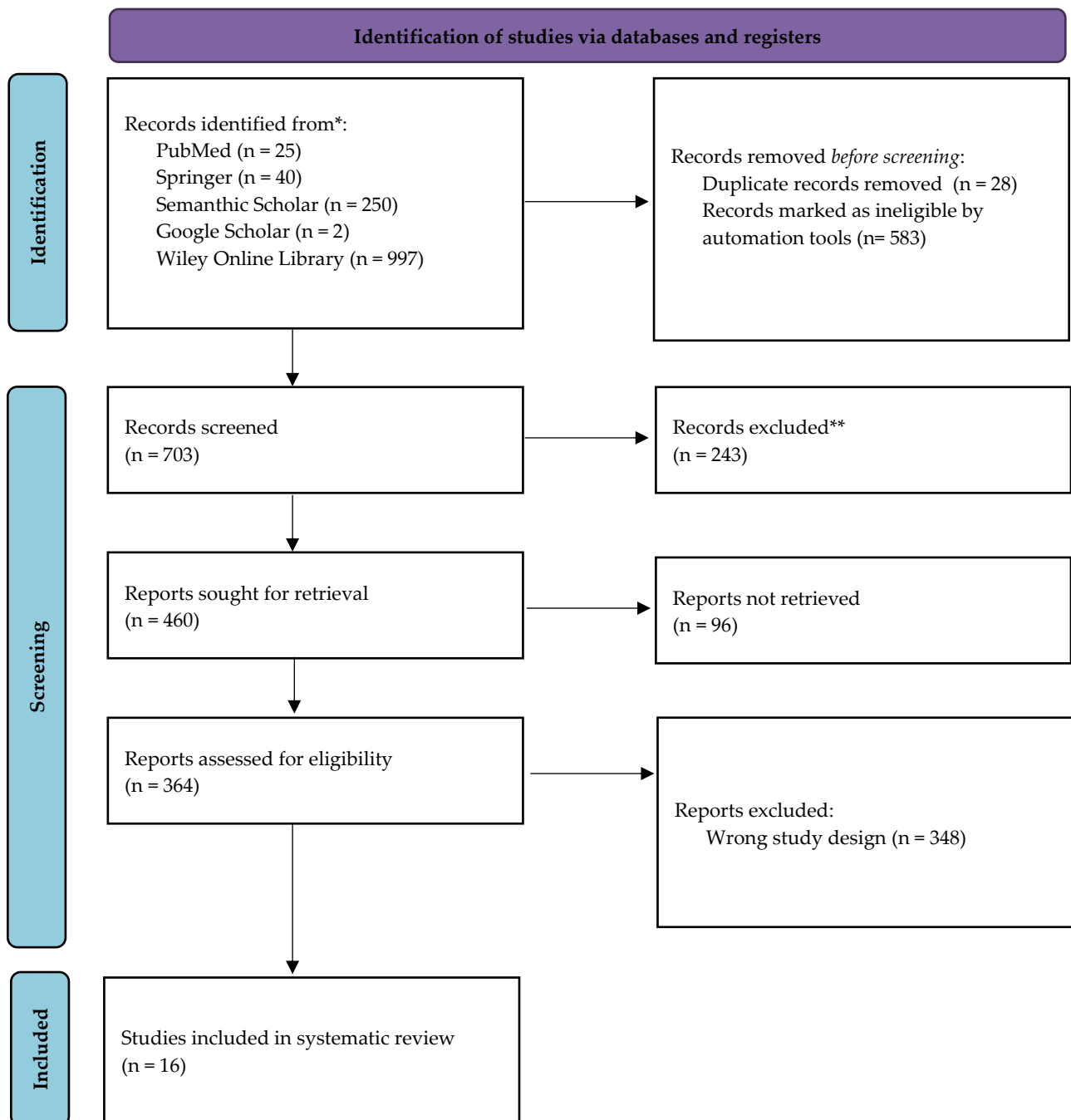


Figure 1. Article search flowchart

RESULTS

Characteristics of Included Studies

The 16 included studies were all observational in design, comprising 13 cross-sectional studies, 2 cohort studies, and 1 systematic review of observational data. The studies were published between 2008 and 2024 and were conducted across a wide range of geographical locations, including Europe, Asia, and North and South America. The total number of participants across all included studies exceeded 10,000.

The study populations varied: 10 studies focused on patients with diagnosed T2DM, examining the overall prevalence of various dermatoses; 4 studies focused on overweight and obese populations (both adult and adolescent); and 2 were broader reviews on skin manifestations of metabolic syndrome or insulin resistance. Of the 10 studies in T2DM populations, none specifically reported KP prevalence as a primary or secondary outcome, and thus did not provide data for this review's central question. The primary data on KP prevalence and its metabolic associations were derived exclusively from the studies conducted in obese and metabolic syndrome cohorts. The detailed characteristics of these 16 key studies are summarized in Table 1.

Table 1: Characteristics of Included Studies

Author (Year)	Study Design	Population	Sample Size (N)	Primary Outcome(s) Measured	Key Quantitative Findings Relevant to KP
Yılmaz et al. (2023)	Cross-sectional	Obese children and adolescents	103	Prevalence of skin lesions; correlation with HOMA-IR	KP prevalence: 64.7%. Significant association between KP and HOMA-IR ().
Pérez et al. (2014)	Cross-sectional	Overweight and obese adults/children	109	Prevalence of skin disorders; correlation with insulin levels	KP prevalence: 42.1%. No significant association found between KP and insulin levels or grade of obesity.
Pavlović et al. (2022)	Review	Obese patients	N/A (Review)	Association between	States KP has been linked to

Author (Year)	Study Design	Population	Sample Size (N)	Primary Outcome(s) Measured	Key Quantitative Findings Relevant to KP
				obesity and skin changes	increased BMI.
Guida et al. (2019)	Cross- sectional	Obese vs. non-obese adults	500	Prevalence and severity of dermatoses	KP incidence and severity increased with the severity of obesity ().
de Oliveira et al. (2024)	Cross- sectional	Patients with Metabolic Syndrome	93	Prevalence of dermatologi cal manifestatio ns	Classified KP as having a "moderate connection" with Metabolic Syndrome.
Niaz, Bashir, and Khan	Cross- sectional	T2DM patients	200	Frequency of cutaneous	Did not report Keratosi s Pilaris.

Author (Year)	Study Design	Population	Sample Size (N)	Primary Outcome(s) Measured	Key Quantitative Findings Relevant to KP
(2019)				manifestations	
Ahmed, Muhammad, and Qayum (2014)	Cross-sectional	T2DM patients	100	Frequency of skin disorders vs. glycemic control	Did not report Keratosis Pilaris.
Mahajan et al. (2012)	Case-control	T2DM patients vs. controls	224	Spectrum of dermatoses in diabetics	Did not report Keratosis Pilaris.
Hosseini et al. (2008)	Cross-sectional	T2DM patients	1135	Prevalence of skin lesions	Did not report Keratosis Pilaris.
Memon et al. (2017)	Cross-sectional	T2DM patients	200	Frequency of skin	Did not report Keratosis Pilaris.

Author (Year)	Study Design	Population	Sample Size (N)	Primary Outcome(s) Measured	Key Quantitative Findings Relevant to KP
				disorders	
Basic-Jukić et al. (2019)	Cross- sectional	T2DM patients	105	Association between skin manifestatio ns and glycemic control	Did not report Keratosis Pilaris.
Ali et al. (2020)	Cross- sectional	T2DM patients	100	Association of skin complicatio ns with duration and control of DM	Did not report Keratosis Pilaris.
Tan et al. (2020)	Cross- sectional	T2DM patients	271	Prevalence of	Did not report Keratosis Pilaris.

Author (Year)	Study Design	Population	Sample Size (N)	Primary Outcome(s) Measured	Key Quantitative Findings Relevant to KP
				cutaneous disorders in primary care	
Kumar and Bose (2024)	Observation al	DM patients	100	Correlation of skin manifestatio ns with HbA1c	Did not report Keratosis Pilaris.
González- Saldivar et al. (2017)	Review	Patients with Insulin Resistance	N/A (Review)	Skin manifestatio ns of insulin resistance	Did not list KP as a primary manifestation of IR, focusing on AN, acrochordons, and acne.
Khan et al.	Prospective	DM patients	(Not	Correlation	Did not report

Author (Year)	Study Design	Population	Sample Size (N)	Primary Outcome(s) Measured	Key Quantitative Findings Relevant to KP
(2024)	Cohort		specified)	of skin disease severity with metabolic markers	Keratosis Pilaris.

Methodological Quality and Risk of Bias within Studies

The risk of bias for the included observational studies was assessed using the ROBINS-I tool and is summarized in Table 2. Of the 16 studies, none were rated as having a "Low" risk of bias. Eleven studies were judged to have a "Moderate" risk of bias. These were typically well-designed cross-sectional studies with clear objectives and systematic data collection, but they were limited by potential for unmeasured confounding and the inherent inability of the design to establish causality. Five studies were rated as having a "Serious" risk of bias due to significant concerns in domains such as confounding (e.g., failure to adjust for age, sex, or atopic status), selection of participants (e.g., convenience sampling from a single clinic), or measurement of outcomes (e.g., non-standardized dermatological assessment). No studies were rated as "Critical." The overall moderate-to-serious risk of bias across the evidence base underscores the preliminary nature of the findings and highlights the need for more methodologically robust research.

Table 2: Risk of Bias Assessment using the ROBINS-I Tool

Author (Year)	D1: Confounding	D2: Selection	D3: Exposure Classification	D4: Deviations from Interventions	D5: Missing Data	D6: Outcome Measurement	D7: Reported Result Selection	Overall Risk of Bias
Yılmaz et al. (2023)	Moderate	Moderate	Low	N/A	Low	Moderate	Low	Moderate
Pérez et al. (2014)	Serious	Moderate	Low	N/A	Moderate	Moderate	Low	Serious
Guida et al. (2019)	Moderate	Moderate	Low	N/A	Low	Moderate	Low	Moderate
de Oliveira et	Serious	Serious	Moderate	N/A	Moderate	Moderate	Low	Serious

al. (2024)								
Niaz et al. (2019)	Moderate	Moderate	Moderate	N/A	Low	Moderate	Low	Moderate

Synthesis of Findings

The results are presented in a narrative synthesis, structured to first address the primary research question and then to explore the indirect evidence gathered from the broadened search.

Direct Evidence Linking Glycemic Control (HbA1c) and Keratosis Pilaris in T2DM

The systematic search of the literature yielded **zero studies** that directly and quantitatively assessed the correlation between HbA1c levels and the severity of Keratosis Pilaris in a population of adult patients with Type 2 Diabetes Mellitus. This absence is the principal finding of this review and represents a definitive gap in the current evidence base. Numerous studies examining the spectrum of dermatoses in T2DM patients were identified and reviewed (Table 1), but none included KP as a reported outcome, precluding any analysis of its relationship with glycemic control in this specific population. Table 3 highlights the studies that specifically investigated dermatoses in T2DM but did not report on KP, underscoring this research gap.

Table 3: Observational Studies of Cutaneous Manifestations in T2DM Populations That Did Not Report on Keratosis Pilaris

Author (Year)	Population	Sample Size (N)	Key Manifestations Reported	Status of Keratosis Pilaris Data
Niaz, Bashir, and Khan (2019)	T2DM patients	200	Infections, xerosis, diabetic dermopathy, acanthosis nigricans	Not Reported
Ahmed, Muhammad, and Qayum (2014)	T2DM patients	100	Infections, diabetic dermopathy, pruritus	Not Reported
Mahajan et al. (2012)	T2DM patients	224	Infections, diabetic dermopathy, ichthyosis, acanthosis nigricans	Not Reported
Hosseini et al. (2008)	T2DM patients	1135	Diabetic dermopathy, infections, acanthosis nigricans	Not Reported

Memon et al. (2017)	T2DM patients	200	Infections, pruritus, diabetic dermopathy, thick/scaly skin	Not Reported
Basić-Jukić et al. (2019)	T2DM patients	105	Infections, xerosis, psoriasis, fibroma molle	Not Reported
Ali et al. (2020)	T2DM patients	100	Fungal infections, xerosis, bacterial infections	Not Reported
Tan et al. (2020)	T2DM patients	271	Infections, diabetic dermopathy, necrobiosis lipoidica	Not Reported
Kumar and Bose (2024)	DM patients	100	Infections, papulosquamous diseases, autoimmune diseases	Not Reported
Khan et al. (2024)	DM patients	(Not specified)	Diabetic dermopathy, acanthosis nigricans, necrobiosis lipoidica	Not Reported

Prevalence of Keratosis Pilaris in Cohorts with Obesity and Metabolic Syndrome

While direct evidence in T2DM is lacking, data from cohorts with related metabolic disorders provide valuable context. The prevalence of KP appears to be notably high in individuals with obesity, often exceeding the general adult population prevalence of approximately 40% (Haveri, Inabnet, and Singh, 2023).

- In a study of 109 overweight and obese individuals (95 adults, 13 children), Pérez et al. (2014) reported a KP prevalence of **42.1%**.
- In a study focused on 103 obese children and adolescents, Yılmaz et al. (2023) found a substantially higher prevalence of **64.7%**.
- Guida et al. (2019), in a large study of 500 adults, observed that both the incidence and the clinical severity of KP increased in direct proportion to the severity of obesity ().

These findings consistently suggest that the metabolic state associated with obesity is a significant risk factor for the presence and severity of KP.

Association between Keratosis Pilaris and Markers of Insulin Resistance

The most compelling indirect evidence linking KP to the core pathophysiology of T2DM comes from studies assessing markers of insulin resistance. The findings, however, are not entirely consistent.

- The study by Yılmaz et al. (2023) stands out as it demonstrated a statistically significant positive association between the presence of KP and the HOMA-IR score () in their cohort of obese adolescents. This provides the strongest quantitative link between KP and insulin resistance currently available in the literature.
- In contrast, the study by Pérez et al. (2014) did not find a statistically significant association between KP and either fasting insulin levels or the grade of obesity, although such associations were found for acanthosis nigricans and acrochordons.
- A broader review by de Oliveira et al. (2024) on skin manifestations of metabolic syndrome

qualitatively described the link to KP as a "moderate connection," suggesting the association is recognized but not as robustly established as that for other dermatoses.

These key quantitative findings are summarized in Table 4.

Table 4: Summary of Quantitative Findings on Keratosis Pilaris in Metabolic Disorders

Study	Population	KP Prevalence (%)	Association Metric	Specific Finding
Yılmaz et al. (2023)	Obese Adolescents	64.7%		Statistically significant association with HOMA-IR score.
Pérez et al. (2014)	Overweight/Obese Adults & Children	42.1%	Not Significant	No significant association with insulin levels or grade of obesity.
Guida et al. (2019)	Obese Adults	(Not specified)		KP incidence and severity increased with the severity of obesity.

de Oliveira et al. (2024)	Metabolic Syndrome Patients	(Not specified)	Qualitative	Described as a "moderate connection" to Metabolic Syndrome.
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DISCUSSION

Summary of Evidence and Interpretation of the Principal Finding: A Definitive Gap in the Literature

This systematic review was initiated to evaluate the correlation between glycemic control and KP severity in T2DM. The most significant and unequivocal finding is the complete absence of primary research addressing this question. Despite a comprehensive search strategy, no studies could be identified that directly measured both HbA1c and KP severity within a T2DM cohort. This void is striking, given the high prevalence of both conditions and the strong biological plausibility of their interaction. The consistent omission of KP from large-scale studies of diabetic dermatoses suggests it is a significant blind spot in both dermatological and endocrinological research. This may be due to its benign nature, leading clinicians to overlook it in favor of more acute complications, or perhaps due to the historical lack of validated scoring systems for KP, which has hindered quantitative research (Wong et al., 2023). Irrespective of the reason, this review formally establishes this gap and provides a robust, evidence-based argument for why it warrants investigation.

Pathophysiological Synthesis: Building the Case for a Correlation

In the absence of direct evidence, a synthesis of indirect clinical data and fundamental pathophysiological principles can be used to construct a compelling model for the hypothesized relationship. The metabolic milieu of poorly controlled T2DM, characterized by concurrent

hyperglycemia and hyperinsulinemia, appears capable of exacerbating the core pathology of KP—follicular hyperkeratosis—through at least two distinct yet synergistic pathways.

The Impact of Hyperglycemia and Advanced Glycation End Products (AGEs) on Epidermal Integrity

Chronic hyperglycemia is the hallmark of poorly controlled T2DM and a primary driver of its long-term complications. A key mechanism of hyperglycemia-induced tissue damage is the non-enzymatic glycation of proteins and lipids, which leads to the formation and accumulation of Advanced Glycation End Products (AGEs) (Kandhwal, 2015). The skin, with its slow-turnover proteins like collagen, is particularly susceptible to the accumulation of AGEs.

The binding of AGEs to their specific cell-surface receptors (RAGE), which are expressed on keratinocytes, triggers a cascade of downstream signaling that promotes a state of chronic oxidative stress and inflammation (Kandhwal, 2015; Rader and St. Surin-Lord, 2021). This pathological environment directly disrupts the tightly regulated process of epidermal homeostasis. Studies in diabetic mouse models have shown that hyperglycemia impairs keratinocyte proliferation, induces the ectopic expression of differentiation markers, and ultimately compromises the integrity of the skin barrier (Basić-Jukić et al., 2019; Rader and St. Surin-Lord, 2021). This can manifest clinically as xerosis (dry skin) and ichthyosiform changes, which are themselves frequently associated with KP (Rader and St. Surin-Lord, 2021). The fundamental pathology of KP is a defect in keratinization. It is therefore highly plausible that the AGE-mediated disruption of normal keratinocyte differentiation and desquamation in a hyperglycemic state would directly worsen the pre-existing tendency for follicular plugging, leading to more severe KP.

The Mitogenic Effects of Hyperinsulinemia and IGF-1 on Follicular Keratinocyte Proliferation

The second, and perhaps more direct, pathway links KP to the insulin resistance that defines T2DM. Insulin resistance in peripheral tissues leads to a state of compensatory hyperinsulinemia as

the pancreas attempts to maintain euglycemia (González-Saldivar et al., 2017). At these supraphysiological concentrations, insulin can exhibit significant cross-reactivity with the receptor for Insulin-like Growth Factor-1 (IGF-1), a potent mitogen involved in cellular growth and proliferation (González-Saldivar et al., 2017).

IGF-1 receptors are expressed on key cells within the pilosebaceous unit, including follicular keratinocytes and hair matrix cells (Su et al., 2021). The activation of these receptors stimulates cellular proliferation through pathways such as the PI3K/Akt cascade (Su et al., 2021). This exact mechanism—hyperinsulinemia leading to increased IGF-1 signaling and subsequent follicular hyperkeratinization—is a well-accepted model for the pathogenesis of acne vulgaris, another common follicular disorder (Melnik, 2015). It is therefore logical to propose that the same mitogenic stimulus that drives comedogenesis in acne could drive the formation of keratotic plugs in KP. This positions KP not as an isolated entity, but as part of a spectrum of "metabolic-driven follicular hyperproliferative disorders," alongside acne and acanthosis nigricans. The significant association between KP and HOMA-IR found by Yılmaz et al. (2023) provides strong clinical support for this hyperinsulinemia-driven hypothesis.

These converging pathways are summarized in Table 5, illustrating how the dual metabolic insults of T2DM could synergistically worsen KP severity.

Table 5: Synthesis of Pathophysiological Mechanisms Linking T2DM and Follicular Hyperkeratinization

Metabolic Disturbance in T2DM	Key Molecular Mediator	Effect on Hair Follicle/Keratinocytes	Potential Manifestation in KP	Supporting Evidence
Hyperglycemia	Advanced Glycation End Products (AGEs)	Binds to RAGE on keratinocytes, inducing oxidative stress and inflammation; impairs normal keratinocyte proliferation/differentiation balance; disrupts epidermal barrier function.	Worsening of follicular plugging due to abnormal desquamation; increased xerosis and perifollicular erythema.	Kandhwal (2015); Rader and St. Surin-Lord (2021); Basić-Jukić et al. (2019)
Hyperinsulinemia / Insulin	Insulin-like Growth Factor-	High insulin levels activate	Increased number and	Melnik (2015); Su et al. (2021); Aoki and

Metabolic Disturbance in T2DM	Key Molecular Mediator	Effect on Hair Follicle/Keratinocytes	Potential Manifestation in KP	Supporting Evidence
Resistance	1 (IGF-1)	IGF-1 receptors on follicular keratinocytes; stimulates cellular proliferation via PI3K/Akt and MAPK/ERK signaling pathways.	size of keratotic papules due to follicular hyperproliferation; exacerbation of follicular plugging.	Murase (2019); Yılmaz et al. (2023)

Clinical Implications and the Role of Dermatological Examination in Diabetes Care

The establishment of a definitive link between glycemic control and KP severity would have significant clinical implications. As a highly prevalent and easily recognizable condition, KP could potentially serve as a non-invasive, visible biomarker for underlying metabolic dysfunction. For an undiagnosed patient, the presence of prominent or worsening KP, particularly in the context of obesity, could prompt a clinician to screen for insulin resistance or prediabetes. In a patient with established T2DM, a noticeable exacerbation of their KP could act as an early warning sign of deteriorating glycemic control, encouraging a timely re-evaluation of their diet, lifestyle, and

medication regimen. This aligns with the broader understanding that the skin often provides the first clues to internal metabolic disease (Sasmaz and Buyukbese, 2015; Basić-Jukić et al., 2019). Integrating a focused assessment of common, benign dermatoses like KP into routine diabetic care could enhance holistic patient monitoring.

Limitations of the Current Evidence Base and This Review

The foremost limitation of this systematic review is the primary limitation of the literature itself: the complete lack of direct evidence. The conclusions drawn regarding the T2DM-KP link are therefore based on inference and the synthesis of indirect evidence, which, while biologically compelling, cannot replace data from direct observational studies. The included studies on related populations suffer from their own limitations, including a moderate-to-serious risk of bias, significant heterogeneity in populations (e.g., adults vs. adolescents) and methodologies, and inconsistent findings regarding the association with insulin resistance markers. Furthermore, the field has been hampered by the historical lack of a standardized, validated scoring system for KP severity, which has made it difficult to conduct and compare quantitative research (Wong et al., 2023). The recent development of tools like the KP-IGA and KPAI may help overcome this barrier in future studies (Wong et al., 2024).

CONCLUSION AND RECOMMENDATIONS

Conclusion

This systematic review confirms a significant and surprising gap in the medical literature concerning the direct correlation between glycemic control, as measured by HbA1c, and the severity of Keratosis Pilaris in patients with Type 2 Diabetes Mellitus. Despite the absence of direct clinical studies, a substantial body of indirect evidence provides a strong, biologically plausible rationale for a positive association. The synthesis of pathophysiological data suggests that the dual metabolic insults of hyperglycemia (via AGEs) and hyperinsulinemia (via IGF-1 signaling) can

synergistically disrupt follicular homeostasis, thereby initiating or exacerbating the hyperkeratotic process central to KP. While the hypothesis remains unproven, the weight of the indirect evidence is compelling and warrants definitive clinical investigation.

Recommendations for Future Primary Research

To address the critical knowledge gap identified in this review, the following primary research studies are strongly recommended, as outlined in Table 6.

Table 6: Recommendations for Future Research on Keratosis Pilaris and T2DM

Research Type	Recommended Study Design	Key Objectives and Methodologies	Expected Outcomes
Clinical Observational	Prospective Cohort Study	- Recruit a large cohort of T2DM patients. - Serially measure HbA1c and KP severity using validated tools (e.g., KP-IGA, KPAI) over several years.	- Establish temporal relationship between changes in glycemic control and KP severity. - Identify predictive value of HbA1c for KP exacerbation.
Clinical Observational	Cross-Sectional Study	- Compare KP prevalence and severity in three groups: T2DM with	- Provide the first robust estimate of the association's magnitude. - Quantify

		poor control (HbA1c >8%), T2DM with good control (HbA1c <7%), and matched non-diabetic controls.	the risk of severe KP in poorly controlled T2DM.
Translational/Mechanistic	Histopathological Study	- Obtain skin biopsies from KP lesions in T2DM patients and controls. - Use immunohistochemistry to quantify the expression of RAGE and IGF-1 receptors in follicular epithelium.	- Provide direct molecular evidence for the proposed pathophysiological pathways (AGEs and IGF-1). - Validate the biological model linking T2DM to KP.

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