



Original Article



Association of Cutaneous Manifestations with Undiagnosed Diabetes Mellitus in Adults

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ABSTRACT

Diabetes mellitus (DM) remains underdiagnosed in resource-limited settings, where access to laboratory screening is constrained. Cutaneous manifestations may serve as visible, cost-effective indicators. **Objectives:** To determine the association between characteristic skin lesions (acanthosis nigricans, skin tags, xerosis) and undiagnosed diabetes in adults. **Methods:** A cross-sectional study involving 400 participants was conducted at a Teaching Hospital with adult patients without known diabetes (aged 18-70) attending dermatology and general medicine clinics. Detailed dermatological examinations documented predefined skin manifestations, while biochemical assessments (fasting plasma glucose, HbA1c, and oral glucose tolerance test) classified participants into normoglycemic, pre-diabetic (IFG/IGT), or diabetic groups per ADA criteria. Statistical analysis was done on SPSS version 26.0. **Results:** The prevalence of cutaneous markers was significantly higher in prediabetes and diabetes groups ($p < 0.001$). Acanthosis nigricans was present in 61.4% of cases, nearly eight times more prevalent than in normoglycemic individuals (8.1%). Similarly, multiple skin tags (≥ 5) affected 52.9% of diabetics compared to just 12.4% of controls, while xerosis showed a fourfold increase from 9.5% in normoglycemic subjects to 44.3% in diabetics. **Conclusions:** It was concluded that specific dermatological manifestations exhibit a robust correlation with undiagnosed diabetes and pre-diabetes. Incorporating cutaneous markers into routine clinical examinations may enhance early detection, particularly in resource-limited settings.

INTRODUCTION

Diabetes mellitus has become a major global health concern in the 21st century, with its prevalence escalating to epidemic levels worldwide. As per the International Diabetes Federation's 2021 data, 537 million adults globally were living with diabetes, a figure expected to rise to 783 million by 2045. In Pakistan alone, rates have increased dramatically, with estimates suggesting that nearly 26.7% of the adult population suffers from this metabolic disorder [1]. Almost half of all diabetes cases are unaware of their condition, in countries with limited healthcare resources

like Pakistan, where access to routine health screening is limited [2]. This diagnostic delay often leads to the development of serious complications, including neuropathy, retinopathy, nephropathy, and cardiovascular diseases before the condition is even recognized [3]. The economic burden of diabetes management and its complications places a substantial strain on healthcare systems, particularly in low-resource settings having limited access to specialized care [4]. The skin, being the largest organ of the human body, frequently manifests



visible signs of systemic diseases, including diabetes mellitus [5]. Numerous dermatological conditions have been strongly associated with insulin resistance and hyperglycemia. These cutaneous manifestations arise through several pathophysiological mechanisms [6]. Chronic hyperglycemia leads to the glycosylation of structural proteins in the skin, resulting in microvascular damage and impaired wound healing [7]. Insulin resistance triggers abnormal proliferation of keratinocytes and fibroblasts, leading to characteristic skin changes [8]. Additionally, the low-grade inflammatory state associated with diabetes contributes to skin barrier dysfunction and altered sebaceous gland activity [9]. Among the most well-documented cutaneous markers of diabetes are acanthosis nigricans (AN), characterized by velvety hyperpigmented plaques; skin tags (acrochordons), which are benign fibroepithelial polyps frequently observed in the neck and axillary regions; and xerosis, presenting as abnormally dry skin that often precedes other diabetic complications [10, 11]. These dermatological findings are particularly relevant in clinical settings, where they may serve as crucial visual clues for early diabetes detection [12]. Early identification of diabetes through cutaneous signs could substantially reduce healthcare costs by minimizing the need for expensive laboratory tests [13]. There is a paucity of data regarding the prevalence and diagnostic value of these cutaneous markers in the local population of Sargodha. Second, most existing studies have focused on patients with already diagnosed diabetes rather than investigating these signs in undiagnosed cases.

This study aims to determine the prevalence of characteristic skin manifestations in adults with undiagnosed diabetes or prediabetes to evaluate their diagnostic accuracy in identifying dysglycemia, and provide evidence for incorporating dermatological examinations into routine diabetes screening protocols in similar healthcare settings. Given the rising burden of diabetes in Pakistan, this research emphasizes the significance of fostering closer collaboration between dermatologists and primary care physicians in diabetes detection strategies.

METHODS

This cross-sectional study was done at the Department of Dermatology and Medicine, Niazi Welfare Foundation Teaching Hospital, Sargodha, from April 1, 2023, to March 31, 2024. The study gained ethical approval from the institutional review committee (Approval No: NM&DC-IRB-66 and Ref Letter No: IRB/NM&DC/203) and followed all ethical regulations during the entire study duration. A written informed consent, along with voluntary participation, was obtained from study participants. A sample size of 400 was calculated using Open Epi software

with an estimated prevalence of skin manifestation in diabetes of 23%, 95% confidence level, 4.12% margin of error [14]. Using a consecutive sampling technique, the study population included adults aged 18–70 years presenting to outpatient departments without known diabetes, excluding those with known diabetes mellitus, pregnancy, chronic steroid use, or severe systemic illnesses that could affect skin manifestations. Participants underwent a comprehensive dermatological examination by trained dermatologists under standardized lighting conditions. The examination focused on identifying specific cutaneous markers: acanthosis nigricans (defined as velvety hyperpigmented plaques in the neck, axillae, or groin), skin tags (≥ 5 lesions in characteristic locations), and xerosis (clinically significant dry skin with scaling). Each finding was documented using a standardized proforma with photographic documentation in suspicious cases. Anthropometric parameters such as body weight, stature, waist circumference, and blood pressure were systematically measured following the WHO STEPS protocol. Body mass index (BMI) was calculated and categorized according to Asian-specific cutoffs. For biochemical assessment, following an 8-hour overnight fast, venous blood samples were obtained. Fasting plasma glucose (FPG) levels were assessed, and HbA1c concentrations were quantified. Participants with FPG 100–125 mg/dL underwent a 75g oral glucose tolerance test (OGTT), measuring glucose levels two hours' post-load. Based on glycemic status, participants were categorized in diabetes (FPG ≥ 126 mg/dL, or HbA1c $\geq 6.5\%$, or 2-hour OGTT ≥ 200 mg/dL), prediabetes (FPG 100–125 mg/dL, or HbA1c 5.7–6.4%, or 2-hour OGTT 140–199 mg/dL) and normoglycemic (FPG <100 mg/dL and HbA1c <5.7%) groups. Data were analyzed using SPSS v26.0. Descriptive statistics (mean \pm SD, frequencies) were computed. Chi-square tests are applied for categorical variables. Significance level was kept at p -value <0.05.

RESULTS

This study presents the demographic and clinical characteristics of 400 participants (mean age 45.2 ± 12.7 years, 58% female) stratified by glycemic status. Age, BMI, and waist circumference were significantly higher in prediabetes/diabetic groups ($p < 0.001$) (Table 1).

Table 1: Participant Profile According to Glycemic Status

Characteristic	Normoglycemic (n=210)	Prediabetes (n=120)	Diabetic (n=70)	p-value
Age (Years)	39.5 \pm 10.2	47.8 \pm 11.5	53.6 \pm 9.8	<0.001*
Female Sex	58.1%	57.5%	58.6%	0.983
BMI (kg/m ²)	24.1 \pm 3.2	27.8 \pm 4.1	29.5 \pm 4.6	<0.001*
Waist Circumference (cm)	84.5 \pm 8.7	92.3 \pm 9.5	96.8 \pm 10.2	<0.001*
Family History of DM	18.6%	35.8%	44.3%	<0.001*

Among participants with confirmed diabetes, acanthosis nigricans was present in 61.4% of cases, nearly eight times more prevalent than in normoglycemic individuals (8.1%). Similarly, multiple skin tags (≥ 5) affected 52.9% of diabetics compared to just 12.4% of controls, while xerosis showed a fourfold increase from 9.5% in normoglycemic subjects to 44.3% in diabetics (all $p < 0.001$) (Table 2).

Table 2: Frequency and Percentage of Cutaneous Markers by Glycemic Status

Cutaneous Markers	Normoglycemic (n=210)	Prediabetes (n=120)	Diabetic (n=70)	p-value
Acanthosis Nigricans	17 (8.1%)	51 (42.5%)	43 (61.4%)	<0.001
Skin Tags (≥ 5)	26 (12.4%)	46 (38.3%)	37 (52.9%)	<0.001
Xerosis	20 (9.5%)	38 (31.7%)	31 (44.3%)	<0.001

DISCUSSION

This study highlights the significance of specific skin conditions—acanthosis nigricans, skin tags (acrochordons), and xerosis as early indicators of undiagnosed diabetes mellitus in Pakistani adults. A clear relationship was observed, with the prevalence of these dermatological manifestations increasing from normoglycemic individuals to those with prediabetes and diabetes. These findings are consistent with existing literature that underscores the role of cutaneous signs in the early detection of diabetes [15]. A pivotal finding of our study was the notably high prevalence of acanthosis nigricans (AN) observed at 61.4% among participants in the diabetes group. This prevalence was significantly higher compared to 42.5% in prediabetes individuals and 8.1% among those with normal glycemic levels. The findings support the pathophysiological understanding that AN develops as a cutaneous marker of hyperinsulinemia and insulin resistance. These results are consistent with other studies [16, 17] and particularly relevant for clinical practice in our setting, where AN is frequently observed but often overlooked as a cosmetic concern rather than a metabolic warning sign. Our findings reinforce the need for routine screening for dysglycemia in all patients presenting with AN, especially those with additional risk factors like obesity or a family history of diabetes. The study highlighted a significant association between the presence of multiple skin tags (≥ 5) and undiagnosed diabetes mellitus. This finding aligns with existing research suggesting that skin tags may serve as external indicators of underlying metabolic disturbances, particularly insulin resistance [18, 19]. Interestingly, our data showed significant concerns when skin tags co-occurred with AN, supporting the clinical practice of considering these markers in combination rather than isolation. This finding has particular relevance for primary care physicians in our region, who may encounter patients with skin tags but lack awareness of their potential metabolic significance. Xerosis was another common dermatological finding

among participants with undiagnosed diabetes, observed in 44.3% of individuals with newly diagnosed diabetes mellitus. This prevalence was notably higher compared to 31.7% in prediabetes participants and 9.5% among normoglycemic individuals. This finding aligns with existing literature indicating that xerosis is a common cutaneous manifestation in diabetic patients [20]. The clinical implications of our findings are substantial for healthcare providers as they support the incorporation of systematic skin examination into routine diabetes screening protocols, particularly in primary care, where resources for laboratory testing may be limited. Second, they highlight the importance of interdisciplinary collaboration between dermatologists and physicians in early diabetes detection. Third, they suggest that patient education about these cutaneous warning signs could improve community awareness and earlier healthcare seeking. We recommend that primary care physicians and dermatologists consider systematic screening for dysglycemia in all patients presenting with these cutaneous markers, particularly when multiple manifestations coexist.

This study is limited by its cross-sectional design, which prevents establishing a causal relationship between cutaneous markers and diabetes mellitus. Additionally, being conducted at a single center may limit the generalizability of the findings to broader populations across Pakistan. Future large-scale, multicenter longitudinal studies are recommended to validate these dermatological markers as predictive tools for early diabetes screening and to assess their role in disease progression over time.

CONCLUSIONS

Our findings establish a significant association between specific cutaneous manifestations, particularly acanthosis nigricans, multiple skin tags (≥ 5), and xerosis and undiagnosed diabetes mellitus in adults. The diagnostic utility of these markers is strongest when they co-occur, with the combination of ≥ 2 signs demonstrating high predictive value. These results underscore the clinical relevance of dermatological examination as a practical, non-invasive screening approach, particularly in resource-limited settings.

Authors' Contribution

Conceptualization: MZ

Methodology: MZ, ZP

Formal analysis: MKM

Writing and Drafting: AG, SN, AB

Review and Editing: MZ, AG, MKM, SN, ZP, AB

All authors approved the final manuscript and take responsibility for the integrity of the work

Conflicts of Interest

All the authors declare no conflict of interest.

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