SKIN

RESEARCH LETTER

Cutaneous Fungal Infections Associated with Pediatric-Onset Diabetes: A Case-Control Study in the All of Us Research Program

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ABSTRACT

Introduction: With the rapidly increasing incidence of pediatric diabetes mellitus (DM) in the United States, an understanding of the risk of long-term cutaneous consequences, particularly the risk of cutaneous fungal infections, is important. In this study, we evaluate the association between pediatric-onset Type 1 diabetes (T1D) and Type 2 diabetes (T2D) with the later development of cutaneous fungal infections.
Methods: Through the All of Us electronic health record database, 300 de-identified participants with a diagnosis of T1D or T2D before the age of 18 were selected at random. These 300 participants, composing our pediatric-onset diabetes cohort, were diagnosed with T1D and/or T2D before the age of 18 and developed cutaneous fungal infections between less than 1 and 24 years later. Each case was age-, race-, and sex-matched to four control participants without T1D or T2D diagnoses, and we compared cutaneous fungal infections between pediatric-onset diabetic cases and controls.
Results: Compared to the control cohort, participants with pediatric-onset diabetes were significantly more likely to present in adulthood with candidiasis of the mouth, onychomycosis, pityriasis versicolor, candidiasis of urogenital sites, and unspecified superficial mycosis, as well as dermatophytosis of the body, feet, and perianal regions than their non-diabetic counterparts.
Conclusion: With the increasing incidence of pediatric DM, it will be important for clinicians to monitor the long-term cutaneous complications, including the risk of fungal infections, to improve dermatology patient outcomes. Further research is warranted to investigate the role of childhood diabetes intervention and glycemic control in mitigating dermatologic fungal complications through adulthood.

INTRODUCTION

With the rapidly increasing incidence of pediatric diabetes mellitus (DM) in the United States,[1] an understanding of the risk of long-term cutaneous consequences, particularly the risk of cutaneous fungal infections, is important. Here, we evaluate the association between pediatric-onset Type 1 diabetes (T1D) and Type 2 diabetes (T2D) with the later development of cutaneous fungal infections in the All of Us research program. This is a National Institutes of Health

database presenting health information on Americans who are historically underrepresented in research.

Through the All of Us electronic health record database, we randomly selected 300 de-identified participants with a diagnosis of T1D or T2D before the age of 18. These 300 participants, composing our pediatric-onset diabetes cohort, were diagnosed with T1D and/or T2D before the age of 18 and developed cutaneous fungal infections between less than 1 and 24 years later. Each case was age-, race-, and sex-matched to four control participants without T1D or T2D diagnoses. Participant demographics are displayed in **Table 1**. We compared cutaneous fungal infections between pediatric-onset diabetic cases and controls. All analyses were performed using R Statistical Software,[2] and the results are depicted as odds ratios (OR) with 95% confidence intervals (CI) in **Table 2**.

Compared to the control cohort, participants with pediatric-onset diabetes were significantly more likely to present with candidiasis of the mouth (OR 8.34, 3.34-20.86 CI), onychomycosis (OR 34.70, 10.37-116.05 CI), pityriasis versicolor (OR 3.56, 1.28-9.90 CI), and unspecified superficial mycosis (OR 16.20, 1.80-145.51 CI) which encompasses dermatophytosis, onychomycosis, and dermal mycosis diagnoses. Additionally, pediatric-onset diabetes participants were significantly more likely to experience localized dermatophytosis of the body (tinea corporis; OR 6.49, 3.00-14.02 CI), feet (tinea pedis; OR 9.01, 3.40-23.92 CI), and perianal region (OR 28.25, 1.46-548.37 CI) than their non-diabetic counterparts. Tinea cruris, a dermatophyte infection localized to the groin, was not clearly increased in the pediatric-onset diabetes cohort (OR 20.12, 0.96-419.99 CI).

Consistent with the findings of a separate study,[3] we observed a significant association between pediatric-onset diabetes and candidiasis of urogenital sites (OR 12.77, 8.16-19.98 CI). Notably, literature suggests that the relationship between pediatric diabetes and vulvovaginal candidiasis may be isolated to postpubescent teenagers, as low estrogen levels during early childhood create a rich, anaerobic flora that inhibits *Candida sp.* growth.[4]

Although participants were randomly selected, our case cohort exhibited female predominance (74%). One potential explanation is that puberty generally begins earlier in females, and physiological insulin resistance during this time gives rise to a higher incidence of T2D in adolescent females over males.[5]

Due to the retrospective nature of this study, a causal relationship between pediatric-onset diabetes and cutaneous fungal infection prevalence cannot be determined. Additionally, this study does not investigate glycemic control and correlation to cutaneous fungal infections. However, the findings do suggest that certain cutaneous fungal infections are more likely to occur in adulthood in those with pediatric-onset DM, including in underrepresented research populations. With the increasing incidence of pediatric DM, it will be important for clinicians to monitor the long-term cutaneous complications, including the risk of fungal infections, to improve dermatology patient outcomes. Further research is warranted to investigate the role of childhood diabetes intervention and glycemic control in mitigating dermatologic fungal complications through adulthood.

Conflict of Interest Disclosures: Dr. Rajani Katta serves on an advisory board for Vichy Laboratories. Emily Strouphauer has no conflicts of interest to disclose.

Table 1. Demographics of pediatric-onset diabetes cases and corresponding controls in *All of Us*

Characteristic	Cases	Controls
n	300	1200
Average age (SD)	30.0 (7.69)	30.0 (7.69)
Race/Ethnicity (%)		
Asian	1 (0.33)	4 (0.33)
Black or African American	79 (26.33)	316 (26.33)
More than one population	13 (4.33)	52 (4.33)
Other	92 (30.66)	368 (30.66)
White	115 (38.33)	460 (38.33)
Ethnicity (%)		
Hispanic or Latino	94 (31.33)	376 (31.33)
Not Hispanic or Latino	195 (65.0)	780 (65.0)
Other	11 (3.66)	44 (3.66)
Sex (%)		
Female	222 (74.0)	888 (74.0)
Male	78 (26.0)	312 (26.0)

SD, standard deviation

Table 2. Cutaneous fungal comorbidities of pediatric-onset diabetes cases and corresponding controls in *All of Us*

Diagnostic count of fungal infections	Cases	Controls	OR (95% CI)	*P* value	
Candidal intertrigo	0	1	1.331 (0.0541-32.745)	0.8613	
Candidiasis of urogenital site	74	30	12.770 (8.163-19.977)	<0.0001	*
Candidiasis of mouth	14	7	8.3427 (3.337-20.860)	<0.0001	*
Dermal mycosis	0	1	1.331 (0.0541-32.745)	0.8613	
Dermatophytosis	48	19	11.840 (6.842-20.488)	<0.0001	*
Dermatophytosis of unspecified region	13	2	27.132 (6.089-120.907)	<0.0001	*
Tinea corporis	17	11	6.493 (3.008-14.016)	<0.0001	*
Tinea cruris	2	0	20.1089 (0.963-419.988)	0.0529	
Tinea pedis	13	6	9.014 (3.397-23.919)	<0.0001	*
Tinea of perianal region	3	0	28.2471 (1.455-548.369)	0.0273	*
Onychomycosis due to dermatophyte	24	3	34.696 (10.374-116.045)	<0.0001	*
Pityriasis versicolor	7	8	3.560 (1.281-9.896)	0.0149	*
Superficial mycosis (unspecified)	4	1	16.203 (1.804-145.506)	0.0129	*
Individuals with more than one fungal diagnosis	Cases	Controls	OR (95% CI)	*P* value	
Number of participants (%)	102 (34%)	63 (5.25%)	9.297 (6.562-13.173)	<0.0001	*

CI, confidence interval; OR, odds ratio
*Denotes significance

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