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Original Research

Association of type 2 diabetes with central-scalp hair loss in a large cohort study of African American women ☆☆☆



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ABSTRACT

Background: Hair loss on the central scalp commonly occurs among African American (AA) women and can pose substantial psychosocial burdens. The causes of hair loss remain obscure, although type 2 diabetes has been hypothesized to increase the risk of hair loss. The objective of the present study was to prospectively estimate the association between type 2 diabetes and severe central hair loss in AA women. **Methods:** The Black Women's Health Study has collected data on medical and lifestyle factors, including diagnosis of type 2 diabetes, biennially since 1995 from AA women across the United States. The present analysis was based on responses from 5389 women to an online hair loss questionnaire in 2015. Respondents indicated severity of central hair loss on a validated six-item photographic scale; the highest levels, levels 3 to 5, were designated as severe. We used Cox proportional hazards models to estimate multivariable hazard ratios and 95% confidence intervals (CIs) for type 2 diabetes in relation to severe central hair loss.

Results: During the follow-up period, 850 cases of severe hair loss occurred. The multivariable hazard ratio for severe hair loss associated with diabetes was 1.68 (95% CI, 1.38–2.06) overall, and 2.05 (95% CI, 1.48–2.85) for diabetes duration of ≥ 10 years.

Conclusion: Type 2 diabetes was associated with an increased risk of severe central scalp hair loss in AA women. Patients with type 2 diabetes should be followed closely for central scalp hair loss so that appropriate treatment can be offered.

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Introduction

Hair loss on the central scalp occurs commonly among African American (AA) women (Alexis et al., 2007; Gathers and Mahan, 2014; Kyei et al., 2011; Olsen et al., 2011) and can pose substantial psychosocial burdens, including negative body image, social anx-

ety, and poor self-esteem (Cash, 1999; Cash et al., 1993). Central scalp hair loss may be due to various conditions (e.g., central centrifugal cicatricial alopecia [CCCA] and androgenetic alopecia; Tanus et al., 2015; Whiting and Olsen, 2008). CCCA is considered the primary form of scarring central alopecia in AA women (Madu and Kundu, 2014; Tanus et al., 2015; Whiting and Olsen, 2008) and has been estimated to affect approximately 5% of AA women (Olsen et al., 2011). CCCA presents as loss of hair on the crown or central scalp that progresses toward the periphery (Tanus et al., 2015; Whiting and Olsen, 2008) and can advance to significant scarring (Herskovitz and Miteva, 2016; Olsen et al., 2011).

Hair loss may be associated with diabetes (Arias-Santiago et al., 2010; Cakir, 2012; El Sayed et al., 2016; Kyei et al., 2011; Miranda et al., 2016). In a cross-sectional study of 326 AA women, the prevalence of type 2 diabetes was higher among women with severe central hair loss (17.6%) than among those without severe

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hair loss (5.7%; [Kyei et al., 2011](#)). In another cross-sectional study ($n = 529$), type 1 and 2 diabetes were described as less common in patients with early compared with late central hair loss ($p = .019$), but diabetes prevalence rates were not provided ([Olsen et al., 2011](#)). In a study of 38 AA patients with biopsy-confirmed CCCA, there was no difference in the prevalence of type 2 diabetes between patients with mild and severe CCCA, but only four patients had diabetes ([Suchonwanit et al., 2016](#)).

Androgenetic alopecia or female pattern hair loss, the most common form of hair thinning in non-Black populations, has been associated with insulin resistance and other manifestations of the metabolic syndrome in studies including predominantly non-AA men ([Arias-Santiago et al., 2010](#); [Banger et al., 2015](#); [Hirsso et al., 2006](#)) and women ([Arias-Santiago et al., 2010](#); [El Sayed et al., 2016](#); [Matilainen et al., 2003](#)). Androgenetic alopecia stems from effects of the testosterone metabolite dihydrotestosterone on androgen-sensitive hair follicles ([Piraccini and Alessandrini, 2014](#)), suggesting that vascular impairment due to hyperglycemia could damage hair follicles ([Miranda et al., 2016](#)) and contribute to hair loss.

The mechanism(s) leading to central hair loss are largely unknown. Peroxisome proliferator-activated receptor gamma (PPAR γ)-mediated signaling is an important modulator of skin homeostasis, and defects in PPAR γ -mediated signaling have been suggested to play a role in CCCA ([Karnik et al., 2009](#); [Ramot et al., 2015](#); [Subash et al., 2018](#)). A role of PPAR γ in lichen planopilaris is supported by biopsy analysis of patients ([Karnik et al., 2009](#)) and a report of a case that improved with use of a thiazolidinedione, a PPAR γ agonist ([Mirmirani and Karnik, 2009](#)). Results on the efficacy of thiazolidinediones have been mixed in other studies ([Baibergerova and Walsh, 2012](#); [Mesinkovska et al., 2015](#); [Spring et al., 2013](#)). If diabetes is associated with CCCA and PPAR γ signaling is involved in CCCA occurrence, then PPAR γ agonists used to treat diabetes (i.e., thiazolidinediones) might counteract an adverse effect of diabetes.

These three prior studies ([Kyei et al., 2011](#); [Olsen et al., 2011](#); [Suchonwanit et al., 2016](#)) on the association of diabetes with central hair loss in AA women were limited by small numbers of participants, lack of information on onset and duration of diabetes and use of diabetes medication, and by their cross-sectional nature, which precludes explication of the timing of diabetes relative to hair loss. Studies on the association of diabetes and other forms of hair loss have been conducted almost exclusively in populations of white men ([Arias-Santiago et al., 2010](#); [Banger et al., 2015](#); [Hirsso et al., 2006](#)) and women ([Arias-Santiago et al., 2010](#); [El Sayed et al., 2016](#); [Matilainen et al., 2003](#)). Only a longitudinal study of a large population of AA women with information on timing of diabetes diagnosis and hair loss can elucidate the temporal association of diabetes with central scalp hair loss.

The Black Women's Health Study (BWHS), a follow-up study of AA women that has collected extensive data on health-related and lifestyle factors biennially since 1995, is positioned to fill these gaps. Since 1995, participants have reported on diabetes diagnosis and use of diabetes medications. Participants reported on hair loss in 2015, including the year hair loss was first noticed and severity of hair loss. Using these data, we prospectively assessed the association of type 2 diabetes with central scalp hair loss and whether an association was modified by the use of thiazolidinediones.

Methods

Black Women's Health Study

The BWHS was established in 1995, and 59,000 AA women age 21 through 69 years were recruited, mainly from subscribers to *Essence* magazine, a general readership magazine that targets AA women ([Rosenberg et al., 1995](#)). The baseline questionnaire elicited information on demographic and lifestyle factors, reproductive

history, and medical conditions. The cohort is followed biennially through mailed and Web-based health questionnaires. Follow up of the baseline cohort has been completed for >85% of the potential years of follow up through 2015.

The study protocol was approved by the Institutional Review Board of Boston University Medical Campus. Participants indicated consent by completing and returning their questionnaires. The present analysis includes data from 20 years of follow-up (1995–2015).

Hair loss

An optional online hair loss questionnaire was included with the health questionnaire for the 2015 follow-up cycle (Online Suppl.). The hair loss questionnaire included 16 multi-part questions about hair loss and hair care practices. Respondents indicated severity of hair loss on a photographic scale developed by investigators of the North American Hair Research Society convened at Duke University, selecting from six photographs representing no hair loss (level 0) through most severe hair loss (level 5; [Olsen et al., 2008](#)). The scalp shown in photographs 3 through 5 has obvious central thinning that is clinically compatible with CCCA ([Olsen et al., 2008](#)).

Reliability of the photographic scale was assessed among 150 women at the Duke Hair Disorders Clinic ([Olsen et al., 2008](#)). Participants and investigators assessed participant hair loss using the photographs. The kappa statistic comparing investigator- and participant-rated hair loss was 0.27 (fair agreement), but there was a tendency for participants to overrate their hair loss ([Olsen et al., 2008](#)). CCCA can be confirmed histopathologically, but we are not aware of a validation study that compares photographic scale results with histopathologic results.

Other questions on the hair loss questionnaire included current and worst hair loss, age when the participant first noticed hair loss on the central scalp, and whether a doctor diagnosed CCCA or took a scalp biopsy. The questionnaire ascertained use of hair relaxers and various hairstyles (e.g., weaves). Hair loss in maternal relatives was ascertained with the hair loss photographic scale; hair loss in male relatives was ascertained with the five-item Hamilton Baldness Scale as modified by Norwood ([Norwood, 1975](#)).

For the current analyses, no hair loss was defined as an answer of no to the question "Have you ever experienced any hair loss on the top of your scalp?" and a selection of level 0 for current and worst hair loss. Participants who chose photographic scale levels 1 to 2 and indicated that their worst hair loss was no greater than level 2 were classified as having mild hair loss. Severe hair loss was defined as photographic scale levels 3 to 5 for current hair loss.

Study population

We compared women who answered the online hair loss questionnaire (responders; $n = 6162$) with 9641 women who responded to the Web-based 2015 follow-up questionnaire but not with the hair loss questionnaire (nonresponders). Responders were similar to nonresponders in terms of age; prevalence of obesity; education; menopausal status; parity; and history of diabetes, cancer, and hypertension (data not shown). The final analysis was based on 5389 women who provided complete and consistent information on hair loss and age at the time of hair loss, whose hair loss did not occur prior to baseline (1995), and who did not have systemic lupus erythematosus.

Exposure and covariate data

We defined a prevalent case of type 2 diabetes as self-report of doctor-diagnosed diabetes at age ≥ 30 years prior to baseline in

Table 1
Characteristics of study population in 2015 by current central scalp hair loss*

	None (n = 3377)	Mild (n = 1162)	Severe (n = 850)
Mean age, years (SD)	54.5 (8.5)	57.2 (8.3)	59.2 (8.3)
Percentage			
Body mass index, kg/m ²			
< 25	19.5	15.8	12.0
25–29	31.5	32.0	32.0
≥ 30	48.0	50.6	55.2
Education, years			
≤ 12	9.6	10.1	10.8
13–15	21.5	23.2	27.7
≥ 16	68.9	66.8	61.5
Smoking status			
Current	6.0	6.2	6.6
Past	24.1	24.1	25.5
Never	67.4	67.1	65.3
Parity			
Nulliparous	28.3	26.9	26.3
1–2	55.8	54.7	56.2
≥ 3	15.7	18.4	17.4
Mother's hair loss			
None	38.8	21.1	20.3
Mild	25.7	41.1	22.4
Severe	17.8	25.9	41.9
Unknown	17.7	12.0	15.3
Father's hair loss			
None	38.9	30.9	27.2
Mild	19.5	25.7	22.2
Severe	21.8	24.8	28.7
Unknown	19.9	18.6	21.9
Ever used hairstyle			
Braids with extensions	21.0	23.0	31.4
Glued weaves	4.7	8.1	15.2
Sewn weaves	12.0	18.2	29.3
Hair relaxer	95.3	96.1	96.4

BMI, body mass index

* Age-adjusted variables in 5-year intervals. Percentages may not add to 100% due to missing data.

1995 or incident diabetes occurring at age ≥ 30 years during the follow-up period through 2015. In a validation study, among 227 participants who met these criteria and whose physicians provided data from their medical records, the diagnosis of type 2 diabetes was confirmed for 96% (Krishnan et al., 2010). Beginning in 1999, participants indicated the specific diabetes drug that they were using on all follow-up questionnaires with the exception of that in 2001.

Self-reported height and weight were ascertained at baseline, and weight was updated on all follow-up questionnaires (validation indicated highly accurate reporting; Wise et al., 2005). Body mass index (BMI) was calculated as weight in kilograms divided by height in meters squared. Smoking history, menopausal status, years of education, and parity were obtained at baseline and updated on various follow-up questionnaires. History of cancer and sarcoidosis was ascertained at baseline and incidence reported on all subsequent questionnaires. Hypertension was ascertained on every questionnaire and was defined as self-report of doctor-diagnosed hypertension together with concurrent use of a diuretic, or report of use of an antihypertensive medication with or without a diagnosis of hypertension (validation study indicated highly accurate reporting; Cozier et al., 2007).

Statistical analyses

Person-years were measured from the beginning of follow-up in 1995 until the onset of hair loss, death, loss to follow-up, diagnosis of diabetes before age 30 (likely type 1), or the end of follow-up (2015), whichever occurred first. We used Cox propor-

Table 2

Association of type 2 diabetes, diabetes duration, diabetes treatment, and age at time of diabetes diagnosis with severe central scalp hair loss* (Black Women's Health Study, 1995–2015)

	Cases/person-years	HR (95% CI)	
		Age-adjusted	Multivariable†
No diabetes	714/89092	1.0	1.0
Diabetes	129/5806	1.87 (1.54–2.28)	1.68 (1.38–2.06)
Duration of diabetes, years			
< 5	48/2499	1.74 (1.29–2.29)	1.56 (1.16–2.11)
5 ≤ 10	39/1870	1.73 (1.25–2.45)	1.55 (1.11–2.15)
≥ 10	42/1437	2.27 (1.64–3.13)	2.05 (1.48–2.85)
Age at diabetes diagnosis, years			
< 50	71/3636	1.92 (1.54–2.39)	1.69 (1.34–1.70)
≥ 50	51/1981	1.51 (1.24–1.84)	1.39 (1.13–1.70)
Use of diabetes medication‡			
No treatment	42/2084	1.84 (1.34–2.52)	1.68 (1.22–2.31)
Used insulin	17/729	1.80 (1.10–2.95)	1.55 (0.94–2.56)
Used pills only	70/2994	1.92 (1.49–2.47)	1.72 (1.33–2.22)

CI, confidence interval; HR, hazard ratio

* No diabetes is reference group for all comparisons.

† Adjusted for age (continuous), body mass index (< 25, 25–29, 30–34, 35–39, ≥ 40, unknown), and years of education (≤ 12, 13–15, 16, ≥ 17)

‡ Among diabetic participants.

tional hazards models, stratified according to age and 2-year questionnaire cycle, to estimate hazard ratios (HRs) and 95% confidence intervals (CIs) for the risk of severe hair loss in relation to type 2 diabetes. Women with mild hair loss were included in the analysis and censored at the cycle when they first noticed hair loss. The analyses were prospective because women reported the year that they first noticed hair loss and only variables (e.g., type 2 diabetes) that occurred prior to that year were considered as independent variables.

We present HRs from an age-adjusted model and a multivariable model adjusted for age (continuous), BMI (< 25, 25–29, 30–34, 35–39, ≥ 40, unknown), and years of education (≤ 12, 13–15, 16, ≥ 17). BMI and education changed the age-adjusted HRs by ≥ 10% in the main analyses. Additional adjustment for smoking status, history of cancer or sarcoidosis, menopausal status, family history of hair loss, and use of various hairstyles or hair relaxers did not materially change the HRs. We calculated HRs for categories of diabetes treatment, duration of diabetes, and age at diabetes diagnosis, with participants without diabetes as the reference group. We conducted prespecified subgroup analyses within strata of BMI, hair loss in participant's mother and father, and use of hair weaves, extensions, and relaxers and tested for interaction on the multiplicative scale with the likelihood ratio test. To check for diagnostic bias, we calculated HRs for hair loss associated with hypertension, a chronic disease that, like diabetes, may increase medical surveillance and therefore the likelihood that hair loss would be brought to a women's attention by a health care provider. We used SAS statistical software, version 9.3 (SAS Institute, Cary, NC).

Results

A total of 850 women (15.7% of 5389) reported current severe hair loss, and 1162 (21.6%) reported current mild hair loss. Among the severe cases, 115 (13.5%) reported that a doctor had

Table 3
Association of diabetes with severe central scalp hair loss according to age when hair loss was first noticed

	Cases/person-years	HR (95% CI)	
		Age-adjusted	Multivariable*
Hair loss noticed age <50 years			
No diabetes	288/82675	1.0	1.0
Diabetes	27/5018	2.35 (1.57-3.52)	1.92 (1.27-2.91)
Hair loss noticed age ≥50 years			
No diabetes	426/86122	1.0	1.0
Diabetes	102/5630	1.78 (1.43-2.23)	1.66 (1.32-2.08)

CI, confidence interval; HR, hazard ratio

* Adjusted for age (continuous), body mass index (<25, 25-29, 30-34, 35-39, ≥40, unknown), and years of education (≤12, 13-15, 16, ≥17)

diagnosed CCA, and 81 (9.5%) reported that the diagnosis was based on biopsy results. As shown in Table 1, women with severe hair loss were more likely to be obese, have fewer years of education, report that their mother or father had severe hair loss, and have used braids with extensions and either glued or sewn hair weaves than were women with no hair loss. The prevalence of these factors among women with mild hair loss was intermediate between participants with no hair loss and those with severe hair loss. As expected, the prevalence of obesity and lower levels of education were greater among women with diabetes than among women without diabetes. Diabetes was not associated with the use of hair styles or hair loss in mother or father (data not shown).

As shown in Table 2, the age-adjusted HR for severe hair loss among women with diabetes was 1.87 (95% CI, 1.54-2.28), and the multivariable HR was 1.68 (95% CI, 1.38-2.06). When we confined the case group to women who reported that CCA had been diagnosed by a physician and/or biopsy result, the multivariable HR was 2.24 (95% CI, 1.35-3.71). The HR for hair loss was greater among women who had diabetes for ≥10 years (multivariable HR: 2.05; 95% CI, 1.48-2.85). Women age <50 years when diabetes was diagnosed had a higher risk of severe hair loss (multivariable HR: 1.69; 95% CI, 1.34-2.12) than women who were age ≥50 years when diagnosed (multivariable HR: 1.39; 95% CI, 1.13-1.70). HRs did not vary according to whether diabetes was untreated or treated with pills or insulin. There was no evidence that treatment with thiazolidinediones reduced the risk of severe hair loss. Among diabetic participants, the multivariable HR among women who ever used a thiazolidinedione relative to women with untreated diabetes was 1.07 (95% CI, 0.64-1.77; based on 26 case users of thiazolidinedione). When use of other diabetes pills and/or insulin was the reference group, the HR among users of thiazolidinedione was 1.12 (95% CI, 0.70-1.78).

The HR for diabetes was higher when hair loss occurred before age 50 years (multivariable HR: 1.92; 95% CI, 1.27-2.91) than when hair loss occurred at age ≥50 years (multivariable HR: 1.66; 95% CI, 1.32-2.08; Table 3).

The multivariable HRs for diabetes did not vary significantly by BMI, use of hair weaves or extensions, or duration of hair relaxer use (Table 4). The HRs for diabetes for women whose mother had no, mild, or severe hair loss were 1.85 (95% CI, 1.21-2.82), 1.92 (95% CI, 1.22-3.01), and 1.54 (95% CI, 1.10-2.16), respectively. The HR was highest among women whose father had no hair loss (HR: 2.37; 95% CI, 1.64-3.41) and lowest among women whose father had severe hair loss (HR: 1.21; 95% CI, 0.76-1.94). The multivariable model HR for diabetes in relation to mild hair loss was 1.09 (95%

Table 4
Association of severe hair loss with diabetes in strata of BMI, use of hair extensions or weaves, use of hair relaxers, mother's hair loss, and father's hair loss

	Cases/person-years	Multivariable HR* (95% CI)
BMI		
BMI <30		
No diabetes	375/55499	1.0
Diabetes	43/1746	2.12 (1.51-2.96)
BMI 30-34		
No diabetes	175/17364	1.0
Diabetes	30/1535	1.37 (0.90-2.08)
BMI 35-39		
No diabetes	84/8752	1.0
Diabetes	27/1220	2.18 (1.36-3.49)
BMI 40+		
No diabetes	74/6664	1.0
Diabetes	29/1262	1.67 (1.04-2.67)
<i>P for interaction</i>		
Use of hair weaves or extensions		
Never used weaves/extensions		
No diabetes	473/70131	1.0
Diabetes	79/4441	1.56 (1.21-2.01)
Ever used weave/extensions		
No diabetes	220/16136	1.0
Diabetes	44/1251	1.50 (1.05-2.14)
<i>P for interaction</i>		
Use of hair relaxer		
Used hair relaxer <6 years		
No diabetes	104/11962	1.0
Diabetes	18/768	1.97 (1.13-3.43)
Used hair relaxer ≥6 years		
No diabetes	597/75485	1.0
Diabetes	108/4970	1.65 (1.32-2.05)
<i>P for interaction</i>		
Hair loss in participant's mother		
Mother had no hair loss		
No diabetes	142/29868	1.0
Yes diabetes	33/2101	1.85 (1.21-2.82)
Mother had mild hair loss		
No diabetes	157/25505	1.0
Diabetes	27/1508	1.92 (1.22-3.01)
Mother had severe hair loss		
No diabetes	296/19342	1.0
Diabetes	49/1239	1.54 (1.10-2.16)
<i>P for interaction</i>		
Hair loss in participant's father		
Father had no hair loss		
No diabetes	183/32412	1.0
Yes diabetes	44/2130	2.37 (1.64-3.41)
Father had mild hair loss		
No diabetes	160/18391	1.0
Diabetes	33/1315	1.57 (1.03-2.39)
Father had severe hair loss		
No diabetes	201/20661	1.0
Diabetes	23/1177	1.21 (0.76-1.94)
<i>P for interaction</i>		
0.07		

BMI, body mass index; CI, confidence interval; HR, hazard ratio

* Adjusted for age (continuous), BMI (<25, 25-29, 30-34, 35-39, ≥40, unknown), except in strata of BMI where it is included as a continuous variable, and years of education (≤12, 13-15, 16, ≥17)

CI, 0.91-1.32) based on 136 women with diabetes among women with mild hair loss.

Finally, the multivariable HR for the association of hypertension with severe hair loss was 0.99 (95% CI, 0.84-1.15).

Discussion

In this study of AA women, type 2 diabetes was associated with a 68% increased risk of severe central-scalp hair loss. The risk was higher among women who had diabetes for at least 10 years and

among those whose hair loss began before age 50 years. We found no beneficial effect of thiazolidinediones.

Two prior studies (Kyei et al., 2011; Olsen et al., 2011) have hinted at an association of diabetes and central scalp hair loss in AA women, but as noted these studies were small and cross-sectional. Because the present study was prospective, we were able to account for the temporal sequence of diabetes and hair loss. Our study was far larger than the prior studies and allowed for more precision in the estimates of association. We adjusted for a range of confounders. Participants were unaware of the study hypotheses, which reduced the possibility of reporting bias. Likewise, the reporting of confounders (e.g., weight) is unlikely to have varied by hair loss, and reporting of these variables has been found to have a high level of accuracy in BWHS (Wise et al., 2005). Likewise, the reporting accuracy of diabetes is quite high in BWHS, and variance by hair loss is unlikely. Evidence against diagnostic bias is provided by the lack of association of hypertension with hair loss.

BWHS responders to the 2015 hair loss questionnaire were more likely to report central scalp hair loss than were nonresponders. Such self-selection would not affect the association under study unless responders to the hair loss questionnaire were also more likely to report diabetes. This is not the case because the prevalence of diabetes was similar among women who did and did not answer the hair loss questionnaire (18.8% vs. 19.4%).

The study was limited by our reliance on self-reported hair loss and inability to classify the particular conditions that resulted in central hair loss. Although the photographic scale levels 3 through 5 are deemed clinically compatible with CCCA (Olsen et al., 2008), that diagnosis requires biopsy confirmation. In the validation study of the photographic scale, women tended to overestimate the severity of their hair loss (Olsen et al., 2008). Thus, women in the BWHS case group of severe hair loss may have included women with mild hair loss, which would have led to underestimation of the magnitude of an association with severe hair loss. When we confined the case group to women reporting doctor- or biopsy-confirmed CCCA, the HR for diabetes was 2.24 compared with 1.68 in the larger case group, which suggests that the association might be greater than estimated. Inaccuracy in reporting of the relative ages at which hair loss and diabetes diagnosis occurred could have led to error in the estimation of the HRs. Because the hypothesis was not known to participants, it is likely that such inaccuracies of memory were random and did not create significant error.

There may be a genetic component to central hair loss (Chumlea et al., 2004; Dlova et al., 2014; Olsen et al., 2011; Whiting and Olsen, 2008). The higher background rate of hair loss among women with a parental history of severe hair loss could explain the lower HRs for diabetes observed among that group; factors that moderately increase the risk are difficult to detect against a high background rate of the outcome. Similarly, the higher risks in women whose diabetes was diagnosed before age 50 years and whose hair loss occurred before age 50 years may be due to the lower background rate of hair loss in younger women.

Conclusion

The findings from this large study support the hypothesis that type 2 diabetes increases the risk of severe central scalp hair loss in AA women. Clinicians should caution women with type 2 diabetes that their risk of severe central hair loss may be increased and should recommend early screening. Conversely, clinicians should screen women with central hair loss for type 2 diabetes. Whether successful treatment of type 2 diabetes might protect AA women from central hair loss remains to be determined.

Appendix A. Supplementary data

Supplementary data to this article can be found online at <https://doi.org/10.1016/j.ijwd.2019.05.010>.

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