

tabulated (Table II). No patient who continued LDOM reported new cardiac diagnoses or morbidity, including pericardial effusions or pericarditis.

Results from this retrospective series indicate increased scalp hair growth (33/51; 65%) and decreased hair shedding (14/51; 27%) with LDOM. Patients with nonscarring alopecia were most likely to acknowledge and exhibit clinical improvement (Supplemental Discussion available via Mendeley at <https://data.mendeley.com/datasets/4sccxmrfzm/1>).

The 5 Cs of LDOM are convenience, cosmesis, cost savings, cotherapy feasibility, and compliance.³ The newly proposed sixth C is “crown efficacy,” exhibited by increased hair growth at this scalp region (Supplemental Figs 1-6, <https://data.mendeley.com/datasets/4sccxmrfzm/1/files/a99ab998-4da1-42d7-926f-e4de7aca4d73>, <https://data.mendeley.com/datasets/4sccxmrfzm/1/files/b67819a9-3e1a-46a9-9637-e001a434cba9>).

Renée A. Beach, MD, FRCPC,^{a,b} Katherine A. McDonald, MD,^c and Bianca Muylaert Barrett, MD^d

From the Faculty of Medicine^a and Division of Dermatology, Department of Medicine,^c University of Toronto; Women's College Hospital, Toronto, Ontario, Canada^b; and Brazilian Medical Association, Sao Paulo, Brazil.^d

Funding sources: None.

Conflicts of interest: None disclosed.

IRB approval status: Approved by University of Toronto Research Ethics Board, protocol 39255.

Reprints not available from the authors.

Correspondence to: Renée A. Beach, MD, FRCPC, 5th Floor, RKS Clinic, Women's College Hospital, 76 Grenville St, Toronto, ON M5S 1B2, Canada

E-mail: renee.beach@wchospital.ca

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<https://doi.org/10.1016/j.jaad.2020.10.032>

Exposure to terbinafine in pregnancy and risk of preterm birth, small for gestational age, low birth weight, and stillbirth: A nationwide cohort study



To the Editor: Terbinafine is a commonly used antifungal agent. Although it is generally well tolerated in the nonpregnant population, data evaluating the fetal safety are limited. We recently provided data not suggestive of a risk of major birth defects or spontaneous abortion when terbinafine is used in early pregnancy.¹ Here, we investigated whether terbinafine exposure during pregnancy is associated with preterm birth, small for gestational age, low birth weight, and stillbirth.

Through linkage of nationwide registries, we identified all pregnancies in Denmark (January 1997 to December 2016), including individual-level data on exposure, outcomes, and covariates. The study was designed as previously conducted.^{1,2} Pregnancy records with overlapping pregnancies, implausible/missing gestational age, and missing information on birth weight (for these analyses) were excluded. Distinct cohorts were constructed for each outcome analysis. Oral terbinafine exposure was defined as filled prescriptions from 2 weeks before and throughout pregnancy. Outcomes were preterm birth (defined as birth before 37 completed gestational weeks), small for gestational age (below the 10th percentile of the gestational-age-specific birth weight), low birth weight (<2500 g), and stillbirth (fetal death after gestational week 22). Terbinafine-exposed pregnancies were compared with unexposed ones to any antifungal drugs from 1 year before through pregnancy, matched (1:10 ratio) on propensity scores (estimated by logistic regression). Associations were assessed by risk ratios (RRs), except for stillbirth, which was assessed by hazard ratio, computed by Cox regression (version 9.4, SAS). Secondary analyses examined the associations by different exposure definitions, as well as in comparison to topical terbinafine-exposed pregnancies. The Danish Data Protection Agency approved the study. Ethical and informed consent was not required.

From a source cohort of 1,650,649 pregnancies, up to 942 oral terbinafine-exposed and 9420 unexposed individuals were included in the matched cohorts (Table I); baseline characteristics were well balanced. In matched analyses, preterm birth occurred in 37 terbinafine-exposed pregnancies (6.2%) and 344 unexposed ones (5.7%) (RR 1.08; 95% confidence interval [CI] 0.77-1.49); small for gestational age in 55 terbinafine-exposed

Table I. Baseline characteristics of matched oral terbinafine–exposed and –unexposed pregnancy study cohorts based on propensity scores*

Characteristics	For analysis of preterm birth [†]		For analysis of SGA and low birth weight		For analysis of stillbirth [‡]	
	Terbinafine (n = 601)	Unexposed (n = 6010)	Terbinafine (n = 611)	Unexposed (n = 6110)	Terbinafine (n = 942)	Unexposed (n = 9420)
GA at first filled prescription, median (IQR)	12 (–2 to 32)		13 (–1 to 34)		13 (–2 to 32)	
Age at pregnancy onset, y						
≤19	9 (1.5)	112 (1.9)	9 (1.5)	97 (1.6)	39 (4.1)	406 (4.3)
20-24	57 (9.5)	607 (10.1)	57 (9.3)	633 (10.4)	112 (11.9)	1143 (12.1)
25-29	180 (30.0)	1703 (28.3)	183 (30.0)	1752 (28.7)	255 (27.1)	2490 (26.4)
30-34	235 (39.1)	2473 (41.2)	237 (38.8)	2474 (40.5)	305 (32.4)	3143 (33.4)
≥35	120 (20.0)	1115 (18.6)	125 (20.5)	1154 (18.9)	231 (24.5)	2238 (23.8)
Married or living with partner	511 (85.0)	5223 (86.9)	520 (85.1)	5283 (86.5)	739 (78.5)	7439 (79.0)
Place of birth						
Denmark	485 (80.7)	4903 (81.6)	496 (81.2)	5018 (82.1)	777 (82.5)	7763 (82.4)
Europe	40 (6.7)	373 (6.2)	39 (6.4)	367 (6.0)	54 (5.7)	511 (5.4)
Outside of Europe	76 (12.7)	734 (12.2)	76 (12.4)	725 (11.9)	111 (11.8)	1146 (12.2)
Region of residence						
Capital Region of Denmark	178 (29.6)	1798 (29.9)	182 (29.8)	1883 (30.8)	507 (53.8)	5169 (54.9)
Region Zealand	68 (11.3)	648 (10.8)	69 (11.3)	710 (11.6)	69 (7.3)	593 (6.3)
Region of Southern Denmark	119 (19.8)	1206 (20.1)	121 (19.8)	1198 (19.6)	122 (13.0)	1213 (12.9)
Central Denmark Region	172 (28.6)	1671 (27.8)	175 (28.6)	1681 (27.5)	180 (19.1)	1837 (19.5)
North Denmark Region	64 (10.7)	687 (11.4)	64 (10.5)	638 (10.4)	64 (6.8)	608 (6.5)
Gross household income, quartile						
1	146 (24.3)	1336 (22.2)	148 (24.2)	1385 (22.7)	232 (24.6)	2221 (23.6)
2	135 (22.5)	1322 (22.0)	136 (22.3)	1398 (22.9)	219 (23.3)	2211 (23.5)
3	151 (25.1)	1599 (26.6)	153 (25.0)	1493 (24.4)	215 (22.8)	2194 (23.3)
4	169 (28.1)	1753 (29.2)	174 (28.5)	1834 (30.0)	276 (29.3)	2794 (29.7)
Education level, y						
<12	135 (22.5)	1327 (22.1)	135 (22.1)	1336 (21.9)	268 (28.5)	2653 (28.2)
12-13	104 (17.3)	1122 (18.7)	105 (17.2)	1032 (16.9)	152 (16.1)	1522 (16.2)
14-15	143 (23.8)	1435 (23.9)	144 (23.6)	1463 (23.9)	212 (22.5)	2162 (23.0)
>15	219 (36.4)	2126 (35.4)	227 (37.2)	2279 (37.3)	310 (32.9)	3083 (32.7)
Year of pregnancy onset						
1997-2000	81 (13.5)	856 (14.2)	79 (12.9)	858 (14.0)	139 (14.8)	1499 (15.9)
2001-2004	125 (20.8)	1214 (20.2)	128 (21.0)	1259 (20.6)	182 (19.3)	1780 (18.9)
2005-2008	152 (25.3)	1599 (26.6)	153 (25.0)	1719 (28.1)	226 (24.0)	2326 (24.7)
2009-2012	139 (23.1)	1409 (23.4)	145 (23.7)	1315 (21.5)	223 (23.7)	2138 (22.7)
2013-2016	104 (17.3)	932 (15.5)	106 (17.4)	959 (15.7)	172 (18.3)	1677 (17.8)
Parity						
1	261 (43.4)	2641 (43.9)	267 (43.7)	2805 (45.9)	NA	NA
2	203 (33.8)	1963 (32.7)	208 (34.0)	2007 (32.9)	NA	NA
≥3	137 (22.8)	1406 (23.4)	136 (22.3)	1298 (21.2)	NA	NA
Multiple-birth pregnancy	17 (2.8)	148 (2.5)	17 (2.8)	160 (2.6)	NA	NA
Smoking during pregnancy	91 (15.1)	985 (16.4)	92 (15.1)	914 (15.0)	NA	NA
Previous pregnancy with same adverse fetal outcome	18 (3.0)	148 (2.5)	61 (10.0)	541 (8.9)	4 (0.4)	21 (0.2)
Antidiabetic drug use in past year	9 (1.5)	76 (1.3)	9 (1.5)	77 (1.3)	11 (1.2)	94 (1.0)
Drugs used for IVF in past 3 mo	29 (4.8)	266 (4.4)	33 (5.4)	387 (6.3)	36 (3.8)	366 (3.9)
No. of drugs used in past year						
1-2	193 (32.1)	1955 (32.5)	198 (32.4)	1906 (31.2)	298 (31.6)	2959 (31.4)
3-4	158 (26.3)	1522 (25.3)	160 (26.2)	1620 (26.5)	248 (26.3)	2559 (27.2)
≥5	198 (33.0)	1990 (33.1)	201 (32.9)	2093 (34.3)	314 (33.3)	3101 (32.9)

Continued

Table I. Cont'd

Characteristics	For analysis of preterm birth [†]		For analysis of SGA and low birth weight		For analysis of stillbirth [‡]	
	Terbinafine (n = 601)	Unexposed (n = 6010)	Terbinafine (n = 611)	Unexposed (n = 6110)	Terbinafine (n = 942)	Unexposed (n = 9420)
No. of hospitalizations in past year						
1	85 (14.1)	719 (12.0)	87 (14.2)	742 (12.1)	136 (14.4)	1328 (14.1)
2	13 (2.2)	108 (1.8)	13 (2.1)	96 (1.6)	24 (2.6)	171 (1.8)
≥3	6 (1.0)	41 (0.7)	6 (1.0)	50 (0.8)	11 (1.2)	88 (0.9)
No. of outpatient contacts in past year						
1	93 (15.5)	805 (13.4)	95 (15.6)	912 (14.9)	155 (16.5)	1480 (15.7)
2	32 (5.3)	305 (5.1)	33 (5.4)	290 (4.8)	54 (5.7)	445 (4.7)
≥3	14 (2.3)	108 (1.8)	14 (2.3)	110 (1.8)	25 (2.7)	207 (2.2)

GA, Gestational age (in days); IQR, interquartile range; IVF, in vitro fertilization; NA, not available; SGA, small for gestational age.

*Values are presented as No. (%) unless otherwise stated. The distinct cohorts for the analyses of preterm birth, small for gestational age, and low birth weight were derived from live birth pregnancies only, whereas the cohort for the stillbirth analysis was derived from all pregnancies.

[†]The exposure window for terbinafine exposure ended on last of gestational week 37 for the analysis of preterm birth.

[‡]The gestational age at first filled prescription (index date) was added as a matching criterion for the analysis of stillbirth (ie, unexposed pregnancies were eligible as matches had they lasted up until the index date).

pregnancies (9.0%) and 589 unexposed ones (9.6%) (RR 0.93; 95% CI 0.72-1.22); and low birth weight in 20 terbinafine-exposed pregnancies (3.3%) and 297 unexposed ones (4.9%; RR 0.67; 95% CI 0.43-1.05) (Table II). Stillbirths occurred in 4 terbinafine-exposed pregnancies (0.4%) and 31 unexposed ones (0.3%) (hazard ratio 1.46; 95% CI 0.52-4.14). Secondary analyses showed similar results while including up to 5715 topical terbinafine-exposed pregnancies (Table II).

This nationwide cohort study found no association between oral or topical terbinafine use in pregnancy and risk of preterm birth, small for gestational age, low birth weight, and stillbirth, thus expanding on previous findings.^{1,3,4} Although the data suggest that terbinafine does not constitute a fetal risk, findings should be confirmed in other independent populations. The stillbirth analysis should be interpreted in light of the low number of cases: 0.4 cases per 100 oral terbinafine-exposed pregnancies compared with 0.3 among unexposed ones. Findings may provide reassurance in situations in which terbinafine exposure in pregnancy has occurred and help inform clinical decision making when treatment is clinically needed.

Limitations include that nonadherence to the dispensed terbinafine would bias toward the null. Also, residual confounding cannot be excluded; particularly, a concern would be a

true association masked by inherited unadjusted factors.

Niklas Worm Andersson, MD,^{a,b} Simon Francis Thomsen, MD, PhD, DMSc,^{c,d} and Jon Trærup Andersen, MD, PhD^{b,d}

From the Department of Epidemiology Research, Statens Serum Institut, Copenhagen, Denmark^a; Department of Clinical Pharmacology, Copenhagen University Hospital Bispebjerg and Frederiksberg, Denmark^b; and Department of Dermatology, Bispebjerg Hospital and Department of Biomedical Sciences^c and Faculty of Health and Medical Sciences,^d University of Copenhagen, Denmark.

Funding sources: None.

Conflicts of interest: Dr Thomsen reports receiving grants and personal fees from Novartis outside the submitted work. Drs Andersson and Andersen have no conflicts of interest to declare.

IRB approval status: Not applicable.

Reprints not available from the authors.

Correspondence to: Niklas Worm Andersson, MD, Department of Epidemiology Research, Statens Serum Institut, Artillerivej 5, Copenhagen S 2300, Denmark

E-mail: nwandersson@gmail.com

Table II. Analyses of the association between terbinafine use and the fetal safety outcomes compared with propensity score–matched comparison pregnancies

	Exposed		Comparison		Relative risk ratio (95% CI)	Absolute risk difference, no. events per 1000 pregnancies (95% CI)
	Pregnancies, no.	Events, no. (%)	Pregnancies, no.	Events, no. (%)		
Preterm birth						
Main analysis (oral terbinafine vs unexposed)	601	37 (6.2)	6010	344 (5.7)	1.08 (0.77 to 1.49)	4.3 (–15.8 to 24.4)
Secondary analyses (oral terbinafine vs unexposed)						
Cumulative oral terbinafine dose >7000 mg	208	13 (6.3)	6010	344 (5.7)	1.09 (0.64 to 1.87)	5.3 (–28.2 to 38.7)
Filled prescriptions for oral terbinafine after pregnancy onset only	476	32 (6.7)	6010	344 (5.7)	1.17 (0.82 to 1.67)	10.0 (–13.3 to 33.2)
Additional comparisons						
Topical terbinafine vs unexposed*	4930	304 (6.2)	49,300	3239 (6.6)	0.94 (0.84 to 1.05)	–4.0 (–11.1 to 3.0)
Oral vs topical terbinafine exposed†	601	37 (6.2)	2277	113 (5.0)	1.24 (0.87 to 1.78)	11.9 (–9.2 to 33.1)
Small for gestational age						
Main analysis (oral terbinafine vs unexposed)	611	55 (9.0)	6110	589 (9.6)	0.93 (0.72 to 1.22)	–6.4 (–30.3 to 17.5)
Secondary analyses (oral terbinafine vs unexposed)						
Cumulative oral terbinafine dose >7000 mg	213	21 (9.9)	6110	589 (9.6)	1.02 (0.68 to 1.55)	2.2 (–38.5 to 42.9)
Filled prescriptions for oral terbinafine after pregnancy onset only	487	41 (8.4)	6110	589 (9.6)	0.87 (0.64 to 1.18)	–12.2 (–38.0 to 13.5)
Additional comparisons						
Topical terbinafine vs unexposed*	5214	482 (9.2)	52,140	5126 (9.8)	0.94 (0.86 to 1.03)	–5.9 (–14.1 to 2.4)
Oral vs topical terbinafine-exposed†	610	55 (9.0)	2318	204 (8.8)	1.02 (0.75 to 1.40)	2.2 (–23.3 to 27.6)
Low birth weight						
Main analysis (oral terbinafine vs unexposed)	611	20 (3.3)	6110	297 (4.9)	0.67 (0.43 to 1.05)	–15.9 (–31.0 to 0.8)
Secondary analyses (oral terbinafine vs unexposed)						
Cumulative oral terbinafine dose >7000 mg	213	9 (4.2)	6110	297 (4.9)	0.87 (0.45 to 1.66)	–6.4 (–21.2 to 33.9)
Filled prescriptions for oral terbinafine after pregnancy onset only	487	16 (3.3)	6110	297 (4.9)	0.68 (0.41 to 1.11)	–15.6 (–32.3 to 1.1)
Additional comparisons						
Topical terbinafine vs unexposed*	5214	203 (3.9)	52,140	2519 (4.8)	0.81 (0.70 to 0.93)	–9.4 (–14.9 to –3.8)
Oral vs topical terbinafine exposed†	610	20 (3.3)	2318	94 (4.1)	0.80 (0.49 to 1.31)	–7.8 (–24.0 to 8.5)

Continued

Table II. Cont'd

	Exposed		Comparison		Relative risk ratio (95% CI)	Absolute risk difference, no. events per 1000 pregnancies (95% CI)
	Pregnancies, no.	Events, no. (%)	Pregnancies, no.	Events, no. (%)		
Stillbirth					Hazard ratio (95% CI)	
Main analysis (oral terbinafine vs unexposed)	942	4 (0.4)	9420	31 (0.3)	1.46 (0.52 to 4.14)	0.9 (−2.0 to 7.6)
Secondary analyses (oral terbinafine vs unexposed)						
Cumulative oral terbinafine dose >7000 mg	305	0	9420	31 (0.3)	NA	NA
Filled prescriptions for oral terbinafine after pregnancy onset only	744	3 (0.4)	9420	31 (0.3)	1.38 (0.42 to 4.50)	0.7 (−2.3 to 8.6)
Additional comparisons						
Topical terbinafine vs unexposed*	5715	18 (0.3)	57150	186 (0.3)	0.95 (0.59 to 1.55)	to 0.1 (−1.6 to 1.4)
Oral vs topical terbinafine exposed ^{†‡}	751	3 (0.4)	1630	8 (0.5)	0.90 (0.24 to 3.39)	to 0.9 (−6.6 to 4.7)

CI, Confidence interval; NA, not applicable.

*Topical terbinafine exposed defined as at least 1 filled prescription after pregnancy onset and throughout the respective exposure windows, matched in a 1:10 ratio with unexposed according to propensity scores. Gestational age at first filled prescription median was 136 days (interquartile range 57-207 days).

[†]Oral terbinafine–exposed pregnancies were matched with up to 4 topical terbinafine–exposed pregnancies.

[‡]Matched on propensity scores and the gestational week at index date, with medians of 3 (interquartile range 1-6) and 5 (interquartile range 3-10) for the matched oral terbinafine– and topical terbinafine–exposed pregnancies, respectively.

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<https://doi.org/10.1016/j.jaad.2020.10.034>

Prevalence of psoriasis among adults in the US 2009-2010 and 2013-2014 National Health and Nutrition Examination Surveys



To the Editor: Recent studies have linked psoriasis with emerging comorbidities, thus requiring up-to-date prevalence of psoriasis to quantify a changing disease burden.¹ As a representative database of health status among US adults, the National Health and Nutrition Examination Survey (NHANES) produces reliable estimates of psoriasis prevalence and

comorbidities. This study aimed to update psoriasis prevalence rates among US adults in the most recent 2013-2014 NHANES cycle.

After National Center for Health Statistics ethics board approval, sample weights were computed to adjust for survey design and nonresponse. Psoriasis diagnosis was determined from definitive (yes/no) responses to the question “Have you even been told by a physician or other health care professional that you had psoriasis?” Using SAS (Version 9.4, SAS Institute Inc, Cary, NC) survey procedures, we reported prevalence and demographic information as percentages or means with 95% confidence intervals (CIs). Logistic regression models were constructed to examine associated factors using the following covariates: age, sex, race, income, educational attainment, and marital status. A χ^2 test was used to determine whether psoriasis prevalence rates varied between the 2009-2010 and 2013-2014 NHANES cycles.

Among 5588 participants aged 20 to 150 years, 5582 participants provided yes/no responses to diagnosis and were analyzed. Psoriasis prevalence was 2.8% (95% CI 2.1%-3.6%) (Table D). The multiracial ethnicity had the highest prevalence of