# Lichen planopilaris and thyroid disease: systematic review and meta-analysis

## Kevin Phan<sup>1</sup>, Saxon D. Smith<sup>2</sup>

<sup>1</sup>Department of Dermatology, Liverpool Hospital, Sydney, Australia; <sup>2</sup>Department of Dermatology, Royal North Shore Hospital, St Leonards, Australia

Correspondence to: Kevin Phan, MD. Department of Dermatology, Liverpool Hospital, Sydney, Australia. Email: kphan.vc@gmail.com.

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Lichen planopilaris (LPP) is a follicular subtype of lichen planus that is characterized by chronic scalp inflammation and scarring, leading to scarring alopecia (1). The etiology of LPP is thought to have an autoimmune pathogenesis, however, the precise mechanisms are not known and there is currently a lack of understanding regarding associated comorbidities. A number of studies have shown a significant association between lichen planus and thyroid disease (2), although the relationship between LPP and thyroid disease is unclear (3-5). We conducted a systematic review and meta-analysis to test the association between LPP and thyroid disease.

Electronic searches were performed using Ovid Medline, PubMed, Cochrane Central Register of Controlled Trials (CCTR), Cochrane Database of Systematic Reviews (CDSR), ACP Journal Club, and Database of Abstracts of Review of Effectiveness (DARE) from their dates of inception to July 2019. Search terms included: "lichen planopilaris" or "frontal fibrosing alopecia", combined with "hyperthyroidism", "hypothyroidism", "thyroid disease", "thyroiditis", "thyroid cancer". Eligible studies were those which compared dyslipidemia in cases of LPP versus controls. Case reports, reviews and studies without controls were excluded. Odds ratio (OR) was calculated using random effects model, heterogeneity was assessed using the I<sup>2</sup> statistic. Analyses were performed using Review Manager Version 5.3 (Cochrane Collaboration, Oxford, United Kingdom). Study quality was assessed using the Newcastle-Ottawa Scale.

A total of 451 references were identified through electronic database searches. After applying exclusion and inclusion criteria, a final 6 studies were included for metaanalysis (*Table 1*). Pooled meta-analysis demonstrated no significant association between LPP and any thyroid disorders [OR 1.23; 95% confidence interval (CI), 0.87–1.73, P=0.24], with no significant heterogeneity ( $I^2$ =40%, P=0.07). Subgroup analysis was performed, with no significant association found between LPP and hyperthyroidism (OR 1.35; 95% CI, 0.91–1.99; P=0.14;  $I^2$ =0%) nor with hypothyroidism (OR 1.64; 95% CI, 0.73–3.70; P=0.23;  $I^2$ =68%), nor with other thyroid disorders (OR 0.85; 95% CI, 0.57–1.27; P=0.43;  $I^2$ =0%) (*Figure 1*).

This pooled analysis of existing case-control studies to date does not support an association between LPP and any thyroid disease, hyperthyroidism or hypothyroidism. Our findings contradict those reported for lichen planus (2). As such, this suggests that there are likely differences in the nuances underlying the pathogenesis of LPP versus lichen planus. Our study has several limitations. The included studies were mostly retrospective in design, thus susceptible to selection and assessment bias. The analysed effect sizes were unadjusted, and as such susceptible to influence by confounder variables. Large database studies may have errors in coding disease parameters, and there is heterogeneity in terms of criteria for diagnosis of thyroid disorders. Prospective studies with larger numbers of patients are required to reaffirm the findings in the present study.

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#### Table 1 Study characteristics

Study	Location	Design	Cases/ controls	Females % (cases/control)	Mean age in years (cases/control)	Adjustment	NOS
Brankov et al., Int J Women's Dermatology, 2018	nen's USA		334/78	93.1/79.5	54.77/52.19	None	7
Fertig et al., Int J Dermatology, 2018	USA	Case-control	206/323	88.35/83.28	NA	Age, gender, ethnicity, race	6
Manatis-Lornell <i>et al., J American</i> Association Derm, 2019	USA	USA Case-control		85.3/85.1	61.7/65	None	7
Moreno-Arrones et al., Clinical and Experimental Derm, 2018	Spain	Case-control	347/308	50.4/49.6	60/58.4	None	7
Nguyen et al., US Endocrinology, 2016	USA	Case-control	28/31	NA	NA	Age, gender, TSH	6
Toosi et al., Iranian J Derm, 2015	Iran	Case-control	26/30	69.2/70	52.5/54.5	None	6

NA, not reported; NOS, Newcastle Ottawa Score for study quality.

			LPP	Control		Odds Ratio	Odds Ratio
Study or Subgroup	log[Odds Ratio]	SE	Total	Total	Weight	IV, Random, 95% C	IV, Random, 95% Cl
Hyperthyroidism							
Brankov 2018 (Hyperthyroidism)	-0.073	1.132	334	78	2.2%	0.93 [0.10, 8.55]	
Fertig 2018 (Hyperthyroidism)	-0.464	0.928	206	323	3.1%	0.63 [0.10, 3.88]	
Manatis-Lornell 2019 (hyperthyroidism)	-0.186	0.713	232	194	4.8%	0.83 [0.21, 3.36]	
Moreno-Arrones 2018 (hyperthyroidism)	0.364643	0.223105	347	308	17.5%	1.44 [0.93, 2.23]	
Toosi 2015 (Hyperthyroidism)	0.936	0.91	26	30	3.2%	2.55 [0.43, 15.17]	
Subtotal (95% CI)			1145	933	30.8%	1.35 [0.91, 1.99]	◆
Heterogeneity: Tau <sup>2</sup> = 0.00; Chi <sup>2</sup> = 1.82, df	f = 4 (P = 0.77); l <sup>2</sup> =	0%					
Test for overall effect: Z = 1.49 (P = 0.14)							
Hypothyroidism							
Brankov 2018 (Hypothyroidism)	1.095	0.359	334	78	12.0%	2.99 [1.48, 6.04]	
Fertig 2018 (Hypothyroidism)	-0.644	0.448	206	323	9.4%	0.53 [0.22, 1.26]	
Manatis-Lornell 2019 (hypothyroidism)	0.476	0.263	232	194	15.7%	1.61 [0.96, 2.70]	
Moreno-Arrones 2018 (hypothyroidism)	0.019803	1.185284	19	58	2.0%	1.02 [0.10, 10.41]	
Toosi 2015 (Hypothyroidism)	3.155	1.489	26	30	1.3%	23.45 [1.27, 434.15]	
Subtotal (95% CI)			817	683	40.5%	1.64 [0.73, 3.70]	◆
Heterogeneity: Tau <sup>2</sup> = 0.48; Chi <sup>2</sup> = 12.61, o	df = 4 (P = 0.01); l <sup>2</sup>	= 68%					
Test for overall effect: Z = 1.20 (P = 0.23)							
Other							
Brankov 2018 (other thyroid disease)	-0.211	0.58	334	78	6.6%	0.81 [0.26, 2.52]	
Manatis-Lornell 2019 (other)	-0.151	0.233	232	194	17.0%	0.86 [0.54, 1.36]	
Nguyen 2016 (Thyroid disease)	-0.198	0.692	28	31	5.1%	0.82 [0.21, 3.18]	
Subtotal (95% CI)			594	303	28.7%	0.85 [0.57, 1.27]	◆
Heterogeneity: Tau <sup>2</sup> = 0.00; Chi <sup>2</sup> = 0.01, df	f = 2 (P = 0.99); l <sup>2</sup> =	0%					
Test for overall effect: Z = 0.79 (P = 0.43)							
Total (95% CI)			2556	1919	100.0%	1.23 [0.87, 1.73]	◆
Heterogeneity: Tau <sup>2</sup> = 0.13; Chi <sup>2</sup> = 19.95, o	df = 12 (P = 0.07): I	² = 40%					
Test for overall effect: $Z = 1.18$ (P = 0.24)							0.002 0.1 1 10 500
Test for subgroup differences: $Chi^2 = 3.50$ ,	df = 2 (P = 0.17), l <sup>2</sup>	<sup>2</sup> = 42.9%					Favours no association Favours association

Figure 1 Forest plot assessing the relationship between lichen planopilaris and thyroid diseases (hyperthyroidism, hypothyroidism, and other thyroid disorders) compared to controls.

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### Footnote

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