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PROFESSOR PETER RIIS HANSEN (Orcid ID : 0000-0002-9056-535X)

DR GREGOR JEMEC (Orcid ID : 0000-0002-0712-2540)

DR CHRISTINA ELLERVIK (Orcid ID : 0000-0002-3088-4375)

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### Thyroid function in psoriasis

P. R. Hansen<sup>a,b</sup>, J. Lynggaard Isaksen<sup>c,d</sup>, G. Borut Jemec<sup>b,e</sup>, C. Ellervik<sup>b,f,g\*</sup> J. Kim Kanthers<sup>c\*</sup>

<sup>a</sup>Department of Cardiology, Herlev and Gentofte Hospital, DK-2900 Hellerup, Denmark.

<sup>b</sup>Department of Clinical Medicine, University of Copenhagen, Copenhagen, Denmark.

<sup>c</sup>Laboratory for Experimental Cardiology, Department of Biomedical Sciences, Panum Institute, DK-2200 Copenhagen N, Denmark.

<sup>d</sup>Department of Health Science and Technology, Aalborg University, DK-9220 Aalborg Oest, Denmark.

<sup>e</sup>Department of Dermatology, Zealand University Hospital, DK-4000 Roskilde, Denmark.

<sup>f</sup>Department of Laboratory Medicine, Boston Children's Hospital, Harvard Medical School, Boston, MA, USA.

<sup>g</sup>Department of Production, Research and Innovation, Region Zealand, DK-4180 Sorø, Denmark.

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Corresponding author: Peter Riis Hansen MD DMSc PhD; prh@dadlnet.dk

Psoriasis has been associated with other autoimmune diseases, e.g. inflammatory bowel disease and autoimmune thyroid disease.<sup>1</sup> These diseases may share genetic susceptibility loci and autoimmune mechanisms including interleukin-17-dependent pathways.<sup>2-4</sup> However, the relationship between psoriasis and autoimmune thyroid disease remains unclear and a recent meta-analysis of available evidence concluded that more data are needed.<sup>5</sup> Therefore, we examined thyroid function in a population-based sample of psoriasis patients.

Thyroid function was assessed in non-fasting blood samples from 21,186 subjects >20 years who participated in the Danish General Suburban Population Study<sup>6</sup> including 1173 (5.5%) with self-reported psoriasis determined by an affirmative response to the question 'Do you suffer from or have you suffered from psoriasis?'. Plasma levels of thyroid-stimulating hormone (TSH), free

thyroxine (fT4), total triiodothyronine (tT3), and thyroid peroxidase antibodies (TPO-Abs) were measured with immunoassays (Cobas 6000 analyzer [Roche, Basel, Switzerland] and Brahms Kryptor [Hennigsdorf, Germany]). TPO-Ab levels greater than 60 U/mL were considered positive. Self-reported information included use of medication for hyper- or hypothyroidism, and answer (yes or no) to the statement that 'according to my general practitioner (GP), I suffer from hyperthyroidism or hypothyroidism'. Subclinical hyperthyroidism and hypothyroidism were defined as TSH<0.4 mIU/L and TSH>3.8 mIU/L, respectively, with normal fT4 and tT3 levels, in absence of self-reported use of thyroid medication or GP diagnosis of hyper- or hypothyroidism. Clinical hyperthyroidism was defined as TSH<0.4 mIU/L and increased fT4 and/or tT3 levels, self-reported use of medication for hyperthyroidism and/or a GP diagnosis of hereof. Clinical hypothyroidism was defined as TSH>3.8 mIU/L and decreased fT4 and/or tT3 levels, self-reported use of medication for hypothyroidism and/or a GP diagnosis hereof. Patients with psoriasis (n=1,127 due to missing data on smoking [n=40] and body mass index [BMI, n=6]) were matched 1:5 for sex, age, BMI, and smoking with controls (n=5,635) without the disease. The study was approved by the regional ethical committee (SJ-113, SJ-114, SJ-191) and the Danish Data Protection Agency.

Characteristics of the two groups are shown in Table 1. Patients with psoriasis had increased levels of tT3 ( $1.69 \pm 0.32$  vs.  $1.72 \pm 0.33$  nmol/L;  $p=0.01$ ). Further adjustment for use of contraceptive pills, lipid levels, albumin, and high sensitive C-reactive protein, respectively, did not considerably change this result. Levels of TSH, fT4 and TPO-Abs were similar and percentages of subjects with TPO-Ab positivity, self-reported use of medication for hyper- or hypothyroidism, self-reported GP diagnosis hereof, and clinical and subclinical hyper- or hypothyroidism, respectively, were not significantly different between the two groups.

In this study, self-reported psoriasis was linked with increased levels of tT3 but not with TPO-Ab positivity and clinical or subclinical thyroid dysfunction. Mechanisms underlying increased tT3 (with normal fT4 and TSH), and its significance in subjects with psoriasis remain to be determined. To our knowledge, the results represent the largest reported data on thyroid function in psoriasis and are in line with recent results from individuals with psoriasis (n=173) in the population-based Rotterdam study where no changes of TSH and fT4, and TPO-Ab positivity was found.<sup>5</sup> In that report, T3 was not measured and an accompanying meta-analysis suggested that TPO-Ab positivity and hyper- or hypothyroidism may be associated with psoriasis, albeit that studies were heterogeneous, e.g. with different definitions of psoriasis/psoriatic arthritis and/or thyroid dysfunction.<sup>5,7,8</sup> Limitations of our study include that psoriasis was self-reported (leaving room for recall bias and information bias), psoriasis severity and treatment were not assessed, and other thyroid function tests, e.g. free T3 and reverse T3 levels were not measured. The results indicate that on a population scale psoriasis may be linked with increased levels of tT3 and more studies of thyroid function in psoriasis are warranted.

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**Table 1. Clinical characteristics of the psoriasis and the matched comparison group.**

	Psoriasis (n=1,127)	Comparison group (n=5,635)	p
Age, years	56.9±12.2	56.9±13.5	0.91*
Males, % (n)	45.1 (508)	45.1 (2540)	1.00*
BMI, kg/m <sup>2</sup>	27.2±5.0	27.2±4.8	0.71*
TSH, mIU/L	2.09±1.70	2.11±2.33	0.83
Total T3, nmol/L	1.72±0.33	1.69±0.32	0.01
Free T4, pmol/L	15.65±2.38	15.60±2.29	0.49
TPO-Abs, U/mL (median [IQR])	19 [12;29]	20 [14;28]	0.16 <sup>#</sup>
TPO-Abs> 60 U/mL, % (n)	11.8 (66)	12.8 (533)	0.57
Medication for hyperthyroidism, % (n)	1.4 (16)	1.1 (59)	0.43
Medication for hypothyroidism, % (n)	5.0 (55)	4.4 (243)	0.34
GP diagnosis of hyperthyroidism, % (n)	2.6 (28)	2.3 (125)	0.64
GP diagnosis of hypothyroidism, % (n)	6.2 (67)	5.3 (289)	0.25
Thyroid status <sup>†</sup> , % (n)			0.72
Clinical hyperthyroidism	2.9 (33)	2.4 (132)	
Subclinical hyperthyroidism	1.4 (16)	1.3 (74)	
Euthyroidism	84.4 (948)	85.7 (4812)	
Subclinical hypothyroidism	5.5 (62)	5.5 (309)	
Clinical hypothyroidism	5.7 (64)	5.2 (290)	
hs-CRP, mg/L (median [IQR])	1.5 (0.8-3.4)	1.5 (0.8-3.2)	0.33 <sup>#</sup>
Use of oral contraceptives, % (n)	4.4 (49)	4.9 (273)	0.53

\*Populations matched on this parameter, <sup>#</sup>Statistics performed on logarithm-transformed data, <sup>†</sup>See text. Data are mean±standard deviation unless otherwise indicated. Continuous and categorical variables were compared using Student's t-test and  $\chi^2$  test, respectively. A larger table including data on smoking, blood pressure, lipids, and albumin is available upon request to the corresponding author. BMI, body mass index; T3, triiodothyronine; T4, thyroxine; TSH, thyroid-stimulating hormone; TPO-Abs, thyroid peroxidase antibodies; GP, general practitioner; hs-CRP, high sensitive-C-reactive protein; IQR, inter-quartile range