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Burden of respiratory comorbidities in patients with atopic dermatitis and psoriasis

Running head

Atopic dermatitis, psoriasis and respiratory comorbidities

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Research letter

Atopic dermatitis (AD), a skin disease with an estimated lifetime prevalence of up to 20%, represents a major global healthcare burden.¹ Patients with AD have a propensity to develop asthma due to a combination of genetic, immunological and environmental factors, yet descriptive studies on the impact of respiratory diseases in adults with AD are scarce.² In contrast, psoriasis, another chronic inflammatory skin disease, has been associated with respiratory comorbidities such as chronic obstructive pulmonary disease (COPD)³, asthma⁴ and obstructive sleep apnea (OSA).⁵ Respiratory diseases cause considerable morbidity and mortality worldwide.⁶ Quantitative assessments of the respiratory comorbidity associated with AD and psoriasis is pivotal, yet this topic remains understudied. We investigated the burden of respiratory diseases in Danish adults with AD compared with patients with psoriasis and general population controls, respectively.

Utilizing data from Danish administrative registries we identified all Danish adults (aged ≥ 18 years) with an inpatient or outpatient (ambulatory) diagnosis of AD or psoriasis during the study period (January 1st 1995 – December 31st 2012). Patients with AD were matched (on age and sex) with 10 general population controls. Patients were classified with severe AD and severe psoriasis,

respectively, if they received appropriate systemic therapy. For detailed description of the methodology, see online supplementary materials.

A total of 7,937 patients with AD, 24,505 patients with psoriasis and 79,370 general population controls were identified. Baseline characteristics are presented in online supplementary materials. Asthma was highly prevalent in the AD group (18.0%) compared with psoriasis (2.8%) and general population controls (2.0%) (Table 1). Logistic regression analyses yielded pronounced associations between asthma and AD, compared with psoriasis (adjusted odds ratio [aOR] 5.95; 5.38-6.59) and general population controls (aOR 8.79; 8.08-9.56). Similar trends were found for status asthmaticus and asthma related therapies (inhaled corticosteroids and inhaled adrenergics). COPD occurred less frequently in patients with AD compared with psoriasis (7.4% vs 2.6%; aOR 0.62; 0.53-0.72), as well as use of COPD related therapies (anticholinergics). In patients with severe AD, however, COPD risk was significantly increased compared with controls (3.5% vs 2.1%; aOR 1.42; 1.17-1.73). Prevalence of OSA was significantly lower in patients with AD compared with psoriasis (1.5% vs 2.2%; aOR of 0.69; 0.56-0.86) yet, increased compared with the general population (1.5% vs 1.0%; aOR 1.24; 1.00-1.53). Lung cancer was less prevalent in the AD group compared with psoriasis (0.9% vs 2.0%; aOR 0.77; 0.59-0.99). Use of smoking cessation drugs was significantly less common in patients with AD compared with patients with psoriasis (5.8% vs 7.0%; aOR of 0.70; 0.62-0.78), but more patients with severe AD had used these drugs compared with general population controls (6.8% vs 4.1%; aOR 1.30; 1.14-1.50). Overall, use of continuous positive airway pressure, non-invasive ventilation and medical ventilator were more prevalent in patients with psoriasis than patients with AD. In patients with severe AD, all in-patient procedures were significantly increased compared with the general population.

The association with asthma was considerably stronger for AD than for psoriasis, suggesting that asthma in psoriasis overall may be more of academic interest than being clinically important.

Smoking related endpoints were more prevalent in patients with psoriasis as expected, yet we found

that patients with severe AD had an augmented smoking-related risk profile compared with general population controls. This indicates that smoking may be regarded as an important risk factor in patients with AD, in particular patients with severe symptoms, which is in line with a recent systematic review.⁷ While cigarette smoking in patients with AD could partially explain the pathway to COPD development, chronic inflammation may also influence the COPD risk.⁸ Although adiposity is most likely the strongest predictor of OSA, an inflammatory component has been suggested as a risk factor. While the association between psoriasis and adiposity is well-established, for patients with AD the association seems to exist in Asians and North Americans but not in Europeans.^{9,10}

Certain limitations apply to interpretation of the present data. Due to the observational and cross-sectional design of the study, causal inference cannot be made. The disease severity definitions were based on systemic therapy as clinical measurements were not available. The measured associations may be underestimated as our access to data was limited to hospital registries and diseases treated in primary care (but not prescribed pharmacotherapy) remain undetected. Lastly, we investigated adults only, and the results cannot be applied to children with AD or psoriasis.

In this nationwide study, we showed that asthma represents a substantial burden in adults with AD, while smoking and obesity-related endpoints dominated in patients with psoriasis. Our results further showed that the burden of smoking-related comorbidities were increased in patients with severe AD compared to general population controls, emphasizing the need of awareness of modifiable risk factors in this patient group.

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Table 1 – Absolute numbers and adjusted odds ratios for association between respiratory disorders and therapy in patients with atopic dermatitis compared with patients with psoriasis and the general population, respectively

	Atopic dermatitis, n (%)	Psoriasis, n (%)	Overall General population, n (%)	AD versus psoriasis			AD versus general population		
				Adjusted OR*	95% CI	p-value	Adjusted OR*	95% CI	p-value
Asthma	1,430 (18.0)	677 (2.8)	1,567 (2.0)	5.95	5.38-6.59	<0.0001	8.79	8.08-9.56	<0.0001
COPD	208 (2.6)	1,818 (7.4)	1,452 (1.8)	0.62	0.53-0.72	<0.0001	1.16	0.99-1.37	0.0730
Unspecified respiratory disease	236 (3.0)	554 (2.3)	437 (0.6)	2.19	1.85-2.58	<0.0001	4.37	3.68-5.20	<0.0001
Status asthmaticus	64 (0.8)	67 (0.3)	76 (0.1)	3.37	2.33-4.88	<0.0001	7.01	4.95-9.94	<0.0001
Obstructive sleep apnea	115 (1.5)	534 (2.2)	751 (1.0)	0.69	0.56-0.86	0.0006	1.24	1.00-1.53	0.0471
Lung cancer	69 (0.9)	491 (2.0)	645 (0.8)	0.77	0.59-0.99	0.0433	0.91	0.69-1.20	0.5103
Inhaled corticosteroids	2,791 (35.2)	4,087 (16.7)	8,522 (10.7)	2.76	2.59-2.93	<0.0001	3.60	3.40-3.82	<0.0001
Inhaled adrenergics	3,859 (48.6)	7,354 (30.0)	14,701 (18.5)	2.30	2.18-2.44	<0.0001	3.19	3.01-3.37	<0.0001
Inhaled anticholinergics	349 (4.4)	1,665 (6.8)	1,550 (2.0)	1.09	0.96-1.24	0.1658	1.86	1.63-2.12	<0.0001
Smoking cessation drugs	462 (5.8)	1,720 (7.0)	3,251 (4.1)	0.70	0.62-0.78	<0.0001	1.11	0.99-1.23	0.0720
Use of CPAP	45 (0.6)	225 (0.9)	219 (0.3)	0.78	0.56-1.08	0.1368	1.54	1.10-2.15	0.0126
Use of NIV	44 (0.6)	410 (1.7)	253 (0.3)	0.51	0.37-0.70	<0.0001	1.36	0.97-1.90	0.0780
Use of mechanical ventilator	186 (2.3)	1,119 (4.6)	1,049 (1.3)	0.73	0.62-0.85	0.0001	1.41	1.19-1.68	0.0001

	Atopic dermatitis, n (%)	Psoriasis, n (%)	Mild disease General population, n (%)	AD versus psoriasis			AD versus general population		
				Adjusted OR*	95% CI	p-value	Adjusted OR*	95% CI	p-value
Asthma	364 (11.0)	364 (2.7)	671 (2.0)	3.21	2.72-3.80	<0.0001	5.21	4.53-6.01	<0.0001
COPD	45 (1.4)	1,074 (7.9)	477 (1.4)	0.33	0.24-0.45	<0.0001	0.76	0.55-1.05	0.0915
Unspecified respiratory disease	21 (0.6)	316 (2.3)	156 (0.5)	0.46	0.29-0.73	0.0009	1.10	0.69-1.75	0.6810
Status asthmaticus	4 (0.1)	38 (0.3)	35 (0.1)	0.57	0.19-1.68	0.3064	0.98	0.35-2.78	0.9690
Obstructive sleep apnea	44 (1.3)	250 (1.8)	288 (0.9)	0.78	0.55-1.09	0.1439	1.28	0.93-1.78	0.1333
Lung cancer	10 (0.3)	265 (2.0)	214 (0.7)	0.30	0.16-0.57	0.0002	0.40	0.21-0.77	0.0059
Inhaled corticosteroids	750 (22.6)	2,201 (16.2)	3,504 (10.6)	1.54	1.39-1.71	<0.0001	2.10	1.90-2.31	<0.0001
Inhaled adrenergics	1,145 (34.5)	3,922 (28.9)	6,104 (18.4)	1.36	1.24-1.48	<0.0001	1.86	1.70-2.03	<0.0001

Inhaled anticholinergics	39 (1.2)	927 (6.8)	521 (1.6)	0.31	0.23-0.44	<0.0001	0.61	0.44-0.86	0.0042
Smoking cessation drugs	146 (4.4)	850 (6.2)	1,361 (4.1)	0.57	0.47-0.68	<0.0001	0.85	0.71-1.02	0.0810
Use of CPAP	15 (0.5)	113 (0.8)	82 (0.3)	0.71	0.41-1.26	0.2427	1.49	0.86-2.61	0.1589
Use of NIV	9 (0.3)	245 (1.8)	88 (0.3)	0.24	0.12-0.48	<0.0001	0.84	0.42-1.68	0.6165
Use of mechanical ventilator	49 (1.5)	659 (4.8)	398 (1.2)	0.46	0.34-0.62	<0.0001	1.02	0.75-1.39	0.9108

	Atopic dermatitis, n (%)	Psoriasis, n (%)	Severe disease						
			General population, n (%)	AD versus psoriasis			AD versus general population		
				Adjusted OR*	95% CI	p-value	Adjusted OR*	95% CI	p-value
Asthma	1,066 (23.1)	313 (2.9)	896 (1.9)	8.16	7.11-9.36	<0.0001	12.41	11.15-13.82	<0.0001
COPD	163 (3.5)	744 (6.8)	975 (2.1)	0.81	0.67-0.97	0.0233	1.42	1.17-1.73	0.0005
Unspecified respiratory disease	215 (4.7)	238 (2.2)	281 (0.6)	3.31	2.72-4.04	<0.0001	6.53	5.34-7.97	<0.0001
Status asthmaticus	60 (1.3)	29 (0.3)	41 (0.1)	5.11	3.21-8.15	<0.0001	12.60	8.22-19.29	<0.0001
Obstructive sleep apnea	71 (1.5)	284 (2.6)	463 (1.0)	0.62	0.47-0.81	0.0005	1.22	0.92-1.61	0.1615
Lung cancer	59 (1.3)	226 (2.1)	431 (0.9)	0.98	0.73-1.32	0.9011	1.21	0.88-1.66	0.2328
Inhaled corticosteroids	2,041 (44.2)	1,886 (17.3)	5,018 (10.9)	3.75	3.46-4.06	<0.0001	5.31	4.92-5.73	<0.0001
Inhaled adrenergics	2,714 (58.7)	3,421 (31.4)	8,597 (18.6)	3.17	2.94-3.42	<0.0001	4.95	4.59-5.33	<0.0001
Inhaled anticholinergics	310 (6.7)	738 (6.8)	1,029 (2.2)	1.54	1.33-1.78	<0.0001	2.64	2.27-3.07	<0.0001
Smoking cessation drugs	316 (6.8)	870 (8.0)	1,890 (4.1)	0.75	0.65-0.87	0.0001	1.30	1.14-1.50	0.0002
Use of CPAP	30 (0.7)	112 (1.0)	137 (0.3)	0.78	0.51-1.18	0.2341	1.55	1.00-2.39	0.0488
Use of NIV	35 (0.8)	165 (1.5)	165 (0.4)	0.73	0.50-1.06	0.0957	1.65	1.10-2.46	0.0148
Use of mechanical ventilator	137 (3.0)	460 (4.2)	651 (1.4)	0.95	0.78-1.16	0.6088	1.69	1.37-2.09	<0.0001

Adjusted for age, sex, socioeconomic status, and number of dermatology visits

CI, confidence interval; COPD, chronic obstructive pulmonary disease; CPAP, continuous positive airway pressure; NIV, non-invasive ventilation; OR, odds ratio