Comorbidity in Atopic Dermatitis

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Saana Kauppi, MD, PhD, conducted her PhD studies at the Department of Dermatology, in Oulu University Hospital, Finland, during the period 2018–2023. Associate Professor Laura Huilaja, MD, PhD, was her main supervisor and the co-supervisors were Professor Kaisa Tasanen-Määttä, MD, PhD, and Professor Markku Timonen, MD, PhD. The opponent was: Associate Professor Maria Lönnrot from the University of Tampere, Finland. The thesis can be found at http://jultika.oulu.fi/Record/isbn978-952-62-3921-7.

Atopic dermatitis (AD) is the most common inflammatory skin disease. Approximately 20% of children and up to 10% of adults carry the disease. The main symptom of the disease is itch, and the clinical picture of AD is characterized by eczematous lesions on typical age-related sites on the skin. Especially severe AD disturbs concentration, working ability and sleep.

The aim of this thesis was to increase knowledge on non-atopic comorbidities associated with AD. Data was obtained from the Finnish Care Register for Health Care (CRHC) and the Finnish Digital Agency (previously Finnish Population Register Centre). CRHC includes all inpatient visits since 1987 and outpatient visits since 1998 in all Finnish hospitals, including psychiatric hospitals. The Finnish Digital Agency maintains registers that include basic information of all Finnish residents.

The thesis was based of three original publications (I–III). The study period started in 1987 and ended in 2014 (I), 2016 (II) or 2018 (III). The ending of the study period was based on the latest data available at the time of statistical analyses. Individuals with at least one (I) or two (II–III) diagnoses of AD recorded in the CRHC were included in AD group. In the original publication I, melanocytic nevi-diagnosed patients served as control population. In the original publications II and III, the control population was formed from a random sample of Finnish residents from the Finnish Digital Agency. The individuals with no recorded information in the CRHC were excluded from the control populations since this group of people may have undiagnosed or unrecorded diseases.

The cases and the controls were searched for psychiatric diseases (I), dermatitis and celiac disease in pediatric age group (II) and eating disorders (III). The final study populations included 57,690 (I), 64,975 (II) and 70,584 (III) AD patients and 40,363 (I), 228,642 (II) and 270,783 control individuals.

At least one mental disorder diagnosis was found in 17.2% of patients with AD compared with 13.1% of melanocytic nevi controls (OR 1.25, 95% CI 1.20–1.30) (I). The most common psychiatric comorbidity diagnosis was depression, found in 10.4% of patients with AD (OR 1.33, 95% CI 1.27–1.39). The association of AD with schizophrenia and bipolar disorders were previously unreported findings of this study. Another new finding was the association between AD and eating disorders (ED), and the strongest associated ED diagnosis at the age of 18 years was bulimia (adjusted OR 2.31, 95% CI 1.54– 3.48) (III). We found a peak onset of eating disorders in adolescence and young adulthood, however the overall prevalence of EDs was relatively low in our study material, being 0.6–0.77%.

In the original publication II, we studied the risk of celiac disease and dermatitis herpetiformis (DH) in pediatric AD population since these autoimmune diseases are highly prevalent in Finland. In addition, no previous publications on the risk of DH in AD patients existed. Significant associations between DH and AD (adjusted OR 9.80, 95% CI 6.15– 15.62), and between celiac disease and AD (adjusted OR 1.92, 95% CI 1.73–2.13) were found. However, the overall prevalence of DH and celiac disease was low in children with AD. Only 71 (0.1%) and 24 (0.01%) DH cases were found in AD vs. control groups, respectively.

From left to right: Professor Kaisa Tasanen-Määttä (supervisor), Associate Professor Laura Huilaja (main supervisor), MD Saana Kauppi (doctoral candidate), Associate Professor Maria Lönnrot (opponent).

The findings of this thesis work increase the knowledge of non-atopic comorbidities associated with AD. The following conclusions can be drawn:

- AD is associated with any psychiatric disorder in adult patients, depression and anxiety being the most common comorbidity diagnoses.
- We found significantly increased risk of DH in pediatric AD patients, however the prevalence of DH is low in this population.
- AD is associated with ED, and the strongest association was found between AD and bulimia nervosa.

LIST OF ORIGINAL PUBLICATIONS

I. Kauppi, S, Jokelainen J, Timonen M, Tasanen K, Huilaja L. Adult patients with atopic eczema have a high burden of psychiatric disease: A Finnish nationwide registry study. Acta Derm Venereol 2019; 99: 647–651. doi: 10.2340/00015555-3165.

II. Kauppi S, Jokelainen J, Timonen M. Tasanen K, Huilaja L. Atopic dermatitis is associated with dermatitis herpetiformis and celiac disease in children. J Invest Dermatol 2021; 141: 191–193. doi: 10.1016/j.jid.2020.05.091.

III. Kauppi S, Jokelainen J, Timonen M, Tasanen K, Huilaja L. (2021). Atopic dermatitis and the risk of eating disorders: A population-based cohort study. J Am Acad Dermatol 2021; 87: 474–476. doi: 10.1016/j.jaad.2021.10.021.