## **Patients and Methods**

The computerized medical records of adult atopic dermatitis (AD) patients who were hospitalized at the dermatology department and followed in the outpatient clinic of Sheba Medical Center between 2009 and 2017 were reviewed for this study.

All patients in the study were adults, aged 18 years and above. Pregnant women were excluded. Detailed medical and medication histories were obtained from all participants. Diagnosis of AD was determined through the presence of a pruritic eczematous eruption with a chronic or chronic-relapsing course lasting at least 6 months that could not be attributed to other eczematous or eczema-mimicking conditions. In all biopsies performed (89 out of 107 cases), the diagnosis was supported by histological findings demonstrating acute, subacute, or chronic eczematous dermatitis with varying degrees of spongiosis or psoriasiform dermatitis and presence of inflammatory infiltrate-containing eosinophils. Cases with the presence of necrotic keratinocytes, which may suggest an irritant contact dermatitis in the pathogenesis, and cases with histological findings suggestive of other conditions (e.g., cutaneous T-cell lymphoma) were all excluded, as other diagnoses could not be ruled out in these cases. To minimize the possibility of unrecognized contact dermatitis or urticarial-stage bullous pemphigoid, patch tests and direct immunofluorescence tests were performed when needed, based on clinical judgment. Personal or family history of atopy and IgE level were documented but were not considered to be diagnostic criteria.

The subjects with AD were classified as COAD and LOAD based on the age of onset of the disease  $(<18 \text{ or } \ge 18 \text{ years}, \text{ respectively})$ . Evaluated characteristics included: the age of onset; sex; ethnicity; skin type according to the Fitzpatrick scale for human skin color; medical history; personal or familial atopic background; and clinical characteristics, laboratory data, and response to treatment. Atopy characteristics included symptoms other than dermatitis, such as family history of atopy, personal history of asthma, allergic rhinitis, conjunctivitis, and various allergies, including drug allergy and positive patch test with no clinical relevance. Clinical characteristics examined included the area affected by the skin eruption (head and neck, ear and retroauricular fold, trunk, upper limbs, lower limbs, palms, and/or soles), type of skin eruption (eczematous, follicular accentuation, or nummular),

and itch severity. Laboratory characteristics evaluated included C-reactive protein, lactate dehydrogenase, IgE, and white blood cell count. Only cases with complete clinical and epidemiological data, in which the differentiation between COAD and LOAD could be determined with absolute certainty, were included.

Evaluation of response to treatment included phototherapy and other systemic treatments. Response to treatment was divided into no response and partial/complete response.

The study was approved by the local ethical committee.

## Statistical Analysis

Categorical variables were reported as both numbers and percentages. Continuous variables were evaluated in comparison to the normal distribution using histograms and reported using median and interquartile range (IQR). Comparison of categorical variables was conducted between the groups using  $\chi^2$  and Fisher's exact tests. Continuous variables were compared between groups using the Mann-Whitney test. All statistical tests were two-sided. The significance value p < 0.05 was defined as statistically significant. SPSS software was used for all statistical analyses (IBM SPSS statistics ver. 24, 2016, IBM Corp., Armonk, NY, USA).