A multicentric study on prevalence of clinical patterns and clinical phenotypes in adult atopic dermatitis

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Atopic dermatitis (AD), also known as atopic eczema, is one of the most common inflammatory skin disease, affecting 15–30% of children and up to 14.3% of adults, about 20% of which have moderate-to-severe disease [1].

Adult patients with AD display different clinical presentations depending on age, ethnicity, and the underlying biologic mechanisms [2]. Typically, the evolution of the disease can occur in 3 different ways: persistent form in which AD appears in childhood and is maintained (with its chronic-recurrent course) until adulthood; relapsing form with childhood onset of the disease and a relapse of symptoms after some symptom-free years; and adult-onset AD in which the disease first appears in adulthood [1]. Moreover, the clinical data and literature suggest the existence of different clinical forms of presentation of AD in adults that can sometimes coexist in the same patient [1].

Therefore, we conducted a study with a primary objective to explore how commonly adult AD occurs and its clinical characteristics.

In this study, we evaluated data collected from an Italian multicenter retrospective cohort. Consecutive adult patients evaluated by highly experienced dermatologists belonging to ten Italian academic dermatological centers during October 2018-February 2020 given AD diagnoses according to ETFAD/EADV recommendations [3] were eligible for this study. The investigators

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performed dermatological examination for characterization of the skin manifestations, aiming to distinguish the different cutaneous phenotypes, as previously described [1].

Patients ≥18 years with AD lasting at least 6 months were assessed for medical history, demographics, allergic comorbidities, and concomitant medications or procedures. Disease severity was assessed by the Eczema Area and Severity Index (EASI) (range: 0-72). Additionally, patient-reported outcomes including peak score on the Numerical Rating Scale (NRS) for pruritus (range: 0-10), peak score on the NRS for sleep (range: 0-10), and Dermatology Life Quality Index (DLQI) (range: 0-30) were collected. Total serum IgE levels and a peripheral blood eosinophil count were also collected.

The study protocol was approved by the principal Ethics Committee nd informed consent was obtained from all patients.

Comparisons between clinical indicators were made with the Fisher's exact test. All statistical analyses were performed with SPSS version 20. The threshold for statistical significance was set at $p<0.05$.

In our cohort, 550 patients with AD were included (detailed in the Supplementary Table 1). In brief, 242 (44.0%) were female and the median ± interquartile range (IQR) for patient age was 38.0±27.0 years. The median±IQR duration of AD was 21.0±21.8 years. The median±IQR scores was 27.0±9.3 for EASI.

In our study population, the persistent form of adult AD occurred in 262 (47.6%) patients, the relapsing form in 86 (15.6%), and the adult-onset AD in 202 (36.8%) (in the Supplementary Table 2).

The most frequent AD phenotype was the classic adult-type with lichenified/exudative flexural dermatitis developed in 267 (48.5%) patients, often associated with head/neck eczema or hand eczema, observed in 45 (8.2%) and 41 (7.5%) patients, respectively, followed by prurigo nodularis (PN)-like pattern in 47 (8.5%) (detailed in the Supplementary Table 2).

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In our cohort, AD had appeared in childhood in 348 (63.3%) patients (persistent form plus relapsing form: childhood-onset AD subgroup), whereas in 202 (36.7%), AD had directly started in adult age (adult-onset AD subgroup). A subanalysis on the differences between the latter two subgroups in terms of prevalence of AD phenotypes was made. Lichenified/exudative flexural dermatitis alone and associated with portrait dermatitis was more common in childhood-onset AD than adult-onset AD (191/348, 54.9% *vs* 76/202, 37.6% [p<0.01]; 14/348, 4.0% *vs* 0/202, 0% [p<0.01], respectively). Nummular eczema (NE)-like phenotype and PN-like pattern appeared to be associated with adult-onset than childhood-onset AD (15/202, 7.4% *vs* 6/348, 1.7% [p<0.01]; 42/202, 20.8% *vs* 5/348, 1.4% [p<0.01], respectively. No statistically significant differences were found regarding the other phenotypes between childhood-onset and adult-onset AD subgroup.

The present study highlighted the heterogeneity of adult AD signs and symptoms.

In our cohort, the proportion of adult-onset AD was 36.7%. Recent studies reported various proportions (range 9-88.0%) of AD patients had onset after 18 years of age [4].

Two adult AD phenotypes predominated in our study lichenified/exudative flexural dermatitis alone or associated with portrait dermatitis, and PN-like AD. These findings are consistent with previous studies showing more flexural involvement in adult AD [4-7]. In our study, lichenified/exudative flexural dermatitis was more common in childhood-onset subgroup. This is in contrast with previous studies that had found lower rates of flexural lesions in childhood-onset when compared to adult-onset AD (119/232, 51.3% vs 14/48, 29.7%; p<0.01) [5] or directly no statistically significant differences between the two subgroups [4,7].

PN-like AD shows distinct, intensely itching papules and nodules mainly affecting the limbs and the upper part of the back. In our study, this clinical phenotype was more common in adult-onset group. In two studies that stratified phenotype by age of AD onset, prurigo was found in 6.3% (4/63) and in 30.5% (11/36) of adult-onset participants, respectively [6,8].

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NE-like phenotype presents with eczematous, sometime oozing areas, and is often associated with cutaneous xerosis. NE can also be the clinical expression of other clinical pathologies such as allergic contact dermatitis due to fragrances or preservatives [9,10]. In our cohort, this clinical phenotype was more common in adult-onset group, supporting the results of a previous study in which adult-onset compared with childhood-onset AD was associated with significantly higher rates of NE lesions (21/149, 15% vs 12/207, 6.4%; $p<0.01$) [5]. This finding did not confirm the study of Son *et al.* [6] which showed no statistically significant differences between the two groups.

Limitation is the relative small sample size, strength are the well collected phenotypes among center since all the investigator were academic in tertiary hospital.

In conclusion, to our knowledge this is the first study to highlight the prevalence of the different clinical forms of adult AD according to recently proposed classifications [1]. Moreover, even though there are many common features, some significant differences between childhood-onset and adult-onset AD subgroups in adult patients with AD can be highlighted. A clear definition of different clinical phenotypes is a key elements for disease recognition, correct treatment and prognosis.

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Conflicts of Interest

All authors declare that they have no conflicts of interest except for:

- Ferrucci SM: she is speaker of Novartis and Sanofi Genzyme; she is Principal Investigator for Eli Lilly, Abbvie, Sanofi Genzyme; she is an advisory board member of Sanofi Genzyme.
- Macchia L: in the past five years accepted a fee for organising education.

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