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An Italian multicentre study on adult atopic dermatitis: persistent versus adult-onset disease

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Abstract Atopic dermatitis (AD) is a chronic, recurrent, inflammatory skin disease which predominantly affects children. However, AD may persist until adulthood (persistent AD), or directly start in adults (adult-onset AD). AD often shows a non-flexural rash distribution, and atypical morphologic variants in adults and specific diagnostic criteria are lacking. Moreover, adult AD prevalence as well as detailed data which can characterize persistent vs adult-onset subtype are scant. The aim of this study was to investigate on the main features of adult AD particularly highlighting differences between persistent vs adult-onset form. An Italian multicentre observational study was conducted between April 2015–July 2016 through a study-specific digital database. 253 adult AD patients were enrolled. Familiar history of AD was negative in 81.0%. Erythemato-desquamative pattern was the most frequent clinical presentation (74.3%). Flexural surface of upper limbs was most commonly involved (47.8%), followed by eyelid/periocular area (37.9%), hands (37.2%), and neck (32%). Hypertension (7.1%) and thyroiditis (4.3%) were the most frequent comorbidities. A subgroup analysis between persistent (59.7%) vs adult-onset AD patients (40.3%) showed significant results only regarding AD severity (severe disease was more common in persistent group, $p < 0.05$), itch intensity (higher in adult-onset disease), and comorbidities (hypertension was more frequent in adult-onset group, $p < 0.01$). Adult AD showed uncommon features such as significant association with negative AD family history and lacking of association with systemic comorbidities respect to general population. No significant differences among persistent vs adult-onset subgroup were registered except for hypertension, itch intensity, and disease severity.

Keywords Atopic dermatitis · Adult · Adult-onset atopic dermatitis · Persistent atopic dermatitis

Introduction

Atopic dermatitis (AD) is a chronically recurrent, pruritic, inflammatory skin disease which predominantly affects children, usually clearing up during infancy or childhood [20, 35]. However, AD may persist with a chronic relapsing course until adulthood (persistent AD), possibly being recalcitrant to different treatments [34]. On the other hand, in some patients, AD directly starts later in life (i.e., after 18 years of age), the so-called adult-onset AD [7]. Adult AD has a major impact on quality of life and working abilities [20]. Since the frequency of AD is constantly increasing worldwide [3], it is also conceivable that both prevalence and incidence of adult AD are rising [3], even if detailed data are lacking; indeed, studies show very variable results, reporting that AD may affect 0.3–14.3% of the

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adult population [3, 12, 13, 19, 20, 22, 27]. Specific diagnostic criteria for adult AD are not available and those used for pediatric patients (Hanifin and Rajka as well as UK criteria above all [4]) have been only adapted to adults, with a consequent reduction of specificity and sensitivity; e.g., in approximately one-fourth of patients, the diagnosis of adult-onset AD was not possible according to UK criteria in its current form [20, 22]. Adult AD diagnosis is also complicated by the fact that in adult patients, AD often shows a non-flexural rash distribution and atypical morphologic variants, such as nummular or prurigo-like lesions [20]. Moreover, literature is constantly enriching of surveys which show adult AD as a possible systemic disease, being associated with metabolic and cardiovascular comorbidities [25, 26, 29, 37]. However, the possible correlation of these comorbidities with AD clinical and morphological forms, persistent vs adult-onset type, as well as the presence of non-cutaneous atopic manifestations have not been investigated so far. Moreover, data regarding systemic treatment effectiveness and long-term safety in adult patients with AD are insufficient and therapy approach widely differs among diverse countries [18]. Despite all these unmet needs, studies on adult AD are still scant; nevertheless, different new treatments for adult AD will be available in the next future [9, 28]. In the current study, we reported the results of an Italian multicentre study on adult AD, highlighting eventual differences on clinical features, involved body sites, past and present medical history, as well as previous and ongoing AD treatments between persistent and adult-onset AD group. This analysis also performed a general overview on adult AD trying to put the basis for the development of specific adult AD diagnostic criteria.

Materials and methods

A multicentre observational study involving 14 dermatological reference centers (mainly university departments) located throughout Italy was conducted between April 2015 and July 2016.

Patients referring to each participating centre were consecutively enrolled. Inclusion criteria were: (1) diagnosis of atopic dermatitis by a high experienced dermatologist (≥15 years) (basing on clinical features, and/or medical history, and/or histological examination, and/or treatment response); (2) disease duration ≥6 months; (3) patients' age ≥18 years. Exclusion criteria were: the presence of current other exogenous and/or endogenous dermatoses, paying particular attention to the most common adult AD stimulants such as allergic contact dermatitis, cutaneous T-cell lymphoma, seborrheic dermatitis, lichen simplex chronicus, and prurigo nodularis. For each patient, the following data were registered in a study-specific digital database using electronic case report forms expressly created to store adult AD characteristics (http://www.dermatiteatopicadulto.it): (1) personal and demographic data; (2) AD past and current history; (3) previous topical and/or systemic AD treatments; (4) current topical and/or systemic treatments; and (5) concomitant diseases Particularly, AD past and current history section explored AD age of onset, family history of AD, personal medical history of atopy (asthma, allergic conjunctivitis, and allergic rhinitis), localization and morphology of AD lesions, AD severity, and pruritus intensity measured through a visual analogue scale (VAS) ranging from 0 to 10 (where "0" means "doesn't itch at all" and "10" means "itch is worse than ever"). As regards the classification of AD lesions morphology, erythemato-desquamative, lichenified, exudative, and diffuse xerosis patterns were chosen. Since adult AD patients may frequently show mixed skin lesions patterns, in each patient, AD morphology was classified following most common clinical aspect (≥50% of existing lesions). AD severity was registered as mild [scoring atopic dermatitis index (SCORAD) <24 and/or objective SCORAD <15 and/or three-item severity score (TIS) <3)], moderate (SCORAD 25–50 and/or objective SCORAD 15–40 and/or TIS 3–6), or severe (SCORAD >50 and/or objective SCORAD >40 and/or TIS ≥6) [33, 35]; each patient signed a written consent form to participate in the study. The study was approved by local ethics committee for every survey participating site and performed in line with declaration of Helsinki guidelines.

Statistical analysis

Fisher's exact test was used for statistical analysis. p values <0.05 were considered statistically significant. All the statistical analyses were performed using GraphPad Prism 4.0 (GraphPad Software Inc., La Jolla, USA).

Results

Persistent vs adult-onset AD

Personal and demographic data

In our study population, persistent AD (onset <18 years of age) was more common than adult-onset disease (onset ≥18 years of age). Indeed, 59.7% (151/253) of patients suffered from persistent AD, whereas in 40.3% (102/253), AD had directly started in adult age (Table 1). Male sex was most frequently affected in both groups, however, without approaching statistical significance (51.6 and 60.8% of males in persistent and adult-onset group, respectively) (Table 1). Significant higher subjects mean

Table 1 Persistent AD vs adult-onset AD group

Feature	Persistent AD group *n* (%)	Adult-onset AD group *n* (%)	*p*
Number	151	102	
Sex			
Male	78 (51.6)	62 (60.8)	0.89
Female	63 (48.4)	50 (49.2)	
Mean age (years) ± sd	31.9 ± 11.6	36.5 ± 12.4	<0.05
Patient residence			
Rural	28 (16.6)	27 (29.4)	0.22
Urban	126 (83.4)	72 (70.6)	
Personal history of non-cutaneous atopic disease	80 (50.3)	52 (48)	0.91
Asthma	37 (24.5)	28 (27.5)	0.77
Allergic conjunctivitis	36 (23.8)	29 (26.5)	0.57
Allergic rhinitis	72 (47.7)	46 (45.1)	0.82
Family history of AD			
Positive	29 (19.2)	19 (18.6)	1
Negative	122 (80.8)	83 (81.4)	
AD severity			
Mild	64 (42.4)	62 (60.8)	0.12
Moderate	59 (39.1)	32 (31.4)	0.45
Severe	28 (18.5)	8 (7.8)	<0.05
Main morphology of skin lesion			
Erythemato-desquamative	118 (78.1)	70 (68.6)	0.55
Lichenified	21 (13.9)	20 (19.6)	0.31
Diffuse xerosis	7 (4.6)	8 (7.9)	0.41
Exudative	5 (3.3)	4 (3.9)	1
Pruritus intensity	4.6 ± 2.5	6.2 ± 2.3	<0.05
(VAS score 0-10: mean ± SD)			
Previous treatments			
Topical			
Corticosteroids	121 (80.1)	75 (73.5)	0.69
Emollients	108 (71.5)	70 (68.6)	0.84
Pimecrolimus	12 (7.9)	5 (4.9)	0.44
Tacrolimus	25 (16.5)	14 (13.7)	0.72
Other	3 (2)	1 (0.9)	0.65
Systemic			
Azathioprine	1 (0.7)	0 (0)	1
Corticosteroids	58 (38.4)	34 (33.3)	0.61
Cyclosporine	18 (11.9)	11 (10.8)	0.84
Methotrexate	2 (1.3)	0 (0)	0.51
NB-UVB phototherapy	24 (15.9)	6 (5.9)	<0.05
Omalizumab	1 (0.7)	0 (0)	1
UVA phototherapy	5 (2.4)	1 (0.9)	0.4
Other	29 (19.2)	11 (10.8)	0.16
Current treatments			
Topical			
Corticosteroids	71 (47)	34 (33.3)	0.18
Emollients	92 (60.9)	66 (64.7)	0.83
Pimecrolimus	4 (2.6)	5 (4.9)	0.49
Tacrolimus	9 (6)	6 (5.9)	1
Other	0 (0)	2 (1.9)	0.16

Table 1 continued

Feature	Persistent AD group *n* (%)	Adult-onset AD group *n* (%)	*p*
Systemic			
Azathioprine	3 (2)	1 (0.9)	0.65
Corticosteroids	9 (6)	5 (4.9)	0.78
Cyclosporine	6 (4)	4 (3.9)	1
Methotrexate	0 (0)	0 (0)	1
NB-UVB phototherapy	13 (8.6)	7 (6.9)	0.81
Omalizumab	0 (0)	0 (0)	1
UVA phototherapy	0 (0)	0 (0)	1
Other	14 (5.5)	6 (5.9)	0.47
Comorbidities			
Celiac disease	2 (1.3)	1 (1)	1
Coronary artery disease	0 (0)	3 (2.9)	0.06
Diabetes	1 (0.7)	2 (2)	0.3
Hypercolesterolemia	2 (1.3)	4 (3.9)	0.23
Hypertension	4 (2.6)	14 (13.7)	<0.01
Hypertriglyceridemia	0 (0)	3 (2.9)	0.06
Obesity	2 (1.3)	2 (2)	1
Stroke	0 (0)	1 (1)	0.4
Thyroiditis	4 (2.6)	7 (6.9)	0.2
Other	6 (4)	7 (6.9)	0.39
Cutaneous comorbidities			
Contact sensitization	10 (6.6)	9 (8.8)	0.63
Psoriasis	4 (2.6)	6 (5.9)	0.32
Vitiligo	1 (0.7)	0 (0)	1
Other	4 (2.6)	1 (1)	0.65

SD standard deviation; *VAS* visual analogue scale

age was registered in AD adult-onset group respect to persistent AD one (36.5 ± 12.4 years vs 31.9 ± 11.6, $p < 0.05$). Urban residence prevailed respect rural one in both groups (see Table 1 for details).

AD past and current history

No significant differences were found for positive personal history of atopy which was present in almost 50% of subjects in both groups; allergic rhinitis was reported as the most frequent non-cutaneous atopic manifestation in both groups (72/151, 47.7% of persistent AD patients vs 46/102, 45.1% of adult-onset AD subjects) (Table 1).

Similar results were observed for positive family history of AD which was negative in 80.8% (122/151) of persistent AD subjects and 81.4% (83/102) of adult-onset AD patients.

As regards morphology of AD lesions, no differences were found: erythemato-desquamative pattern was the most common clinical presentation in both groups (118/151, 78.1% in persistent AD group and 70/102, 68.6% in adult-onset AD), followed by lichenified pattern (21/151, 13.9 vs 20/102, 19.6%). Exudative pattern was registered as the less frequently observed being reported in only 3.3% (5/152) and 3.9% (4/102) of persistent and adult-onset disease group, respectively (Table 1). No statistically significant differences were found regarding AD lesion localization between persistent and adult-onset AD group. Flexural region of upper limbs was reported as the most commonly affected site (44/102, 43.1 vs 77/151, 51%, in adult AD and persistent group, respectively), followed by eyelid—periocular area (33/102, 32.4 vs 63/152, 41.7%), hand (dorsal surface) (36/102, 35.5 vs 58/152, 38.4%), neck (26/102, 25.5 vs 55/151, 36.4%), and labial—perioral area (22/102, 21.6 vs 53/151, 35%). Conversely, plants (2/102, 1.9 vs 2/151, 1.3%), elbow (5/102, 4.9 vs 12/151, 7.9%), knee (6/102, 5.9 vs 13/151, 8.6%), and scalp (7/102, 6.9 vs 12/151, 7.9%) were the less frequently involved body areas in both groups (data not shown).

Analyzing AD severity, a higher percentage of patients with mild disease was found in the adult-onset AD group compared to the persistent AD group (62/102, 60.8 vs 64/151, 42.4%), whereas opposite results were observed for patients with severe disease (8/102, 7.8 vs 28/151, 18.5%),

even if results reached statistical significance only for severe disease ($p < 0.05$).

Pruritus intensity was significantly higher in adult-onset group respect persistent one (6.2 ± 2.3 vs 4.6 ± 2.5, $p < 0.05$).

Previous topical and/or systemic AD treatments

Emollients and corticosteroids were the most common previous topical treatments in both groups (from 68.6 to 80.1% of subjects, Table 1). As regards systemic treatments, brief course of systemic corticosteroids was the most frequently prescribed (58/151, 38.4 vs 34/102, 33.3%, Table 1). There was not any significant differences between persistent vs adult-onset AD except for narrow band (NB)-UVB which was more common in persistent AD past medical history (24/151, 15.9 vs 6/102, 5.9%, $p < 0.05$).

Current topical and/or systemic treatments

Emollients were the main ongoing topical treatment in both groups (92/151, 60.9 vs 66/102, 64.7%), followed by topical corticosteroids (71/151, 47 vs 34/102, 33.3%), whereas NB-UVB prevailed among the systemic therapies (13/151, 8.6 vs 7/102, 6.9%) in persistent and adult-onset AD group (Table 1). The comparison between ongoing treatments did not show any statistically significant differences between persistent and adult-onset AD.

Concomitant diseases

Comorbidities were much more frequent in the adult-onset AD group respect to persistent AD group; particularly, this trend was registered for coronary artery disease, hypertension, hypercholesterolemia, hypertriglyceridemia, and autoimmune thyroiditis with statistical significance reached only by hypertension (4/151, 2.6 vs 14/102, 13.7%; $p < 0.01$). However, hypertriglyceridemia and coronary artery disease almost approached statistical significance (0/151, 0 vs 3/101, 2.9%, $p = 0.06$ in both cases. The rate of skin diseases linked to AD was comparable between the two groups. Contact sensitization and psoriasis were the most common in both groups (Table 1). Particularly, as regard contact sensitization, involved haptens are displayed in Table 2; no significant differences were observed between persistent and adult-onset disease group.

Total adult AD study population analysis

Personal and demographic data

The study population consisted of 253 adult AD patients [140 male (55.3%) and 113 female (44.7%), mean age 33.8 ± 14.8 years] (Table 3). Gender did not appear to be a relevant marker of AD in adults. Mean age of AD onset was 16.2 ± 18.8 years. Patients residence was more commonly urban than rural (198/253, 78.3 vs 55/253, 21.7%).

AD past and current history

A positive personal history of non-cutaneous atopic disease was present in half of the patients (132/253, 52.2%); particularly 65/253 (25.7%) patients suffered from asthma, 65/253 (25.7%) from allergic conjunctivitis, and 118/253 (46.6%) from allergic rhinitis, which was hence observed as the most common atopic manifestation linked to adult AD. Interestingly, 81% (205/253) of subjects presented a negative familiar history of AD.

As regards principal AD features, the main clinical morphology of AD lesions was represented by erythemato-desquamative pattern (188/253, 74.3%), followed by lichenified one (41/253, 16.2%); exudative lesions were the less frequently registered (10/253, 4%) (Table 3). AD lesions more frequently involved the flexural surface of upper limbs (121/253, 47.8%), followed by eyelid and periocular area (96/253, 37.9%), hands (dorsal surface) (94/253, 37.2%), neck (81/253, 32%), and labial and perioral area (75/253, 29.6%) (see Fig. 1 for detailed data regarding skin lesions localization).

Analyzing global disease severity, it was rated as mild in 125/253 (49.4%), moderate in 91/253 (36%), and severe in 37/253 (14.6%) of cases. In general, itch was a frequent symptom in adult AD patients with a mean VAS-pruritus intensity was 5.8 ± 2.87.

Previous topical and/or systemic AD treatments

Obviously, topical corticosteroids and emollients resulted as the mainstay of previous treatments, being reported by 196/253 (77.5%) and 178/253 (70.3%) patients, respectively, followed by brief course of systemic corticosteroids (92/253, 36.4%).

Current topical and/or systemic AD treatments

Topical emollients were reported as the most common ongoing therapy (158/253, 62.4%), followed by topical corticosteroids (105/253, 41.5%) and NB-UVB phototherapy (20/253, 7.9%) (Table 3).

Concomitant diseases

Obesity was not frequent in our group of patients (4/253, 1.6%), with hypertension and autoimmune thyroiditis being the most frequent reported comorbidities (18/253, 7.1 and 11/253, 4.3% respectively) (Table 3). Not surprisingly,

Table 2 Contact sensitization in persistent vs adult-onset AD group

Hapten	Persistent AD group *n* (%)	Adult-onset AD group *n* (%)	*p*
Balsam of Peru	2 (1.3)	1 (0.9)	1
Cobalt	0 (0)	1 (0.9)	1
Corticosteroids	1 (0.7)	0 (0)	1
Fragrance mix	2 (1.3)	1 (0.9)	1
Kathon CG	2 (1.3)	1 (0.9)	1
Nickel	3 (0)	2 (1.9)	1
Para-phenylenediamine	0 (0)	1 (0.9)	1
Potassium dichromate	0 (0)	1 (0.9)	1

contact sensitization was registered as the principal skin disease associated with adult AD (7.5%); psoriasis was observed in 10/253 (4%) of adult AD patients.

Discussion

AD lifetime prevalence has shown a worldwide increase in the past 30 years, seeming to reach a plateau at 10–20% in developed countries, whereas it continues to increase in many developing countries [5, 32]. AD usually starts during the first year of age (up to 60% of cases), but it may begin at any age [7, 10]. Several studies have suggested that AD may greatly improve or disappear until late childhood in up to 70% of cases, with early and severe onset, family history of AD, and early allergen sensitizations being risk factors for a longer course [10, 23]. Therefore, it is not surprising that adult AD prevalence is rising worldwide even if detailed data are still lacking; indeed, studies show very variable results, reporting that AD may affect 1–10% of the adult population, with findings from pediatric registries suggesting that the prevalence of persistent or adult-onset disease is underestimated and higher than previously assumed [3, 12, 13, 17, 19, 20, 22]. Therefore, we conducted an Italian multicentre study on adult AD enrolling 253 subjects. Surprisingly, even if positive family history of AD is commonly reported as a risk factor for persistent AD [10, 23], it was found in only 19% (48/253) of adult AD patients suggesting that it could be less important respect to childhood AD where a positive family history of the disease is generally reported in 54.2–68% of cases [8, 14]. Therefore, it may be suggested that adult-onset AD form did not tend to show a significant association with positive AD family history respect to classical AD of childhood. Our findings are only partially in line with the previous studies which report variable percentages of positive family history of AD (17–35%) in adult AD patients [2, 6, 22, 31]. However, we believe that this hypothesis needs to be further investigated and eventually confirmed in future studies, also because a sub-analysis between persistent AD and adult-onset AD group did not reveal significant difference in positive AD family history percentage (19.2 vs 18.6%). Moreover, it should also be stated that this result may be influenced by possible uncorrected personal medical history (AD patients are not always able to remember their infantile or early AD, especially in mild cases). As regards AD skin lesions morphology, erythemato-desquamative skin manifestations were the most commonly observed (188/253, 74.3%), followed by lichenified lesions (41/253, 16.2%), diffuse xerosis (14/253, 5.5%), and exudative lesions (10/253, 4%). No differences were found between persistent AD and adult-onset AD sub-groups of patients (Table 1). Interesting data came from the analysis of AD skin lesions localization (Fig. 1). Flexural region of upper limbs was the body area most frequently involved (121/253, 47.8%), supporting the results of previous studies which proposed flexural area involvement as one of the main possible important criteria for adult AD identification [14, 22]. Other frequently involved areas were represented by eyelid and periocular area (96/253, 37.9%), hands (dorsal surface) (94/253, 37.2%), neck (81/253, 32%), and labial and perioral area (75/253, 29.6%). Particularly, the common involvement of hands in adult AD patients was also supported by the previous investigations [2, 11, 14] as the case of eyelid/periocular, neck and labial/perilabial lesions predominance [36], appearing as interesting data which may guide future research trying to establish adult AD-specific diagnostic criteria. Indeed, diagnostic criteria usually used (Hanifin and Rajka and UK criteria) are not completely adaptable in adult patients with a consequent reduction of specificity and sensitivity [14, 20, 22]. Persistent and adult-onset AD did not present any significant differences regarding skin lesions localizations (data not shown), suggesting that separate clinical diagnostic criteria for these two adult AD forms may not be needed. Finally, as concerns AD severity, there were no significant differences between persistent vs adult-onset AD except for severe disease which was more common in persistent AD group; however, mild disease was the most common form in both groups, followed by moderate disease and severe forms, confirming the results of Kulthanan et al. [14]. Patients with childhood AD often have personal and/or family history of other atopic diseases such as asthma, allergic rhinitis, and allergic conjunctivitis [24]. This strong association is confirmed also in adult AD subjects. Half (132/253, 52.2%) of our study population showed a personal history of atopic diseases with allergic rhinitis being the most commonly observed (118/253, 46.6%), in line with the previous studies [14]. No differences were found between the subset of persistent vs adult-onset adult AD forms. It has been proposed that AD is a systemic

Table 3 Main features of the study population

Feature	Study population *n* (%)
Number	253 (100)
Sex	
Male	140 (55.3)
Female	113 (44.7)
Mean age (years) ± sd	33.8 ± 14.8
Patient residence	
Rural	55 (21.7)
Urban	198 (78.3)
Personal history of non-cutaneous atopic disease	132 (52.2)
Asthma	65 (25.7)
Allergic conjunctivitis	65 (25.7)
Allergic rhinitis	118 (46.6)
Familiar history of AD	
Positive	48 (19)
Negative	205 (81)
AD severity	
Mild	125 (49.4)
Moderate	91 (36)
Severe	37 (14.6)
Main morphology of skin lesion	
Erythemato-desquamative	188 (74.3)
Lichenified	41 (16.2)
Diffuse xerosis	14 (5.5)
Exudative	10 (4)
Pruritus intensity (VAS score 0-10: mean ± SD)	5.8 ± 2.87
Previous treatments	
Topical	
Corticosteroids	196 (77.5)
Emollients	178 (70.3)
Pimecrolimus	17 (6.7)
Tacrolimus	39 (15.4)
Other	4 (1.6)
Systemic	
Azathioprine	1 (0.4)
Corticosteroids	92 (36.4)
Cyclosporine	29 (11.5)
Methotrexate	2 (0.8)
NB-UVB phototherapy	30 (11.9)
Omalizumab	1 (0.4)
UVA phototherapy	6 (2.4)
Other	40 (15.8)
Current treatments	
Topical	
Corticosteroids	105 (41.5)
Emollients	158 (62.4)
Pimecrolimus	9 (3.6)
Tacrolimus	15 (5.9)
Other	2 (0.8)
Systemic	
Azathioprine	4 (1.6)
Corticosteroids	14 (5.5)
Cyclosporine	10 (4)
Methotrexate	0 (0)
NB-UVB phototherapy	20 (7.9)
Omalizumab	0 (0)
UVA phototherapy	0 (0)
Other	20 (7.9)
Comorbidities	
Celiac disease	3 (1.2)
Coronary artery disease	3 (1.2)
Diabetes	3 (1.2)
Hypercolesterolemia	6 (2.4)
Hypertension	18 (7.1)
Hypertriglyceridemia	3 (1.2)
Obesity	4 (1.6)
Stroke	1 (0.4)
Thyroiditis	11 (4.3)
Other	13 (5.1)
Cutaneous comorbidities	
Contact dermatitis	19 (7.5)
Psoriasis	10 (4)
Vitiligo	1 (0.4)
Other	4 (1.6)

SD standard deviation; *VAS* visual analogue scale

disease where the skin manifestations are only a part of the disorder [16, 25, 26, 37]. Therefore, we also focused on evaluating the possible presence of systemic as well as skin comorbidities in adult AD patients. Our results showed that hypertension was the most frequent systemic comorbidity in adult AD patients (18/253, 7.1%) followed by autoimmune thyroiditis (11/253, 4.3%). Hypertension appeared also to be more associated with adult-onset than persistent AD (14/102, 13.7 vs 4/151, 2.6%; $p < 0.01$). However, it should be stated that adult-onset group showed a higher mean age respect to persistent AD, possibly influencing the frequency of systemic comorbidities. Conversely, obesity was very uncommon, being found in only 4/253 (1.6%) of subjects. This finding did not confirm the previous studies which showed that obesity was associated with AD in adults [25, 37], supporting the results of Sybilski et al. which reported obesity as a risk factor for asthma but not for AD in a cohort of 18,617 subjects [30]. Further studies are needed to deeply clarify this relationship, since

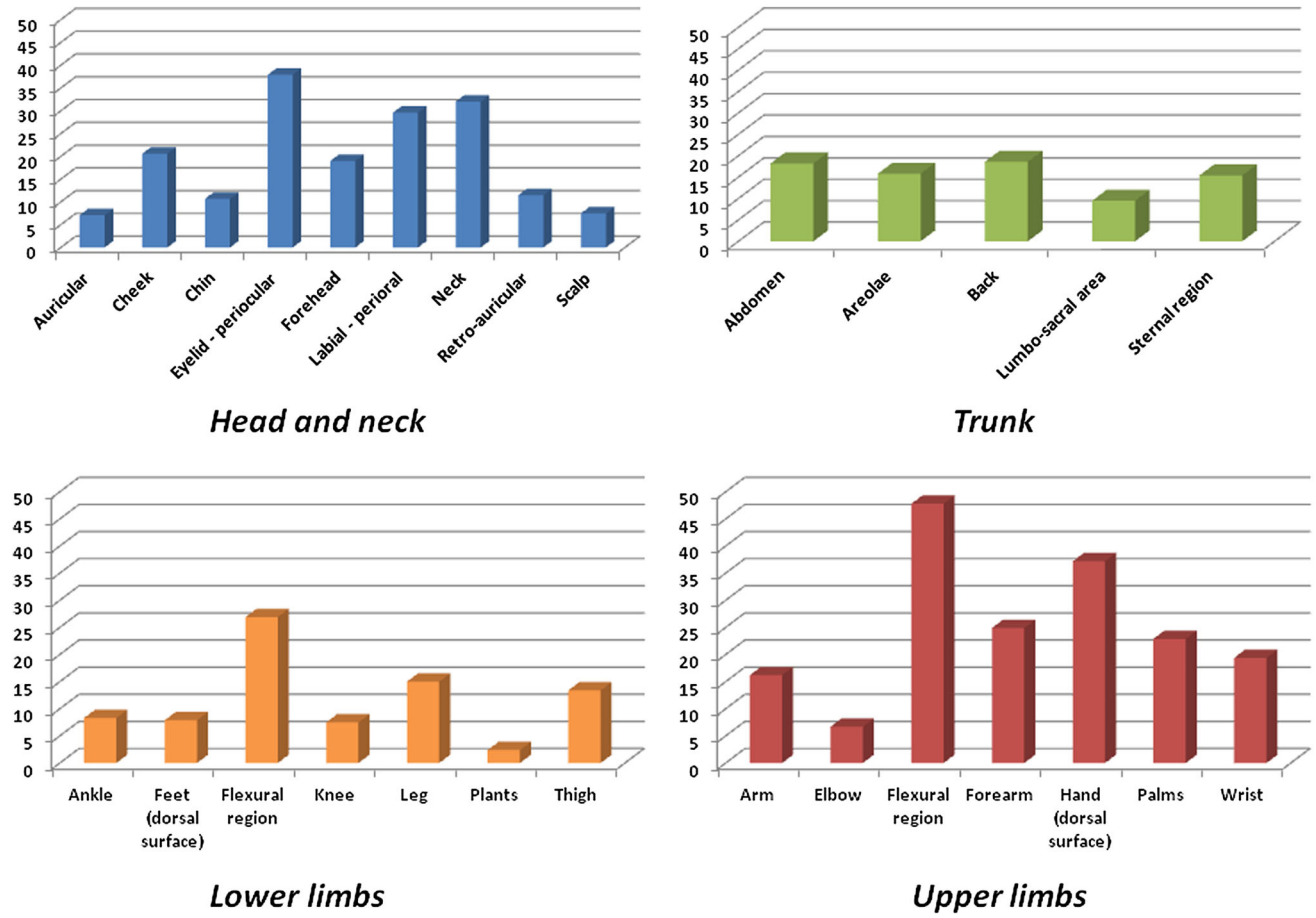

Fig. 1 AD lesion localization in the study population

literature is constantly enriching of surveys showing different and debatable results like the very recent cross-sectional study with a nationwide sample of the Korean population conducted by Lee et al. which suggested that obesity was related to AD in adult women, but not in men [15]. As regards skin comorbidities, it is not surprisingly that contact sensitization was found in 19/253 (7.5%) of adult AD subjects, being, therefore, frequent in this class of patients as previously suggested [11, 14]. Interestingly, psoriasis, a Th1–Th17-mediated disease [1], was found in 4% of our patients (10/253), a percentage which is similar to the psoriasis prevalence in general population, suggesting a possible overlap between Th1–Th17 and Th-2 pathways in AD, especially in adult-onset or persistent chronic forms as reported by a study conducted among Korean adults visiting health service centre in Seul [13]. Indeed, the importance of Th1–Th17 pathway in AD course is further supported by a very recent study which showed that the profile of Cutaneous Mesenchymal Stem Cells, obtained from patients suffering from chronic AD, retraces a Th1–Th17 environment [up-regulation of interleukin (IL)6, IL8, IL12, IL13, IL17A, IL17F, transforming growth factor-β, interferon-γ, whereas Th2 chemokines such as IL2, IL4, IL5, and IL23A were down-regulated) [21].

In conclusion, epidemiological and clinical studies on adult AD are still poor. We have performed an Italian multicentre pilot study on adult AD patients reporting that persistent and adult-onset AD did not show substantial differences except for disease severity (severe disease was more common in persistent AD group), pruritus intensity (higher in adult-onset disease), and comorbidities (hypertension was more frequent in adult-onset group with also hypertriglyceridemia and coronary artery disease almost approaching significance). Further research with greater study population is needed to deeply study the epidemiological and clinical features of adult AD, underline eventual differences between adult-onset and persistent AD subset, and to put the basis to establish specific adult AD diagnostic criteria.

Our study showed some limitations such as the relatively small sample size which may limit the generalizability of the results and the comparison between adult-onset vs persistent AD groups particularly regarding the frequency of comorbidities.

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Compliance with ethical standards

Conflict of interest The authors declare that they have no conflict of interest.

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