Eczema distribution in girls and boys during infancy: A cohort study on atopic dermatitis

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Clinical Implications

- Different eczema distribution in girls and boys during infancy may reflect differences in sex-related factors in early atopic dermatitis. With eczema being prevalent on the trunk, we suggest adding truncal eczema to the diagnostic criteria for atopic dermatitis in infants.

Atopic dermatitis (AD) is a common chronic inflammatory skin disease characterized by eczematous skin lesions, pruritus, and dry skin.[1] The distribution of the eczema lesions in AD patients is known to vary with age and ethnicity.[2] We are not aware of data on possible differences in the clinical distribution of eczema in girls and boys during infancy. Furthermore, the clinical distribution of eczema during infancy may not be suitable for the 2 most commonly used diagnostic criteria sets for AD—the UK Working Party (UKWP) and Hanifin & Rajka (H&R) criteria.[3]

We aimed to determine prevalence and clinical distribution of eczema at 3, 6, and 12 months of age in girls and boys. Also, we aimed to determine sensitivity and specificity of fulfilling the UKWP and/or H&R criteria for AD using the areas most commonly affected by eczema.

From the PreventADALL (Preventing Atopic Dermatitis and Allergies) randomized controlled trial in a mother-child birth cohort study in Norway and Sweden,[3] we included all 1,834 infants (966 boys and 868 girls) who attended study visits at 3, 6, and 12 months of age. Skin assessment of the infants was performed by trained health care personnel. The primary outcome was eczema, defined as the presence of eczematous skin lesions, clinically excluding the differential diagnosis to AD (eg, seborrheic and contact dermatitis). Eczema on 11 specific areas of the skin[3] was registered at all 3 clinical follow-up visits. The secondary outcome, atopic dermatitis, was defined as fulfilling the UKWP and/or H&R criteria for AD. The UKWP criteria were used at all visits, whereas the H&R criteria were used at 12 months only. Comparing the occurrence of eczematous skin on different locations in girls and boys was performed using the chi-squared statistic in SPSS software version 26.0 (IBM, Armonk, NY). The sensitivity and specificity of the 2 sets of diagnostic criteria were calculated based upon the 3 areas most commonly affected with eczema.

Eczema was observed more often in boys (n = 355; 37%) than in girls (n = 273; 31%) ($P = .02$) by 12 months of age. Likewise, AD, by fulfilling 1 or both sets of diagnostic criteria at any timepoint, was diagnosed more often in boys (n = 126; 13%) than in girls (n = 86; 10%) ($P = .04$). Eczema was most often found on the cheeks, the extensor surfaces of the extremities, and the trunk (Table I, Figure 1, and Figures E1 and E2; available in this article's Online Repository at www.jaci-inpractice.org). More boys than girls had eczema on the cheeks—44% versus 31% at 3 months ($P = .04$), 51% versus 33% at 6 months ($P = .001$), 39% versus 29% at 12 months ($P = .08$), and 51% versus 37% ($P = .001$)—overall in infancy. However, more girls than boys had eczema on flexor surfaces of the extremities at 3 months (45% vs 31%; $P = .03$) (Table I, Figure 1, and Figures E1 and E2). Eczema on the trunk did not differ at any timepoint and was observed in 58% of girls and 53% of boys ($P = .29$). Sensitivity and specificity for the UKWP and/or H&R criteria using at least 1 observation of eczema at each location, independent of timepoint, were 47% and 95% for the cheeks, 43% and 97% for the extensor surfaces, and 51% and 98% for the trunk, respectively.

To the best of our knowledge, this is the first study to report the clinical distribution of eczema separately for boys and girls during infancy. Eczema on the cheeks was more common in boys at both 3 and 6 months of age, and with a trend also at 12 months of age, as was AD, whereas eczema on the flexor surfaces was more common in girls than in boys at 3 months of age. These findings are in line with studies in older children showing a slightly higher prevalence of AD in boys than in girls with a reversal after puberty.[4] Our study also adds to the recent finding of other sex-specific patterns of AD.[5] With cheeks being more exposed to wear and tear by local triggers,[6] sensitivity to such factors may play a more important role in the pathogenesis of infantile AD in boys than in girls, possibly contributing to the higher prevalence of AD observed in boys.

In all infants, regardless of sex, eczema was common in flexural areas of the extremities during infancy. This is in line with a study of AD in 12-month-old infants identifying flexural involvement to be as common as involvement of the cheeks, outer arms, and legs,[7] but, according to the authors, in contrast to others suggesting that typical flexural involvement often does not develop until about 2 years of age.[7]

In our study, the trunk was a common site for eczema during the first year of life, and had a somewhat higher sensitivity and specificity for a criteria-based diagnosis of AD than both cheeks and extensors. In the modified UKWP criteria for AD in infants, anatomical sites other than the trunk were chosen partly in order to separate infantile seborrheic dermatitis from infantile AD.[8] Although sometimes affecting the umbilical area,[9] infantile seborrheic dermatitis is not as common on the trunk as AD in infants and may also involve the sites already included in the criteria. Our findings may provide a rationale to add eczema localized on the trunk to the diagnostic criteria for AD.

The strengths of our study include the high number of infants from the general population in 3 different geographic areas in Norway and Sweden. Limitations include that the H&R criteria were used at 12 months only; we might have underestimated the total number of infants with criteria-based AD. The fluctuating

TABLE I. The clinical distribution of eczema by age and sex in the 628 infants with at least one observation of eczema in infancy

	At 3 months			At 6 months			At 12 months			During infancy		
Localization of eczema	**Girls n/N (%) (n = 105)**	**Boys n/N (%) (n = 135)**	***P****	**Girls n/N (%) (n = 162)**	**Boys n/N (%) (n = 197)**	***P****	**Girls n/N (%) (n = 140)**	**Boys n/N (%) (n = 189)**	***P****	**Girls n/N (%) (n = 273)**	**Boys n/N (%) (n = 355)**	***P****
Scalp	10 (10)	22 (16)	.13	14 (9)	15 (8)	.72	4 (3)	6 (3)	.87	23 (8)	39 (11)	.29
Cheeks	33 (31)	60 (44)	**.04**	53 (33)	100 (51)	**.001**	41 (29)	73 (39)	.08	102 (37)	180 (51)	**.001**
Head and neck (excluding scalp and cheeks)	43 (41)	54 (40)	.88	70 (43)	83 (42)	.84	37 (26)	51 (27)	.91	109 (40)	142 (40)	.99
Trunk (abdomen, back, shoulders, and chest)	54 (51)	69 (51)	.96	78 (48)	100 (51)	.62	75 (54)	88 (47)	.21	157 (58)	189 (53)	.29
Extensors of arms and legs	72 (69)	85 (63)	.37	71 (44)	100 (51)	.19	83 (59)	111 (59)	.92	166 (61)	229 (65)	.34
Flexors of arms and legs	47 (45)	42 (31)	**.03**	54 (33)	64 (33)	.87	43 (31)	68 (36)	.32	123 (45)	141 (40)	.18
Flexor of elbows and knees	40 (38)	36 (27)	.06	49 (30)	61 (31)	.88	40 (29)	43 (23)	.23	105 (38)	114 (32)	.10
Dorsum of hands and wrists	27 (26)	28 (21)	.36	26 (16)	21 (11)	.13	30 (21)	26 (14)	.07	65 (24)	64 (18)	.08
Plantar side of hands and wrists	4 (4)	7 (5)	.61	4 (3)	3 (2)	.52	9 (6)	10 (5)	.66	15 (5)	19 (5)	.94
Ankles and feet	19 (18)	35 (26)	.15	30 (19)	34 (17)	.76	27 (19)	24 (13)	.10	65 (24)	73 (21)	.33
Nappy area†	4 (4)	8 (6)	.46	5 (3)	6 (3)	.98	6 (4)	11 (6)	.53	14 (5)	24 (7)	.40

*P values $< .05$ are given in bold. A conservative level of statistical significance by Bonferroni's correction for multiple testing: $P = .05/11 \times 3 = .0015$.
†Nappy area indicates the area of the skin covered by a standard sized diaper.

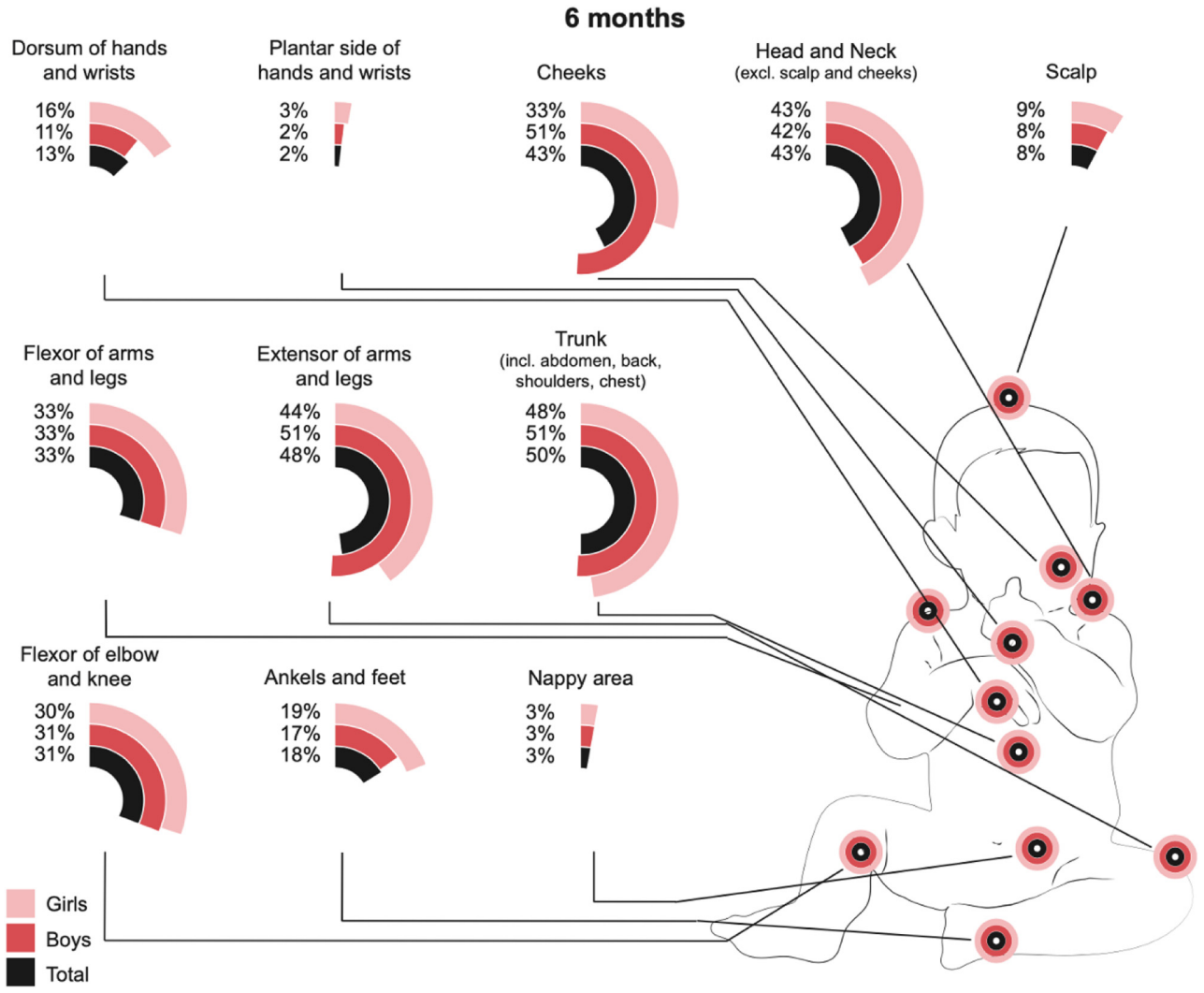

FIGURE 1. The distribution of eczema in the 359 girls and boys with observed eczema at 6 months of age. (Illustration by Ine Eriksen, University of Oslo, Oslo, Norway.) *Nappy area indicates the area of the skin covered by a standard sized diaper.

nature of AD and treatment effects during the study period may also have contributed to an underestimation of the prevalence of eczema. Although recruiting from the general population, parents with higher education and atopic disease were somewhat overrepresented,[3] which may limit the generalizability of the results.

In conclusion, the clinical distribution of eczema in infants differed between girls and boys, which may be relevant for our understanding of the pathogenesis of AD in boys and girls. With the finding of the trunk being a predilection site for infantile eczema, we suggest adding the trunk to the diagnostic criteria for AD in infants.

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The PreventADALL study is approved by the Regional Committee for Medical and Health Research Ethics in Norway (2014/518) and Sweden (2014/2242-31/4) and is registered at clinicaltrials.gov (NCT02449850).

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Conflicts of interest: K. M. A. Endre has received honorary for presentations from AbbVie. M. LeBlanc has received honorary for presentations from MSD. E. M. Rehbinder has received honoraria for presentations from Sanofi Genzyme, Novartis, MEDA and Omega Pharma. The rest of the authors declare that they have no relevant conflicts of interest.

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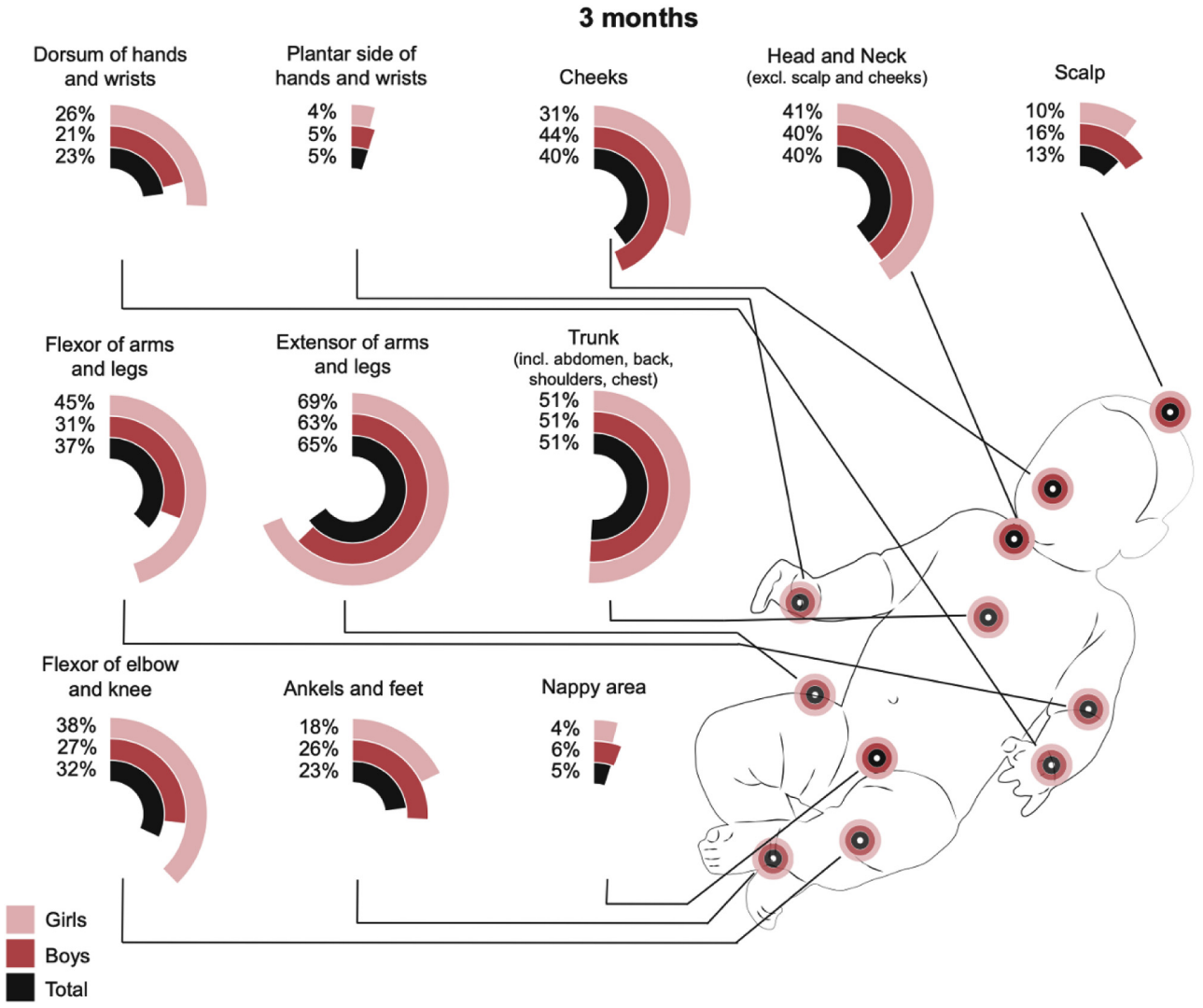

FIGURE E1. The distribution of eczema in the 240 girls and boys with observed eczema at 3 months of age. (Illustration by Ine Eriksen, University of Oslo, Oslo, Norway.) (Illustration by Ine Eriksen, University of Oslo, Oslo, Norway.) *Nappy area indicates the area of the skin covered by a standard sized diaper.

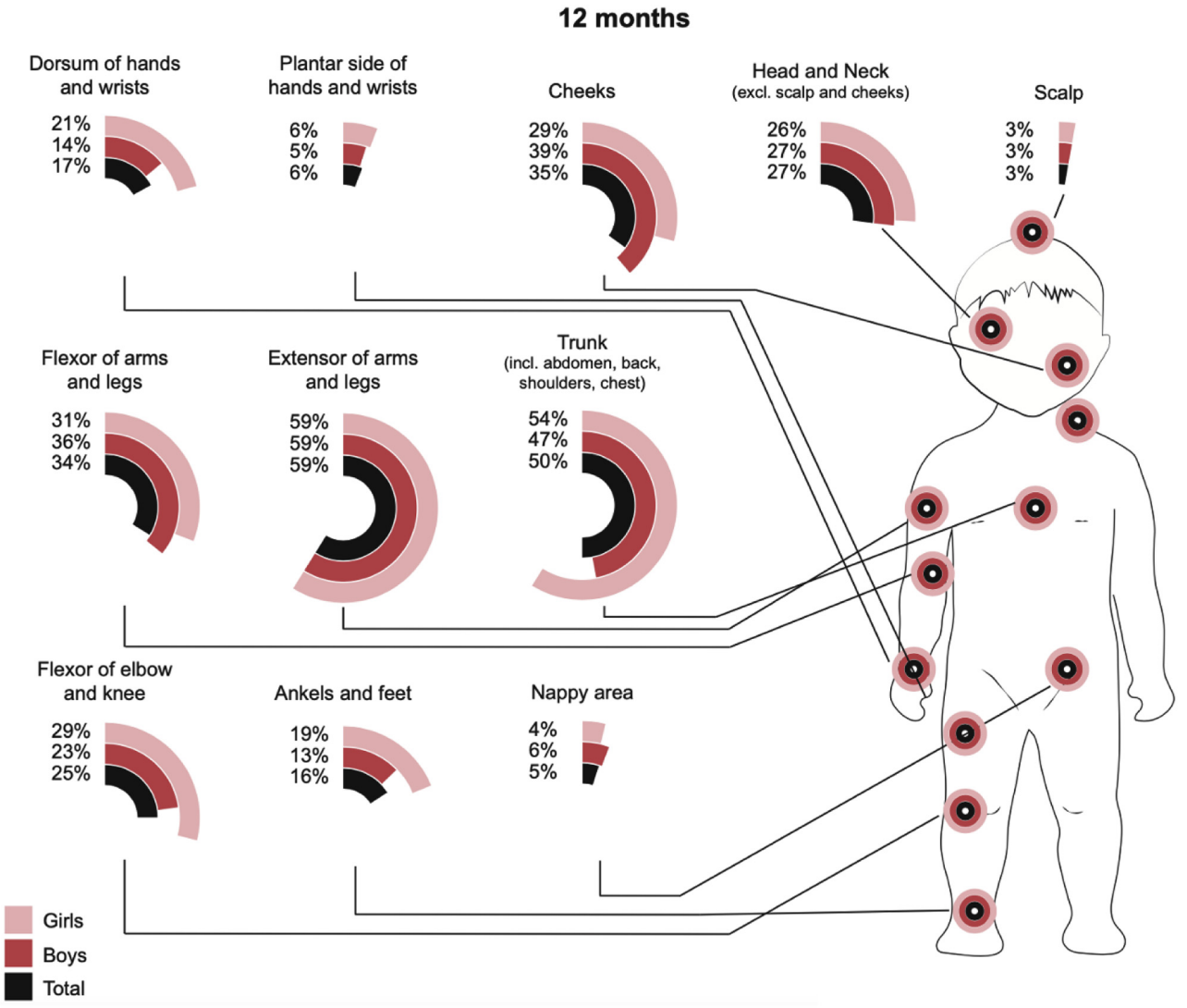

FIGURE E2. The distribution of eczema in the 329 girls and boys with observed eczema at 12 months of age. (Illustration by Ine Eriksen, University of Oslo, Oslo, Norway.) *Nappy area indicates the area of the skin covered by a standard sized diaper.