Br J Dermatol 2023; **189**:129–147
https://doi.org/10.1093/bjd/ljad085
Advance access publication date: 22 March 2023

Investigator Global Assessment for impetiginization in atopic dermatitis: development and initial reliability testing

Dear Editor, Secondary infections with *Staphylococcus aureus* (i.e. impetiginization) are common in patients with atopic dermatitis (AD).[1] However, owing to a lack of definition and standardized outcome measures, research investigating the prevalence and treatment of impetiginization in AD is lacking.

We sought to develop an Investigator Global Assessment scale (IGA) for impetiginization in AD. To develop the scale, a team of five dermatologists (S.G.M.A.P., R.A.T., M.L.A.S., M.dG., T.R.), specialized in AD, from five hospitals reviewed the literature, consulted other dermatologists and further elucidated the concept of IGA for impetiginization over six online, structured, consensus-based meetings. The need for a simple IGA for impetiginization in which the degree of impetiginization relates to treatment intensity was expressed. Unanimous consensus was achieved for an IGA scale with three outcome options: absent impetiginization; limited impetiginization; or extensive impetiginization (Figure 1). After development, we pilot tested the comprehensibility and relevance of the IGA for impetiginization among five clinicians, two of whom were involved in its development.

We next developed online surveys to evaluate the inter- and intra-rater reliability of the IGA for impetiginization. Surveys contained an instruction section and 36 cases of AD. Case information included several photographs and the patients' ages. All cases were selected by three AD experts (S.G.M.A.P., R.A.T., M.L.A.S.) from two existing academic hospital databases that contain images of patients with AD. Cases were selected to represent the full spectrum of both AD severity and degree of impetiginization across all age groups (58% paediatric cases) and skin types (81% Fitzpatrick skin type I–III). For analysis purposes, the three experts selected cases at an approximate ratio of 1 : 1 : 1 for absent, limited and extensive impetiginization, respectively. All cases were presented to dermatologists at two time points (survey 1 and survey 2). Cases from survey 1 were duplicated and randomized to develop survey 2. At least 6 weeks after the completion of survey 1, dermatologists assessed survey 2. Attending Dutch dermatologists were recruited using the contact lists of four academic hospitals and one public one. Dermatologists who developed the IGA did not participate in the surveys.

We used intraclass correlation ($ICC_{2,1}$), weighted kappa (linear) and the Kendall coefficient of concordance (*W*) to assess reliability and agreement.[2] We calculated the overall, positive and negative agreement for absent vs. any degree of impetiginization.[3] Furthermore, we investigated specific agreement to evaluate the agreement between all possible outcomes.[4] Based on our assumptions (expected reliability 0.65) a sample size of 36 cases and 20 dermatologists was deemed sufficient to reject the null hypotheses of poor reliability ($ICC < 0.5$).

This study was exempt from the Dutch Medical Research Involving Human Subjects Act according to the institutional review board of Erasmus MC (MEC-2020-0369).

Twenty-two and 14 dermatologists participated in the first and second surveys, respectively. The median years of experience of the dermatologists was 8.5 years (interquartile range 1–14) and the majority worked in public hospitals (59%). General dermatology (84%), inflammatory dermatology (64%) and paediatric dermatology (46%) were the most common subspecialties. Overall reliability parameters indicated moderate reliability and agreement {ICC 0.68 [95% confidence interval (CI) 0.57–0.79]; Kendall *W* [0.75]; weighted kappa 0.59 [95% CI 0.57–0.61]}. Additionally, overall agreement was high (81%). Specific agreement was highest for absent vs. extensive impetiginization (91%) and lowest for limited vs. absent impetiginization (59%), suggesting that dermatologists may have disagreed more in distinguishing patients with mild-to-absent impetiginization. Furthermore, we found good intra-rater reliability [ICC 0.81 (95% CI 0.75–0.87); weighted kappa 0.74 (95% CI 0.66–0.81)].

Based on these results, we assumed moderate-to-substantial inter-rater reliability and good intra-rater reliability for the IGA for impetiginization.

Compared to other clinical outcome measures for AD such as the Eczema Area and Severity Index (EASI), similar inter- and intra-rater reliabilities were found.[5] Keeping in mind that the EASI is one of the most reliable outcome measures in AD assessment, this adds support to the IGA for assessing impetiginization in AD. However, ideally, the reliability of both the EASI and IGA impetiginization should be higher. For the IGA impetiginization, discrepancy between raters was largely due to differences in the judgement of limited impetiginization. Agreement on extensive impetiginization was high, which is more important for clinical decision-making. More training could help increase reliability. Although we have conducted the initial validation of the IGA for impetiginization, more research is needed to further validate the IGA for impetiginization among other dermatologists and in real-life settings. Furthermore, the IGA for impetiginization could be compared to definitive measures (i.e. cultures).

Use of the IGA for impetiginization in AD will help us to investigate the prevalence of impetiginization in AD and the effects of treatment. In turn, this will help with the development of treatment guidelines for impetiginization in AD.

Accepted: 15 March 2023

Investigator Global Assessment for Impetiginization in Atopic Dermatitis

Instructions:

The IGA score for impetiginization in atopic dermatitis is selected using the morphological description and extent that best describe overall appearance of the lesions at a given time point. It is not necessary for all features to be present.

Score	Morphological description	Extent of impetiginization
0 – Absent	No signs of impetiginization	-
1 – Limited	Mild yellow crusting and/or mild (yellow) exudate/oozing	Restricted area
2 – Extensive	Mild yellow crusting and/or mild (yellow) exudate/oozing OR Severe yellow crusting and severe (yellow) exudate/oozing	Large area or multiple areas Irrespective of the extent of the area

Figure 1 The Investigator Global Assessment for impetiginization in atopic dermatitis. Expert consensus was achieved using a 3-point scale based on morphological features and extent of impetiginization.

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Acknowledgments:We would like to thank Dirk-Jan Hijnen, Elodie Mendels and Claire van Eijsden, in particular, for providing their views on the concept on an Investigator Global Assessment for impetiginization in atopic dermatitis. Additionally, we thank Karin Fieten for her contribution to the realization of the ABC project (ZonMw: 843004017) of which this study is a part. Finally, we thank all the dermatologists who participated in the study.

Funding sources: ZonMw (Netherlands Organisation for Health Research and Development), grant number 843004017.

Conflicts of interest: the authors declare they have no conflicts of interest.

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