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Clinical epidemiology of hand eczema in patients accessing dermatological reference centers: results from a Mediterranean Country

Short title

Epidemiological and Clinical aspects of Hand Eczema.

Authors:

L. Scalone[1,2], P.A. Cortesi[1,2], L.G. Mantovani[2,3], A. Belisari[2], F. Ayala[4], A.B. Fortina[5], D. Bonamonte[6], G. Borroni[7], S.P. Cannavò[8], F. Guarneri[8], A. Cristaudo[9], O. De Pità[10], R. Gallo[11], G. Girolomoni[12], M. Gola[13], P. Lisi[14], P.D. Pigatto[15], R. Satta[16], A. Giannetti[17] for the Italian Hand Eczema Study Group.

1 Research Centre on Public Health, University of Milan-Bicocca, Monza, Italy;

2 CHARTA Foundation, Milano, Italy;

3 Faculty of Pharmacy, Federico II University of Napoli, Napoli, Italy;

4 Department of Dermatology, University of Naples Federico II, Napoli, Italy;

5 Pediatric Dermatology Unit, Department of medicine, University of Padua, Padova, Italy;

6 Department of Biomedical Science and Human Oncology, Unit of Dermatology, University of Bari "Aldo Moro", Bari, Italy;

7 Clinical-Surgical, Diagnostic and Pediatric Science, Dermatology Unit, University of Pavia, Fondazione IRCCS Policlinico San Matteo, Pavia, Italy;

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8 Department of Clinical and Experimental Medicine-Unit of Dermatology, University of Messina, Messina, Italy;

9 Department of Allergological and Occupational Dermatology, San Gallicano Dermatologic Institute, IRCCS, Roma, Italy;

10 Laboratory of Immunology, Istituto Dermopatico dell'Immacolata (IDI)-IRCCS, Rome, Italy;

11 Section of Dermatology, DISSAL - Department of Health Sciences, University of Genoa, Genoa, Italy.

12 Department of Medicine, Section of Dermatology and Venereology, University of Verona, Verona, Italy;

13 Allergological and Occupational Dermatology Unit, Department of Critical Care Medicine and Surgery University of Florence, Firenze, Italy;

14 Department of Medical and Surgical Specialities and Public Health, Section of Clinical, Allergological and Venereological Dermatology, University of Perugia, Perugia, Italy;

15 Department of Biomedical Science for Health IRCCS Galeazzi Hospital, University of Milan, Milano, Italy;

16 Institute of Dermatology, University of Sassari, Sassari, Italy;

17 Division of Dermatology, University of Modena and Reggio Emilia, Modena, Italy;

Corresponding author (name, address, email):

Paolo A Cortesi
CESP - Research Centre On Public Health
Department of Statistics and Quantitative methods
University of Milano - Bicocca
Villa Serena, Via Pergolesi 33 - I-20052 Monza
phone: +39 0392333097/8
fax: +39 02700536422
E-mail address: p.cortesi@campus.unimib.it

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All authors of this paper have contributed to the conception and design of the project, interpretation of the result, critical revision and final approval. LS and PAC have also analysed the data and have written the manuscript.

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Members of the Italian Hand Eczema Study Group: Dr. Ilaria Romano (University of Padua, Padova, Italy), Dr. Giuseppe Pellegrini (University of Bari "Aldo Moro", Bari, Italy), Dr. Donatella Schena (University of Verona, Verona, Italy), Dr. Mirko Frasca (Institute San Gallicano, IRCCS, IFO, Roma, Italy), Dr. Angelo Massimiliano D'erme and Dr. Nicola Milanesi (University of Florence, Firenze, Italy), Dr Valerio Pedrelli (University of Milan, Milano, Italy), Dr. Konstantina Christana (University of Genoa, Genoa, Italy), Dr. Katharina Hansel and Prof. Luca Stingeni (University of Perugia, Perugia, Italy), Dr. Patriza Pepe (University of Modena and Reggio Emilia, Modena, Italy), Dr. Arianna Ruggiero (Istituto Dermopatico dell'Immacolata (IDI)-IRCCS, Roma, Italy), Dr. Michela Castello (Institute of Dermatology, Pavia, Italy), Dr. Donata Martellotta and dr. Cataldo Patruno (University of Naples Federico II, Napoli, Italy).

What's already known about this topic?

- *Hand eczema (HE) is a frequent dermatological disorder that can develop to a chronic, severe and refractory stage.*

What does this study add?

- *Chronic HE is common among patients accessing dermatological reference centers in a Mediterranean country. One-fifth are severe and one-tenth are also refractory to standard therapy.*
- *Severe Chronic HE is more common among men, 41-50 years and lower education. Severe and Refractory Chronic HE is also associated with atopic dermatitis and unemployed patients.*

ABSTRACT

Background: data on epidemiological impact and clinical characteristics of chronic hand eczema in Southern Europe are lacking.

Objectives: to estimate prevalence of chronic hand eczema and its different stages of severity and refractoriness to standard therapy among patients accessing Italian dermatological reference centers, and to evaluate socio-demographic and clinical factors associated with each different stage.

Methods: A cross-sectional multicenter study was conducted. Adult hand eczema patients, consecutively accessing 14 centers through a 6-month period, were enrolled. Patients were classified according to disease duration, severity and response to standard therapy with potent

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topical corticosteroids. Logistic regression analyses were performed to investigate relationship between socio-demographic and clinical data with different stages of eczema.

Results: 981 patients participated. Hand eczema was chronic in 83.5% of patients. Among them, 21.3% were severe, 62% of these patients being refractory to standard therapy. Food processing and related works, health professions, craft and related trades works (builders, plumbers, electricians), hairdressers/beauticians and handicraft works were the jobs most frequently associated with having chronic hand eczema. Severe chronic hand eczema was more likely to be among men, older patients and those with lower education. Severe and refractory hand eczema was also more likely among unemployed and patients with allergic rhinitis and/or atopic dermatitis.

Conclusions: Chronic hand eczema is frequent among hand eczema patients accessing dermatology centers. Many patients were severe and refractory to standard therapy. The appropriate identification of hand eczema is a first step necessary to implement effective and efficient treatments.

KEYWORDS: Hand Eczema, Chronic Hand Eczema, Severe Hand Eczema, Refractoriness to therapy, Epidemiology.

INTRODUCTION

Hand eczema has been identified as one of the most frequent dermatological disorders encountered in clinical practice, most frequently in cool moist climates. It is usually long-lasting[1-4], with a mean duration of 11.6 years from the time of first appearance to the time of clinical examination[1]. It is caused by a combination of endogenous (individual susceptibility, atopy, other genetic factors) and exogenous (exposure to contact irritants and allergens) factors[5], and has been reported to be more common among women and in young age groups[6].

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The point prevalence estimated for hand eczema in the general population is around 4%, the 1-year prevalence nearly 10%[6]. However, some authors underline that only 44% or less of hand eczema individuals actually seek medical consultation and treatment[7,8].

A number of hand eczema patients develop chronic hand eczema, with eczematous lesions persisting even when the initial causative agents are avoided to the greatest practical extent[9]. Chronic hand eczema is a subset of hand eczema that usually has a multifactorial aetiology. Consequently, it is rarely possible to identify all causative factors and remove them entirely[11,12]. Clinical signs and symptoms of chronic hand eczema include erythema, oedema, vesiculation/blistering, hyperkeratosis, fissuration, pruritus and pain[12-14]. Chronic hand eczema patients can be managed with emollients, topical corticosteroids and avoidance of irritants/allergens, but some severe cases are refractory to this standard therapy[9]. Severe chronic hand eczema may lead to severe impairment of quality of life, prolonged sick leave, loss of job and early retirement[15-17].

The incidence of chronic hand eczema is reported to be 0.7 cases per 1,000 people per year in high-risk occupational groups[18,19]. The proportion of patients with severe chronic hand eczema is estimated to be 5% to 7% of all patients with hand eczema, and those who are considered to be refractory to potent topical corticosteroids are estimated to represent 2% to 4 %, potentially representing up to 0.14% to 0.48% of the total population, in countries where the disease is most prevalent[9]. In a recent registry project of the German Dermatological Society, conducted in 66 German Centers, 23.4% of all chronic hand eczema cases were graded as severe and 47.0% as moderate[20]. Noteworthy, data on the epidemiologic impact and characteristics of chronic hand eczema mainly refer to Northern European countries, while data on Southern Europe are not available.

The aim of this study was twofold: 1) to estimate prevalence of chronic hand eczema among patients with hand eczema accessing dermatological reference centers in Italy, with focus on its

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different stages of severity and responsiveness to treatment, 2) to evaluate socio-demographic and clinical factors associated with each different stage.

MATERIALS AND METHODS

Subjects and setting

We conducted a cross-sectional, multicenter study in 14 dermatological reference centers located all over the Italian territory, in the period between October 2009 and October 2010. Most of the dermatology centers that participated in the study are university departments and some are also acknowledged as IRCCS (Istituto di Ricovero e Cura a Carattere Scientifico), i.e., Institute of treatment and research, which are Institutes recognised by the Italian Ministry of Health as Scientific Institutes that carry out biomedical research as well as clinical activities of relevant national interest.

All patients consecutively accessing each participating center within a time frame of six months were enrolled. The patients accessed the centers without any interference due to the study, i.e., only because they were referred by their general practitioner or by a specialist for reasons related to their condition. The time frame of six months was chosen under the assumption that it was sufficient to take into account all the possible climatic conditions potentially affecting the occurrence of signs and symptoms. To be considered eligible for the study, inclusion criteria were: age older than or equal to 18 years, diagnosis of hand eczema, absence of psoriasis, active infections of the hands (fungal, viral or bacterial) or any other confounding skin conditions and having signed an informed consent to participate in the study. Patients were not considered eligible if any of the above inclusion criteria was not satisfied.

The study was performed in accordance with the guidelines of the International Conference on Harmonization for Good Clinical Practice as stipulated in the Declaration of Helsinki[21]. Local Ethics Committees approval was obtained at each of the participating study sites.

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Assessments

Data on socio-demographic characteristics and clinical status were collected by means of a case report form. Socio-demographic data were on patients' gender, age, education, family and working status at the time of enrolment. Employed patients were sub-grouped, according to their occupation, in working categories. The classification by Senghal et al.[22] was used to help perform this classification. Clinical data consisted of diagnosis of hand eczema, duration of disease from appearance of symptoms, duration of disease from diagnosis, disease chronicity, severity, refractoriness to standard therapy and presence of concomitant atopic diseases (asthma, allergic rhinitis and/or atopic dermatitis). The data necessary to classify the participants as chronic or acute were collected in the full sample, while the data useful to identify severe patients were collected only among patients with chronic hand eczema, and data on refractoriness to standard therapy were collected among chronic and severe patients.

To perform classifications according to chronicity, severity and refractoriness to standard therapy, we basically used the same criteria used in the clinical trial by Ruzicka et al.[23]. However, the clinical investigators considered the criteria used by Ruzicka et al. not always sufficient to classify correctly the target patients for our study, hence some modifications were adopted, as below specified.

Namely, to be defined as chronic, patients had to have symptoms of hand eczema for 6 months or more, in the absence of external causative factors (e.g., contact with allergens or irritants); chronic patients with current relapse were further classified as chronic and relapsed patients.

To define the disease as severe, each physician evaluated the general clinical status of the patient, the functional impact of the disease on the patient's professional and everyday activity, and used as a guide the Physician's Global Assessment (PGA) score combined with the modified Total Lesion Symptom Score (mTLSS)[23] and with the photographic guide[24]. Hence, differently from the approach used in the study by Ruzicka et al.[23], the decision to classify a patient as severe was not

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driven only by the PGA score, but also by the functional impact of the disease on the patient's professional and everyday activity, and by the general clinical status that was assessed by the physician during the visit.

PGA and mTLSS were developed as verbal descriptions of the different chronic hand eczema severity grades depicted in the photographic guide[24]. PGA consists of a five level scale: clear, almost clear, mild disease, moderate disease and severe disease. Each level is associated with a description of hand eczema intensity and a percentage of hand surface involved. The mTLSS consists of 7 items: 1) erythema, 2) scaling, 3) lichenification/hyperkeratosis, 4) vesiculation, 5) edema, 6) fissures, 7) pruritus/pain. Each item ranges from 0 (none) to 3 (severe). These item scores are summarized in a summary score ranging from 0 to 21, with a higher score indicating a more severe condition. The photographic guide classifies the severity of hand eczema in 5 levels: clear, almost clear, moderate, severe, very severe. Each level is represented by 4 photographs showing both dorsal and palmar views of hands.

Finally, patients were defined as refractory to standard therapy with potent topical corticosteroids when they fulfilled all the following criteria: (i) had avoided irritants and allergens, if identified, without significant improvement, (ii) other disorders that may mimic chronic hand eczema had been excluded, (iii) had received standard skin care, including emollients and barrier protection as appropriate, without significant improvement, and (iv) they had also received treatment with topical corticosteroids for at least 8 weeks in total, within 6 months before enrolment, with either no response or only a transient response. The previous 8 weeks of treatment had to include 4 weeks of therapy with the most potent class of topical corticosteroids, e.g., clobetasol propionate.

Due to lack of an adequate system for hand eczema classification and to the frequent coexistence of different possible etiologies (irritant, allergic, endogenous, mixed), sub-diagnoses, e.g. allergic, irritant, atopic or vesicular hand eczema, were not taken into account and we preferred to focus on the morphology and severity of the disease as defined by two validated scoring systems.

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Statistical analyses

Socio-demographic and clinical characteristics of the sample were described using proportions for categorical data, mean and/or median as central tendency parameters for continuous data, standard deviation (SD), minimum (min) and maximum (max) values as dispersion parameters.

Multivariable logistic regression analyses were conducted in order to investigate the relationship between socio-demographic and clinical data (age, gender, educational level, concomitant atopic diseases and unemployment status, included as independent variables in the model) with the different stages of chronic hand eczema (included as dependent variable). In particular, we assessed these relationships by comparing severe with not severe cases, and refractory and severe were compared with not severe cases within the group of chronic hand eczema patients. With the logistic regression analyses we estimated the Odds Ratio (OR) as a measure of risk increase (OR > 1) or decrease (OR < 1) of having each form of chronic hand eczema related with the independent variables. The magnitude of the OR indicates the magnitude of the association between the independent and dependent variables.

A stepwise procedure was adopted to investigate and select the most efficient models. To select the models we considered the following features: statistical significance of the regression coefficients, the parsimony criterion and the goodness of fit assessed using the AIC (Akaike information criterion) and BIC (Bayesian information criterion). We used the AIC and the BIC because they are two popular measures to assess the goodness of fit estimated considering the number of parameters and the likelihood function for the model. Given two models with different information criterion values, the model with the smaller value of the AIC and BIC is considered to be better.

Although several models were investigated, only the most efficient ones are specified in the paper. P-values <0.05 (two-tailed tests) were considered for statistical significance. All analyses were performed using IBM SPSS software version 18 (IBM, Somers, NY, USA).

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RESULTS

Sample description

A flow chart (Figure 1) shows the number of patients recruited and sub-grouped according to the stage of severity and responsiveness to treatment. A total of 984 patients were enrolled. Three patients were identified as not eligible for the study because they did not meet the inclusion criteria. Hence, the valid study sample included 981 patients.

Hand eczema was classified as chronic or chronic and relapsed in 83.5% of the sample. Around 6.5% of chronic hand eczema patients reported only the data on their chronicity but not on the severity and refractoriness to therapy, hence these patients were excluded from the analyses focusing on the severe and severe and refractory subgroups. Accordingly, the valid study sample of patients that were severe and refractory to standard therapy actually included 766 chronic hand eczema patients. Among these patients, 21.3% (N=163) were classified as severe and 62.6% (N=102) of chronic severe patients were refractory to standard therapy.

Table 1 shows the description of patients belonging to each subgroup of patients. In the patients with chronic hand eczema, the mean difference between appearance of symptoms and diagnosis was 1.7 years and 19.2% were at first visit in a contact clinic due to hand eczema. The average (±SD) mTLSS summary score was 8.1 (±4.5) and, according to the PGA scale, 9.9% of the chronic patients were severe (Figure 2). The mean difference between appearance of symptoms and diagnosis is similar of what found in the chronic group when we considered the severe and the severe and refractory chronic hand eczema patients. Chronic patients underwent more dermatological tests than severe and severe and refractory group, while these last two subgroups reported more concomitant atopic diseases. Considering the patients with severe chronic hand eczema, 98.8% did not show any other condition which may mimic chronic hand eczema, 77.2% had avoided irritants and allergens, if identified, without significant improvement, 82.3% had received standard skin care, including emollients and barrier protection, without significant

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improvement, and 71.6% had received treatments with topical corticosteroids for at least 8 weeks during the six months before the enrolment, with either no response or only a transient response.

Table 2 shows details on the working status of employed patients, according to chronicity, severity and refractoriness of hand eczema. Food processing and related works, health professions, craft and related trades works (builders, plumbers, electricians), hairdressers/beauticians and handicraft works were the jobs most prevalent in the acute and chronic hand eczema patients group. The patients included in these five job categories were 45% of all employed patients. The prevalence of hairdressers/beauticians decreased from the acute hand eczema to the severe and severe refractory hand eczema patients, while the prevalence of the handicraft workers increased. Further, in the severe and severe and refractory hand eczema groups the percentage of patients included in the previous five job categories was 49.6% and 46.6%, respectively, similar of what found in the chronic group.

Factors associated with chronic hand eczema and its different stages of severity and refractoriness

Results from the logistic regression analyses, reported in Table 3, show that having severe or severe and refractory chronic hand eczema was more likely to be (i.e., with OR>1) among men (statistically significant for severe patients), among older patients (statistically significant for both subgroups of patients in 41-50 years old patients), among those with lower educational level (significant in both subgroups of patients), among unemployed patients (statistically significant among severe and refractory patients), and among those with allergic rhinitis and/or atopic dermatitis. Each result is to be considered adjusted for all the other variables specified in the model and reported in the table.

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DISCUSSION

To the best of our knowledge, this is the first cross-sectional study on hand eczema conducted in a Mediterranean European country. The centers involved were allocated all over the Italian territory, including the two major islands, in order to account for geographical and climatic differences. According to our results, the prevalence of chronic hand eczema among patients with hand eczema accessing dermatological reference centers is as high as 83.5%, and this condition is more frequent in women (63.5% of cases). The percentage of severe condition among chronic hand eczema patients was 21.3%, similar to what was found in a study recently conducted in a different setting of Germany[20]. The proportion of patients with a severe PGA score was 6.6%, less than the proportion of severe patients (21.3%) classified as severe according to a combination of assessments.

Among our chronic patients, we found a mean duration of 6 years from the appearance of symptoms and of 4 years from the diagnosis, which is shorter than that found in German patients (7.6 years), however, it confirms that chronic hand eczema is a long lasting disease[20]. Also, we found that more than 60% of severe chronic hand eczema patients were refractory to standard therapy, around 11.0% of all hand eczema patients. This result shows the relatively high presence of patients, among those with hand eczema accessing the dermatological reference centers to receive medical assistance, having a condition that is difficult to manage and related to severe impairment of quality of life and high direct and indirect costs[15,17,25].

Investigations on hand eczema in the general population found that it is associated with female sex, young age, lower education and occupational status[6,26]. According to other authors, hand eczema frequency is higher among health professionals and cleaners, but this relation it is still not clear[1,27,28]. Our results show that compared to the not severe ones, the subgroup of severe patients appears to be more common among men and in the 41-50 years age group, and to be associated with lower education, after adjusting for the other factors included in the analyses. In studies on general population conducted in North European countries, the hand eczema risk was

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higher in female aged below 30 or between 30-39 years old[3,26,27,29]. When comparing the general population without hand eczema with the HE population, the ORs for reporting HE was significantly higher for woman and individuals with lower education[26,27,29]. Our results show that not severe CHE is more frequent among women and in people aged below 40; while men, people aged 41-50 years and people with a lower education reported a higher risk to have severe CHE.

Further, our study shows that the percentage of unemployed patients was higher in severe (6.8%) and in severe and refractory chronic hand eczema (8.8%) than in not severe chronic hand eczema (3.6%); furthermore, the presence of severe and refractory chronic hand eczema was found to be significantly related with being unemployed adjusting for the other patients' characteristics. Other studies, on the general population, showed that subjects with HE had a higher period of sick leave, a higher probability to change their job or to lose it[1,16,30-32]. Therefore, one interpretation of our results is that more severe patients are likely to lose their job, due to their condition. In addition, both severe chronic hand eczema and severe and refractory chronic hand eczema were also found significantly associated with having atopic dermatitis and allergic rhinitis. Also other studies conducted on the general population found that atopic dermatitis is significantly associated with hand eczema[1,3,31-33], but effect seems to level off with increasing age; while respiratory atopy was associated with hand eczema even with increasing age[32,34]. A study conducted in Finland showed that atopic dermatitis and especially respiratory atopy are correlated with the continuation of hand eczema[32]. Our study reports a higher prevalence of allergic rhinitis compared to atopic dermatitis; furthermore, our results seem to show that atopic dermatitis and allergic rhinitis are more strongly associated with severe and refractory condition. This could be explained in the light of the reduced efficacy of the cutaneous/mucosal barrier function, together with the aspecific and, in many cases, also specific (allergic) hyper-reactivity to environmental conditions and substances, in atopic persons.

In the study we also compared chronic and acute patients, but no significant differences were found. In particular, the results showed a similar distribution in the working status categories

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and in the education levels, and a similar percentage of male and concomitant diseases. Because this study was conducted in highly specialized centers, the acute patients who access these departments are the most severe and difficult to treat. We could not consider these patients as a representative sample of Italian acute hand eczema subjects and a comparison with the chronic sample is not correct because it could include a big selection bias.

Finally, we found that food processing and related works, health professions, craft and related trades works (builders, plumbers, electricians), hairdressers/beauticians and handicraft works were the jobs most frequently associated with having chronic hand eczema, as shown in other studies[21]. While, no specific type of work was found to be associated with any of the different chronic hand eczema subgroups. Our results are in line with what found in the general population studies where nursing, medical work, service work, and in general daily occupational exposure to water, detergents, chemicals or dirt, resulted in a higher prevalence of hand eczema[1,20,27].

Our study has some limitations: it was conducted in patients spontaneously accessing dermatological reference centers and it does not allow estimating the epidemiological features of chronic hand eczema in the general population. The criteria used to classify patients as chronic differ in some aspects from those used in other recent studies[17,20] and can generate results not totally comparable. Augustin et al.[17] define as chronic patients with initial diagnosis at least 12 months before enrolment while Apfelbacher et al.[20] define as chronic patients with a disease duration of at least 3 months or with more than 2 flares within the last 12 months. A further criticism could rise on the approach used to classify the patients as severe. In previous researches, only the PGA score was used to identify severe patients, while in our study clinicians considered more appropriate using a combination of parameters: the functional impact of the disease on the patient's professional and everyday activity and the general clinical status of the patient, using the PGA score combined with the mTLSS and the photographic guide. Finally, although we planned to cover all the climatic conditions in the target context, adopting an observational period of 6 months, data collection was performed through different periods of time and seasons by the different participating centers, and,

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actually, in some cases the enrollment time span of 6 months might have been insufficient to observe the effect of changing climatic condition on chronic hand eczema patients, with possible implications on the study sample enrolled.

Despite its limitations, this study offers a picture of the epidemiological aspects related with hand eczema among patients accessing dermatological reference centers in a Mediterranean country. Chronic hand eczema is common among these patients. One fifth of chronic patients are severe and more than one-tenth are also refractory to standard therapy with potent topical corticosteroids. Severe chronic hand eczema and especially refractory severe chronic hand eczema are burdensome conditions[25], requiring to medical and policy decision special attention aimed to appropriately identify and manage these patients.

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TABLES AND FIGURES

Table 1: Patients' socio-demographic and clinical characteristics

Variable description		Entire sample (N=981)	Acute hand eczema (N=162)	Chronic hand eczema (N=819)	Severe chronic hand eczema (N=163)*	Severe and refractory chronic hand eczema (N=102)*
Proportion of patients within the more general subgroup, %		_	**16.5**	**83.5**	**21.3**	**62.6**
Age in years	Median (min-max) Mean (SD)	39.1 (18.0-90.1) 41.3 (15.1)	36.7 (18.8-83.3) 40.5 (15.6)	41.5 (18.0-90.1) 39.5 (15.0)	42.9 (18.0-79.9) 44.4 (14.6)	42.6 (18.0-79.9) 44.0 (15.0)
Age group, %	18-30 years	25.5	26.5	25.3	16.0	14.7
	31-40 years	26.7	30.9	25.9	25.2	27.5
	41-50 years	20.9	16.7	21.7	27.5	31.3
	51-60 years	13.8	11.7	14.2	15.3	10.8
	>60 years	13.1	14.2	12.9	16.0	15.7
Gender, %	Male	36.1	34.0	36.5	48.5	41.2
Education, %**	Primary school	10.4	10.5	10.4	14.4	14.7
	Lower secondary school	29.4	28.4	29.5	39.4	40.2
	Upper secondary school	44.9	39.5	46.0	35.6	33.3
	Graduate	14.4	21.0	13.0	10.0	8.8
	Postgraduate	0.9	0.6	0.1	0.6	1.0
Working status, %	Employed	64.8	66.7	64.4	61.3	58.8
	Housewife	15.9	13.6	16.4	17.8	18.6
	Retired	8.7	8.0	8.8	10.4	9.8
	Student	6.3	6.8	6.2	3.7	3.9
	Unemployed	4.3	4.9	4.2	6.8	8.8
Years from appearance of symptoms	Median (min-max) Mean (SD)	2.0 (0.0-50.0) 5.0 (7.2)	0.2 (0.0-0.49) 0.2 (0.1)	3.0 (0.5-50.0) 6.0 (7.5)	3.0 (0.5-30.0) 6.3 (6.4)	3.5 (0.5-30.0) 6.3 (6.5)
Years from diagnosis	Median (min-max) Mean (SD)	1.0 (0.0-50.0) 3.6 (6.3)	0.1 (0.0-0.5) 0.1 (0.1)	1.5 (0.0-50.0) 4.3 (6.8)	2.0 (0.0-30.0) 4.8 (5.9)	3.0 (0.0-30.0) 5.2 (6.0)
First visit in a dermatology center due to hand eczema, %**		25.8	59.8	19.2	20.2	20.6
Dermatological test (e.g., patch and prick), %		74.7	60.2	77.5	71.8	68.6
Results of dermatological tests: positive, %		64.1	68.8	63.4	65.0	67.1
Patch test, %		70.2	55.5	73.1	69.9	65.7
Results of patch test: positive, %		58.3	62.2	57.3	59.7	62.7
Prick test, %		25.7	19.2	27.0	16.9	30.4

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Results of prick test: positive, %		52.0	67.7	48.9	44.7	48.4
Concomitant diseases, %**	Patients with at least one concomitant atopic disease	27.4	25.0	27.5	37.3	41.0
Concomitant atopic diseases, %**	Allergic rhinitis	17.8	16.2	18.3	23.6	24.0
	Atopic dermatitis	10.8	6.3	11.8	14.9	18.6
	Asthma	8.4	8.8	8.4	10.6	11.0

* Around 6.5% of chronic hand eczema patients did not report data on their severity and refractoriness (we only know they were chronic), hence they were excluded from these subgroups: then, the valid study sample for the severity and refractoriness analyses was 766.
** Up to 9 patients did not provide one or more data. Percentages were estimated excluding patients with data missing from calculation.

Table 2: Type of work conducted by patients with employed work.

Working categories	**Entire sample**	**Acute hand eczema**	**Chronic hand eczema**	**Severe chronic hand eczema**	**Severe and refractory chronic hand eczema**
Number of patients*	636	108	528	100	60
Food processing and related workers	11.8%	9.3%	12.3%	10.4%	12.1%
Health professionals	9.8%	14.8%	8.7%	7.2%	10.3%
Craft and related trades workers (builders, plumbers, electricians)	8.4%	7.4%	8.5%	12.4%	8.7%
Hairdressers/beauticians	8.2%	12.0%	7.5%	3.1%	-
Handicraft workers	7.7%	6.5%	7.9%	16.5%	15.5%
Teaching professionals	5.9%	5.6%	6.0%	4.1%	5.2%
Computing professionals	5.3%	2.8%	5.8%	8.2%	5.2%
Cleaners	3.9%	2.8%	4.2%	2.1%	3.4%
Office clerks	3.7%	3.7%	3.7%	1.0%	-
Mechanical machinery assemblers	3.4%	-	4.0%	3.1%	3.4%
Computer associated professionals	3.1%	-	3.7%	3.1%	3.4%
Shop salespersons and demonstrators	2.6%	3.7%	2.4%	1.0%	1.7%
Cashiers and related clerks	2.1%	2.8%	2.0%	3.1%	5.2%
Agricultural workers	1.9%	2.8%	1.8%	4.1%	5.2%
Merchants	1.3%	0.9%	1.4%	2.1%	-
Stall and market sales persons	1.3%	0.9%	1.4%	1.0%	1.7%
Motor vehicles drivers	1.0%	1.9%	0.8%	3.1%	5.2%
Gardeners and florists	0.6%	-	0.8%	-	-
Printing and related trade workers	0.6%	-	0.8%	1.0%	-
Launderers	0.5%	-	0.6%	2.1%	3.4%
Electronics and telecommunications engineering and related technicians	0.5%	-	0.6%	2.1%	-
Professionals	0.5%	0.9%	0.4%	-	-
Armed forces	0.3%	-	0.4%	1.0%	1.7%
Other working categories	15.6%	21.3%	14.3%	8.2%	8.7%

*Percentages are calculated using as denominator the number of employed patients in each subgroup.

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Table 3. Results from the Multivariable logistic regression analyses.

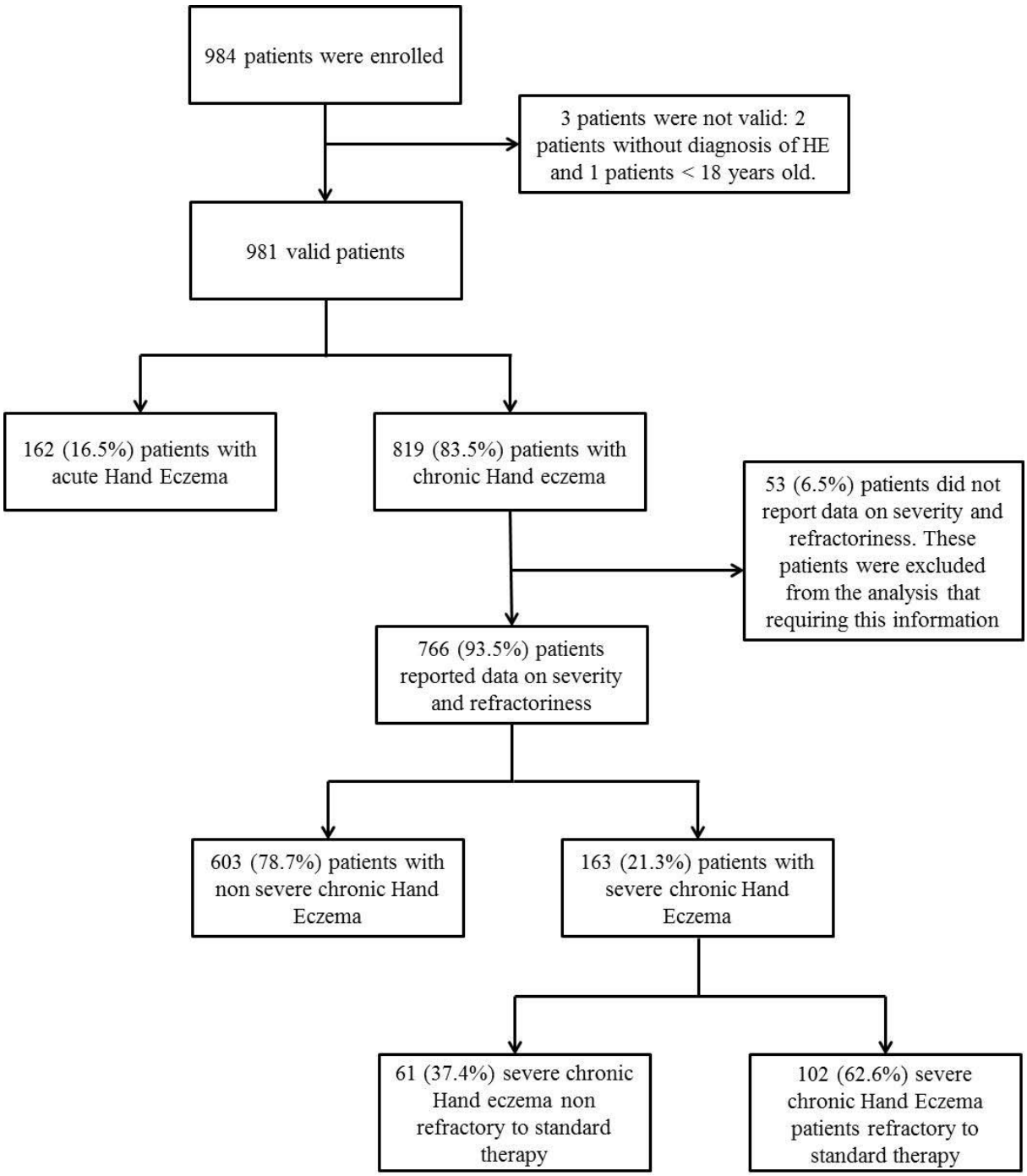
Description of independent variables		Chronic Hand Eczema Patients			
		Severe *versus* non severe		Severe and refractory *versus* non severe	
		OR* (IC 95%)	**p-value**	**OR* (IC 95%)**	**p-value**
Gender	Female	*1 (Reference)*	.	*1 (Reference)*	.
	Male	1.69 (1.15-2.50)	*0.008*	1.20 (0.75-1.93)	*0.447*
Age	18-30	*1 (Reference)*	.	*1 (Reference)*	.
	31-40	1.61 (0.89-2.92)	*0.114*	1.91 (0.93-3.94)	*0.079*
	41-50	2.38 (1.31-4.31)	0.004	3.32 (1.61-6.81)	0.001
	51-60	1.81 (0.91-3.63)	0.093	1.54 (0.61-3.86)	0.363
	≥ 61	1.79 (0.88-3.62)	0.106	2.32 (0.98-5.49)	0.056
Education	upper secondary school or graduate/postgraduate	*1 (Reference)*	.	*1 (Reference)*	.
	primary or lower secondary school	2.00 (1.35-2.96)	*0.001*	2.24 (1.39-3.58)	*0.001*
Working status	employed/housewife/student /retired	*1 (Reference)*	.	*1 (Reference)*	.
	Unemployed	2.19 (0.93-5.17)	*0.072*	3.30 (1.31-8.34)	*0.012*
Atopy	Absence of allergic rhinitis	*1 (Reference)*	.	*1 (Reference)*	.
	Allergic rhinitis	1.61 (0.99-2.60)	*0.055*	1.55 (0.87-2.76)	*0.137*
	Absence of atopic dermatitis	*1 (Reference)*	.	*1 (Reference)*	.
	Atopic dermatitis	1.61 (0.89-2.92)	*0.114*	2.16 (1.12-4.17)	*0.021*
Number of observations		593 (non severe) 158 (severe)		593 (non severe) 98 (severe and refractory)	
AIC		221.1		189.5	
BIC		267.3		239.5	

* OR = 1 indicates that the condition or event under study is equally likely to occur in the reference group and in the group compared with the reference (e.g. Male comparing to female (reference group)). OR > 1 indicates that the condition or event is more likely to occur in the group compared with the reference group. OR < 1 indicates that the condition or event is less likely to occur in the group compared with the reference group.

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Figure 1. Enrolment and stages distribution.

Figure 2: PGA score in chronic hand eczema patients (N=766)



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