



Contact dermatitis: Clinical practice findings from a single tertiary referral hospital, a 4-Year retrospective study

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ABSTRACT

Background: It is estimated that 20% of the general population is sensitized to some kind of contact allergen. Contact dermatitis is one of the major occupational diseases worldwide. This disease has a higher prevalence in the female gender and is more frequently observed in the third or fourth decade of life. The main objective of this study was to describe the main sociodemographic and clinical characteristics of patients with contact dermatitis treated in the Allergy Unit of the San Juan De Dios Hospital - Caja Costarricense de Seguro Social.

Methods: Clinical records of contact dermatitis outpatients from a single hospital were analyzed, in a 4-year retrospective observational study.

Results: At the time of the patch testing, patients showed a mean age of 42.2 years. Disease frequency was higher in the female population (female/male ratio of 4.2:1) and in patients mostly dedicated to household workchores. Most patients presented several years of disease history, and the hands were the highest affected body part. Patch testing revealed that nickel sulfate, CI+Me-Isothiazolinone (Kathon CG), and thimerosal were allergens regularly associated with contact dermatitis in the analyzed population.

Conclusions: To a great extent, sociodemographic and clinical characteristics identified in these patients resemble what is reported in other regions, including the Americas and worldwide. It is worth highlighting a high female proportion rate probably related to cultural aspects, a smaller percentage of irritant contact dermatitis that may be associated to institutional patient management, and a slight difference in the most common allergens when compared to other published studies.

Keywords: Contact dermatitis, Allergens, Tertiary referral hospital

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INTRODUCTION

Contact dermatitis is any disorder of the skin caused by contact with an exogenous substance, which causes an irritating and/or allergic reaction.¹ This condition is quite frequent, and although it can occur at any age, it is commonly observed in the adult population. It is one of the main causes within occupational diseases, and it represents an associated annual cost of close to US\$1 billion.^{2,3} Irritative contact dermatitis corresponds to 80% of cases; the remaining percentage is associated with allergic contact dermatitis in which the external agent activates a classic delayed hypersensitivity response type IV.⁴ Non-allergic contact dermatitis is caused by the irritating action of an external precipitating agent (physical or chemical), establishing a chronic effect of the substance on the skin. The result on skin usually occurs by the effect of acids, bases, detergents, soaps, and topical medicinal products.⁵

In both allergic and irritant contact dermatitis, its main affection occurs in the hands; it has been reported that 5% of patients with hand-level contact dermatitis develop a chronic and disabling disease.⁶

It is estimated that 20% of the general population is sensitized when in contact with an allergen,⁷ and more than half of the identified chemicals, have the potential to become contact allergens.⁸ The development of contact dermatitis is determined by individual susceptibility, the physicochemical properties of the allergen, and the dose.⁸

Patch tests are the gold standard to diagnose contact dermatitis. In this test, the patient is exposed to various allergens, causing a skin reaction when the patient is sensitive to the allergen. The North American Contact Dermatitis Group (NACDG), part of the American Society of Contact Dermatitis,⁹ recommends the use of TRUE (Thin-Layer Rapid Use Epicutaneous) TEST; a test made by a panel of 35 antigens and a negative control, which provides highly reproducible results.

In recent years, different regions have reported an increase in the incidence and prevalence of contact dermatitis,¹⁰⁻¹² North America reported nickel, the CI + Me-Isothiazolinone (Kathon CG),

and the mixture of fragrances as the main causal agents of allergic contact dermatitis;⁹ some of these agents coincide with what has been reported in Latin American studies.^{13,14} The Latin American Region has reported a predominance in the involvement of hands, as well as a higher frequency of the condition in females^{13,14}

At a Central American level there are no recent studies describing the percentage of patients affected by this disease, its evolution, or prevention measures. In the same way, Costa Rica has a lack of current local data describing the population with contact dermatitis. This research aims to carry out a description of the main clinical and epidemiological characteristics of patients with clinical diagnosis of contact dermatitis, seen in the outpatient Allergy Clinic at the *Hospital San Juan de Dios* part of *Caja Costarricense de Seguro Social, CCSS in Spanish*) between 2012 and 2018. Also, in this study, the major allergens responsible for allergic contact dermatitis in our population are specified.

METHODOLOGY

This was an observational retrospective study based on medical records of patients over the age of 13 with a clinical diagnosis of contact dermatitis who were treated in the Allergy Unit of the *Hospital San Juan de Dios - CCSS*, between 2012 and 2018.

During the study period, at least one TRUE TEST was performed on each patient. Of the 622 tests performed, 228 cases correspond to repeated assessments of the TRUE TEST in the same patient or patients with incomplete records (clinical records with more than 50% of missing information). For patients with multiple assessments, results from the most recent tests were considered, while patients with incomplete records were excluded from this investigation. The data from the remaining 394 patients were incorporated into the study. The patch test reading was performed 48 h after been applied to the patient's back; if the first result was negative a second reading was scheduled 24 h later (72 h in total).

Distributions of frequency and measures of central tendency for the variables studied were established according to their nature. Unless

stated otherwise, these values were expressed as: absolute number and percentage (qualitative variable), and mean \pm standard deviation (quantitative variable). The contrasts of hypothesis for qualitative variables were performed using Chi-square test or Fisher's exact test using a significance level of 0.05, using SPSS Statistics Program 23[®]. This research was developed in accordance with the international bioethics treaties, respecting both international and national regulations, and was approved by the Scientific Ethics Committee of the *Hospital San Juan de Dios* within the Social Security System named "Caja Costarricense de Seguro Social".

RESULTS

At the time the TRUE TEST was applied, the analyzed population presented an average age of 42.2 years (95% CI 40.7-43.8), with a range between 13 and 86 years. Those with ages between 30 and 34 years and 45-49 years, correspond to the ranges where a greater number of tests can be observed, this increase is exhibited in both sexes (Fig. 1).

Distribution according to sex shows a noticeable female predominance, where 318 (80.7%) of the records correspond to women while only 76 (19.2%) belong to men. The above, generates a female/male relationship of 4.2:1.

According to the common features regarding the type of occupation for each patient, 8 categories were considered: home/domestic work, office work, health, craftwork, aesthetics, agro-industry, and others. Patients who did not indicate occupation in their file were categorized in the "not indicated" classification. The distribution according to work can be seen in Table 1.

Regarding the main comorbidities associated with hypersensitivity reactions in these patients; 12.9% (51) documented asthma, and the same percentage presented allergic rhinitis. At the same time, we identified a small rate of atopic dermatitis 5.6% (22), allergic conjunctivitis 0.8% (3) and chronic rhino sinusitis 0.5% (2). There was no statistically significant correlation between these comorbidities and the presence of contact dermatitis.

Manifestations of the disease with a disease history of more than 3 years were the most common (31.5%). Conditions with a clinical course disease period between 1 and 3 years and those with less than 6 months presented similar frequencies of 20.6% and 20.3%, respectively; while contact dermatitis with a clinical course period between 6 months and 1 year represented 9.8% of the population. In 70 cases, the years of disease history were not registered.

The affected anatomic location varies between patients, and a significant percentage had multiple areas compromised. It should be noted, as shown in Fig. 2, in which the hands were the most commonly affected area (37.1%), followed by the face (25.6%) and the arms (21.8%). Areas such as chest, abdomen, legs, and eyelids also showed considerable affection; while nose and genitals constitute minor alteration anatomical locations. Fifteen (3.8%) analyzed cases reported a generalized condition.

Fig. 3 shows the main allergens that cause a dermal reaction through the TRUE TEST within the Allergy Clinic's outpatient population. Out of all patients in 155 cases (corresponding to 39.3%), despite having a clinical diagnosis of contact dermatitis did not show reaction to the test.

A remarkable finding is the existence of a difference within the major allergens that cause the disorder and the participant's gender. While in females the main allergen reported was nickel sulfate, in men the amount of positive reactions produced by Cl + Me-isothiazolinone (Kathon CG) ($n = 12$) is almost equivalent to those produced by nickel sulfate ($n = 11$). The distribution of other allergens which trigger a reaction at the dermis level did not vary according to the sex of patients with allergic contact dermatitis.

Table 2 compares the most important positive allergens identified in this study with the main studies of allergic contact dermatitis published recently.

A multivariate analysis between the 3 main allergens and the different anatomical locations of affection identified a series of statistically significant correlations. Evidence of association was found between: nickel sulfate and eyelid

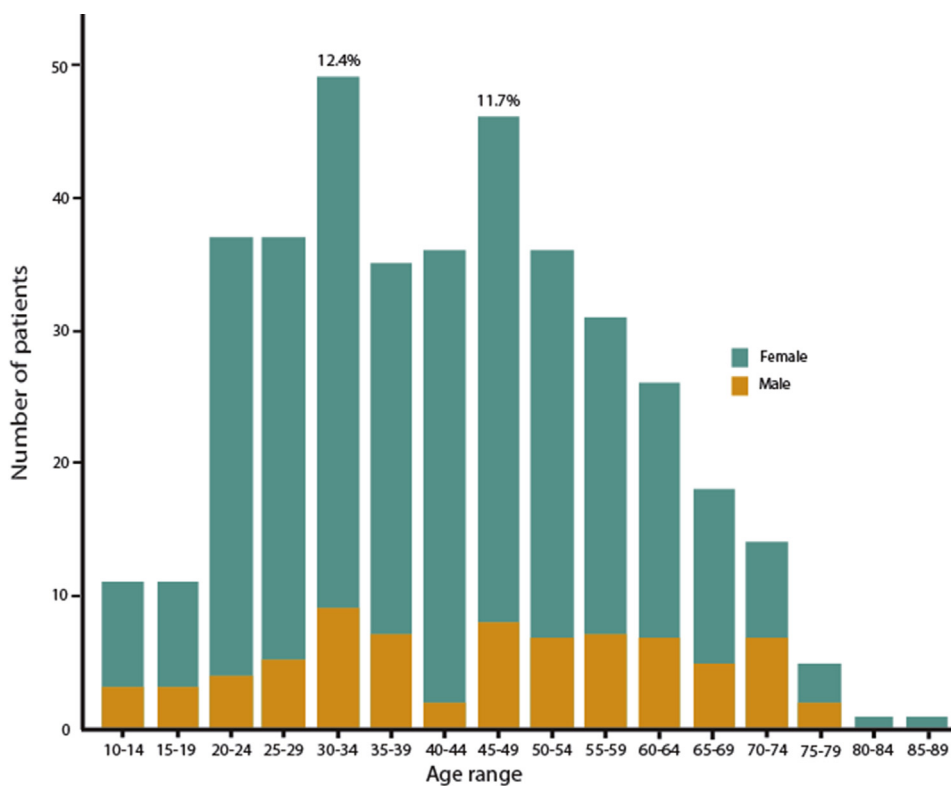


Fig. 1 Number of TRUE TESTs according age and sex, in patients diagnosed with contact dermatitis treated in the Allergy Clinic in Hospital San Juan de Dios - CCSS from 2012 to 2018

involvement ($p = 0.002$) and armpits ($p = 0.009$); Cl+Me-Isothiazolinone (Kathon CG) and the development of a dermal reaction in ears ($p = 0.04$) and fingers ($p = 0.01$) and thiomersal and nose-level alterations ($p = 0.04$) and genitals ($p = 0.04$).

Analysis regarding the association between the type of occupation self-reported by study participants and the various allergens showed a statistically significant correlation between patients who work in the field of aesthetics and mixture of parabens ($p < 0.001$), as well as with mercapto-benzothiazole ($p = 0, 007$). In the same way, there is a statistically significant correlation between patients who engage in the agro-industry with black rubber mix or PPD mix ($p = 0.007$), Quaternium 15 ($p = 0.007$), the *para*-phenyldiamine ($p = 0,008$), and formaldehyde ($p = 0.001$). There is also evidence of an association between individuals that perform manual work (craftwork) and the Cl + Me-Isothiazolinone (Kathon CG) ($p = 0.004$), and those who carry out office work and are in contact with formaldehyde ($p = 0, 001$).

The contrast between the type of occupation reported by study participants and the main anatomical regions affected identified a statistically significant correlation between patients working in the health industry and lesions in hands ($p = 0.02$). The abdominal area also showed a higher frequency in this population ($p = 0.02$). In contrast, patients who performed manual work presented a tendency of greater lesions in the arms.

DISCUSSION

Knowing the characteristics of a population that suffers from a certain disorder is essential for adequate management. This study constitutes an initiative including a large population from a single facility in which the main socio-demographic and clinical characteristics of patients diagnosed with contact dermatitis are described, as well as the main allergens involved.

In this study, the average age for a diagnostic confirmation identified by the TRUE TEST panel, is similar to that reported in other countries such as Spain,¹⁶ Chile,¹⁵ and Malaysia.¹⁷ Possible

Type of occupation	Frequency, n (%)
Home/domestic work	125 (31,7%)
Others	79 (20,1%)
Office work	53 (13,5%)
Health	51 (12,9%)
Craftwork	46 (11,7%)
Aesthetics	5 (1,3%)
Agro-industry	3 (0,8%)
Not indicated	32 (8,1%)
Total	394 (100%)

Table 1. Main occupation self-reported by patients diagnosed with contact dermatitis seen by the Hospital San Juan de Dios (CCSS) allergy outpatient consultation

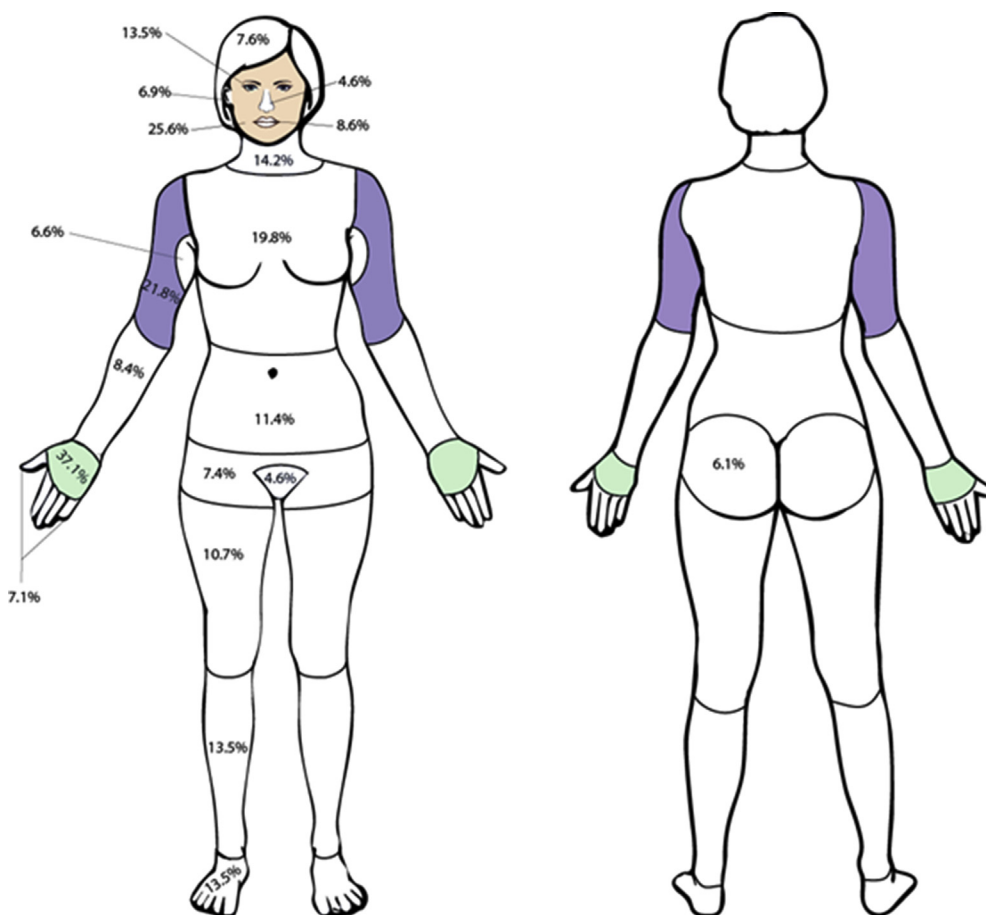


Fig. 2 Main affected body areas by percentage of patients with allergic contact dermatitis seen by the Hospital San Juan de Dios (CCSS) Allergy outpatient consultation

differences with other regions,^{14,18} could be related to the fact that a considerable proportion of patients presented clinical manifestations during a specific period of time and were initially diagnosed and treated in a primary or secondary level of care, up until a partial treatment response requiring a referral to a third level of care.

In general, it is still unclear why it is common to observe a higher prevalence of contact dermatitis in the age groups between 30 and 34 years and 45 and 49 years. The time required to develop

sensitization to one or several allergens as well as the repeated exposure to them are suggested as possible explanations.¹⁹ It is important to consider that both identified groups represent a major part of the workforce, a characteristic previously described for this condition²⁰

Regarding the socio-demographic features, and consistent with the majority of contact dermatitis studies, this research identified a higher prevalence in women; however, the defined woman/man relationship in this study is slightly higher than the one described worldwide.^{9,17,21-23} Although

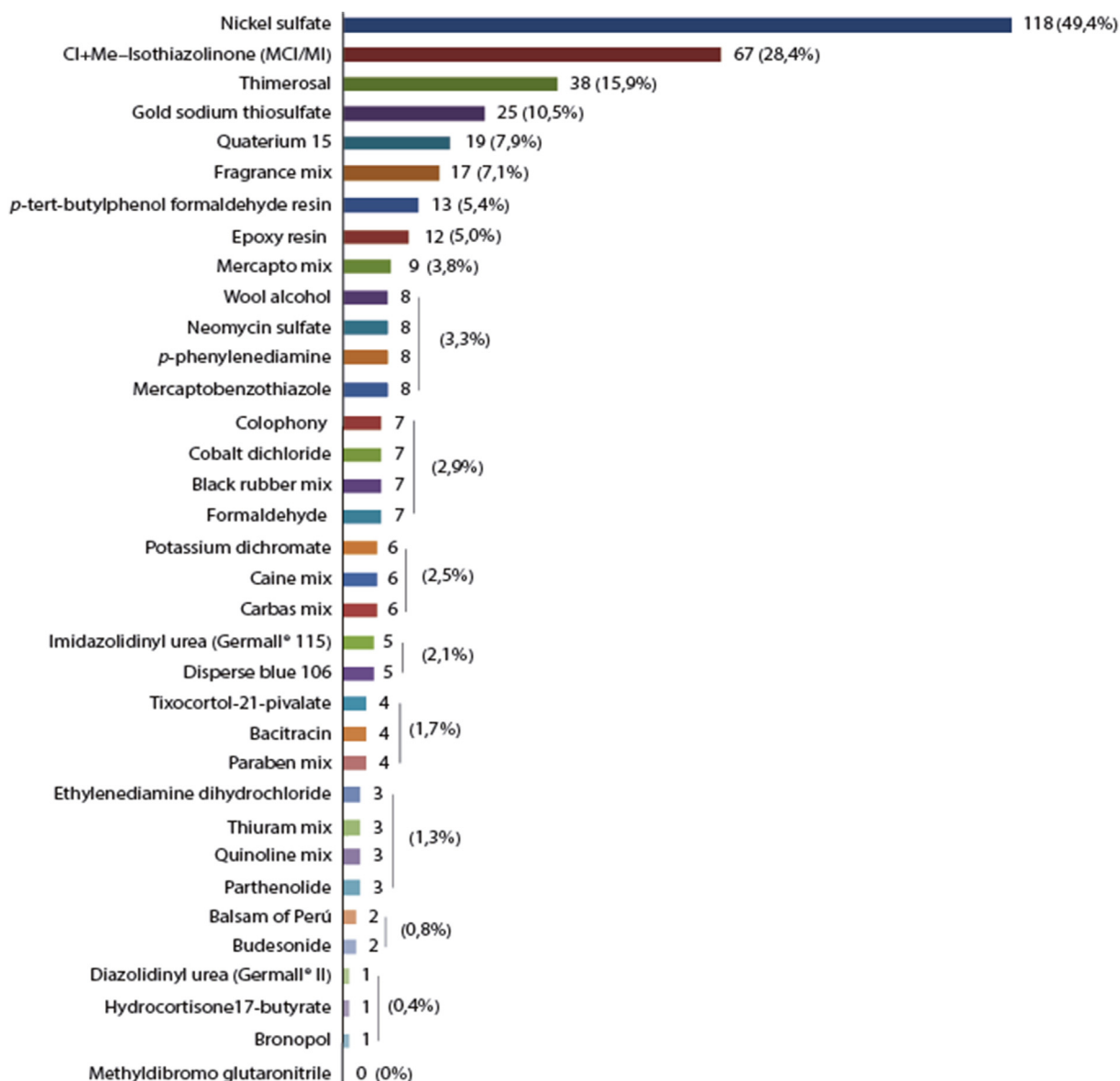


Fig. 3 Major allergens that cause dermal reaction through the TRUE TEST in patients with allergic contact dermatitis seen by the Hospital San Juan de Dios (CCSS) Allergy outpatient consultation

the influence of gender within this disorder is not entirely understood, a reason commonly accepted for the female dominance has been greater exposure to cosmetic and/or personal care products. Recently, hormone influence has also been identified as a factor that could relate to this condition^{24,25} The observed increase may in turn respond to specific cultural factors. It is more common for women to attend medical appointments and have better health control; therefore, the condition is diagnosed more frequently.²⁶

The presence of hypersensitivity associated comorbidities in one third of the analyzed patients is similar to that found by other authors.^{9,14,27} This could illustrate the susceptibility of such population to concomitantly be affected by related diseases, even though this might be controversial. The origin that may explain the

association between these diseases is probably multifactorial and may include genetic and environmental predispositions, as well as risk factors related to lifestyle and behavior.²⁸

The relationship between atopic dermatitis and contact dermatitis is not entirely clear; publications both in favor and against exist, and have shown different correlations between them.^{30,31} In contrast to what was described by Sunquist et al,²⁵ our study identified that the number of contact dermatitis patients who also had a diagnosis for atopic dermatitis was lower.

The main affected areas in patients with contact dermatitis, identified in this study are comparable to what has been described in recent publications and in accordance with world literature.³³⁻³⁵ The main anatomical localization is in hands, in 37.1% of cases. The high percentage of this condition's

	This study	Kasumagic et al. ⁴⁸	Dekoven et al. ⁹	Alinaghi et al. ⁵⁰
1.	Nickel sulfate	Nickel sulfate	Nickel sulfate	Nickel sulfate
2.	Cl+ Me-Isothiazolinone (MCI/MI)	Cobalt dichloride	Methylisothiazolinone 0.2% aq	Fragrance mix I
3.	Thimerosal	Thimerosal	Fragrance mix, 8%	Cobalt
4.	Gold Sodium Thiosulfate	Colophony	Formaldehyde 2% aq	Myroxylon pereirae resin (Balsam of Peru)
5.	Quaterium 15	Carba mix	Methylchlorisothiazolinone/ Methylisothiazolinone mix 0.01%	Chromium
6.	Fragrance mix	Potassium dichromate	Myroxylon pereirae resin (Balsam of Peru)	<i>p</i> -Phenylenediamine
7.	<i>p</i> -terc-butylphenol formaldehyde resin	Chromic acid	Neomycin	Cl+ Me-Isothiazolinone (MCI/MI)
8.	Epoxi resin	Fragrance mix	Bacitracin	Colophonium
9.	Mercapto mix	Balsam of Peru	Formaldehyde 1% aq	Formaldehyde
10.	Wool alcohols, neomycin sulfate, <i>p</i> -phenylenediamine	Formaldehyde	<i>p</i> -Phenylenediamine	<i>p</i> -tert-butylphenol formaldehyde resin.

Table 2. Comparison between the main positive allergens obtained in this study and the main studies of allergic contact dermatitis published today

presence in this anatomical region could be explained by the fact that the hands are the body part most often used in daily activities, and which are repeatedly exposed to a large number of allergens.³³ This high involvement of the hands would have a considerable impact in work related aspects and patients' quality of life.

Due to a high exposure rate, a thinner skin, a significant accumulation of allergens, and frequent contact with fingers (which are constantly exposed to multiple substances),^{36,37} eyelids are considerably susceptible to the action of irritants and/or allergens, which was shown in this study.

Regarding employment, patients who perform domestic work constitute the most affected group (31.7%). This association has been described elsewhere. In Turkey for example, 65% of the nickel contact dermatitis occurred in people who do domestic work.²⁷ In our particular case, this figure might be influenced by the presence of determined groups showing a higher proportion related to domestic chores.³⁸

The incidence of irritant contact dermatitis fluctuating from what has been described in world literature⁴ could be related to circumstances such as these: In the majority of cases, patients are previously assessed by physicians who carried out a clinical diagnosis of irritant contact dermatitis and do not consider the TRUE TEST employed by the Allergy Outpatient Clinic to be necessary.

The main allergens causing contact dermatitis vary depending on the region; large countries may have differences in allergens between regions¹⁵ (see Table 2). However, in general terms, the major European studies described nickel, cobalt, and chromium sulfate as the main triggers. Meanwhile, in the United States of America nickel sulfate, Cl + Me-Isothiazolinone (Kathon CG), and the mixture of fragrances are the most important.^{18,21}

As shown in Table 2, and in accordance with the vast majority of reports,^{17,24,43,48,49} nickel sulfate was identified as the substance to which a higher percentage of patients were sensitive. The high percentage is based on the fact that metals are the most sensitizing elements in the case of allergic contact dermatitis.⁴² Of particular

interest, in our study is the association identified between nickel sulfate and the eyelids as an area of involvement, similar to other studies that have documented nickel sulfate as a trigger agent in allergic contact dermatitis in the eyelid for 53.33% of cases.⁴⁰

Because of its low molecular weight, iso-thiazolinone mixture constitutes an ideal hapten, which would explain why it is the second allergen mostly associated with contact dermatitis in this study (see Table 2). Also, this mixture was the main allergen found in the male population. DeKoven et al reported a similar finding during the screening of 70 allergens in a population from 13 North American centers.⁹ As a widely used preservative, especially within the cosmetics industry, this allergen should be considered in patients with a history of allergic reactions to makeup and sunscreen.²³

Concerning the most affected anatomical locations, the Cl+Me-Isothiazolinone (Kathon CG) was mainly associated with lesions in face and hands,^{43,44} an aspect that has previously been referred to by Scherrer et al in a series of Brazilian patients with positive tests for this allergen where 50% presented involvement of hands and scalp and 40% showed face lesions.⁴⁵

As in the present investigation, Kasumagic et al report that thiomersal was the third most common allergen in patients with allergic contact dermatitis in their study population.⁴⁶ Thiomersal is commonly found in cosmetics such as eye shadows, eye mascaras, lotions, and ophthalmology solutions. This preservative with antimicrobial properties is also used in vaccines and many other products. The heterogeneity of products in which this allergen is utilized implies a high exposure population and would explain the elevated rate of positive reactions to the patch test.⁴⁶

Health care workers are exposed to a variety of agents that are capable of leading to a disease spectrum that includes allergic contact dermatitis (ACD), irritant contact dermatitis (ICD), and allergic contact urticarial (ACU). Permanent hand washing in health personnel favors the repeated exposure to different allergens,^{47,48} which would explain the identification of a statistically significant correlation between the two variables. This association is often

described in different regions and populations worldwide.^{47,49}

This work describes the principal triggers of allergic contact dermatitis and analyzes the main clinical and socio-demographic characteristics for a Central American population, supporting both similarities and differences in the pattern for this condition with regard to other regions worldwide.

Abbreviations

NACDG: North American Contact Dermatitis Group; TRUE Test: Thin-Layer Rapid Use Epicutaneous Test; CCSS: Caja Costarricense de Seguro Social; Aq: Aquosus

Funding

This study did not have external sponsorship; the researchers solved by their own means the necessary resources to carry out the protocol.

Availability of data and materials

The database and materials are not available to the public because they are property of the Caja Costarricense de Seguro Social. The permit for publication of the database wasn't granted by the institutional IRB.

Author contributions

Dr. Giovanni Sedó: Data collection, article writing and editing, communication with journal, study design.
Dr. Andrés Soto: Database management, statistical analysis, article writing and editing, graph and illustrations, study design.
Dra. Patricia Monge: Data collection, article reviewing and editing.
Dra. Caridad Pino: Data collection, article reviewing and editing.
Dr. Alfredo Sanabria: Statistical analysis, editing, study design.

Ethics approval

Ethics approval was given by the Hospital San Juan de Dios' IRB on August 14 of 2018 by the protocol number CEC-HJSD-11-2018.

Consent for publication

The consent for publication was given on August 28 of 2019 by the CENDEISS.

Declaration of competing interest

The authors have nothing to declare.

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