

Epidemiological and clinical data for allergic contact dermatitis in Kosovo during 2010-2020

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Abstract

Introduction: Allergic Contact Dermatitis is a form of eczema or dermatitis on the skin which appears as a delayed-type IV hypersensitivity reaction that manifests 48-72 hours after exposure to the allergen (low molecular weight chemical) with social, psychological, occupational, and familial by having an impact on the patient's quality of life.

Objectives: The purpose of the study is to show the epidemiological and clinical situation of Allergic Contact Dermatitis in Kosovo by identifying the most at-risk patients.

Patients and Methods: The study is of a retrospective cohort, clinical-analytical type. The study population consists of 1201 pediatric, adult, and elderly patients who presented to the Allergy Clinic, University Hospital Center (UHCK), and the Allergy-Asthma Specialist Office in Prishtina, Kosovo with suspicion of Contact Dermatitis and from which 536 were diagnosed with ACD during 2010-2020.

Results: Of the 355 cases, 59 patients were male (11.03%) and 477 were female (88.97%). The youngest patient in the study was 1 year old and the oldest was 85 years of age. The most common allergens from our study are Nickel sulphate 5% in 404 cases (57.7%), P-phenyl diamine 1% in 97 cases (13.86%), Cobalt chloride 1% in 46 cases (6.57%), Potassio Bicromato 0.5% in 23 cases (3.29%), Thiuram-mix in 19 cases (2.7%), Paraben mix 16% in 13 cases (1.86%).

Conclusion: 12% of patients who come to the Allergy Clinic for skin problems have Allergic Dermatitis Contact and Prevalence to have a positive result in at least one allergen is high 44.6%. The most affected age group is 25-29 years (102 cases or 19.3% of cases with Allergic Contact Dermatitis). For each year of increasing age, the likelihood of Allergic Contact Dermatitis increases by a factor of 1.01; the presence of allergic diseases increases the likelihood by a factor of 0.511, the female gender has a 3,084 times greater risk of contracting Allergic Contact Dermatitis in a lifetime.

Keywords: Allergic Contact Dermatitis, Chemical Substances.

Introduction

Allergic Contact Dermatitis (ACD) is a delayed-type hypersensitivity reaction mediated by T cells. In these studies, inflammation of the skin was caused by topical application to the epidermis of chemical sensitizing agents that act as haptens. [1]. Although antibody-mediated reactions may be a factor, ACD depends primarily on allergen-specific T cell activation and is considered a prototype of delayed hypersensitivity, as classified by Turk, Gell, and Coombs (type IV hypersensitivity) [2-4]. The sensitization phase involves events after the first contact with the allergen and ends when the individual is sensitized and able to give a positive reaction (dermatitis). The effector phase begins with elicitation and results in the clinical manifestation of ACD. The

whole induction phase process requires at least 3 days to several weeks, while the effector phase reaction takes place completely within 1-2 days [5].

The purpose of the study is to show the epidemiological and clinical situation of ACD in Kosovo by identifying the most at-risk patients.

Material and Methods

The study is of a retrospective cohort, clinical-analytical type. The study population consists of 1201 pediatric, adult, and elderly patients who presented to the Allergy Clinic, University Hospital Center (UHCK), and the Allergy-Asthma Specialist Office in

Prishtina, Kosovo with suspicion of Contact Dermatitis and from which 536 were diagnosed with ACD during 2010-2020.

Admission criteria in the study

The sample was selected from patients who visited this clinic voluntarily. The patients who were taken into the study are patients who have been with a Contact dermatitis on a clinic basis and who have agreed to be tested to determine their sensitivity to chemicals as the cause of their disease.

Exclusion criteria from the study

Patients who did not apply the Patch Test who had pathology or were under treatment that could not be tested were excluded from the possibility of testing. This group includes: Patients who are under continuous treatment with corticosteroids or drugs that affect the immune system; Patients with a history of severe allergic reactions (local or systemic); Patients with sore skin; Patients who have had skin exposure to UV rays very close to the visit; Patients who have changes in the surface of the skin where they should be tested; Patients who use topical corticosteroids in the test area; Pregnancy and Breastfeeding Women.

Technical data of the Patch Test procedure

Patch Test was performed using 20-22 reagents from the substances that are most often the cause of ACD. These substances during the 10 years were not only from one manufacturer but depending on the possibility of import for different periods were used manufacturers: Stalergens, Lofarma, Brial, Torlak, Chemotechnique diagnostics, but diagnostic kits with the same substances have always been selected. After 2 days the patients had the Patch test removed and their reading was done. Reading after 24 hours was mandatory and this was the real result that was recorded. They were advised to be notified during a week if a new reaction occurs. The intensity of erythematous changes was taken as a criterion for reading the test, vesicular and bullous papillomatosis at the site of application of each haptens as international criteria for the evaluation of the Patch test.

1. Negative-no changes in the location of the haptens
2. +slight positive-with slight erythematous changes and some slight papules
3. ++strong positive with erythematous changes, papillomatosis, and any possible vesicles
4. +++strong positive numerous vesicular or even bullous changes

This reading was done on the 3rd day, i.e after 24 hours that the patch tests were removed, but the patient was advised to be informed even during the 7 days if there are any new changes, especially in those patients who were negative. After informed consent, relevant history was taken and clinical examination was performed. The following factors were considered: sex, age,

group-age, time of patch Test, Place of Residence, Concomitant diseases, Treatment.

Statistical Analysis

SPSS 23 software was used for the conduction of the statistical analysis. Descriptive Statistics were conducted to summarize data for the central tendency (Mean) and variability (Standard Deviation). We have used Inferential Statistics through probability theory to conclude. Concretely Logical Linear Regression for estimating a model of age, gender, allergic diseases, and atopic dermatitis as factors for Allergic Contact Dermatitis and survival analysis for probability of sensitization with Nickel sulphatis 5%> We use Line and Bar graphs for the presentation of our data. Statistical significance was defined as $p < 0.05$.

Results

During the period 2010-2020, 4522 patients with skin problems were presented. After the clinical visit, the number of patients with Atopic Dermatitis was 990, the number of patients with food and respiratory allergies was 2331, while the Patch Test was performed on 1201 patients (from which 536 were diagnosed with ACD and 665 with ICD). If we see all the visits made during these years to the Allergology Clinic in Prishtina we noticed that the number of visits for skin touch has also increased and the number of patients diagnosed with ACD (increase 17.0% for 11 years or 1.5% increase per year. We note that the number of patients with ICD has been greater than those with ACD (excluding 2012 and 2016) thus giving us a ratio greater than 1 in recent years reaching up to 1.9 in 2019. In table 1 we are giving data for patients with ACD.

Of the 355 cases, 59 patients were male (11.03%) and 477 were female (88.97%). The youngest patient in the study was 1 year old and the oldest was 85 years of age. The commonest age group affected was 25-29 years (102 cases or 19% of the total) while the Attac rate for ACD or Prevalence to have a positive result in at least one allergen in each age group tells us that there is a risk group- age 40-44 years. The disease was more frequent in Spring with April the month of more cases (66 cases or 12.3%). The mean age of all the patients was 35.1 ± 11.3 years, while for males was higher 37.06 ± 11.6 years. According to the place of residence, the patients were 40% from Prishtina and 60% from other municipalities.

Out of 536 patients with ACD, the positive responses were in at least one allergen in 417 patients (78%), in two allergens in 84 cases (16%), in three allergens in 25 cases (4%), and in four allergens in 10 cases or 2%. The prevalence of having a positive result on at least one allergen is 44.6%. The risk for ACD in women who perform Patchhstest is 0.4 or 40% of women who perform a Patch test, while in men it is 0.2 or 20% of men who perform Patch Test.

Table 1: General data for patients with ACD (n=536).

Number total, n (%)	536(100)
F,n(%)	477(88.97)
M,11 (%)	59(11.03)
Age, mean(SD)	35.10(11.3)
Female, age, mean(SD)	34.79(11.2)
Male, age, mean(SD)	37.06(11.6)
Group-ages, n(%)	
0-10	3(0.56)
10-14	1 (0.19)
15-19	27(5.04)
20-24	63(11.75)
25-29	102(19.03)
30-34	82(15.3)
35-39	83(15.49)
35-40	1 (0.19)
40-44	71 (13.25)
45-49	42(7.84)
50-54	30(5.60)
55-59	19(3.54)
60-64	5(0.93)
65-69	6(1.12)
85-89	1 (0.19)
Time of the disease, n(%)	
January	45(8.4)
februaiy	44(8.21)
March	54(10.07)
April	66(12.31)
May	56(10.45)
June	48(8.96)
July	49(9.14)
August	36(6.72)
September	32(5.97)
October	36(6.72)
November	26(4.85)
December	44(8.21)

To analyze the frequency of each chemical allergen we enumerated all the positivity results for cases that had two or three positive allergens simultaneously. Thus the total number of positive Patch Test results was 700 out of 536 patients with ACD. Out of 700 positive results, 613 analyzes were of female patients and 87 were male.

Allergens by frequency were Nickel sulphate 5% in 404 cases (57.7%), P-phenyl diamine 1% in 97 cases (13.86%), Cobalt

chloride 1% in 46 cases (6.57%), Potassio Bicromato 0.5% in 23 cases (3.29%), Thiuram-mix in 19 cases (2.7%), Paraben mix 16% in 13 cases (1.86%), Neomicin sulphate 20% in 10 cases (1.43%), Mercaptobenzotiazolo-2 2% and Epoxy resin 1% from 9 cases (1.29%), Fragrance mix and Ethylene diamine dihydrochloride from 8 cases (1.14%), PPD black ruber, Lanolin 30% and Disperso yellow 3 1% from 6 cases (0.86%), Benzocaina 5% and Balsamo del peru 25% from 5 cases (0.71%), Lyril 5% 4 cases (0.57%), Colophony 20%, Dibromocianobutano 0.3% and Carba mix (1-3

d-guanidine) from 3 cases (0.43%), Octyl gallate, Merkpto mix, Tertiary butylphenol p, ptB.formadeidica Resin from 2 cases (0.29%), Thiomersal, Methylidibromo glutalonitrile, Hydrochinon, Germal and Formaldehyde with only one case or 0.14% (Table 2 and Figure 1).

The prevalence of sensitization with Nickel is 33.6% of patients who perform Patch Test, ie higher, while the risk for sensitization by Nickel is 0.75 which indicates increased values where women

have 0.8 or 78% of cases with ACD in women are from Nickel. Since gender has an important role not only in clinical but also in statistical significance, we decided to analyze the probability of sensitization by this allergen through the Survival Function (in our case the possibility to escape sensitization with these allergens) by marking "Status variable" (sensitization=1 and not sensitization=0), "Dependent variable" (age as a continuous variable) and "factor variable" (groups according to gender M, F). below we are giving the statistical results for Nickel (Figure 2).

Table 2: Results of sensitization by chemical substances.

Allergens	Numri	%
Formaldehid	1	0.14
Germal	1	0.14
Hydrochinon	1	0.14
Methylidibromo glutalonitrile	1	0.14
Thiomersal	1	0.14
p-t-B .formadeidica Resina	2	0.29
Butilfenol p terciar	2	0.29
Merkpto mix	2	0.29
Octyl gallate	2	0.29
Carba mix (1-3 d-guanidin)	3	0.43
Dibromocianobutano 0.3%	3	0.43
Colophony 20%	3	0.43
Lyral 5%	4	0.57
Balsamo del peru 25%	5	0.7 1
Benzocaina 5%	5	0.7 1
Disperso yellow 3%	6	0.86
Lanolin 30%	6	0.86
PPD black ruber	6	0.86
Etilen diamin dihidrochlorid	8	1.14
Fragrance mix	8	1.14
Epoxy resin 1%	9	1.29
Mercaptobenzotiazolo- 22%	9	1.29
Neomicin sulphate 20%	10	1.43
Paraben mix 16%	13	1.86
Thiuram-mix	19	2.7 1
Potassio Bicromato 0.5%	23	3.29
Cobalt chloride 1%	46	6.57
P-phenil di.amine 1%	97	13.86
Nickel sulphate 5%	404	57.71
Grand Total	700	

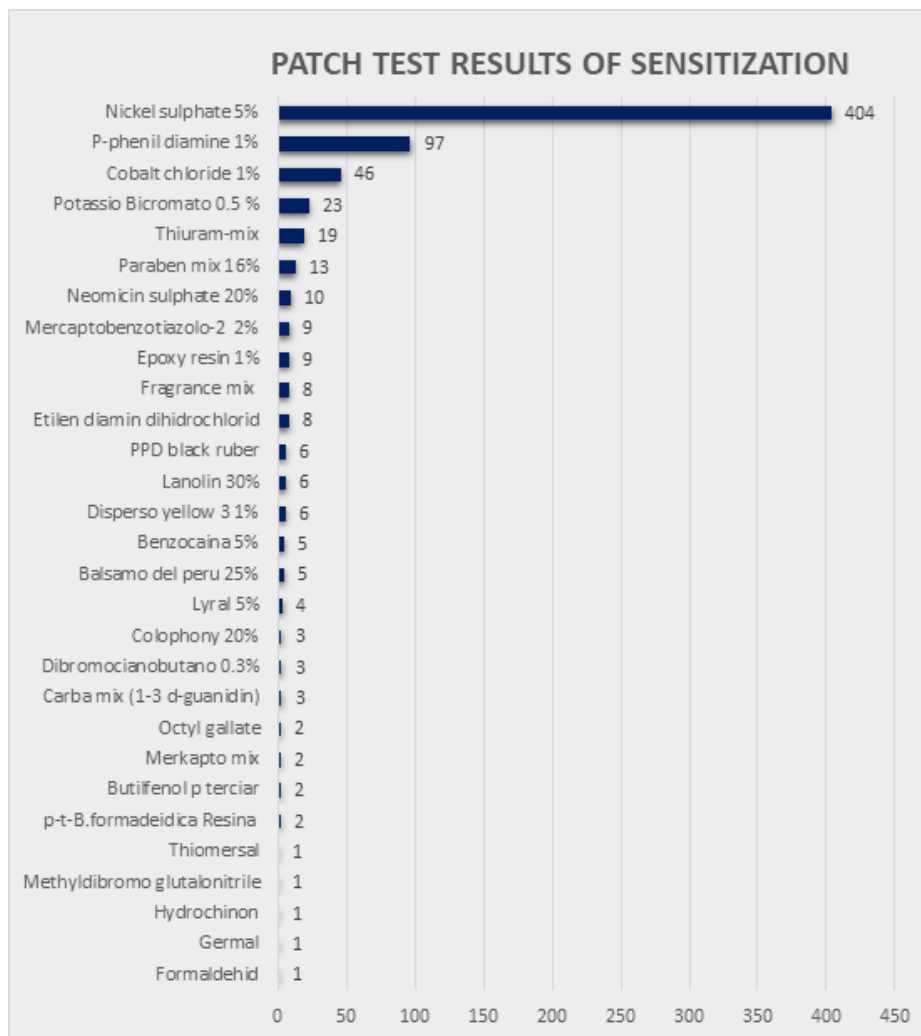


Figure 1: Results of epicutaneous patch testing.

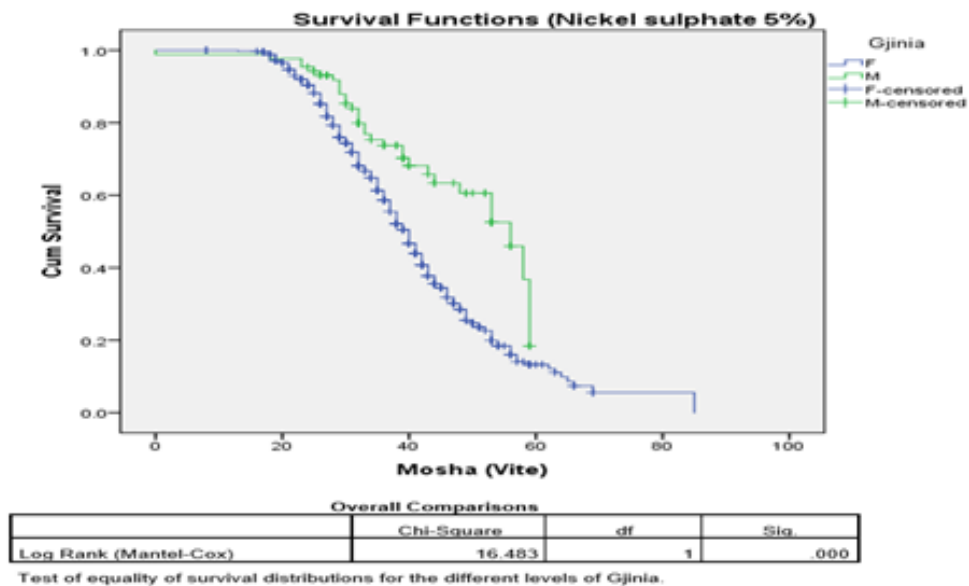


Figure 2: Kaplan-Meier function for sensitization by Nickel sulphate 5%.

Sensitization from this allergen was present in 404 cases (F=372 and M=32). The mean age of the affected F was 34.8 ± 10.2 almost the same as those intact (35.5 ± 12.2), while the mean age of males was 35.7 ± 13.1 therefore much younger than the age of the uncensified (39.7 ± 10.1). The probability of surviving sensitization to Nickel Sulphate 5% in males was higher than in females with statistical significance (Figure 2). The survival distribution for the two groups (M and F) was $\chi^2(1) = 16.483$, $p < 0.0001$ (Log-Rank test).

To analyze whether factors together such as age, gender, atopic dermatitis, and allergic diseases affect the possibility of occurrence or not of ACD (1=ACD; 2=ICD) we use logistic regression (Figure 3). We had 700 positive test results (ACD) and 665 cases with negative Patch test (ICD) a total of 1365 test results.

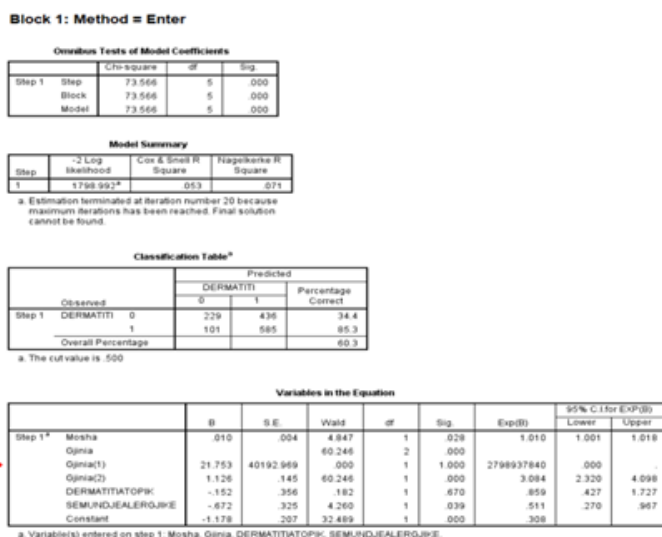


Figure 3: Logistic regression for the possibility of ACD by analyzing: age, gender, allergic diseases, and atopic dermatitis.

From the Regression we notice that the model has statistical significance.

$$\chi^2(5, N=1365) = 73,566, p < 0.001.$$

- Age has significance ($p=0.028$) and for each year of increasing age the probability of being sensitized with ACD increases by a factor of 1.01.
- Females are significant ($p < 0.001$) and have a risk of ACD 3,084 times higher than males.
- Atopic dermatitis has no significance as the only factor.
- Allergic diseases have significance ($p=0.039$) and their presence increases the likelihood of ACD by a factor of 0.511.

Discussion

Allergic Contact Dermatitis is a form of eczema or dermatitis on the skin which appears as a delayed-type IV hypersensitivity reaction that manifests 48-72 hours after exposure to the allergen (low molecular weight chemical) with social, psychological,

occupational, and familial by having an impact on the patient's quality of life.

From our data, about 12% of patients who present at the Allergy Clinic for skin problems have Allergic Contact Dermatitis, while 14.7% have Irritant Contact Dermatitis. According to the place of residence, the patients were 40% from Prishtina and 60% from other municipalities, which shows that the study is of national importance. The prevalence of having a positive result on at least one allergen is 44.6% which is higher than European countries like Portugal (20%), Holland (17.5%), Italy 16.9%, Germany 15.4%), Sweden (8.5%) but comparable to countries in the region such as Bosnia and Herzegovina (62.2%) [6-9].

We notice that our patients have had a young average age, specifically the mean age has been 35.1 ± 11.3 years which is less than in the literature where it exceeds the age of 40 years [10,11]. In our cases, the most affected age group is again young 25-29 years old (102 cases or 19.3% of cases with ACD).

The most affected gender is female (89% of cases with ACD), the time of ACD diagnosis is spring where most cases are seen in April. The literature also speaks of the female predominance of 51.9% in Turkey, 54.9% in a study in Europe, 58.9% in Bosnia-Herzegovina, and 80.7% in Costa Rica [6,10,11,18].

Allergy-related comorbidities have been only 30% of cases with concomitant diseases. According to the literature they can make up 1/3 of all patients [11]. On the other hand, atopic dermatitis does not result as a factor in the occurrence of ACD, although in the literature there are different opinions for and against [11,12]. Also, some studies have shown the coexistence of allergic contact dermatitis with asthma although various actions [13].

The most common allergens from our study are Nickel sulphate 5% in 404 cases (57.7%), P-phenyl diamine 1% in 97 cases (13.86%), Cobalt chloride 1% in 46 cases (6.57%), Potassio Bicromato 0.5% in 23 cases (3.29%), Thiuram-mix in 19 cases (2.7%), Paraben mix 16% in 13 cases (1.86%). Methyl dibromo glutalonitrile, Hydrochinon, Germal, and Formaldehyde are the chemicals to which our population exposure has been minimal.

According to the literature Nickel is considered the most common allergen in our study in Bosnia, Turkey, Czech Republic, Hong Kong, and Ethiopia [10,14-17,18]. While the ranking of other allergens occurs according to the characteristics of the place. Thus, in our country, the second chemical in terms of frequency is P phenylenediamine followed by Cobalt and Potassio while in Bosnia Cobalt is found, in Turkey Potassium, in Hong Kong, and Ethiopia Fragrance mix, etc. [10,14-17,18].

From our survival analysis both sexes are affected by sensitization with the chemical substance Nickel sulphate 5% (How many more are women) certainly men have a higher probability of surviving sensitization than women with statistical significance.

From our Logistic Regression analysis, the model formed with factors (age, gender, allergic diseases, and concomitant atopic dermatitis) has statistical significance, as well as separate factors for each year of increasing age the likelihood of ACD increases by a factor of 1.01; the presence of allergic diseases increases the likelihood by a factor of 0.511, the female gender has a 3,084 times greater risk of contracting ACD in a lifetime.

Conclusion

12% of patients who come to the Allergy Clinic for skin problems have Allergic Dermatitis Contact and Prevalence to have a positive result in at least one allergen is high 44.6%.

The most affected age group is 25-29 years (102 cases or 19.3% of cases with ACD) while the Attac rate for ACD or Prevalence to have a positive result in at least one allergen in each age group tells us that there is a risk group- age 40-44 years.

For each year of increasing age, the likelihood of ACD increases by a factor of 1.01; the presence of allergic diseases increases the likelihood by a factor of 0.511, the female gender has a 3,084 times greater risk of contracting ACD in a lifetime.

In our country, the prevalence of sensitization with Nickel is 33.6% of patients who perform Patch Test, i.e higher than in European countries where there is protection legislation. Men have a higher probability of surviving sensitization from Nickel sulphatis 5% than women with statistical significance.

Positive Side and Limitations of the Study

In European countries since the implementation of legislation regarding the amount of Nickel to which people should be exposed has created a decrease in the prevalence of nickel sensitization. Perhaps this paper is modest data but that should direct policy attention towards the possibilities of reducing allergies to Nickel and other substances. The middle-aged and elderly have been sensitized before and are allergic already according to the cohort effect. Preventive measures regarding the reduction of sensitization to Nickel should be directed to the young age group.

It would be of interest to include in the study patients who suffer from leg ulcers or as it is called Venous Stasis Dermatitis to sensitize doctors towards avoiding substances that are sensitizing. The use of chemicals that are strong sensitizers with closed-bandage treatment, repeatedly and long-term are considered together with skin damage as the main protective barrier, factors for sensitization of these patients.

The study would be more complete if it analyzed in particular Dermatitis related to the profession which is one of the important aspects where they aim at training policies that aim to increase the work culture in terms of health.

References

1. Eisen HN, Orris L, Belman S (1952) Elicitation of delayed allergic skin reactions with haptens; the dependence of elicitation on hapten combination with protein. *J Exp Med* 95(5):473-487.
2. Bergstresser PR (1989) Sensitization and elicitation of inflammation in contact dermatitis. In: Norris DO (ed) *Immune mechanisms in cutaneous disease*. Dekker, New York, 219-246.
3. Turk JL (1975) *Delayed hypersensitivity*, 2nd eds. North-Holland, Amsterdam.
4. Gell PDH, Coombs RRA, Lachman R (1975) *Clinical aspects of immunology*, 3rd eds. Blackwell, London
5. Vanderbilt RJ, van Loveren H (2010) Non-animal sensitization testing: state-of-the-art. *Crit Rev Toxicol* 40:389-404.
6. Schuttelaar MLA, Ofenloch RF, Bruze M, Cazzaniga S, Elsner P, Gonçalo M, et al. (2018) Prevalence of contact allergy to metals in the European general population with a focus on nickel and piercings: The EDEN Fragrance Study. *Contact Dermatitis* 79:1-9.
7. Teixeira V, Coutinho I, Gonçalo M (2014) Allergic contact dermatitis to metals over 20 years in the Centre of Portugal: evaluation of the effects of the European directives. *Acta Med Port* 27:295-303.
8. Rossi M, Coenraads PJ, Diepgen T, et al. (2010) Design and feasibility of an international study assessing the prevalence of contact allergy to fragrances in the general population: the European Dermato-Epidemiology Network Fragrance Study. *Dermatology* 221:267-275.
9. Diepgen TL, Ofenloch RF, Bruze M, et al.(2016) Prevalence of contact allergy in the general population in different European regions. *Br J Dermatol* 174:319-329.
10. Acer E, Erdogan HK, Batan T, Saracoglu ZN (2020) European Standard Series Patch Test Results in Contact Dermatitis Patients in a Tertiary Care Hospital. *Sisli Etfal Hastan Tip Bul* 54(2):206-210.
11. Sedó-Mejía G, Soto-Rodríguez A, Pino-García C, Sanabria-Castro A, Monge-Ortega OP (2020) Contact dermatitis: Clinical practice findings from a single tertiary referral hospital, a 4-Year retrospective study. *World Allergy Organ J* 13(7):100440.
12. Tagka A, Lambrou GI, Nicolaidou E, Gregoriou SG, Katsarou-Katsari A, Rigopoulos D (2020) The Effect of Atopy in the Prevalence of Contact Sensitization: The Experience of a Greek Referral Center. *Dermatol Res Pract* 2020:3946084.
13. Kolberg L, Forster F, Gerlich J, et al. (2020) Nickel allergy is associated with wheezing and asthma in a cohort of young German adults: results from the SOLAR study. *ERJ Open Res* 6(1):00178-2019.
14. Machovcova A, Dastychova E, Kostalova D, Vojtechovska A, Reslova J, Smejkalova D, et al. (2005) Common contact sensitizers in the Czech Republic. Patch test results in 12,058 patients with suspected contact dermatitis. *Contact Dermatitis* 53:162-166.

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15. Lam WS, Chan LY, Ho SC, Chong LY, So WH, Wong TW (2008) A retrospective study of 2585 patients patch tested with the European standard series in Hong Kong (1995-99). *Int J Dermatol* 47:128-133.
 16. Lazarov A (2006) European Standard Series patch test results from a contact dermatitis clinic in Israel during the 7 years from 1998 to 2004. *Contact Dermatitis* 55:73-76.
 17. Bilcha KD, Ayele A, Shibeshi D, Lovell C (2010) Patch testing and contact allergens in Ethiopia-results of 514 contact dermatitis patients using the European baseline series. *Contact dermatitis* 63:140-145.
 18. Kasumagic-Halilovic E, Ovcina-Kurtovic N (2018) Analysis of Epicutaneous Patch Test Results in Patients with Contact Dermatitis. *Med Arch* 72(4):276-279.

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