ORIGINAL ARTICLE



Analysis of patch testing results in patients with contact dermatitis in Istanbul, Turkey, from 2012 to 2022

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Abstract

Revised: 4 April 2023

Background: Allergens responsible for allergic contact dermatitis (ACD) differ between populations. They can even change over the years with the effect of environmental factors.

Aims: To evaluate the results of patch testing performed in our center.

Methods: In this study, the thin-layer rapid-use epicutaneous (T.R.U.E.) test results of patients with a diagnosis of ACD between 2012 and 2022 were retrospectively evaluated.

Results: In 431 (42.5%) of the total 1012 patients, a positive reaction to at least one allergen was detected in the patch test. Allergen positivity was most detected for nickel sulphate (16.8%), gold sodium thiosulfate (GST) (6.9%), thimerosal (4.2%), fragrance mix (3.4%), carba mix (3.2%), and cobalt dichloride (2.9%). Nickel sulfate and GST sensitivity was found to be significantly higher in women, fragrance mix sensitivity in men, thimerosal sensitivity in individuals aged under 40 years, colophony and balsam of Peru sensitivity in head and neck dermatitis, and carba mix and thiuram mix sensitivity in atopic individuals.

Conclusions: This study presents comprehensive data from Turkey concerning the sensitivity frequencies for allergens included in the T.R.U.E. test.

KEYWORDS

allergic contact dermatitis, contact allergy, contact dermatitis, patch testing

1 | INTRODUCTION

Allergic contact dermatitis (ACD) is a common inflammatory skin disease presenting with pruritic, eczematous lesions. ACD results from a T cell-mediated, delayed type hypersensitivity reaction elicited by the contact of the skin with the offending chemical in individuals who have been previously sensitized to the same chemical. Patch testing is an important diagnostic tool used to detect responsible allergens in the diagnosis of ACD. Allergens responsible for contact sensitization are affected by genetic, geographical, occupational, and socioeconomic factors, as well as atopy, age, gender, and individual factors. Therefore, a standard series has been determined as a patch test in many countries, and it is revised from time to time. However, there is no standard series designed for this purpose in Turkey. Therefore, the European baseline series (EBS) is used in all studies conducted in Turkey to report patch test results in patients with ACD.¹⁻¹⁰ The thin-layer rapid-use epicutaneous (T.R.U.E.) test is a ready-to-use patch test containing 35 allergens. The primary aim of the current study was to identify the most frequent contact sensitizing agents between 2012 and 2022 in Istanbul, the largest industrial

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city in Turkey. The secondary aim was to determine sensitivity frequencies to allergens included in the T.R.U.E. test but not in EBS in order to draw attention to the allergens that are most commonly seen in this geographical area.

2 | MATERIALS AND METHODS

The study included 1012 patients aged 18 years and older, who presented to the dermatology clinic of University and underwent patch testing with a preliminary diagnosis of ACD between January 2012 and March 2022. Patch testing was not performed in pregnant and lactating women. Age, gender, disease duration, localization of lesions, and presence of personal atopy history (hay fever/allergic rhinitis, asthma, and atopic eczema) were retrospectively recorded by screening the patient files. The ethics committee of our university approved the study protocol (approval number: 2022/312).

In all the patients, the T.R.U.E. test (Smart Practice Denmark) materials containing 35 allergens and one negative control were used. Patch testing was not performed in patients using systemic steroids or any other immunosuppressive medication. These drugs were discontinued at least 1 month before the test procedure. Topical steroids applied to the test area were discontinued at least 7 days before the procedure.¹¹ The patch test was adhered to a clean, dry, hairless, and lesion-free area on the upper back of the patients for 2 days (application day, Day 0 [D0]). The patches remained in place for 48 h. The first and second patch test readings were performed at 48h and 72–168h, respectively, after initial test placement by a dermatologist. Reactions were assessed according to the International Contact Dermatitis Research Group criteria on D2, D3 or D4, and D7 and recorded as follows: no reaction, (-); only slight erythema, doubtful reaction; possible erythema, infiltration, and papules, (+); erythema, infiltration, papules, and vesicles, (++); and intense erythema, infiltration, confluent vesicles, and bullae, (+++). At least 1+ reaction was considered a positive patch test result.¹¹

Cross-tabs and descriptive statistics were used in statistical analyses. Data analyses were performed using IBM Statistical Package for the Social Sciences Statistics v. 26.0. A $p \le 0.05$ was considered statistically significant.

3 | RESULTS

Of the 1012 patients, 433 (42.8%) were male and 579 (57.2%) were female. The mean age was 37.97 (18–87) years. The mean disease duration was 28.36 (1–120) months. In 431 (42.5%) of the 1012 patients, a positive reaction to at least one allergen was detected in the patch test. The most frequently positive allergens were nickel sulphate (16.8%), gold sodium thiosulfate (GST) (6.9%), thimerosal (4.2%), fragrance mix (3.4%), carba mix (3.2%), and cobalt dichloride (2.9%). The contact sensitivity rate was 47.1% in women and 36.4% in men. When the distribution of contact sensitivity to allergens was examined according to gender, it was determined that the rates of

sensitivity to nickel sulfate, fragrance mix, and GST significantly differed (p < 0.05). While sensitivity to nickel sulfate and GST was significantly higher in women, sensitivity to fragrance mix was more common in men. Sensitivity to neomycin sulfate, diazolidinyl urea, mercaptobenzothiazole, and bacitracin was detected only in the female patients. Table 1 presents the positive patch test frequencies by gender.

Of the patients included in the study, 636 were aged 18-40 years, and 376 were over 40 years. When the frequency of sensitivity to allergens was examined according to age, there were significant differences in relation to the rates of sensitivity to fragrance mix, formaldehyde, thimerosal, imidazolidinyl urea, and budesonide (p < 0.05). Sensitivity to fragrance mix, formaldehyde, imidazolidinyl urea, and budesonide was significantly higher in the patients aged over 40 years, while thimerosal sensitivity was more common in those aged 40 years and under. The most common localization of dermatitis was the hands (34.9%), followed by head and neck (22.2%), generalized (18.9%), trunk (7%), palmoplantar (5.1%), genital (4.6%), legs (3.4%), feet (2.2%), and arms (2.0%). Table 1 shows the patch test positivity rates with at least one positive result according to the dermatitis localizations of the patients. The highest positivity rate was observed in head and neck involvement. In 230 patients with head and neck dermatitis, the involvement areas were periorbital (41.7%), generalized (32.2%), perioral (10.4%), ears (7%), neck (6.1%), and scalp (2.6%). When the frequency of contact sensitivity in the head and neck region was evaluated, it was determined that the rates of sensitivity to colophony and balsam of Peru significantly differed (p < 0.05). Both allergens showed more positivity in headneck localization. The rates of positivity in the head and neck region are shown in Table 2.

Of all the patients, 33.2% had a history of atopy. When the positive patch test results of the patients with and without atopy were compared, it was found that the positivity rates significantly differed for the carba mix, thiuram mix, and disperse blue 106 allergens (p < 0.05). The carba mix and thiuram mix positivity rates were significantly higher in the patients with atopy, while disperse blue 106 positivity was significantly more common in those without atopy (Table 3).

4 | DISCUSSION

ACD is the classical response of T cell-mediated, delayed-type hypersensitivity reaction to exogenous agents.¹² Medical history and dermatological examination may be helpful in identifying suspected allergens in patients with ACD. The patch test is the main method used to detect specific allergens in ACD or, in some cases, to diagnose ACD. Some countries have their own standard series, which refers to a patch test designed to include the most common allergens responsible for ACD in a given area. Standard series is revised as new allergens are identified as the cause of ACD. In Turkey, there is no specific standard series, and EBS is frequently used for this purpose. EBS results were also reported

TABLE 1 Distribution of allergen sensitivity by gender.

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	Male (n = 433)	%	Female (n = 579)	%	Total (N = 1012)	%	p-value
Nickel sulfate	41	9.5	129	22.3	170	16.8	0.000 ^a
Wool alcohols	11	2.5	10	1.7	21	2.1	NS
Neomycin sulfate	0	0.0	3	0.5	3	0.3	NS
Potassium dichromate	7	1.6	14	2.4	21	2.1	NS
Caine mix	4	0.9	5	0.9	9	0.9	NS
Fragrance mix	20	4.6	14	2.4	34	3.4	0.005ª
Colophony	3	0.7	13	2.2	16	1.6	NS
Paraben mix	4	0.9	10	1.7	14	1.4	NS
Balsam of Peru	8	1.8	9	1.6	17	1.7	NS
Ethylenediamine dihydrochloride	7	1.6	2	0.3	9	0.9	NS
Cobalt dichloride	13	3.0	16	2.8	29	2.9	NS
p-tert-Butylphenol formaldehyde resin	5	1.2	9	1.6	14	1.4	NS
Epoxy resin	4	0.9	7	1.2	11	1.1	NS
Carba mix	12	2.8	20	3.5	32	3.2	NS
Black rubber mix	6	1.4	7	1.2	13	1.3	NS
Cl ⁺ Me-isothiazolinone	10	2.3	7	1.2	17	1.7	NS
Quaternium-15	7	1.6	5	0.9	12	1.2	NS
Methyldibromo glutaronitrile	1	0.2	1	0.2	2	0.2	NS
p-Phenylenediamine	9	2.1	11	1.9	20	2.0	NS
Formaldehyde	1	0.2	4	0.7	5	0.5	NS
Mercapto mix	7	1.6	5	0.9	12	1.2	NS
Thimerosal	10	2.3	32	5.5	42	4.2	NS
Thiuram mix	4	0.9	3	0.5	7	0.7	NS
Diazolidinyl urea	3	0.7	7	1.2	10	1.0	NS
Quinoline mix	0	0.0	1	0.2	1	0.1	NS
Tixocortol-21-pivalate	2	0.5	3	0.5	5	0.5	NS
Gold sodium thiosulfate	13	3.0	57	9.8	70	6.9	0.001 ^a
Imidazolidinyl urea	4	0.9	3	0.5	7	0.7	NS
Budesonide	3	0.7	2	0.3	5	0.5	NS
Hydrocortizone-17-butyrate	5	1.2	3	0.5	8	0.8	NS
Mercaptobenzothiazole	0	0.0	2	0.3	2	0.2	NS
Bacitracin	0	0.0	4	0.7	4	0.4	NS
Parthenolide	4	0.9	7	1.2	11	1.1	NS
Disperse blue 106	8	1.8	5	0.9	13	1.3	NS
Bronopol	3	0.7	2	0.3	5	0.5	NS
Total	158		273		431		

^aStatistically significant at 0.05.

Abbreviation: NS, not significant.

in all studies conducted in Turkey in which patients with ACD were evaluated.¹⁻¹⁰ The T.R.U.E. test is a commercially available, readyto-use kit containing 35 allergens and one negative control and commonly used by dermatologists and allergists. As a patch test available in our clinic, we used the T.R.U.E. test. The advantages of the T.R.U.E. test are that it is easy to apply, the test tape better adheres to the skin, it involves less mistakes and errors caused by the human factor due to its standard features, and the standard limited amount of allergens used minimizes undesirable consequences associated with other tests, such as extending beyond the test area and excessive reactions. Our polyclinic is a health center in which a very high number of patients are examined

TABLE 2 Distribution of allergen positivity according to the presence of head-neck involvement.

	No head-neck involvement (n=782)	%	Head-neck involvement present (n = 230)	%	Total (N = 1012)	%	p-value
Nickel sulfate	130	41.0	40	35.1	170	39.4	NS
Wool alcohols	16	5.0	5	4.4	21	4.9	NS
Neomycin sulfate	2	0.6	1	0.9	3	0.7	NS
Potassium dichromate	16	5.0	5	4.4	21	4.9	NS
Caine mix	7	2.2	2	1.8	9	2.1	NS
Fragrance mix	25	7.9	9	7.9	34	7.9	NS
Colophony	6	1.9	10	8.8	16	3.7	0.001 ^a
Paraben mix	9	2.8	5	4.4	14	3.2	NS
Balsam of Peru	8	2.5	9	7.9	17	3.9	0.012 ^a
Ethylenediamine dihydrochloride	9	2.8	0	0.0	9	2.1	NS
Cobalt dichloride	24	7.6	5	4.4	29	6.7	NS
p-tert-Butylphenol formaldehyde resin	9	2.8	5	4.4	14	3.2	NS
Epoxy resin	7	2.2	4	3.5	11	2.6	NS
Carba mix	21	6.6	11	9.6	32	7.4	NS
Black rubber mix	8	2.5	5	4.4	13	3.0	NS
Cl ⁺ Me-isothiazolinone	15	4.7	2	1.8	17	3.9	NS
Quaternium-15	8	2.5	4	3.5	12	2.8	NS
Methyldibromo glutaronitrile	2	0.6	0	0.0	2	0.5	NS
p-Phenylenediamine	14	4.4	6	5.3	20	4.6	NS
Formaldehyde	2	0.6	3	2.6	5	1.2	NS
Mercapto mix	11	3.5	1	0.9	12	2.8	NS
Thimerosal	35	11.0	7	6.1	42	9.7	NS
Thiuram mix	5	1.6	2	1.8	7	1.6	NS
Diazolidinyl urea	8	2.5	2	1.8	10	2.3	NS
Quinoline mix	0	0.0	1	0.9	1	0.2	NS
Tixocortol-21-pivalate	4	1.3	1	0.9	5	1.2	NS
Gold sodium thiosulfate	45	14.2	25	21.9	70	16.2	NS
Imidazolidinyl urea	6	1.9	1	0.9	7	1.6	NS
Budesonide	3	0.9	2	1.8	5	1.2	NS
Hydrocortizone-17-butyrate	6	1.9	2	1.8	8	1.9	NS
Mercaptobenzothiazole	1	0.3	1	0.9	2	0.5	NS
Bacitracin	4	1.3	0	0.0	4	0.9	NS
Parthenolide	9	2.8	2	1.8	11	2.6	NS
Disperse blue 106	11	3.5	2	1.8	13	3.0	NS
Bronopol	4	1.3	1	0.9	5	1.2	NS
Total	317		114		431		

^aStatistically significant at 0.05.

Abbreviation: NS, not significant.

daily. Therefore, the T.R.U.E. test is primarily used in our clinic due to its ease of use and other advantages. However, although it is easy to apply, there are studies reporting that its sensitivity may be lower than standard series.¹³

To the best of our knowledge, this is the first study to report the results of the T.R.U.E. test in Turkey. In studies performed with the EBS patch test in Turkey, positivity rates for at least one allergen have been reported to vary between 31.3% and 57.8%, while the

TABLE 3 Distribution of allergen positivity according to the presence of atopy.

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Carba mix142.1185.4323.20.004*Black rubber mix60.972.1131.3NSCl* Me- isothiazolinone121.851.5171.7NSQuaternium-1571.051.5121.2NSMethyldibromo glutaronitrile00.020.620.2NSp-Phenylenediamine142.161.8202.0NSFormaldehyde20.330.950.5NSMercapto mix71.051.5121.2NSThimerosal314.6113.3424.2NSDiazolidinyl urea81.220.6101.0NSQuioline mix00.010.350.5NSGold sodium thiosulfate477.0236.87.06.9NSImidazolidinyl urea60.910.350.5NSBudesonide40.610.350.5NSHydrocortizone-17-butyrate60.920.680.8NSMercaptobenzothiazole20.300.020.2NSBacitracin30.410.340.4NSBudesonide40.610.350.5NSBudesonid		7	1.0	7	2.1	14	1.4	NS
Black rubber mix60.972.1131.3NSCl' Me-isothiazolinone121.851.5171.7NSQuaternium-1571.051.5121.2NSMethyldibromo glutaronitrile00.020.620.2NSp-Phenylenediamine142.161.8202.0NSFormaldehyde20.330.950.5NSMercapto mix71.051.5121.2NSThimerosal314.6113.3424.2NSDiazolidinyl urea81.220.6101.0NSQuinoline mix00.010.310.1NSGold sodium thiosulfate477.0236.8706.9NSImidazolidinyl urea60.910.350.5NSBudesonide40.610.350.5NSHydrocortizone-17-butyrate60.920.680.8NSMercaptobenzothiazole20.300.020.2NSBacitracin30.410.311.1NSDisperse blue 106121.810.3131.30.048*Bronopol30.420.650.5NS <td>Epoxy resin</td> <td>7</td> <td>1.0</td> <td>4</td> <td>1.2</td> <td>11</td> <td>1.1</td> <td>NS</td>	Epoxy resin	7	1.0	4	1.2	11	1.1	NS
Cl' Me-isothiazolinone121.851.5171.7NSQuaternium-1571.051.5121.2NSMethyldibromo glutaronitrile00.020.620.2NSp-Phenylenediamine142.161.8202.0NSFormaldehyde20.330.950.5NSMercapto mix71.051.5121.2NSThimerosal314.6113.3424.2NSDiazolidinyl urea81.220.6101.0NSQuinoline mix00.010.310.1NSGold sodium thiosulfate477.0236.8706.9NSBudesonide40.610.350.5NSHydrocortizone-17-butyrate60.920.680.8NSMercaptobenzothiazole20.300.020.2NSBacitracin30.410.340.4NSParthenolide91.320.6111.1NSDisperse blue 106121.810.3131.30.04888Bronopol30.420.650.5NS	Carba mix	14	2.1	18	5.4	32	3.2	0.004 ^a
Quaternium-1571.051.5121.2NSMethyldibromo glutaronitrile00.020.620.2NSp-Phenylenediamine142.161.8202.0NSFormaldehyde20.330.950.5NSMercapto mix71.051.5121.2NSThimerosal314.6113.3424.2NSDiazolidinyl urea81.220.6101.0NSQuinoline mix00.010.310.1NSGold sodium thiosulfate477.0236.8706.9NSImidazolidinyl urea60.910.350.5NSIdedesonide40.610.350.5NSIdedesonide60.920.680.8NSHydrocortizone-17-butyrate60.920.680.8NSMercaptobenzothiazole20.300.020.2NSBacitracin30.410.340.4NSParthenolide91.320.6111.1NSDisperse blue 106121.810.330.5NSBacitracin30.420.650.5NS	Black rubber mix	6	0.9	7	2.1	13	1.3	NS
Methyldibromo glutaronitrile00.020.620.2NSp-Phenylenediamine142.161.8202.0NSFormaldehyde20.330.950.5NSMercapto mix71.051.5121.2NSThimerosal314.6113.3424.2NSThiuram mix20.351.570.70.30%Diazolidinyl urea81.220.6101.0NSQuinoline mix00.010.310.1NSGold sodium thiosulfate477.0236.8706.9NSImidazolidinyl urea60.910.350.5NSIdedsonide420.610.350.5NSIdedsonide60.920.680.8NSHydrocortizone-17-butyrate60.920.680.8NSMercaptobenzothiazole20.300.020.2NSBacitracin30.410.340.4NSParthenolide91.320.6111.1NSDisperse blue 106121.810.3131.30.4488Bronopol30.420.650.5NS	Cl ⁺ Me- isothiazolinone	12	1.8	5	1.5	17	1.7	NS
p-Phenylenediamine142.161.8202.0NSFormaldehyde20.330.950.5NSMercapto mix71.051.5121.2NSThimerosal314.6113.3424.2NSDiazolidinyl urea81.220.6101.0NSQuinoline mix00.010.310.1NSTixocortol-21-pivalate40.610.350.5NSImidazolidinyl urea60.910.370.7NSGold sodium thiosulfate477.0236.8706.9NSImidazolidinyl urea60.910.350.5NSHydrocortizone-17-butyrate60.920.680.8NSMercaptobenzothiazole20.300.020.2NSBacitracin30.410.3111.1NSDisperse blue 106121.810.4130.40.4NSBronopol30.420.650.5NS	Quaternium-15	7	1.0	5	1.5	12	1.2	NS
Formaldehyde20.330.950.5NSMercapto mix71.051.5121.2NSThimerosal314.6113.3424.2NSThiuram mix20.351.570.70.030°Diazolidinyl urea81.220.6101.0NSQuinoline mix00.010.310.1NSTixocortol-21-pivalate40.610.350.5NSGold sodium thiosulfate477.0236.8706.9NSImidazolidinyl urea60.910.370.7NSBudesonide40.610.350.5NSHydrocortizone-17-butyrate60.920.680.8NSMercaptobenzothiazole20.300.020.2NSBacitracin30.410.340.4NSParthenolide91.320.6111.1NSDisperse blue 106121.810.3131.30.448°Bronopol30.420.650.5NS	Methyldibromo glutaronitrile	0	0.0	2	0.6	2	0.2	NS
Mercapto nix71.051.5121.2NSThimerosal314.6113.3424.2NSThiuram mix20.351.570.70.303°Diazolidinyl urea81.220.6101.0NSQuinoline mix00.010.310.1NSTixocortol-21-pivalate40.610.350.5NSGold sodium thiosulfate477.0236.8706.9NSImidazolidinyl urea60.910.350.5NSBudesonide40.610.350.5NSHydrocortizone-17-butyrate60.920.680.8NSBacitracin30.410.340.4NSParthenolide91.320.6111.1NSDisperse blue 106121.810.3131.30.048°Bronopol30.420.650.5NS	p-Phenylenediamine	14	2.1	6	1.8	20	2.0	NS
Thinrosal314.6113.3424.2NSThiuram mix20.351.570.70.30°Diazolidinyl urea81.220.6101.0NSQuinoline mix00.010.310.1NSTixocortol-21-pivalate40.610.350.5NSGold sodium thiosulfate477.0236.8706.9NSImidazolidinyl urea60.910.370.7NSBudesonide40.610.350.5NSHydrocortizone-17-butyrate60.920.680.8NSMercaptobenzothiazole20.300.020.2NSBacitracin30.410.340.4NSParthenolide91.320.6111.1NSDisperse blue 106121.810.3131.30.48*Bronopol30.420.650.5NS	Formaldehyde	2	0.3	3	0.9	5	0.5	NS
Thiuram mix20.351.570.70.030°Diazolidinyl urea81.220.6101.0NSQuinoline mix00.010.310.1NSTixocortol-21-pivalate40.610.350.5NSGold sodium thiosulfate477.0236.8706.9NSImidazolidinyl urea60.910.350.5NSBudesonide40.610.350.5NSHydrocortizone-17-butyrate60.920.680.8NSMercaptobenzothiazole20.300.020.2NSBacitracin30.410.3111.1NSDisperse blue 106121.810.3131.30.048°Bronopol30.420.650.5NS	Mercapto mix	7	1.0	5	1.5	12	1.2	NS
Diazolidinyl urea81.220.6101.0NSQuinoline mix00.010.310.1NSTixocortol-21-pivalate40.610.350.5NSGold sodium thiosulfate477.0236.8706.9NSImidazolidinyl urea60.910.370.7NSBudesonide40.610.350.5NSHydrocortizone-17-butyrate60.920.680.8NSBacitracin30.410.340.4NSParthenolide91.320.6111.1NSDisperse blue 106121.810.3130.48*Bronopol30.420.650.5NS	Thimerosal	31	4.6	11	3.3	42	4.2	NS
Quinoline mix00.010.310.1NSTixocortol-21-pivalate40.610.350.5NSGold sodium thiosulfate477.0236.8706.9NSImidazolidinyl urea60.910.370.7NSBudesonide40.610.350.5NSHydrocortizone-17-butyrate60.920.680.8NSMercaptobenzothiazole20.300.020.2NSBacitracin30.410.340.4NSParthenolide91.320.6111.1NSBonopol30.420.650.5NS	Thiuram mix	2	0.3	5	1.5	7	0.7	0.030 ^a
Tixocortol-21-pivalate40.610.350.5NSGold sodium thiosulfate477.0236.8706.9NSImidazolidinyl urea60.910.370.7NSBudesonide40.610.350.5NSHydrocortizone-17-butyrate60.920.680.8NSMercaptobenzothiazole20.300.020.2NSBacitracin30.410.340.4NSParthenolide91.320.6111.1NSDisperse blue 106121.810.350.5NSBronopol30.420.650.5NS	Diazolidinyl urea	8	1.2	2	0.6	10	1.0	NS
Gold sodium thiosulfate477.0236.8706.9NSImidazolidinyl urea60.910.370.7NSBudesonide40.610.350.5NSHydrocortizone-17-butyrate60.920.680.8NSMercaptobenzothiazole20.300.020.2NSBacitracin30.410.340.4NSParthenolide91.320.6111.1NSDisperse blue 106121.810.350.5NSBronopol30.420.650.5NS	Quinoline mix	0	0.0	1	0.3	1	0.1	NS
Imidazolidinyl urea60.910.370.7NSBudesonide40.610.350.5NSHydrocortizone-17-butyrate60.920.680.8NSMercaptobenzothiazole20.300.020.2NSBacitracin30.410.340.4NSParthenolide91.320.6111.1NSDisperse blue 106121.810.3130.048°Bronopol30.420.650.5NS	Tixocortol-21-pivalate	4	0.6	1	0.3	5	0.5	NS
Budesonide40.610.350.5NSHydrocortizone-17-butyrate60.920.680.8NSMercaptobenzothiazole20.300.020.2NSBacitracin30.410.340.4NSParthenolide91.320.6111.1NSDisperse blue 106121.810.3131.30.048³Bronopol30.420.650.5NS	Gold sodium thiosulfate	47	7.0	23	6.8	70	6.9	NS
Hydrocortizone-17-butyrate60.920.680.8NSMercaptobenzothiazole20.300.020.2NSBacitracin30.410.340.4NSParthenolide91.320.6111.1NSDisperse blue 106121.810.3131.30.048 ^a Bronopol30.420.650.5NS	Imidazolidinyl urea	6	0.9	1	0.3	7	0.7	NS
Mercaptobenzothiazole20.300.020.2NSBacitracin30.410.340.4NSParthenolide91.320.6111.1NSDisperse blue 106121.810.3131.30.048³Bronopol30.420.650.5NS	Budesonide	4	0.6	1	0.3	5	0.5	NS
Bacitracin 3 0.4 1 0.3 4 0.4 NS Parthenolide 9 1.3 2 0.6 11 1.1 NS Disperse blue 106 12 1.8 1 0.3 13 1.3 0.048 ^a Bronopol 3 0.4 2 0.6 5 0.5 NS	Hydrocortizone-17-butyrate	6	0.9	2	0.6	8	0.8	NS
Parthenolide 9 1.3 2 0.6 11 1.1 NS Disperse blue 106 12 1.8 1 0.3 13 1.3 0.048 ^a Bronopol 3 0.4 2 0.6 5 0.5 NS	Mercaptobenzothiazole	2	0.3	0	0.0	2	0.2	NS
Disperse blue 106 12 1.8 1 0.3 13 1.3 0.048 ^a Bronopol 3 0.4 2 0.6 5 0.5 NS	Bacitracin	3	0.4	1	0.3	4	0.4	NS
Bronopol 3 0.4 2 0.6 5 0.5 NS	Parthenolide	9	1.3	2	0.6	11	1.1	NS
	Disperse blue 106	12	1.8	1	0.3	13	1.3	0.048 ^a
Total 288 143 431 NS	Bronopol	3	0.4	2	0.6	5	0.5	NS
	Total	288		143		431		NS

^aStatistically significant at 0.05.

Abbreviation: NS, not significant.

most common allergen has been identified as nickel sulphate (12.2%-29.6%) in all studies.¹⁻¹⁰ In the current study, 431 patients (42.5%) had a positive reaction to at least one allergen in the patch test, and the most frequently positive allergen was nickel sulphate (16.8%), which is consistent with previous studies from Turkey. Nickel sulphate is the most common sensitizing allergen in Europe and North America, with

the frequency of sensitization varying from one country to another (6%–18.6%).^{14–19} These results indicate that nickel sulphate sensitivity is an important public health problem not only in Turkey but also across the world, and there is a need for strict regulations in this regard.

An important characteristic of this study is that sensitivity to GST was investigated for the first time in Turkey. In our study, the

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second most common allergen detected after nickel sulphate was GST (6.9%). GST was removed from routine testing by the North America Contact Dermatitis Group (NACDG) after the 2003-2004 study period. Since the frequency of irritant reactions to GST is high, sensitivity reaction is very strong, and a long duration of exposure can be discomforting for the patient, and therefore, it has been recommended to be evaluated only when jewelry allergy is suspected or in cases of the dermatitis of the head and neck region.²⁰ GST is also not included in EBS. In a study using the Japanese baseline series published in 2021 in Japan, the most common allergen was reported to be GST (25.7%).²¹ In our study, nickel sulphate and GST were the most frequently detected allergens and found to have significantly higher frequencies in women than in men. The traditional use of gold and imitation jewelry, ear, and body piercings by women in our country can explain these high sensitivity rates. NACDG recommends that GST sensitivity should not be routinely investigated, but it is indicated in patients with contact dermatitis in the head and neck region.²⁰ In this study, the frequencies of allergen sensitivities in the head and neck region were compared with the regions outside the head and neck, and no significant difference was found in the frequency of GST sensitivity. These results indicate that GST sensitivity is frequently seen in Turkey, but it can often be overlooked because it is not included in the EBS patch test, and therefore, there is a need for prospective studies investigating the frequency of GST sensitivity in Turkey.

In this study, thiomersal sensitivity was found to be the third most common reaction (4.2%), and its frequency was found to be significantly higher under 40 years of age. Thiomersal is an organic mercury compound with antibacterial and antifungal effects, widely used in contact lens solutions, eve drops, eve cosmetics, and antiseptic materials. Although the production of vaccines containing thiomersal was stopped in the United States in 2001, it is still used as a preventative in hepatitis B and tetanus-diphtheria vaccines in Turkey. We found few studies from Turkey reporting the frequency of thiomersal sensitivity. Ada et al. determined the thiomersal sensitivity rate as 2.2% in their study and reported thiomersal sensitivity as the second most common cosmetic allergen after octyl gallete. Boyvat et al. determined the rate of thiomersal sensitivity as 1.6% in 308 patients.²² In another study published in 2022 from Slovenia, Bizjak et al.²³ reported the rate of thiomersal sensitivity as 3.6% and found its frequency to be significantly higher in those under 40 years, which is in agreement with our findings. Thiomersal still being used as a preservative in some vaccines in Turkey may be the reason for this sensitivity reaction. Similarly, contact lenses being preferred especially by individuals under 40 years may explain the higher incidence of this reaction in this age group. Since thiomersal is not included in the EBS patch test series, there are not sufficient data sharing the frequency of sensitivity to this agent in Turkey. The high sensitivity rate in the current study reveals the necessity of detailed studies on the frequency of thiomersal sensitivity in Turkey, as in GST.

We found the rate of fragrance mix sensitivity to be 3.4%, and it was significantly higher in men and individuals over 40 years of age.

In other studies conducted in Turkey, sensitivity rates have been reported to range from 2.1% to 6.4%.^{4-8,24} Similar to our study, in the literature, it is stated that fragrance mix sensitivity increases with age.²³⁻²⁶ This increase is considered to be due to the decrease in the protection of the skin-barrier and the increase in the use of topical moisturizers and cosmetics with advancing age. Similarly, in our study, we found that sensitivities to formaldehyde, imidazolidinyl urea, and budesonide, which are frequently used in cosmetics, were at significantly higher rates in the group aged over 40 years, which may be related to the same reason. The use of cosmetics in Turkey is increasing rapidly every year. Although the use of cosmetics is more common in women, our finding indicating that its frequency was significantly higher in male patients may be due to the frequent use of cologne after shaving and as a traditional treat, especially among middle and older men in Turkey.

Carba mix (3.2%) is another allergens to which our patients had frequent sensitivity reaction. Carba mix is not included in EBS. The only study in Turkey in which the frequency of carba mix sensitivity was investigated belongs to Akasya-Hillenbrand and Ozkaya-Bayazit,³ who reported this rate as 4.8%. The authors noted that the frequency of carba mix sensitivity increased in hospital workers, and there was a significantly higher frequency of sensitivity in non-atopic patients. In contrast, we found that carba mix sensitivity was significantly higher in atopic patients. In another study comparing the patch test results between atopic and non-atopic patients, Jurakić Tončić et al.²⁷ reported the frequency of carba mix sensitivity as 4% in atopic patients and did not detect a significant difference between the two groups. Carba mix is often found in rubber and elastic materials, such as medical gloves, car tires, balloons, condoms, and erasers. Due to the high frequency of sensitivity, it is important that patients with intense exposure to these materials such as healthcare personnel are informed about the methods of protection.

In Turkey, cobalt chloride susceptibility has also been detected at high rates (5.3%–13.6%) in studies using the EBS patch test.^{1–10} NACDG reported the rate of sensitivity to cobalt chloride as 6.2%– 8.2%.²⁸ In our study, we found a lower rate (2.9%) compared to other studies reported from Turkey. This may be related to the low sensitivity of the T.R.U.E. test panel used in our study in detecting cobalt chloride sensitivity compared to EBS. There is a need for comparative studies investigating sensitivity to cobalt chloride using the T.R.U.E. test.

In this study, contact dermatitis was most frequently localized on the hands, followed by the head and neck region. We found the most common patch test positivity rate in head and neck dermatitis (49.3%). Similarly, Akyol et al.⁴ reported the highest sensitivity rate in face (40%) and neck (45%) dermatitis. In addition, in our study, we found that colophony and balsam of Peru sensitivities were significantly higher in head and neck dermatitis compared to other localizations. In a study published in 2021, Koca et al.¹ determined an increase the frequency of colophony sensitivity in recent years (1.7%) and noted that this sensitivity was especially common in housewives. We found a similar colophony sensitivity rate in our study (1.6%) and observed that it was more common in women, although not at a statistically

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significant level. The frequency of balsam of Peru sensitivity has also increased in Turkey in recent years,⁶ which can be associated with the increased use of cosmetic products.

Our results showed that there was less than 1% sensitivity to the following allergens: neomycin sulphate (0.3%), caine mix (0.9%), ethylenediamine dihydrochloride (0.9%), methyldibromo glutaronitrile (0.2%), formaldehyde (0.5%), imidazolidinyl urea (0.7%), budesonide (0.5%), hydrocortizone-17-butyrate (0.8%), mercaptobenzothiazole (0.2%), bacitracin (0.4%), and bronopol (0.5%). We consider that this information will be valuable in the preparation of a local standard series for Turkey.

Concerning the limitations of the study, first, as a standard patch test, the T.R.U.E. test was applied to all patients included in the study, and no additional extended series was used or no test was performed on the personal products used by the patients; therefore, some allergen sensitivities might not have been detected. In addition, due to the retrospective nature of the study, the clinical relevance of patients with allergen sensitivity could not be determined, and the MOAHLFA index could not be calculated since occupational information was not available in the patient files.

5 | CONCLUSION

This study provides a comprehensive profile of agents found responsible for ACD in Turkey and included in the T.R.U.E. test. In our study, we detected high sensitivity rates for the GST, thiomersal, and carba mix allergens that are not included in EBS. The sensitivity rates of common allergens in EBS and T.R.U.E. tests were comparable to those reported in the literature. We can conclude that due to its ease of use, the T.R.U.E. test is a reliable patch test, especially in busy healthcare facilities like our clinic. Lastly, the T.R.U.E. test is an important alternative patch test, particularly in suspected allergen susceptibility to GST, thiomersal, or carbamix, which are not included in EBS. The results of this study should be considered in standard series to be established for Turkey and confirmed by further studies.

ACKNOWLEDGMENTS

None declared.

FUNDING INFORMATION

None declared.

CONFLICT OF INTEREST STATEMENT

None declared.

DATA AVAILABILITY STATEMENT

Data sharing is not applicable to this article as no new data were created or analyzed in this study.

ETHICS STATEMENT

The ethics committee of İstanbul Medipol University approved the study protocol (approval number: 2022/312).

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SUPPORTING INFORMATION

Additional supporting information can be found online in the Supporting Information section at the end of this article.

How to cite this article: Ünal A. Analysis of patch testing results in patients with contact dermatitis in Istanbul, Turkey, from 2012 to 2022. *J Cosmet Dermatol*. 2023;22:2831-2838. doi:10.1111/jocd.15791