

Characteristics of patch test patients in Yogyakarta, Indonesia, 2011-2020 Study Period

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Abstract

Introduction Patch tests are performed to identify allergens that cause contact dermatitis. There were varying results on the prevalence of contact dermatitis to specific allergens from different countries.

Methods A retrospective study was conducted over a 10-year period from January 2011 to December 2020 on patch test patients performed at Dr. RSUP. Sardjito, Yogyakarta.

Results During 2011-2020, 616 patients underwent 735 different patch test series. The percentage of female patients was higher than the male patients. The most common diagnoses were drug eruption, allergic contact dermatitis (ACD) due to cosmetics, nummular dermatitis, hand eczema, ACD due to hair dye, ACD due to footwear, ACD due to metals, pigmented contact dermatitis, and atopic dermatitis. The most common allergens were nickel sulphate, cobalt chloride, potassium dichromate, Peru balsam, neomycin sulphate, fragrance mix I, paraben mix, colophony, carba mix, and p-phenylenediamine (PPD).

Conclusion Sensitization to metals, namely nickel sulphate, cobalt chloride, and potassium dichromate, became the largest proportion of allergen results in this study.

Key words

Patch test, allergen, diagnosis, Indonesia.

Introduction

Patch test is an examination performed to identify the cause of allergic contact dermatitis (ACD). Contact allergy is classified as type IV delayed hypersensitivity. This patch test is performed by attaching an allergen with a

standard concentration to an area of the body for a certain period of time. Reactions observed during the patch test are carefully assessed and interpreted so that a positive result is systematic confirmation of sensitization to allergens. If a positive result is found in the allergen tested on the patch test, the patient is then advised to avoid the ingredients containing the allergen. Allergens in patch testing are divided into several series, such as standard series, rubber series, dental series, textile series, and shoe series. The patch test series is performed according to the indications after history and physical examination data are obtained.^{1,2}

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This study aimed to describe the characterization

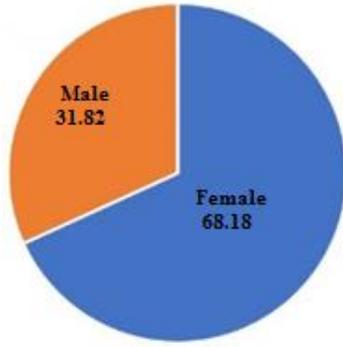


Figure 1a Patient gender.

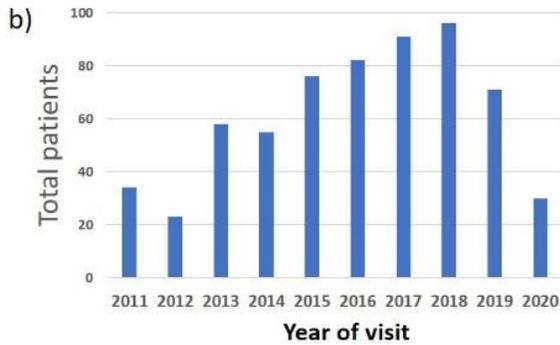


Figure 1b Distribution of the number of patch test patients each year during 2011-2020.

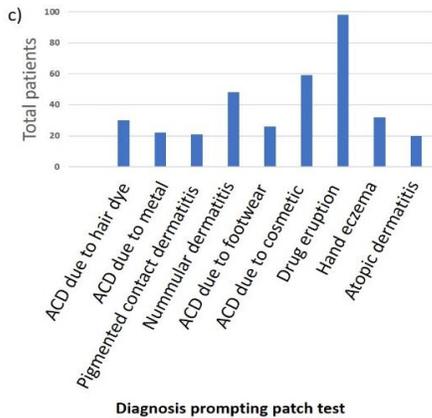


Figure 1c The most common diagnoses of patch test patients during 2011-2020.

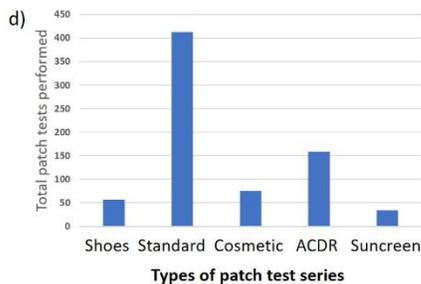


Figure 1d The most common type of patch test series

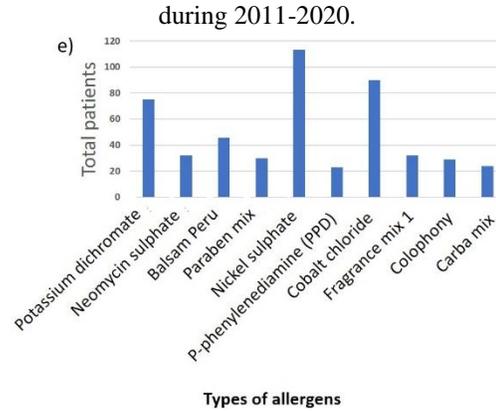


Figure 1e The top ten most common allergens in patch test patients during 2011-2020.

of patch test patients in a ten-year period from 2011 to 2020 in Yogyakarta, Indonesia.

Methods

This research was conducted at RSUP Dr. Sardjito, Yogyakarta, a referral hospital in the Special Province of Yogyakarta. A retrospective study with secondary data was conducted on patients who came to the Dermatology and Venereology Polyclinic from January 2011 to December 2020. Patch testing was done according to international recommendations. The readings of the patch test reactions were conducted at 48, 72, and 96 hours after attachment. Reaction readings with + (weak/ non-vesicular), ++ (strong/ vesicular), or +++ (very strong/ bulla) were classified as positive (allergic) and other skin lesions as negative. Types of allergens are categorized into several international allergen series, such as standard series, adverse cutaneous drug reaction series, shoes series, and rubber series.^{1,3}

Results

From January 2011 to December 2020 there were 616 patients who underwent patch testing. The highest proportion occurred in 2016-2018, there were 82 patients in 2016, 91 patients in

Table 1 The percentage of patch test patients with the most common allergens to the most frequent diagnosis at RSUP Dr. Sardjito during 2011-2020

	<i>ACD due to metal</i>	<i>Atopic dermatitis</i>	<i>ACD due to hair dye</i>	<i>ACD due to footwear</i>	<i>ACD due to cosmetic</i>	<i>Pigmented contact dermatitis</i>	<i>Hand eczema</i>	<i>Drug eruption</i>	<i>Nummular dermatitis</i>
Potassium dichromate	6.67	0.00	6.67	8.00	5.33	5.33	13.33	0.00	9.33
Neomycin Sulphate	3.13	0.00	6.25	3.13	12.50	0.00	12.50	3.13	21.88
Balsam Peru	0.00	0.00	6.52	0.00	6.52	2.17	13.04	0.00	17.39
Paraben mix	0.00	6.67	10.00	0.00	10.00	3.33	3.33	3.33	13.33
Nickel sulphate	7.96	0.88	9.73	4.42	7.08	1.77	13.27	1.77	13.27
p-phenylenedia mine (PPD)	13.04	0.00	13.04	0.00	0.00	4.35	4.35	0.00	13.04
Cobalt Chloride	4.44	1.11	3.33	3.33	6.67	3.33	6.67	2.22	16.67
Fragrance mix I	3.13	0.00	3.13	0.00	9.38	3.13	12.50	0.00	15.63
Colophony	6.90	3.45	6.90	13.79	10.34	0.00	3.45	3.45	24.14
Carba mix	4.17	0.00	8.33	0.00	8.33	4.17	8.33	0.00	29.17

2017, and 96 patients in 2018, while only 23 patients underwent patch testing in 2012 (**Figure 1b**). Of these 616 patients, 735 patch tests were performed, indicating that some patients had more than one type of patch tests.

The percentage of female patients was 68.18% (420 people), with 31.82% male patients (196 people) (**Figure 1a**). The mean age of the patients was 36.5 years with the youngest age being 4 years and the oldest 76 years old (two people) diagnosed as drug eruption and ACD with eye drops.

During that period, there were 57 types of diagnosis and the most common diagnoses for patients who were patch tested were drug eruption as many as 98 people, possibly ACD due to cosmetic (59 people), nummular dermatitis (48 people), hand eczema (32 people), ACD due to hair dye (30 people), ACD due to footwear (26 people), ACD due to metal (22 people), pigmented contact dermatitis (21 people), and atopic dermatitis (20 people) (**Figure 1c**).

For the most common type of patch test, the

standard series were performed 413 times, adverse cutaneous drug reaction series (159 times), cosmetics (76 times), shoes (56 times), and sunscreen (34 times) (**Figure 1d**).

For the standard series, the most common allergens were 113 patients positive to nickel sulphate (18.34%), 90 people to cobalt chloride (14.61%), 75 people to potassium dichromate (12.18%), 46 people to Balsam Peru (7.47%), 32 people to neomycin sulphate (5.19%), 32 people to fragrance mix I (5.19%), 30 people to paraben mix (4.87%), 29 people to colophony (4.71%), 24 people to carba mix (3.90%), and 23 people to p-phenylenediamine (PPD) (3.73%). For the adverse cutaneous drug reaction series, the most common allergens were captopril (28 people), cefradine (8 people), and amoxicillin (7 people). Only one patient was found positive for allergens included in the sunscreen series, namely octocrylene, octyltriazone, 2-ethylhexyl-4-dimethylaminobenzoate (octyl dimethyl PABA) and 2-hydroxy-4-methoxybenzophenone (benzophenone-3). In patch test with standard series allergens, the largest number of allergens that showed positive results in one patient was 17 allergens.

The most common allergens in the standard series were grouped with patients with the most common positive diagnoses for these allergens (**Figure 1e**). Patients with the most common diagnoses in this study showed positive results for nickel sulphate and cobalt chloride (**Table 1**). There were two patients with a diagnosis of ACD due to metal who showed positive results for metal-based nickel sulphate, cobalt chloride, and potassium dichromate. In this study, eight patients with a diagnosis of ACD due to nickel showed positive patch test results for nickel sulphate.

Discussion

Patch testing is a test to determine the allergen that causes contact dermatitis.^{1,2} Previous studies have shown that the prevalence of contact dermatitis to specific allergens from several countries has varying results, for example, sensitization to chromium in Nigeria.⁴ In this study, from the most frequent diagnoses of patients (drug eruption, ACD due to cosmetic, nummular dermatitis, hand eczema, ACD due to hair dye, ACD due to footwear, ACD due to metal, pigmented contact dermatitis, and atopic dermatitis) (**Figure 1c**), six diagnoses of which are allergic contact dermatitis with different causes (cosmetic, footwear, metal, hair dye and drug eruption) and manifestations (pigmented contact dermatitis).

This study shows that the most common allergens during the ten-year period from 2011 to 2020 were metal allergens, respectively, namely nickel sulphate, cobalt chloride, and potassium dichromate (**Figure 1e**). These results are in accordance with previous studies in several countries which also showed that metal allergens included in this standard series have a moderately large percentage of positive results on patch tests.^{3,5} Previous research has stated that people adults and children are often

sensitized by metals, for example sensitization to nickel and other metallic jewelry associated with piercing. In adults, ACD due to metals was also frequently associated with occupational dermatitis.⁶

Nickel is a metal commonly found in jewelry, zippers, belt heads, eyeglass frames, and keys.⁷ Coins in some countries contain nickel. Nickel was also frequently found in household accessories, which can cause sensitization to nickel.¹ Cobalt is also a metal that is often found together with nickel. These two metals are also found in prosthetic joint replacements and dental accessories and are often found to be positive in the same patient due to co-sensitization by both allergens.² Co-sensitization itself is different from cross-reaction. Poly-sensitization is divided into two categories, namely cross-reaction (the same IgE binds to several different allergens with similar structural characteristics) and co-sensitization (the presence of different IgE that bind almost simultaneously to allergens that do not necessarily have similar characteristics).⁸ This study also supports the statement regarding co-sensitization with some patients having positive results for both allergens.

Potassium dichromate is another metal that can be found in wet cement and leather, including leather shoes.² These three metals can also be found in everyday materials, such as detergents and cosmetics, which can then cause sensitization.⁶ Most of the common diagnoses in this study also indicated that some patients had positive results for nickel sulphate, cobalt chloride, and potassium dichromate (**Table 1**). This pattern shows that positive results for the three metal allergens can be found in patients with different diagnoses. Sensitization to metals can cause various skin lesions, such as systemic contact dermatitis, granulomas, erythema multiforme, and lichen planus. Systemic contact dermatitis to nickel occurs after consuming a

nickel-containing diet.¹ Nickel is also frequently correlated with lymphomatoid type of ACD.²

Neomycin, which belongs to the aminoglycoside group, is one of the most common topical antibiotics found to show positive results in contact dermatitis. This antibiotic is often used as a topical drug on the skin, ears, and eyes.² In this study, 21.88% of patients sensitized by neomycin sulphate were patients previously diagnosed with nummular dermatitis (**Table 1**). Patients who had early skin lesions of nummular dermatitis might purchase self-medicating drugs and became sensitized to topical drugs containing neomycin. This was also consistent with previous studies showing that nummular dermatitis was associated with sensitization by neomycin.⁹

There were several patients with a diagnosis of nummular dermatitis, hand eczema, Riehl melanosis and ACD due to cosmetic in this study who showed positive results with fragrance mix I and II. Previous research has shown that the frequency of contact allergies to fragrance mix is higher in women than men,¹⁰ which is also in accordance with the results in this study, namely a total of 33 female patients (64.71%) were sensitized to fragrance mix I and II compared to 18 male patients (35.29%). Fragrance mix I contains oak moss absolute, geraniol, cinnamic aldehyde, hydrocitronellal, cinnamic alcohol, isoeugenol, alpha-amyl cinnamic alcohol and eugenol; whereas fragrance mix II contains lylal, hexyl, cinnamic aldehyde, citral, coumarin, farnesol, and citronellol.¹ It was possible to find elements in fragrance mix I or II in the type of fragrance product used by the patients.

Balsam Peru is also one of the ingredients in fragrance. This balsam Peru extracted from plants which can also be found in the medication.¹ Previous studies reported that 8.5%

of patients with clinical manifestations were sensitized to Balsam Peru,⁵ with 4.7% in patients scheduled for hip arthroplasty. In this study, 7.46% of patients with clinical manifestations showed positive results for Balsam Peru (**Figure 1e**). There was one patient, diagnosed with dermatitis intertrigo, who was sensitized to Fragrance Mix II and Peru Balsam. This was in accordance with previous research which showed that the axilla, as one of the intertriginous areas, is one of the most common areas with fragrance allergens.²

p-Phenylenediamine (PPD) is a potent allergen contained in permanent hair dye. Sensitization to PPD can be seen characteristically on the face, neck, and eyelids, without any abnormalities on the scalp.² In this study, the earliest sensitization to PPD was found in patients aged 21-30 years (3 patients, 13.04%), there was also one patient in the age range of 31-40 years old (4.35%), eight patients in the group 41-50 years old (34.78%), six patients in the fifth decade (26.09%), three patients in the age range 61-70 years old (13.04%) and two patients in the seventh decade (8.7%). The age range of 41-50 and 51-60 years had the highest number of patients who showed positive results for PPD from a total of 23 patients. The results of this study were different from previous studies which showed that the prevalence of sensitization to PPD increases with age, at the time gray hair begins to appear.¹¹ This difference can be explained by the working age of the Indonesian people. In both of these age ranges, when the gray hair began to increase, the patient was still working so she/he tried to improve their appearance by dyeing their hair.¹²

Parabens are one of the ingredients for preservatives in the drug, food, and cosmetic industries.¹ There were three patients with a diagnosis of ACD due to cosmetics who were sensitized by paraben mix. This result could be

due to the difficulties in the history of contactants used by the patient previously so that it was not possible to explore the conditions that caused the sensitization. It was mentioned in previous studies that patients who were sensitive to parabens should not avoid cosmetics containing parabens because patients would tolerate them and did not show sensitization to these allergens so that they did not cause skin lesions. This phenomenon was called the paraben paradox.^{1,13}

Colophony is a natural resin that is commonly found in topical medications.¹ In this study, 24.14% of patients who tested positive for the allergen colophony were diagnosed as nummular dermatitis (**Table 1**). In patients with nummular dermatitis, it is mentioned that patch testing was necessary to determine allergen from contact sensitivity as an etiologic factor. Allergens that are usually associated with nummular dermatitis were nickel, fragrance, neomycin, and colophony.⁹ In patients who were sensitized to these allergens, patients diagnosed as nummular dermatitis have a percentage of more than 10%, namely 13, 27% for nickel, 15.63% for fragrance mix I, 21.88% for neomycin, and 24.14% for colophony (**Table 1**).

Carba mix consists of the following three allergens, diphenylguanidine, zincdibutyldithiocarbamate, and zincdiethyldithiocarbamate.¹ These allergens are usually contained in rubber chemicals that often cause sensitization to ACD due to footwear or ACD in the feet.^{1,2} In this study, there was one patient with an initial diagnosis of palmoplantar keratoderma who showed positive results on thiuram mix and carba mix. These two allergens were the most common allergens in the rubber series.^{1,2} The results of this study were also consistent with previous studies which showed that subjects sensitized to carbamates also showed positive reactions to thiuram. This

phenomenon is known as cross-reaction.^{1,14} Rubber, apart from being commonly found in shoes, is also contained in gloves, balloons, and other rubber-based tools that can cause sensitization. Rubber can cause hand and foot dermatitis.^{1,15} The palmoplantar keratoderma in this study may be a chronic hand and foot dermatitis in the form of lichenification, hyperkeratosis, and fissures resembling palmoplantar keratoderma.

In this study, data were obtained for 159 patch tests (21.63%) with adverse cutaneous drug reaction series. The largest proportion of allergens that showed positive results was captopril with 28 patients out of 159 patients (17.61%). Previous studies have shown that captopril can cause several types of drug eruptions, such as drug-induced pemphigus, lichen planus pemphigoides, linear IgA bullous dermatoses, Drug Reaction With Eosinophilia and Systemic Symptoms (DRESS), eczematous eruptions, exfoliative dermatitis, palmoplantar psoriasis and palmoplantar pustulosis, Toxic Epidermal Necrolysis (TEN), onycholysis, and buccal ulceration.¹⁶ In this study, the proportion of sensitization to captopril is still difficult to explain because in all patch test patients who were diagnosed with a suspected drug eruption, it turned out that there was no history of treatment with captopril at all. Meanwhile, the possibility of a cross reaction between captopril and the tested drug allergen has not been previously reported.

Conclusion

This paper reported the characteristics of patch test patients conducted at Dr. Sardjito in the 2011-2020 period. The results of this study were in accordance with the results of previous studies which showed that the most common allergens were caused by metals, namely nickel sulphate, cobalt chloride, and potassium

dichromate. The results of this study can be used as a reference in predicting allergens in patients when patch testing is not available, according to the patient's diagnosis.

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