

STUDY OF COMMON ALLERGENS IN PATIENTS WITH ALLERGIC CONTACT DERMATITIS: A HOSPITAL BASED STUDY

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ABSTRACT

Allergic contact dermatitis (ACD) is one of the most common diseases presenting to the Dermatology department. The one and only method of preventing as well as treating this disease is avoidance of the allergen causing it. The identification of the allergen causing the ACD is possible by performing patch testing. The purpose of this study was to identify common allergens among patients with ACD using Indian standard series (ISS) of patch test. Clinically suspected cases of ACD were included in the hospital based cross-sectional study from January to December 2017. These cases underwent patch testing with the ISS. The study assessed the following variables: sex, age, occupation, site and positive patch test results. There were a total of 58 patients among which, 36.2% were males and 63.8% were females with a mean age of 32.36 ± 12.51 years. Positive patch test reactions were seen in 63.0% of patients. The most common allergens were nickel sulphate (51.4%), fragrance mix (37.8%), potassium dichromate (8.1%), colophony (8.1%) and black rubber mix (8.1%). Among male, most common allergens were fragrance mix (57.1%), nickel sulphate (28.6%) and potassium dichromate (21.4%) while in female, most common allergens were nickel sulphate (65.2%) and fragrance mix (26.1%). In our study, majority of the allergens were positive. Hence, the ISS used in the study might be suitable in the context of Nepalese population. However, further similar studies on large number of patients with multiple allergens are required to determine the exact number of contact allergens prevalent in our population.

KEYWORDS

Allergic contact dermatitis; allergen; patch test, Nepal

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DOI: <https://www.doi.org/10.3126/nmcj.v23i1.36222>

INTRODUCTION

Allergic contact dermatitis (ACD) should be suspected in any patient with ongoing dermatitis. Once the detected allergens are removed from the patient's environment, it results in clearing of the dermatitis.¹ One in five individuals from the general population have contact allergy.² A study in rural village development community of Nepal showed ACD in 7.7% of the population.³ ACD is a type IV, delayed type reaction where there is activation of antigen specific T cells in a sensitized individual.^{1,4} Patch testing is considered the gold standard in the diagnosis of ACD.⁴ It creates an allergic response to non-irritating concentrations of allergens, which are applied directly on the skin.¹

Standard series of allergens are recommended for use in patch testing. It contains different allergens that most commonly cause ACD in the general population being patch tested. According to the differences in regional allergen exposure, there are different patch test series such as British standard series, North American standard series, European standard series, Korean standard series and Indian standard series (ISS).⁵ These different patch test series vary in number as well as in the type of allergen. Nepal doesn't have a standard patch test series. So, ISS was used in this study for patch testing. This study was done with the aim of finding out the common allergens in patients clinically diagnosed with ACD.

MATERIALS AND METHODS

This was a hospital based cross-sectional study conducted in the department of dermatology, Nepal Medical College Teaching Hospital from January to December 2017. Ethical approval was obtained from Institutional Review Committee of Nepal Medical College. All the patients clinically suspected to have ACD were included in the study. Patients with acute eczema and those who had lesions on the upper back (patch test site) were excluded from the study. An informed and written consent was taken from all patients.

Patch testing was performed using ISS, approved by Contact and Occupational Dermatitis Forum of India (CODFI). The test panel consisted of the following allergens: vaseline (as control), wool alcohol, balsam of Peru, formaldehyde, mercaptobenzothiozole, potassium dichromate, nickel sulphate, cobalt sulphate, colophony, epoxy resin, paraben mix, paraphenylenediamine (PPD), parthenium,

neomycin, benzocaine, chlorocresol, fragrance mix, thiuram mix, nitrofurazone and black rubber mix.

Finn chambers were used and allergens were applied in round chambers of aluminium, which was mounted on adhesive tapes free from colophony. Patch tests were applied on the upper half of the back of the patient after cleaning with spirit, and the patches with the allergens were applied in vertical rows beginning from the left scapula and continuing over the right, but avoiding the skin over the vertebral column. Patients were instructed to leave (keep) the patches in place for 48 hours and to avoid taking a bath or washing the back during this period. They were advised to avoid any activity that may cause excessive sweating. Readings of patch tests were done at 48 hours and at 96 hours. These readings were recorded according to the scoring system of International Contact Dermatitis Research Group (ICDRG) (Table 1).⁶ The diagnosis of ACD was confirmed based on a positive patch test reaction to an allergen.

Table 1: Recording of patch test reactions according to the ICDRG scoring system.⁶

Score	Description
-	Negative
?+	Doubtful reaction; faint erythema only
+	Weak positive reaction; palpable erythema, infiltration, possibly papules
++	Strong positive reaction; erythema, infiltration, papules, vesicles
+++	Extreme positive reaction; intense erythema, infiltration and coalescing vesicle
IR	Irritant reaction of different types
NT	Not tested

Recordings of demographic variables, clinical history, examination findings and patch test results were taken in the prepared proforma. Data was entered and analysed in Statistical Package for the Social Sciences (SPSS) version 16. Descriptive statistics was interpreted in terms of percentage, mean and standard deviation.

RESULTS

A total of 58 clinically diagnosed patients of ACD underwent patch test with ISS. Among

them, 36.2% (21/58) were males and 63.8% (37/58) were females, thus showed a female preponderance. The age group of the patients ranged from 7-73 years with the mean age of 32.36±12.51 years. Maximum numbers of patients were in the age group 26-35 years (Fig. 1). Occupation wise, homemakers constituted the majority 37.9% (22/58) followed by office workers 24.1% (14/58) (Others included shopkeeper 3.4% (2/58), driver 1.7% (1/58) and carpenter 1.7% (1/58) [Fig. 2].

Of the total 58 patients, most of the patients had ACD localized to the hands 51.8% (30/58) followed by feet 20.7% (12/58) and face 15.5%

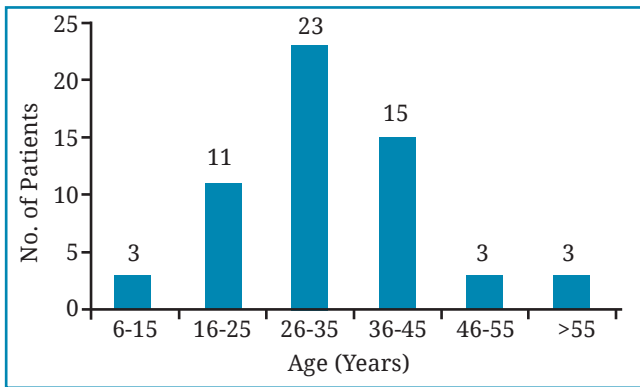


Fig. 1: Distribution of patients according to the age group

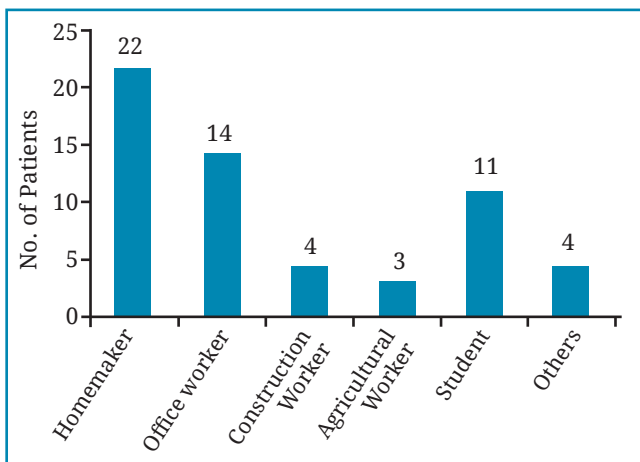


Fig. 2: Distribution of patients according to the occupation

(9/58). Scalp was the least involved site and affected only two patients (Table 2). Out of 58 patients undergoing patch testing, 63% (37/58) of them tested positive to either one or more allergens. Among them, 56.7% (21/37) reacted to a single allergen and remaining 43.3% (16/37) to more than one allergen (Table 3).

Out of 37 patients, 51.4% (19/37) showed positive reaction to nickel sulphate and 37.8%

Table 2: Distribution of patients according to the site of ACD (n=58)

Sites	Number of patients	%
Hands	30	51.8
Feet	12	20.7
Face	9	15.5
Generalized	6	10.3
Extremities	5	8.6
Neck	5	8.6
Trunk	5	8.6
Scalp	2	3.4

Note 1: Results do not add upto 100% since each patient generally had more than one lesion on the same or different parts of body; 2. Extremities exclude hands and feet.

Table 3: Frequency of allergens in patients with positive patch test reactions (n=37)

Number of Allergens	Number of patients with positive patch test	%
1	21	56.7
2	13	35.1
3	2	5.4
5	1	2.7
Total	37	100

Table 4: Results according to Indian standard series of patch test (n=37)

Allergens	positive reactions	
	(n)	(%)
Nickel Sulphate	19	51.4
Fragrance mix	14	37.8
Potassium dichromate	3	8.1
Colophony	3	8.1
Black rubber mix	3	8.1
Cobalt	2	5.4
Epoxy resin	2	5.4
PPD	2	5.4
Neomycin	2	5.4
Chlorocresol	2	5.4
Wool alcohol	1	2.7
Formaldehyde	1	2.7
Mercaptobenzothiazole	1	2.7
Parthenium	1	2.7
Benzocaine	1	2.7
Thiuram mix	1	2.7

Table 5: Distribution of patients with positive patch test reactions according to gender

Allergens	Patients with positive reactions	Male (%) (n=14)	Female (%) (n=23)
Nickel sulphate	19	4 (28.6)	15 (65.2)
Fragrance mix	14	8 (57.1)	6 (26.1)
Potassium dichromate	3	3 (21.4)	0 (0.0)
Colophony	3	0 (0.0)	3 (13.0)
Black rubber mix	3	1 (7.1)	2 (8.7)
Cobalt	2	0 (0.0)	2 (8.7)
Epoxy resin	2	2 (14.3)	0 (0.0)
PPD	2	0 (0.0)	2 (8.7)
Neomycin	2	2 (14.3)	0 (0.0)
Chlorocresol	2	0 (0.0)	2 (8.7)
Wool alcohol	1	0 (0.0)	1 (4.3)
Formaldehyde	1	0 (0.0)	1 (4.3)
Mercaptobenzothiazole	1	1 (7.1)	0 (0.0)
Parthenium	1	1 (7.1)	0 (0.0)
Benzocaine	1	0 (0.0)	1 (4.3)
Thiuram mix	1	0 (0.0)	1 (4.3)

Table 6: Comparison of common allergens in different studies

Author	Country	Common Allergens		
		1 st	2 nd	3 rd
Watts et al ¹² (2018)	United Kingdom	Nickel Sulphate	PPD	Cobalt
Freireich-Astman et al ¹⁹ (2007)	Israel	Nickel Sulphate	Potassium dichromate	Fragrance mix
Yu et al ¹⁶ (2017)	Korea	Nickel Sulphate	Cobalt	Potassium dichromate
Hassan et al ⁹ (2013)	India	Potassium dichromate, Nickel Sulphate	Cobalt	Thiuram mix
Parajuli et al ⁷ (2017)	Nepal	Nickel Sulphate	Fragrance mix, Parthenium	Multiple allergens
Bhattarai et al ¹⁸ (2016)	Nepal	Nickel Sulphate	Gentamicin	Fragrance mix
Present study	Nepal	Nickel Sulphate	Fragrance mix	Potassium dichromate, Colophony, Black rubber mix

(14/37) showed positive reaction to fragrance mix. Potassium dichromate, colophony and black rubber showed positive reactions in 8.1% (3/37) of the patients while cobalt, epoxy resin, PPD, neomycin and chlorocresol were positive in 5.4% (2/37) (Table 4). Among males,

most common allergens were fragrance mix 57.1% (8/14) nickel sulphate 28.6% (4/19) and potassium dichromate 3 (21.4%). Among females, most common allergens were nickel sulphate 15 (65.2%) and fragrance mix 6 (26.1%) (Table 5).

DISCUSSION

In our study, 58 patients underwent patch testing for the diagnosis of ACD. Among them, over one-third were males and nearly two-third were females, showing a female preponderance. This is in concordance with the study done by Parajuli *et al*,⁷ where there were 42.8% males and 57.2% females. A study by Sudhashree *et al*⁸ which used ISS containing 29 allergens also showed a female preponderance. Moreover, a systematic review and meta-analysis on prevalence of contact dermatitis also showed higher prevalence in females.² But, other studies done by Hassan *et al*⁹ and Bajaj *et al*¹⁰ showed a male preponderance. The reason for female preponderance in our study can be due to the fact that females have greater contact with the allergens, as they are exposed to household activities, cosmetics, farming and wet works than the males.

The age group of the patients ranged from 7-73 years with the mean age of 32.36 ± 12.5 years in our study. Maximum number of patients was in the age group of 26-35 years. Similarly, in the study by Singhal and Reddy¹¹ most of the patients were young adults between 20 and 39 years old. A study by Watts *et al*¹² which used patch testing with extended British standard series included patients 18-77 years with mean age of 36.9 ± 14.4 years. The age distribution in our study is representative of our demographic profile, where younger population outnumbered the elderly.¹³

Majority of the patients in our study were homemakers, which was similar to the study done by Parajuli *et al*⁷ in Nepal. Similar results were seen in the studies from India.^{9,11} On the other hand, study conducted in United Kingdom by Watts *et al*¹² had office work as the major occupation of the patients. In countries like Nepal and India, a significant number of females are homemakers. Besides, in our custom females are exposed to the common allergens from early age like in the form of wearing artificial jewellerys, cosmetics, fragrances, etc.

Most common site of ACD in our study was the hands (51.8%). Other common sites were feet and face which were involved in 20.7% and 15.5%, respectively while the least common site was scalp (3.4%). Similarly, in the study by Singhal and Reddy,¹¹ hands were the commonest site involved. Studies from the Czech Republic¹⁴ and Kuwait¹⁵ also reported hands as the common site of involvement. However, in the study done by Yu *et al*,¹⁶ the most common site were face and trunk followed by hands and

extremities. Frequent involvement of hand in our study may be due to the fact that the hand is the most exposed part of the body which comes in regular contact with the allergens, especially in homemakers, farmers and constructional workers. Other reason might be that the people from our country are not habituated to wearing gloves.

In this study, 63.0% of patients showed positive patch test result among 58 patients. Another study from Nepal by Parajuli *et al*⁷ reported 54.3% of patients with positive patch test result among 35. Similar results were also noted in the study done by Sudhashree *et al*⁸ which showed 64.7% of patients with patch test positive among 85. Patch test positivity of 65.3% by using ISS of 28 allergens were noted in the study by Singhal and Reddy.¹¹ Another study which used European standard series for patch testing in Pakistan by Hussain *et al*¹⁷ showed patch test positivity of 61%. This percentage of patch test positivity was comparable to that of patch testing using ISS.

In our study, 56.7% reacted to only one allergen and remaining 43.3% reacted to more than one. In the study by Parajuli *et al*,⁷ 89.4% patients reacted positive to a single allergen. In the study by Sudhashree *et al*,⁸ 74.5% showed positive reactions to multiple allergens and 25.5% were positive for single allergen. Similar result of higher positivity for multiple allergens (55.8%) were noted in study done by Yu *et al*.¹⁶ In the same study, single allergen was positive in 16.7%. This difference could be due to higher number of allergens in patch test series used in their study as well as different prevalence of ACD in different geographical location.

Nickel sulphate was the most common allergen in various studies including the two studies from Nepal (Table 6).^{7,9,12,16,18,19} Nickel sulphate (51.4%) and fragrance mix (37.8%) were the most common allergens in our study. Nickel sulphate followed by fragrance mix were also the most common allergens seen in the systematic review and meta-analysis study of Alinaghi *et al*.² Both Hussain *et al*¹⁷ and Freireich-Astman *et al*¹⁹ also showed nickel sulphate to be the most common allergen. However, potassium dichromate was the second most common allergen in contrast to fragrance mix seen in our study. Similarly, in other studies by Hassan *et al*⁹ and Boonchai *et al*²⁰ potassium dichromate was the most common allergen. In the study done by Watts *et al*¹² and Shakoor *et al*²¹ the most common allergen was nickel sulphate like ours. However, second most common allergen in their study was PPD.^{12,21} In our experience, patients with sensitivity

to cement and hair dye are more confident of association of their dermatitis and exposure to respective allergens, and hence are not inclined to undergo patch testing. This could be a cause of less number of positive patch test results to PPD and potassium dichromate in our study.

In this study the most common allergens among females were nickel sulphate (65.2%) and fragrance mix (26.1%), while, in male fragrance mix (57.1%) was the most common allergen followed by nickel sulphate (28.6%). A study done by Bhattarai *et al*¹⁸ among patients with hand eczema, also showed nickel sulphate to be the commonest allergen among females. Alinaghi *et al*² also showed nickel sulphate followed by fragrance mix as the most common allergens in both the gender. In the study done by Hassan *et al*⁹ the most common allergen in male was potassium dichromate followed by thiuram mix, however in females, the most common allergen was nickel sulphate followed by cobalt. Most common allergens in males and females in the study by Shakoor *et al*²¹ were PPD and nickel sulphate respectively. The reason for nickel sensitivity among females in our study can be due to the fact that females are naturally expected to have greater contact with nickel which is commonly found in jewellery and utensils.

Parthenium is abundantly found growing around major urban areas such as Kathmandu, Hetauda, Bharatpur, Butwal, Pokhara, Dang, Surkhet and Nepalgunj.²² However, our study showed only 2.7% of positive reaction to parthenium. Similar results of less positive reactions to parthenium (2.8%) were seen in the study done in Nepal by Paudel *et al*.²³ This

is in contrast to the study done by Parajuli *et al*⁷ in our country, where parthenium was the second most common allergen. Other studies in India also showed higher rates of parthenium positive reactions.^{11,24} This differences regarding frequency of positive reactions to parthenium in our study as compared to others in similar geographical area should be further explored in future studies.

However, the limitations of this study were the small sample size and the use of the patch test kit developed elsewhere. Till date, a Nepalese standard series for patch testing is lacking.

ACD is one of the frequently encountered conditions in the Dermatology Department. The identification of the allergen is important for the management of the ACD, as avoidance of the allergen is pivotal to both prevention and treatment of the condition. This is possible by performing patch testing. In our study, majority of the allergens were positive. Hence, the ISS of patch testing used in the study might be considered suitable for Nepalese population. Future studies could focus on conducting large scale, multi-centre studies including different standard series or multiple allergens to determine the set of allergens that could be used in the development of Nepalese standard series tailored for Nepalese population.

ACKNOWLEDGEMENTS

We would like to thank Mr. Prem Prasad Panta Lecturer, from Department of Community Medicine of Nepal Medical College for his help in data analysis.

REFERENCES

- Mowad CM, Anderson B, Scheinman P, Pootongkam S, Nedorost S, Brod B. Allergic contact dermatitis: Patient diagnosis and evaluation. *J Am Acad Dermatol* 2016; 74: 1029-40. doi: 10.1016/j.jaad.2015.02.1139.
- Alinaghi F, Bennike NH, Egeberg A, Thyssen JP, Johansen JD. Prevalence of contact allergy in the general population: A systematic review and meta-analysis. *Contact Dermatitis* 2018; 80: 77-85. doi: 10.1111/cod.13119.
- Shrestha R, Lama L, Gurung D, Shrestha DP, Rosdahl I. Pattern of skin diseases in a rural village development community of Nepal. *Nepal J Dermatol Venereol Leprol* 2014; 12: 41-4.
- Uyesugi BA, Sheehan MP. Patch Testing Pearls. *Clin Rev Allerg Immunol* 2019; 56: 110-8. doi: 10.1007/s12016-018-8715-y.
- Davis MD, Scalf LA, Yiannias JA *et al*. Changing trends and allergens in the patch test standard series: a mayo clinic 5-year retrospective review, January 1, 2001, through December 31, 2005. *Arch Dermatol* 2008; 144: 67-72. doi: 10.1001/archdermatol.2007.2
- Wilkinson DS, Fregert S, Magnusson B, *et al*. Terminology of contact dermatitis. *Acta Derm Venereol* 1970; 50: 287-92.
- Parajuli S, Paudel V, Paudel U, Pokhrel DB. Pattern of patch test reactivity among patients with clinical diagnosis of contact dermatitis: a hospital-based study. *Our Dermatol Online* 2017; 8: 389-92. doi: 10.7241/ourd.20174.111.
- Sudhashree VP, Parasuramalu BG, Rajanna MS. A clinico-epidemiological study of allergens in patients with dermatitis. *Indian J Dermatol*

- Venereol Leprol* 2006; 72: 235-7. doi: 10.4103/0378-6323.25793.
9. Hassan I, Rather PA, Jabeen Y *et al.* Preliminary experience of patch testing at Srinagar, Kashmir. *Indian J Dermatol Venereol Leprol* 2013; 79: 813-6. doi: 10.4103/0378-6323.120737.
 10. Bajaj AK, Saraswat A, Mukhija G, Rastogi S, Yadav S. Patch testing experience with 1000 patients. *Indian J Dermatol Venereol Leprol* 2007; 73: 313-8. doi: 10.4103/0378-6323.34008.
 11. Singhal V, Reddy BS. Common contact sensitizers in Delhi. *J Dermatol* 2000; 27: 440-5. doi: 10.1111/j.1346-8138.2000.tb02202.x
 12. Watts TJ, Watts S, Thursfield D, Haque R. A patch testing initiative for the investigation of allergic contact dermatitis in a UK allergy practice: a retrospective study. *J Allergy Clinical Immunol Pract* 2018; 7: 89-95. doi: 10.1016/j.jaip.2018.08.030.
 13. Dhakal B. An analytical study on present status of age-sex structure of Nepal. *Asia Pac J Edu Art Sc* 2014; 1: 20-6.
 14. Machovcova A, Dastychova E, Kostalova D *et al.* Common contact sensitizers in the Czech Republic: patch test results in 12,058 patients with suspected contact dermatitis. *Contact Dermatitis* 2005; 53: 162-6. doi: 10.1111/j.0105-1873.2005.00676.x
 15. Almutairi N, Almutawa F. Allergic contact dermatitis pattern in Kuwait: nickel leads the pack. In-depth analysis of nickel allergy based on the results from a large prospective patch test series report. *Adv Dermatol Allergol* 2017; 34: 207-15. doi: 10.5114/ada.2017.67843.
 16. Yu DS, Kim HJ, Park YG, Bae JM, Kim J-W, Lee YB. Patch-test results using Korean standard series: a 5-year retrospective review. *J Dermatol Treat* 2017; 28: 258-62. doi: 10.1080/09546634.2016.1219015.
 17. Hussain I, Rani Z, Rashid T, Haroon TS. Suitability of the European standard series of patch test allergens in Pakistani patients. *Contact Dermatitis* 2002; 46: 50-1. doi: 10.1034/j.1600-0536.2002.460111.x
 18. Bhattarai S, Rijal A, Agrawal S. Common contact sensitizers among patients with hand eczema: A multicenter-study in Nepal. *Nepal J Dermatol Venereol Leprol* 2016; 14: 14-7. doi: 10.3126/njdvl.v14i1.15809.
 19. Freireich-Astman M, David M, Trattner A. Standard patch test results in patients with contact dermatitis in Israel: age and sex differences. *Contact Dermatitis* 2007; 56: 103-7. doi: 10.1111/j.1600-0536.2007.01004.x
 20. Boonchai W, Iamtharachai P, Sunthonpalin P. Prevalence of allergic contact dermatitis in Thailand. *Dermatitis* 2007; 19: 142-5. doi: 10.2310/6620.2008.07112.
 21. Shakoor Z, Al-Mutairi AS, Al-Shenaifi AM, Al-Abdulsalam AM, Al-Shirah BZ, Al-Harbi SA. Screening for skin-sensitizing allergens among patients with clinically suspected allergic contact dermatitis. *Saudi Med J* 2017; 38: 922-7. doi: 10.15537/smj.2017.9.19864.
 22. Shrestha, BB, Shabbir, A & Adkins, SW. Parthenium hysterophorus in Nepal: a review of its weed status and possibilities for management. *Weed Res* 2015; 55:132-44. doi: 10.1111/wre.12133.
 23. Paudel S, Pun G, Parajuli N, Paudel S, Sharma R. Patch testing in Nepalese population: A single center study from Kathmandu, Nepal. *Nepal J Dermatol Venereol Leprol* 2019; 17: 12-6. doi: 10.3126/njdvl.v17i1.23118.
 24. Sharma VK, Chakrabarti A. Common contact sensitizer in Chandigarh, India. *Contact Dermatitis* 1998; 38: 127-31. doi: 10.1111/j.1600-0536.1998.tb05677.x.