

# Contact sensitisation pattern of patients with eczema at the face and neck region: A retrospective study in Kuala Lumpur

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## ABSTRACT

**Introduction:** Allergic contact dermatitis (ACD) involving the face and neck region (FNR) is not uncommon. We aimed to determine the sensitisation pattern among patients with dermatitis involving FNR who underwent skin patch tests between 2016 and 2022.

**Materials and Methods:** This is a 7-year retrospective review on contact sensitisation patterns in patients with dermatitis over the FNR who underwent skin patch tests between 2016 and 2022 in the Department of Dermatology Hospital Kuala Lumpur.

**Results:** There were 291 patients (female-to-male ratio of 7.8:1; mean age of  $34.1 \pm 14.0$  years) with dermatitis at the FNR who underwent patch tests. The majority ( $n = 116, 39.9\%$ ) were aged between 20 and 29 years. About 8% were below 19 years of age. Nearly 50% had dermatitis over the perioral region, 8.6% at the periorbital area and 50.6% at the other parts of the face and neck region. The clinical diagnoses included contact dermatitis ( $n = 145, 49.8\%$ ), cheilitis ( $n = 81, 27.8\%$ ), endogenous eczema ( $n = 28, 9.6\%$ ) and others. All were tested with European baseline series, with 91.4% and 77.0% tested with extended series, and own products, respectively. About 70.1% were sensitised to at least one allergen. The most common sensitizing allergen was nickel sulfate (34.0%), followed by cobalt chloride (11.7%), fragrance mix (10.7%), methylchloroisothiazolinone/methylisothiazolinone (8.9%), and formaldehyde (8.9%). Clinical relevance was documented in 58.8% of them.

**Conclusion:** Contact sensitisation was detected in about 70% of patients with dermatitis at the FNR who were patch-tested. Nickel, cobalt chloride and fragrance mix were the most common sensitising allergens in these patients.

## KEYWORDS:

Allergic contact dermatitis, dermatitis, face and neck region, skin patch test, European baseline series

## INTRODUCTION

Allergic contact dermatitis (ACD) is an inflammatory dermatosis caused by a type IV hypersensitivity reaction to an allergen, which leads to a subsequent T-cell-mediated

response.<sup>1</sup> The face and neck region (FNR), being more susceptible to environmental stressors, is a common site for ACD. The triggering factors include aeroallergens, ultraviolet radiation, and cosmetic products.<sup>2</sup> Patch testing is the gold standard to diagnose ACD. It is performed when ACD is suspected in patients with FNR dermatitis.<sup>3</sup> The findings of patch testing will identify the culprit allergen. Avoidance of future exposure eventually will result in the resolution of clinical symptoms. There is limited local data on the sensitisation pattern of FNR dermatitis in our region. This study aimed to determine the sensitisation pattern among patients with suspected allergic contact dermatitis over the FNR who had undergone patch testing in Dermatology Clinic, Hospital Kuala Lumpur from the year 2016 to 2022.

## MATERIALS AND METHODS

This was a retrospective, single-centre study conducted at Hospital Kuala Lumpur, Malaysia. We retrieved data from the clinical record of all patch tests done between January 2016 and December 2022. Those patients with dermatitis involving their face and neck including the perioral and periorbital region were included. Subsequently, medical records were retrieved from the Medical Record Unit, hospital Kuala Lumpur with permission. Demographic data, clinical characteristics of the FNR and the initial diagnosis were recorded. The patch tests included were European baseline series, extended series such as cosmetic series, dental series, and hairdressing series. The patch test was done over 5 days with patching of the allergen on day 1, followed by reading on day 3 and day 5. Information on the patch test series done and their finding were obtained. Descriptive analysis and inferential analysis were performed using SPSS Version 26.0

## RESULTS

There was a total of 1224 patch testing done between 2016 and 2022. Of these, 291 (23.8%) of the patients had dermatitis at the FNR. Their clinical characteristics were summarised in Table I. The mean age of the patients was  $34.1 \pm 14.0$  years when they were patch-tested. The youngest patient patch-tested was 11 years old. The female-to-male ratio was 7.8:1. White collar workers (110, 37.8%) and healthcare workers (61, 21.0%) were the two most common occupations in the cohort.

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Table I: Characteristics of 291 patients who underwent patch test for FNR dermatitis (2016-2022)

Characteristic	Total n = 291	Female n = 258	Male n = 33	P-value
Age (range)	34.1 (11- 77)	33.6 9 (11- 77)	37.8 (15- 72)	0.104
Age group in years, n(%)				
10- 19	22 (7.6)	20 (7.9)	2 (6.1)	1.000
20- 29	116 (39.9)	104 (40.3)	12 (36.4)	0.710
30- 39	85 (29.2)	77 (30.6)	8 (24.2)	0.547
40- 49	19 (6.5)	18 (7.1)	1 (3.0)	0.708
50 -59	25 (8.6)	19 (7.5)	6 (18.2)	0.053
60 -69	17 (5.8)	14 (5.6)	3 (9.1)	0.428
70 -79	7 (2.4)	6 (2.4)	1 (3.0)	0.582
Ethnicity, n(%)				
Malay	172 (59.1)	155 (60.1)	17 (51.5)	0.346
Chinese	81 (27.8)	68 (26.4)	13 (39.4)	0.116
Indian	32 (11.0)	30 (11.6)	2 (6.1)	0.336
Others	6 (2.1)	5 (1.9)	1 (3.0)	0.678
Occupations, n(%)				
White collar workers	110 (37.8)	98 (38.0)	12 (36.4)	0.857
Healthcare workers	61 (21.0)	59 (22.9)	2 (6.1)	0.026
Blue collar	25 (8.6)	16 (6.2)	9 (27.3)	<0.001
Pink collar	15 (5.2)	14 (5.4)	1 (3.0)	0.558
Unemployed	80 (27.5)	71 (27.5)	9 (27.3)	0.976
Provisional diagnosis, n (%)				
Cheilitis	81 (27.8)	77 (29.8)	4 (12.1)	0.032
Contact dermatitis	145 (49.8)	124 (48.1)	21 (63.6)	0.092
Endogenous eczema	28 (9.6)	24 (9.3)	4 (12.1)	0.605
Face dermatitis	22 (7.6)	19 (7.4)	3 (9.1)	0.724
Photodermatitis	8 (2.7)	7 (2.7)	1 (3.0)	0.916
Others	7 (2.4)	7 (2.7)	0 (0.0)	0.338
Sites involved, n (%)				
Face (except perioral, periorbital area)	148 (50.9)	125 (48.4)	23 (69.7)	0.022
Perioral	136 (47.4)	131 (50.8)	7 (21.2)	0.001
Periorbital	25 (8.6)	22 (8.5)	3 (9.1)	0.913
Non facial area (trunk, upper and lower limbs)	70 (24.1)	60 (23.3)	10 (30.3)	0.372

FNR = Face and neck region

The clinical diagnoses before the patch test include contact dermatitis (145, 49.8%), cheilitis (81, 27.8%), endogenous eczema (28, 9.6%), non-specific facial dermatitis (22, 7.6%) and others. The majority of patients had involvement of the face other than perioral and periorbital area (n = 148, 50.9%), followed by perioral (n = 136, 47.6%), and periorbital (n = 25, 8.6%) region. About a quarter of them reported dermatitis involving other parts of the body as well.

All were tested with the European Baseline Series (Table II). About 91% (n = 266) were also tested with at least one extended series. Among these, 76.6% (n = 223) were tested with cosmetic series. Other extended series used include dental series (25, 8.6%), hairdressing series (20, 6.9%), rubber series (15, 5.2%), metal series (14, 4.8%), medicaments (13, 4.5%), photoallergen series (10, 3.4%), shoe chemical series (4, 1.4%), textile and leather dye (2, 0.7%) and plastic and glue series (1, 0.3%). Own products were also tested in 224 (77%) of the patients.

About 70.1% (n = 204) developed at least one positive reaction (range 1 to 12 allergens). Of these, more than 80% (n = 169) had at least one positive reaction in the European baseline series. About 54.4% (n = 111) and 19.6% (n = 40) of them had positive reactions to the extended series and their products. There was about 12.7% (n = 26) of them had a negative reaction in the European baseline series but a positive reaction in the extended series. There were nine

patients (4.4%) who only tested positive for their own product but had negative reactions in the European Baseline Series and extended series. Clinical relevance was found in 58.8% (n = 120) of the patients with positive reactions. The positivity of the patch tests was not significantly associated with ethnicity, occupations, pretest diagnoses and site of involvement.

The most frequently tested positive allergen was nickel sulfate (99, 34.0%), followed by cobalt chloride (34, 11.7%), fragrance mix (31, 10.7%), kathon CG (Methylchloroisothiazolinone/methylisothiazolinone) (26, 8.9%) and formaldehyde (n = 26, 8.9%) (Table III). A similar pattern of sensitisation was found in the sub-analysis among the female patients. In male patients (n = 33), nickel sulfate remained the most common sensitising allergen detected (n = 7, 21.2%). This was followed by para-phenylenediamine (PPD) (4, 12.1%), and textile dye mix (3, 9.1%).

Female patients (Mean age = 33.6 years) were younger than their male counterparts (mean age 37.8 years) although it was not statistically significant (Table I). In terms of occupations, a higher proportion of females worked as healthcare workers (22.9% vs 6.1%, p = 0.026) whereas a higher proportion of male patients were blue-collar workers (27.3% vs 6.2%, p < 0.001) compared to their counterparts. For the pretest diagnosis, there were significant differences in the cheilitis group (29.8% in females vs 12.1% in males). No

Table II: Patch test findings among patients with FNR dermatitis (2016 to 2022)

Patch testing	Total n = 291	Female n = 258	Male n = 33	p-value
Patch test series used				
European baseline	291 (100)	258 (100)	33 (100)	
Own products	224 (77.0)	207 (80.2)	17 (51.5)	
Cosmetic	223 (76.6)	208 (80.6)	15 (45.5)	
Dental	25 (8.6)	24 (9.3)	1 (3.0)	
Hairdressing	20 (6.9)	18 (7.0)	2 (6.1)	
Rubber	15 (5.2)	13 (5.0)	2 (6.1)	
Metal	14 (4.8)	8 (3.1)	6 (18.2)	
Medicaments	13 (4.5)	10 (3.9)	3 (9.1)	
Photoallergen	10 (3.4)	10 (3.9)	0 (0.0)	
Shoe chemicals	4 (1.4)	4 (1.6)	0 (0.0)	
Textile and leather dye	2 (0.7)	2 (0.8)	0 (0.0)	
Plastic and glue	1 (0.3)	1 (0.4)	0 (0.0)	
Number with ≥1 positive reaction (%)	204 (70.1)	187 (72.5)	17 (51.5)	0.013
1 allergen	54 (18.6)	51 (19.8)	3 (9.1)	0.160
2 allergens	63 (21.6)	58 (22.5)	5 (15.1)	0.500
3 allergens	37 (12.7)	31 (12.0)	6 (18.2)	0.401
>3 allergens	50 (17.2)	47 (18.2)	3 (9.1)	0.229
Number with positive reaction in European baseline series (%), n = 204	169 (82.8)	153 (81.8)	16 (94.1)	0.316
Number with positive reaction in extended series (%), n = 204	111 (54.4)	98 (52.4)	13 (76.5)	0.009
Number with positive reaction with testing own products (%), n = 204	40 (19.6)	38 (20.3)	2 (11.8)	1.000
Number with negative reaction in European baseline but positive in extended series (%), n = 204	26 (12.7)	25 (13.4)	1 (5.9)	0.697
Number with negative reaction in European baseline & extended series but positive reaction with testing own products (%), n = 204	9 (4.4)	9 (4.8)	0 (0.0)	1.000
Clinical relevance	120/204 (58.8)	108/187 (57.8)	12/17 (70.6)	0.040

FNR = Face and neck region

Table III: The sensitisation pattern among patients with FNR dermatitis 2016 to 2022 (Top 10 allergens)

No	All (n = 291)		Female (n = 258)		Male (n = 33)	
	Types of allergen	n(%)	Types of allergen	n(%)	Types of allergen	n (%)
1	Nickel sulfate	99 (34.0)	Nickel sulfate	92 (35.7)	Nickel sulfate	7 (21.2)
2	Cobalt chloride	34 (11.7)	Cobalt chloride	33 (12.8)	4-Phenylenediamine	4 (12.1)
3	Fragrance mix	31 (10.7)	Fragrance mix	29 (11.2)	Textile dye mix	3 (9.1)
4	Kathon CG	26 (8.9)	Kathon CG	25 (9.7)	Fragrance mix	2 (6.1)
5	Formaldehyde	26 (8.9)	Formaldehyde	25 (9.7)	Colophony	2 (6.1)
6	Thimerosal	25 (8.6)	Thimerosal	25 (9.7)	Tea tree oil	2 (6.1)
7	Methylisothiazolinone	20 (6.9)	Methylisothiazolinone	19 (7.4)	2,5-Diaminotoluene sulfate	2 (6.1)
8	Colophony	19 (6.5)	Colophony	17 (6.6)	hexahydro-1,3,5-tris-(2-hydroxyethyl)triazine	2 (6.1)
9	Balsam Peru	17 (5.8)	Balsam Peru	16 (6.2)		
10	gallate mix	16 (5.5)	gallate mix	16 (6.2)		

FNR = Face and neck region

significant differences were found in the other diagnosis groups. For the site of involvement, there was a significantly higher proportion of male patients with FNR (non-periorbital and perioral) involvement (69.7% in males vs 48.4% in females,  $p = 0.022$ ). On the other hand, significantly more female patients had perioral involvement compared to male patients (50.8% vs 21.2%,  $p = 0.001$ ). No differences were found for the periorbital or other body site groups.

There was a significantly higher rate of positive patch test reaction among the females (72.5% vs 51.5%,  $p = 0.013$ ) compared to males. More male patients reported a positive

reaction in the extended series ( $n = 13$ , 76.5% vs  $n = 98$ , 52.4%,  $p = <0.009$ ) compared to female patients (Table II).

## DISCUSSION

This study population had a mean age of 34.1 years which is similar to other studies done earlier in China, Thailand, India and Turkey.<sup>4-7</sup> The female-to-male ratio was as high as 7.8:1. A similar observation was reported by Kasemsarn et al., with a female-to-male ratio of 9.1:1.<sup>6</sup> Others had a female-to-male ratio of 2.5 to 6.3:1.<sup>4-8</sup> This was likely due to females applying more cosmetics than their male counterparts.<sup>9</sup> Use of

**Table IV: Comparison of different studies on patch testing among patients with facial dermatitis or cosmetic allergy**

Country	Malaysia	Turkey <sup>4</sup>	India <sup>5</sup>	Thailand <sup>6</sup>	China <sup>7</sup>	United State <sup>8</sup>
Authors	Teo et al.	Adisen et al.	Garg et al.	Kasemsarn et al.	Li et al	Katz et al.
Study year	2016 - 2022	2001 -2007	2013 -2015	2006 -2011	2003 -2005	1995- 1997
n	291	404	58	244	92	85
Mean age	34.7	33	36.3	37.3	35.3	47.0
F: M	7.8:1	-	6.25:1	9.1:1	2.5:1	4.6:1
Test series	European baseline and extended series	European baseline series only	ISS, ICFS	SiSS, cosmetic series (44.9%)	Modified European standard series	NACDG standard series
Top 3 allergens	Nickel sulfate 34% Cobalt chloride 11.7% Fragrance mix 10.7	NA	Cetrimide 20.7%	Thimerosal 15.5% Nickel 13.8%	Nickel sulfate 28.5% Benzalkonium chloride 20.3% Gold sodium Thiosulfate 18.5% Nickel sulfate-26.1% Thimerosal 15.2% Potassium dichromate 8.7%	NA

ISS: Indian standard series (ISS), ICFS: Indian cosmetic and fragrance series, SiSS: Siriraj Standard Series, NACDG: Northern America contact dermatitis group

**Table V: The sensitisation pattern of the top 10 allergens according to age groups**

		All patients	Nickel sulfate	Cobalt chloride	Fragrance mix	Kathon CG	Formaldehyde	Thimerosal	MI	Colophony Peru	Balsam	Gallate mix
Age group	10-19	22	7	2	1	0	0	1	0	1	2	1
	20-29	116	43	11	7	11	14	11	8	7	3	10
	30-39	85	30	16	13	3	6	11	4	5	7	4
	40-49	19	6	0	4	8	1	1	5	4	2	0
	50-59	25	6	1	4	1	2	1	1	1	1	0
	60-69	17	4	3	0	2	3	0	1	1	0	0
	70-79	7	3	1	2	1	0	0	1	0	2	1
Total	291	99	34	31	26	26	25	25	19	17	16	
p -Value		0.829	0.149	0.048	<0.001	0.365	0.444	0.025	0.271	0.06	0.330	

MI = Methylisothiazolinone

cosmetics was found to be a trigger factor for sensitive skin.<sup>10</sup> Females with sensitive skin also have higher use of moisturisers and facial products to improve the sensation of skin sensitivity, thus rendering them more vulnerable to allergic contact dermatitis.<sup>10</sup> On the other hand, females are more likely to report any allergic dermatitis and seek treatment due to concern about their appearance.<sup>11</sup>

Nickel sulfate (34.0%), cobalt chloride (11.7%) and fragrance mix (10.7%) were the three most common allergens with positive reactions in the current study (Table IV). Most of the other studies reported similar findings as well.<sup>5,7</sup> Kasemsarn et al. reported benzalkonium chloride and gold sodium thiosulfate as the common allergens after nickel among 244 patients with facial allergic contact dermatitis in Thailand.<sup>6</sup> Li et al. found that thimerosal and potassium dichromate were common allergens after nickel in their study among 92 patients in China with facial contact dermatitis.<sup>7</sup> On the other hand, Garg et al. reported cetrimide, thimerosal and nickel as the commonest allergens in their study.<sup>5</sup> The differences among these studies were partly due to the different target populations and test series used in different centres.

Nickel allergies are mostly caused by non-occupational exposures (jewellery, clothing, metal tools and medical devices), although occupational exposures are common as well for those who work as mechanics, platers, hairdressers and metal and construction workers.<sup>12</sup> It was also found in cosmetics, eyeshadow, and beauty tools, predisposing to facial and neck region ACD.<sup>13,14</sup> However, due to the abundance of nickel in the environment, it was difficult to determine the relevance of nickel in patients with FNR dermatitis. On the other hand, most cases of cobalt sensitisation are associated with nickel co-sensitisation and many products that contain nickel will also contain cobalt.<sup>15</sup> Studies showed that both nickel and cobalt can be present in inorganic pigments rich in iron and manganese used in cosmetics such as eyeshadow. Cobalt was detected in yellow, purple and black pigments.<sup>15</sup> Silverberg et al. reported an 11.9% positive patch test to cobalt in children, with facial involvement in 10.6% of their patients.<sup>16</sup> Previous studies had revealed that fragrance mix are present in 15 to 100% of cosmetic products, and these included deodorants and fine fragrances.<sup>16</sup> It is difficult to avoid fragrance exposure as even products labelled as 'fragrance-free' may contain fragrance ingredients as preservatives or the use of botanicals.<sup>17</sup>

The most common allergens that tested positive beyond European baseline series were thimerosal (8.6%) and gallate mix (5.5%). Thimerosal is an organic mercurial that has been used as a preservative and it has been incorporated into vaccines, test solutions and topical creams.<sup>18</sup> Many studies reported a high rate of sensitisation to thimerosal, but they were of little clinical relevance.<sup>19</sup> It has been removed from most of the childhood vaccines in the United States since 2001. Currently, thimerosal use in cosmetics has been diminished and may be found in ophthalmic solutions.<sup>20</sup> Gallate mix is a preservative commonly found in food products and cosmetics such as lipstick, and facial products and may contribute to allergic cheilitis.<sup>21</sup> However, it is difficult to determine the presence of gallate mix in processed food as labelling in the food industry is not strictly regulated.

Sub-analysis showed that PPD and textile dye mix were the important sensitising allergens in male patients after nickel sulphate. In three out of the four patients with positive reactions to PPD, hair dye was identified as the likely source of reagents. None of these cases were occupational-related. In patients with PPD sensitisation or hair dye allergies, apart from the face, dermatitis can also be found on the side of the neck and hands.<sup>22</sup> Scalp is sometimes spared due to the thickness of the skin in these areas, protective sebum production and moderation by hair follicle regulation which promotes tolerance.<sup>23</sup> Interestingly, the three patients with positive reactions to textile dye mix were co-sensitised to PPD. PPD had been reported to have cross-reactivity with other dyes such as textile dye, local anaesthetics and rubber chemicals.<sup>24</sup>

In current study, 70.1% of patients had at least one positive reaction in the patch test. This finding is comparable to earlier studies which reported at least one positive reaction in 41.8 to 69.0% of the patients.<sup>4,5,25</sup> Kasemsarn et al. reported a higher positive patch test reaction at 81.6% in their study as it was conducted in a contact dermatitis clinic among patients with likely diagnosis of allergic contact dermatitis. We reported a high clinical relevance among patients with positive reactions (120 out of 204 patients, 58.8%). In addition, patch testing with extended series and own products was important as it increased the sensitivity of the patch tests. Otherwise, patch tests with the European standard series alone may lead to misdiagnosis in nearly 20% of cases.

The present study showed significantly more patients in the age group of 20 to 39 to have positive patch tests on fragrance mix ( $p = 0.048$ ), Kathon CG ( $p = <0.001$ ), and methylisothiazolinone ( $p = 0.025$ ) (Table V). These allergens are commonly found in cosmetic products that are used more often by young patients than older ones.<sup>26</sup> There were significantly more females who experienced cheilitis compared to their male counterparts (29.8% vs 12.1%,  $p = 0.032$ ). For the area of involvement, females also had significantly higher involvement of perioral (50.8% vs 21.2%,  $p = 0.001$ ) compared to males. On the other hand, FNR dermatitis in males tends to involve facial areas other than periorbital and perioral such as cheek and forehead, compared to females (69.7% vs 48.4%,  $p = 0.001$ ). Cheilitis is commonly caused by allergic hypersensitivity especially to

cosmetic and hygiene products.<sup>27</sup> Other culprits include personal care products and toiletries like toothpaste, musical instruments, and others. Female patients tend to use more cosmetic products on the lips such as lipstick, lip balm, lip gloss, lip serum and lip paint compared to males, which could explain their higher prevalence of allergic cheilitis. Getachew et al. reported that 80.1% of females had a habit of using cosmetic products and 86.8% of them used lipstick, lotion, toothpaste or eye makeup.<sup>26</sup>

The study is limited by the single-centred data from a tertiary hospital in an urban area. A prospective multicentre study will be more informative to compare the differences in sensitisation patterns in different regions of Malaysia. The male patients in the current study remain low ( $n = 33$ , 11.3%). As a result, several trends of differences were observed but did not reach statistical significance. Given the retrospective nature of the study, there is a likelihood of incomplete data, particularly in terms of demographic information, clinical findings, and the objective assessment of clinical response.

## CONCLUSION

In summary, contact sensitisation was detected in about 70% of patients with dermatitis at the face and neck region (FNR) who were patch-tested. Nickel sulfate, cobalt chloride and fragrance mix were the most common allergens in the current study. Females had a significantly higher rate of positive patch tests compared to males. The addition of an extended series and patients' own products helps to improve the sensitivities of the patch test.

## ETHICAL APPROVAL AND CONSENT TO PARTICIPATE

This study was registered to the National Medical Research Register, Ministry of Health Malaysia (RSCH ID-23-03846-TXV)

## CONFLICT OF INTEREST

The authors declare no competing interests

## FUNDING

The authors declare no financial disclosure

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