

Nickel Sensitization in Patients with Hand Eczema: A Cross-Sectional Study from Northeast India

Running title: *Nickel sensitization in hand eczema*

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Abstract: ***Background:** Nickel is one of the commonest causes of allergic contact sensitization and remains an important trigger of hand eczema. Exposure to jewellery, piercings and other metal-containing consumer products makes nickel particularly relevant in younger individuals. **Objectives:** To describe the pattern of nickel sensitization among patients with hand eczema, with particular emphasis on age, sex and clinical phenotype. **Methods:** This cross-sectional study included 126 consecutive patients with hand eczema attending a tertiary care centre between February 2023 and January 2025. Patch testing was performed using the Indian Standard Series, with readings at 48 and 96 hours according to International Contact Dermatitis Research Group criteria. **Results:** Patch-test positivity was observed in 71/126 patients (56.3%). Among patch-positive patients, 59 (83.0%) belonged to the 18–35-year age group, 11 (15.5%) to the 36–55-year group and 1 (1.4%) to the 56–70-year group. Nickel sulfate was the most frequent individual allergen, occurring in 16/71 patch-positive patients (22.5%). Fourteen of the 16 nickel-positive patients were female. Nickel was also present in combination with cobalt, potassium dichromate and fragrance mix. Recurrent vesicular eczema was the commonest morphological pattern among patch-positive patients and was reported in the thesis analysis as being frequently associated with nickel sensitization. **Conclusion:** Nickel was the leading individual allergen in this cohort and was predominantly observed among women. The concentration of patch-positive patients in the younger age group, shows the recent shift from occupational exposure related allergens to lifestyle related allergens in the current society.*

Keywords: nickel sensitization; nickel allergy; hand eczema; allergic contact dermatitis; patch testing; lifestyle

1. Introduction

Nickel is one of the most frequent contact allergens encountered in dermatological practice.¹ Repeated exposure to jewellery, watches, clothing fasteners, body-piercing materials and other everyday metal objects can result in sensitization, often beginning at a relatively young age.^{2–4}

Nickel allergy has a clear female predominance in many population studies. Previous piercing and multiple piercings have been consistently associated with nickel sensitization, suggesting an important contribution from consumer and lifestyle exposures.^{5–7}

Children and adolescents are also frequently sensitized to nickel. A systematic review of pediatric patch-test studies identified nickel among the leading allergens in both children and adolescents, while a more recent meta-analysis involving 11,593 children found nickel to have the highest pooled prevalence of contact allergy at 11.9%.^{8,9}

Nickel sensitization is clinically relevant in hand eczema, previous studies have described an association between nickel allergy and dyshidrotic or vesicular hand eczema, and metal exposure may act as an important trigger in susceptible patients.^{10,11}

The present study was undertaken to describe the pattern of nickel sensitization in patients with hand eczema, with particular attention to age, sex, associated clinical patterns and nickel-containing combination reactions.

2. Materials and Methods

Study design and participants

This cross-sectional observational study included 126 consecutive patients with clinically diagnosed hand eczema attending the dermatology outpatient department of a tertiary care centre from February 2023 to January 2025. Patients aged 18–70 years were included after written informed consent. Patients with other causes of hand dermatoses were excluded clinically and, where indicated, by potassium hydroxide examination or biopsy. Patients with active dermatitis at the time of patch testing and those receiving systemic corticosteroids or immunosuppressive treatment were excluded. The study received approval from the Research Ethics Board, Regional Institute of Medical Sciences, Imphal (Approval No. A/206/REB-Comm (SP)/RIMS/2015/1002/33/2023).

Patch testing

Patch testing was performed using the Indian Standard Series containing 20 allergens. Aluminium chambers mounted on microporous tape were applied to uninvolved upper-back skin. Patches were removed after 48 hours and readings were recorded at 48 and 96 hours according to International Contact Dermatitis Research Group criteria.

Assessment of nickel sensitization

The primary outcome was a positive patch-test reaction to nickel sulfate. Nickel-containing combination reactions were recorded separately. Age and sex were reviewed in relation

to the overall patch-test findings and the nickel-positive group.

Statistical analysis

Categorical variables were expressed as frequencies and percentages. Associations were assessed using the chi-square test or Fisher exact test as appropriate. A p-value <0.05 was considered statistically significant.

3. Results

Age distribution and patch-test positivity

Of the 126 patients, 89 (70.6%) were aged 18–35 years, 30 (23.8%) were aged 36–55 years and 7 (5.6%) were aged 56–70 years. Overall patch-test positivity was observed in 71 (56.3%) patients. The younger age group accounted for the large majority of patch-positive patients: 59 of 71 (83.0%) patch-positive patients were aged 18–35 years, compared with 11 (15.5%) aged 36–55 years and 1 (1.4%) aged 56–70 years. Thus, contact sensitization was concentrated in younger adults (Table 1).

Nickel sensitization

Nickel sulfate was the most frequent individual allergen in the study, producing a positive reaction in 16 of 71 patch-positive patients (22.5%) (Table 1).

There was a marked female predominance among nickel-positive patients. Fourteen of the 16 patients with a nickel-positive reaction were female (87.5%), while two were male (12.5%) (Table 1).

Nickel also occurred as part of multiple sensitization patterns. Nickel and cobalt were detected together in seven patients (9.9% of patch-positive patients), potassium dichromate and nickel in five (7.0%), and fragrance mix and nickel in four (5.6%) (Table 1).

The concentration of patch-test positivity in younger adults is particularly notable in the context of nickel sensitization, because nickel was the leading allergen in the cohort. However, the aggregate dataset does not provide the number of nickel-positive patients within each individual age group; therefore, an age-specific nickel odds ratio or p-value cannot be calculated from the available data. The observed age pattern should consequently be interpreted as a pattern of overall contact sensitization rather than proof of an age-specific increase in nickel sensitization.

Nickel and clinical phenotype

Recurrent vesicular eczema was the commonest morphological subtype among patch-positive patients, accounting for 26 of 71 (36.6%) patch-positive cases. The thesis analysis identified nickel sulfate as one of the leading allergens in this clinical pattern, supporting the recognized relationship between metal sensitization and vesicular hand eczema.

Nickel was also repeatedly identified among the predominant allergens in chronic fissured and hyperkeratotic hand eczema. These findings suggest that nickel sensitization is not restricted to a single morphological

phenotype, although recurrent vesicular disease appears particularly relevant.

Nickel and polysensitization

More than one allergen was identified in a substantial proportion of patch-positive patients. Nickel was most often combined with cobalt, followed by potassium dichromate and fragrance mix (Table 1). The frequent nickel–cobalt combination may reflect shared exposure to metal-containing jewellery or other consumer products.

4. Discussion

Nickel sulfate was the leading individual allergen in our cohort, with a positive reaction in 22.5% of patch-positive patients (Table 1). This finding is consistent with previous studies of hand eczema in which nickel has remained one of the most frequent sensitizers.^{12,13}

The marked female predominance in our nickel-positive group is also in keeping with population-based studies. The European EDEN study demonstrated strong associations between nickel sensitization, female sex and piercing, while North American Contact Dermatitis Group data similarly found higher nickel sensitivity among women and identified jewellery as an important source of exposure.^{5–7}

The age distribution in our study is noteworthy. Although 18–35-year-olds comprised 70.6% of the study population, they accounted for 83.0% of all patch-positive patients. This indicates that contact sensitization was concentrated in younger adults (Table 1). It does not, however, establish that nickel sensitization itself was statistically higher in this age group because age-specific nickel counts were not available. This finding is nevertheless relevant when considered alongside pediatric literature. Nickel is consistently reported as one of the leading contact allergens in children and adolescents, and recent pooled data from 11,593 children identified nickel as the most prevalent allergen.^{8,9} The predominance of nickel among younger adults in our cohort may reflect exposures acquired earlier in life, particularly jewellery use and piercing. Piercing has repeatedly been associated with nickel allergy, and the risk appears to increase with repeated or multiple piercings.^{5,7,14}

The association with recurrent vesicular hand eczema is also clinically relevant. Previous studies have described an increased likelihood of contact allergy in recurrent vesicular hand eczema, and nickel exposure has been implicated as a possible trigger of vesicular disease in sensitized individuals.^{10,11}

Nickel–cobalt co-sensitization was the most frequent nickel-containing combination in our study. This is clinically useful because patients who react to nickel may also encounter cobalt in the same metal-containing products. Asking specifically about jewellery, watches, belt buckles, clothing fasteners, mobile accessories and previous piercing can therefore help identify relevant sources.

From a practical standpoint, a positive nickel patch test should be interpreted in the context of exposure history. Avoidance of relevant nickel-containing products, together

with appropriate skin care and reduction of irritant exposure, may help reduce recurrent hand eczema.

5. Limitations

The principal limitation of this analysis is the absence of patient-level age-specific nickel results. The study can demonstrate that younger adults had a higher proportion of overall patch-test positivity and that nickel was the leading allergen, but it cannot establish a statistically significant age-related increase in nickel sensitization.

6. Conclusion

Nickel sulfate was the most frequent individual contact allergen in this cohort of patients with hand eczema and showed a marked female predominance. Most patch-positive patients were young adults, and nickel was frequently associated with recurrent vesicular hand eczema and with cobalt co-sensitization.

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Tables and Figures

Table 1: Nickel-related findings in the study cohort (N= 71 patch positive patients)

Findings of the study (N= 71)	Result n (%)	Interpretation
Age 18–35 years	59 (83.0%)	Majority of the patch positives belonged to younger age group
Age 36–55 years	11 (15.5%)	
Age 56–70 years	1 (1.4%)	
Nickel sulfate positivity	16 (22.5%)	Nickel is the most common allergen showing patch positivity
Nickel-positive patients	Females: 14 (87.5%)	Females showed more patch positivity compared to males
	Males: 2 (12.5%)	
Nickel + cobalt	7 (9.9%)	Most common allergen combination
Potassium dichromate + nickel	5 (7.0%)	
Fragrance mix + nickel	4 (5.6%)	
Recurrent vesicular eczema	26 (36.6%)	More chance of patch test positivity

Figures

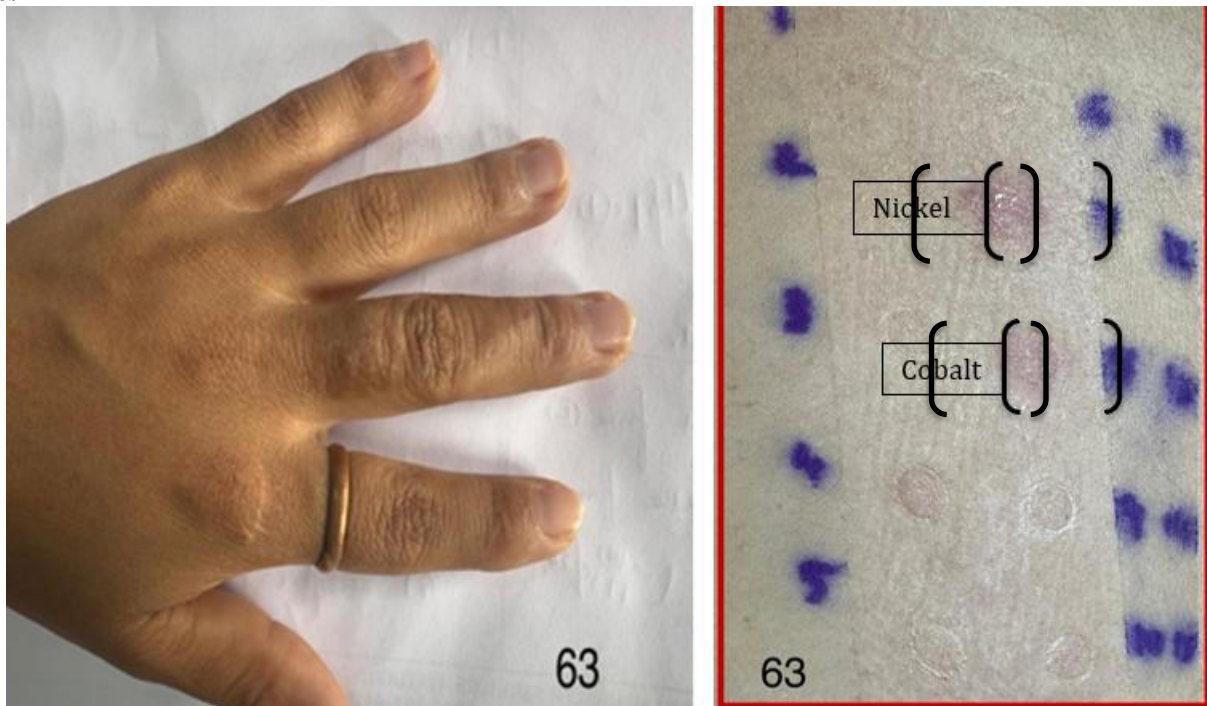


Figure 1: Ring eczema with a 1+ nickel and cobalt patch-test reaction on day 4.



Figure 2: Recurrent vesicular hand eczema with a 1+ nickel patch-test reaction on day 2.