

Prevalence of Type I Allergy to Latex and Type IV Allergy to Rubber Additives in Turkish Healthcare Workers

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ABSTRACT Introduction: Glove-induced dermatoses are frequently seen among healthcare workers (HCWs) and are often mistakenly defined as latex allergy.

Objectives: To determine the prevalences of (i) the symptoms of immediate type hypersensitivity reactions, (ii) the symptoms of hand eczema, (iii) latex sensitization detected using skin prick test (SPT), and (iv) contact hypersensitivity to rubber additives or glove pieces detected using patch test, in Turkish HCWs.

Methods: Ninety-eight HCWs were included in the study. All subjects completed a questionnaire. All participants were skin prick tested for latex, and foods previously identified as concomitant allergens in latex-sensitive individuals; patch tested for 7 rubber additives, 3 additional haptens, and glove pieces.

Results: The mean age was 32.1 (\pm 9.4) years, and 71 (72.4%) participants were nurses. Eighty-four (85.7%) subjects had a history of mucocutaneous symptoms of immediate-type hypersensitivity occurring within the first 24 hours after latex glove contact, while 9 (9.2%) subjects demonstrated SPT positivity for latex. Eighty (81.6%) subjects had a history of glove-induced hand eczema symptoms, while patch test positivity for the rubber additives or glove pieces was in 17.3%.

Conclusions: About one-tenth of those with a history of glove-induced type I hypersensitivity symptoms had true latex allergy, and one-quarter of those with a history of glove-related hand eczema symptoms had contact hypersensitivity to glove products. Therefore, rote avoidance of latex use is generally ineffective in the management of glove-related skin complaints. Individual measures should focus on reducing the use of soaps and disinfectants, and promoting the use of moisturizers, rather than glove choice.

Introduction

During the novel Coronavirus disease of 2019 (COVID-19) pandemic, implementation of several hygiene measures have gained importance among healthcare workers (HCWs). The Centers for Disease Control (CDC) published guidelines highlighting the importance of using personal protective equipment, including gloves¹. In this unusual situation, HCWs had exposed to gloves, water, soaps, disinfectants, and hand sanitizers more frequently than before, leading to an increase in the prevalence of occupational irritant contact dermatitis [1-5].

Skin complaints that manifest after exposure to latex examination gloves are often attributed to contact with natural rubber latex (NRL) [6]. Although the majority of medical staff misidentify their dermatose as “latex allergy”, previous studies show that more than two-thirds of those with glove-related symptoms do not have any allergies to latex or rubber chemicals [7-10]. This fact necessitates the detection of hypersensitivity to NRL and rubber additives and illumination of HCWs about the correct management of their occupational dermatoses.

The prevalence of latex allergy among Turkish HCWs has previously been investigated via measuring the serum levels of latex-specific IgE [11]. However, there is no study evaluating latex allergy by skin prick test (SPT) and contact hypersensitivity to rubber additives using patch test in Turkish HCWs.

Objectives

In the present study, we aimed to determine

- the prevalence of latex hypersensitivity assessed by SPT,
- the prevalence of delayed type hypersensitivity to rubber additives assessed by patch test,
- glove usage and hand washing habits, symptoms of type I allergy, and symptoms of hand eczema using a self-administered questionnaire; in our hospital staff.

Methods

We designed a cross-sectional study among 98 healthcare professionals working in our hospital. Ethics approval was

obtained from the local ethics committee (decision number: 2019/0046). An informed consent was obtained from all subjects. All participants filled out a questionnaire including the following information: (i) age, (ii) gender, (iii) occupation, (iv) workstation (internal, surgery, laboratory, radiology, intensive care unit, emergency), (v) duration of exposure to gloves (years), (vi) length and frequency of glove usage (per day), (vii) frequency of hand washing (per day), (viii) history of contact with irritants, (ix) history of atopy and food/drug allergy, (x) history of type I allergy-related symptoms developing within 24 hours of contact with a latex glove, and (xi) history of symptoms related to hand eczema.

Skin prick test was performed on all participants using standardized commercial extracts of natural non-ammoniated latex and of foods to which individuals with latex hypersensitivity are often simultaneously hypersensitive including banana, kiwi, chestnut, apple, melon, tomato, and pineapple (ALK-Abelló A/S, Hørsholm, Denmark). The SPT for avocado was performed using fresh avocados, by prick-to-prick technique. Histamine dihydrochloride was used as positive control while normal saline was used as negative control. SPTs were performed on the anterior aspect of the participants' forearm using a standardized device (MedBlue 10®, Asistan Medikal), and evaluation was done 15 minutes after application. A wheal with a mean diameter of 2 mm or more was interpreted as a positive reaction, also considering the positive and negative controls.

All participants were patch tested with 7 rubber additives (thirum mix, colophony, mercapto mix, carba mix, mercapto-benzothiazole, 1,3-diphenylguanidine, N-isopropyl N-phenyl 4 phenylenediamine), 3 additional haptens (methylidibromo glutaronitrile, quaternium-15, formaldehyde), and 1 cm² pieces of two types of (powdered/non-powdered latex) gloves. The IQ Chambers and haptens were purchased from Chemotechnique MB Diagnostics AB. The chambers were placed on the upper back and removed after two days. Readings were performed 48 and 72 hours after application and reactions were interpreted in accordance with the European Society of Contact Dermatitis guidelines [12].

SPSS (Statistical Package for Social Sciences) v17.0 was used to perform statistical analysis. Continuous data were expressed as means (\pm standard deviation, SD). Chi-square

techniques were performed for categorical variables, and continuity correction or Fisher exact test was used when necessary. P value < 0.05 was considered significant.

Results

Of the 98 participants, 87 (88.8%) were female and 11 (11.2%) were male. The mean age was 32.1 (\pm 9.4) years. Seventy-one (72.4%) of the subjects were nurses, and those working in the internal and surgical divisions were 31 (31.6%) and 34 (34.7%), respectively (Table 1).

Duration of occupational exposure to gloves was 9.5 (8.1) years. The frequency of latex glove use was 94.9%, and powdered glove use was 80.6%. Of the participants, 60.2% were using gloves >4 hours/day, 63.3% were changing the gloves >10 times a day, and 45.9% were washing their hands

>20 times a day (Table 1). Thirty-seven (37.8%) cases had a history of at least one atopic disease (Table 1), 84 (85.7%) had a history of any mucocutaneous symptom of type I hypersensitivity which developed within the first 24 hours after latex glove exposure (Table 2), and 80 (81.6%) had a history of any symptom of hand eczema (Table 3).

Nine (9.2%) subjects had positive SPT to natural rubber latex. All of these 9 cases were among those with a history of immediate type hypersensitivity symptoms. Besides, SPTs were positive for tomato in 12 (12.2%), for kiwi in 8 (8.2%), for banana in 8 (8.2%), and for apple in 8 (8.2%) subjects (Table 4). One case revealed dermographism. No adverse reactions were observed in any subjects during the test procedure. The presence of the history of urticaria, redness, scaling, eye redness/lacrimation, and rhinorrhea within the first 24 hours after latex exposure

Table 1. Characteristics of the participants.

Characteristics	Value	Characteristics	Value
Age		duration of exposure to gloves	
mean (\pm SD [years])	32.14 (\pm 9.39)	mean (\pm SD [years])	9.49 (\pm 8.14)
range (years)	21-60		
Gender	N(%)	exposure time to gloves	N (%)
female	87 (88.8%)	>4 hours a day	59 (60.2%)
male	11 (11.2%)	>4 hours a day	37 (37.8%)
Job title	N (%)	weekly	1 (1%)
nurse	71 (72.4%)	monthly	1 (1%)
laboratory technician	9 (9.2%)		
physician	5 (5.1%)	frequency of glove change	N (%)
radiology technician	4 (4.1%)	1-5 pair daily	14 (14.3%)
anesthetic technician	3 (3.1%)	6-10 pair daily	22 (22.4%)
physiotherapist	1 (1.0%)	>10 pair daily	62 (63.2%)
other	5 (5.1%)		
Division	N (%)	frequency of hand-washing	N (%)
surgical	34 (34.7%)	<10 times per day	9 (9.2%)
internal	31 (31.6%)	10-20 times per day	44 (44.9%)
laboratory	12 (12.2%)	>20 times per day	45 (45.9%)
radiology	6 (6.1%)		
intensive care unit	6 (6.1%)	personal history of atopy/allergy	N (%)
emergency	4 (4.1%)	no atopy	61 (62.2%)
other	5 (5.1%)	at least one atopic disease	37 (37.8%)
Type of glove used	N (%)	atopic dermatitis	13 (13.3%)
powdered	79 (80.6%)	allergic rhinitis	17 (17.3%)
non-powdered	88 (89.8%)	allergic conjunctivitis	3 (3.1%)
latex	93 (94.9%)	asthma	6 (6.1%)
vinyl	30 (30.6%)	urticaria/angioedema	8 (8.1%)
nitrile	18 (18.4%)	food/drug allergy	11 (11.2%)

SD = standard deviation.

Table 2. Prevalence of immediate-type hypersensitivity symptoms and SPT positivity for latex.

	SPT positive for latex N =9	SPT negative for latex N =89	Total N=98	
Immediate type allergy symptoms	rate (%) within the cases SPT positive for latex	rate (%) within the cases SPT negative for latex	rate (%)	P
urticaria	5/9 (55.6%)	16/89 (18.0%)	21/98 (21.4%)	0.02
itching	8/9 (88.9%)	65/89 (73.0%)	73/98 (74.5%)	0.441
redness	9/9 (100%)	41/89 (46.1%)	50/98 (51.0%)	0.003
scaling	8/9 (88.9%)	37/89 (41.6%)	45/98 (45.9%)	0.011
eye redness/ lacrimation	4/9 (44.4%)	6/89 (6.7%)	10/98 (10.2%)	0.00
rhinitis	3/9 (33.3%)	4/89 (4.5%)	7/98 (7.1%)	0.016
respiratory symptoms	0/9 (0%)	1/89 (1.1%)	1/98 (1.0%)	1.0
at least one symptom	9/9 (100%)	75/89 (84.3%)	84/98 (85.7%)	0.35

SPT = skin prick test.

Table 3. Prevalence of hand eczema symptoms and patch test positivity for rubber additives/glove pieces.

	Patch test positive for rubber additive/glove pieces N=17	Patch test negative for rubber additive/glove pieces N =81	Total N=98	
Hand eczema symptoms	rate (%) within the patch test positive cases	rate (%) within the patch test negative cases	rate (%)	P
itching	11/17 (64.7%)	48/81 (59.3%)	59/98 (60.2%)	0.789
burning	8/17 (47.1%)	26/81 (32.1%)	34/98 (34.7%)	0.270
redness	9/17 (52.9%)	39/81 (48.1%)	48/98 (49.0%)	0.793
fissure	11/17 (64.7%)	34/81 (42.0%)	45/98 (45.9%)	0.111
exudation	4/17 (23.5%)	5/81 (6.2%)	9/98 (9.2%)	0.046
dyshidrosis	3/17 (17.6%)	10/81 (12.3%)	13/98 (13.3%)	1.0
at least one symptom	14/17 (82.4%)	66/81 (81.5%)	80/98 (81.6%)	1.0

was significantly higher in those with positive SPT for NRL compared to those without (55.6% versus 18% P = 0.02; 100% versus 46.1% P = 0.003; 88.9% versus 41.6% P = 0.011; 44.4% versus 6.7% P = 0.006; 33.3% versus 4.5% P = 0.016; respectively) (Table 2). Eight (88.9%) of latex-sensitive subjects had a frequency of glove change >5 times a day and all (100%) were washing their hands >10 times a day.

There were 25 positive patch test results in 19 cases. The most common patch test positivity had detected for powdered latex gloves (N = 7; 7.1%), non-powdered latex gloves (N = 5, 5.1%), mercapto mix (N = 3, 3.1%), and 1,3-diphenylguanidine (N = 3, 3.1%) (Table 5). Seventeen (17.3%) cases had a positive patch test for at least one of the rubber additives or glove pieces (Table 3). Irritant

reaction developed to the fixation tape in three cases and to the chamber in one case. In participants with a positive patch test, history of hand eczema symptoms and length and frequency of glove usage were not different than those without (Table 3).

Conclusions

Natural rubber latex is a raw material obtained from the rubber tree (*Hevea Brasiliensis*), widely used in gloves and several medical devices [13]. The term “latex allergy” not only defines glove-related localized dermatological symptoms on hands, and encompasses immediate-type hypersensitivity reactions, which can be induced by any latex-containing product such as gloves, catheters, balloons, or pads [14,15].

Therewithal symptoms that develop after the use of latex-containing gloves correspond to 3 types of reactions:

1. Irritant contact dermatitis, a nonspecific response to chemical or mechanical factors, can be defined as a non-immunologic reaction.
2. Allergic contact dermatitis, occurs due to contact with rubber additives present in gloves and is an example of delayed type (type IV) hypersensitivity reaction.
3. True latex allergy, which may present with a spectrum of clinical manifestations from contact urticaria to anaphylaxis, is a kind of immediate type (type I, IgE mediated) hypersensitivity reaction [15].

Contrary to the glove-choice behaviour of many HCWs, in the presence of irritant or allergic contact dermatitis, avoidance of latex products (especially latex gloves) is usually ineffective, unnecessary, and even –economically- problematic. While protecting HCWs from serious reactions caused by

latex exposure, to avoid unnecessary restriction of the latex use is one of the goals of management of glove-related occupational dermatoses [16].

We found the latex hypersensitivity in 9 (9.2%) of our participants. All these nine subjects had a history of type I allergy symptoms, and the frequency of SPT positivity for NRL in symptomatic cases was 10.7%. In previous studies conducted on HCWs of various professions, latex sensitization was found to be between 4.2% and 18.2% [6,9-11,17-20]. Previously, Nettis et al found latex sensitization in 9.1% of the 295 symptomatic, prick-tested subjects [8]. In another study by Tang et al on 313 HCWs, the prevalence of latex sensitivity determined using SPT was 9.6% [18]. In a study of Turkish HCWs like ours, latex sensitization was found in 4.2% of 1115 subjects [11]. The prevalence of latex hypersensitivity was lower in above-mentioned study because it was determined only by the measurement of latex-specific IgE levels.

Glove-related dermatological symptoms are quite common in HCWs. In a study of 98 laboratory workers, 36.9% of subjects reported hand dermatitis, and 24.6% reported immediate hypersensitivity symptoms including urticaria [7]. In another study on 1584 HCWs, 24.4% of participants reported glove-induced dermatological complaints, either hand dermatitis symptoms or urticaria/angioedema [8]. In the present study, the presence of the history of any mucocutaneous symptom of type I hypersensitivity and any symptom of hand eczema was 85.7% and 81.6%, respectively. The higher frequencies in our study can be explained by taking the history using a questionnaire without deepening the anamnesis, an expected disability of the participants to differentiate the eczema symptoms from type I hypersensitivity symptoms, and the possibility of the participants' experiencing these symptoms at least once in their professional life. On the other hand, in our study and previous studies, the prevalences of glove-related symptoms are 3 to 8 times higher than the prevalence of latex sensitization. These findings suggest that the majority of glove-related symptoms are not caused by true latex allergy and therefore cannot be controlled by avoidance of latex glove use.

The history of urticaria, redness, and scaling within the first 24 hours after exposure to latex was significantly higher in latex-sensitive individuals compared to those without. This result was consistent with that of previous studies. Liss et al found the prevalence of skin rash, hives, and itchy skin, Diéguez et al found the proportion of urticaria and dermatitis, Tang et al found the frequency of the history of glove-related urticaria, Nettis et al found the prevalence of localized and generalized hives significantly higher in subjects with latex hypersensitivity than in those without [8,18-20]. Although a minority of HCWs with glove-related symptoms have latex sensitization, it is an expected finding that the prevalence of latex sensitization is higher in those

Table 4. Skin prick test results.

Allergen	N (%)
tomato	12 (12.2)
natural rubber latex	9 (9.2)
kiwi	8 (8.2)
banana	8 (8.2)
apple	8 (8.2)
melon	7 (7.1)
pineapple	5 (5.1)
chestnut	3 (3.1)
avocado	1 (1.0)

Table 5. Patch test results.

Allergen	N (%)
powdered latex glove piece	7 (7.1)
non-powdered latex glove piece	5 (5.1)
mercapto mix	3 (3.1)
1,3-diphenylguanidine	3 (3.1)
carba mix	2 (2.0)
mercapto-benzothiazole	2 (2.0)
colophony	1 (1.0)
quaternium-15	1 (1.0)
formaldehyde	1 (1.0)
thiruam mix	0 (0)
N-isopropyl N-phenyl 4 phenylenediamine	0 (0)
methyl dibromo glutaronitrile	0 (0)

with a history of glove-related urticaria or erythema compared to those without.

We also investigated SPT positivity for foods that have been previously identified as concomitant allergens in latex-sensitive individuals [21,22]. Twelve per cent of the cases were sensitive to tomato, 8% to kiwi, 8% to banana, and 8% to apple. In our study, sensitization to any food was not more frequent in latex-sensitive subjects, and our results did not exemplify the phenomenon previously defined as “latex-fruit syndrome”.

Although 81.6% of the subjects had a history of glove-related hand eczema symptoms, only 17.3% of them demonstrated patch test positivity for any of the rubber additives or glove pieces. In previous studies performed by Miri et al and Nettis et al, only those with glove-related symptoms were patch-tested, and patch test positivity for rubber additives and/or glove pieces was found to be 27.1% and 10.5%, respectively [8,10]. In other studies by Japundžić et al and de Groot et al, the prevalences of dermatological symptoms were 56.1% and 36.9%, and the rates of patch test positivity for glove products were 4.8% and 6.6%, respectively [6,7]. The results of our study and previous data indicate that the frequency of glove-related symptoms was 6-10 times the rate of patch test positivity. Therefore we can say that the majority of glove-related dermatological symptoms seen in HCWs are not caused by contact allergy to any hapten contained in the glove.

During the COVID-19 pandemic, healthcare workers faced an occupational risk of infection and were exposed to gloves and increased hygiene procedures more frequently than before. In a recent study of 270 HCWs, 76.5% reported symptoms of irritant contact dermatitis on their hands, 99.3% had increased the frequency of washing their hands, and 45.4% had not used any moisturizer². Likewise, in our study, 81.6% of the participants reported hand eczema symptoms. Among these, 81.3% had a negative patch test, 57.5% were using gloves >4 hours/day, 62.5% were changing the gloves >10 times a day, and 45% were washing their hands >20 times a day. These data suggest that the most frequent glove-related dermatosis in HCWs, irritant contact dermatitis, results from increased frequency of hand-washing and glove pair change, increased exposure time to gloves, and not using any emollient.

Our study has several limitations. Although we constituted a detailed form questioning the symptoms of immediate type allergy and hand eczema, some items of two different entities were similar, therefore some participants might have been confused about making the appropriate choice. The records of glove-related manifestations were questionnaire-based, neither glove provocation tests nor dermatological examination during the symptomatic period

was performed. Lastly, we did not measure the serum levels of latex-specific IgE.

In summary, our study investigates whether glove-related dermatoses in Turkish HCWs are caused by a true allergy to latex or rubber additives utilizing both the skin prick test and patch test. Approximately one-tenth of those with a history of glove-induced immediate type hypersensitivity symptoms demonstrated SPT positivity to latex. Again, about one-quarter of those with a history of glove-related hand eczema symptoms showed patch test positivity for rubber additives or glove pieces. We can speculate that the majority of glove-related dermatoses correspond to irritant contact dermatitis, and contrary to popular belief, avoidance of latex gloves is unnecessary and ineffective. Moreover, from an economic point of view, latex is still an indispensable raw material for gloves and many medical devices. Therefore the development of glove-induced skin disorders in HCWs should rather be attributed to high frequency of hand-washing and glove-change, high exposure time to gloves, and insufficient use of moisturizers; and individual measures at the workplace should target these mentioned causes.

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