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The prevalence of latex sensitisation and allergy and associated risk factors among healthcare workers using hypoallergenic latex gloves at King Edward VIII Hospital, KwaZulu-Natal South Africa: A cross sectional study

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ARTICLE SUMMARY

ARTICLE FOCUS

- The use of hypoallergenic latex gloves has been adopted as policy in different healthcare settings globally.
- However, information with regard to their use and the development of latex sensitisation and allergy among exposed healthcare workers is limited.
- We hypothesised that there is latex sensitization and allergy in healthcare workers using hypoallergenic latex gloves in a South African hospital.

KEY MESSAGE

- In the presence of powder free hypoallergenic gloves, latex sensitisation and latex allergy is still an important occupational health effect in healthcare workers.
- Healthcare workers should be continuously monitored for the development of latex sensitisation and allergy.
- There is a need for a national policy accompanied by clear implementation plans as well as sustainable education and training programmes to address latex sensitisation and allergy among HCWs.

STRENGTH AND LIMITATIONS

- Strength of the study included the presence of a control group providing a background prevalence of latex sensitisation in this population and random selection of participants which minimised the potential of participant bias that arises with a volunteer approach.
- This study was limited by the cross sectional study design as it only allowed for the determination of the prevalence of latex sensitisation; recall bias with regard to the number of gloves used in the past 7 working days and the self-reporting of personal and family atopic disorders may have resulted in the misclassification of exposure and atopy respectively.

What this paper adds

- In the presence of powder free hypoallergenic gloves, latex sensitisation and latex allergy is still an important occupational health effects in healthcare workers
- Healthcare workers should be continuously monitored for the development of latex sensitisation and allergy
- There is a need for a national policy accompanied by clear implementation plans as well as sustainable education and training programmes to address latex sensitisation and allergy among HCWs

ABSTRACT

Objectives

The present study describes latex sensitisation and allergy prevalences and associated factors among healthcare workers using hypoallergenic latex gloves at King Edward VIII Hospital in KwaZulu-Natal South Africa.

Design

Cross sectional study

Setting

A tertiary hospital in eThekwini municipality, KwaZulu Natal, South Africa

Participants

600 healthcare workers were randomly selected and 501(337 exposed and 164 unexposed) participated. Participants who were pregnant, less than one year of work as healthcare worker and history of anaphylactic reaction were excluded from the study.

Primary and secondary outcome measures

Latex sensitisation and latex allergy were the outcome of interest and they were successfully measured

Results

Prevalence of latex sensitisation and allergy was observed among exposed workers (7.1% and 5.9%) and unexposed workers (3.1% and 1.8%). Work related allergy symptoms were significantly higher in exposed workers (40.9%, $p<0.05$). Duration of employment was inversely associated with latex allergy (OR: 0.9; 95% CI: 0.8-0.9). The risk of latex sensitisation (OR: 4.2; 95% CI: 1.2-14.1) and allergy (OR: 5.1; 95% CI: 1.2-21.2) increased with exclusive use of powder-free latex gloves. A dose –response relationship was observed for powdered latex gloves (OR: 1.1; 95% CI: 1.0-1.2). Atopy (OR: 1.5; 95% CI: 0.7-3.3 and OR: 1.4; 95% CI: 0.6-3.2) and fruit allergy (OR: 2.3; 95% CI: 0.8-6.7 and OR: 3.1; 95% CI: 1.1-9.2) also increased the risk of latex sensitisation and allergy.

Conclusion

This study adds to previous findings that healthcare workers exposed to hypoallergenic latex gloves are at risk for developing latex sensitisation highlighting its importance as an occupational hazard in healthcare. More research is needed to identify the most cost effective way of implementing a latex free environment in resource limited countries, such as South Africa. In addition more cohort analysis is required to better understand the chronicity of illness and disability associated with latex allergy.

INTRODUCTION

Latex allergy (LA) as an occupational disease among healthcare workers (HCWs) gained recognition after Nutter published a case report of contact urticaria in a HCW in 1979.[1] The increase in prevalence coincided with the emergence of the Human Immunodeficiency Virus/ Acquired immunodeficiency syndrome (HIV/AIDS) epidemic and the introduction of "universal precautions" in the healthcare industry which had resulted in the increased use of latex gloves among HCWs .[2]

Latex gloves are preferred due to their superior barrier and physical properties as compared to the non-latex gloves.[3] International epidemiological studies have reported the prevalence of latex allergy among HCWs to range between 2-22% depending on the population and diagnostic methods used.[4-11] The prevalence in the general population has been reported to range between 1-6%.[12 13]

In South Africa studies amongst HCWs reported a latex sensitisation prevalence of between 2.7 to 20.8%.[14-16] Latex allergy in HCWs is a compensable disease in South Africa in terms of the Compensation of Occupational Injuries and Diseases Act No. 130 of 1993.[17] Latex allergy comprised an estimated 1.4 % of all occupational diseases reported by the Surveillance of Work Related and Occupational Respiratory Diseases of South Africa programme (SORDSA) between 1996 and 1998.[18] In 2000 De Beers and De Villiers documented a high prevalence (20.8%) of latex sensitisation among theatre and laboratory staff (n=277) employed at Tygerberg hospital in the Western Cape Province.[15] Potter and colleagues conducted a latex allergy screening survey among Groote Schuur hospital employees. They reported latex sensitisation of 11.9% among 969 respondents with the majority of sensitised HCWs being nursing staff (64%) followed by doctors (10%), technologists (8%), paramedics (7%) and cleaners (6%).[16] A 2001 survey at the Red

Cross childrens hospital in Cape Town reported a latex sensitisation prevalence of 7% amongst the HCWs working in clinical and laboratory areas of the hospital.[14]

Powdered latex gloves were identified as an important risk factor for latex sensitisation and allergy in HCWs as they were found to contain a high allergenic protein content.[19] Following these findings, hypoallergenic gloves with low allergen content namely, low powdered and powder free latex gloves were introduced. The European definition of powder free gloves is gloves with powder content not exceeding 2 mg per glove and leachable latex protein which is as low as is reasonably practical.[20]

Hypoallergenic gloves have been associated with reduced latex aeroallergen concentrations, reduced conversion rates and a subsequent decrease in clinic visits, and compensation claims for latex induced occupational asthma and allergic contact dermatitis among HCWs.[19, 21] As much as the use of low or powder free gloves has been shown to reduce latex related symptoms, other studies have shown that exposed HCWs still exhibit symptoms at very low levels of measureable airborne latex allergens.[22] Most studies have reported on the airborne levels and inhalational route of exposure hence the recommendation on low powdered or powder free latex gloves. There is little consideration given to the dermal route of exposure despite the fact that exposure is as a result of direct contact in these instances.[23] Eliminating the cornstarch powder only removed the carrier and not the source of allergen which is in the latex itself. Therefore workers using powder free gloves are still exposed to the allergenic content of latex gloves. It has been shown that different brands from different suppliers contain differing levels of protein due to a lack of standards in latex glove manufacture.[24] A South African study reported that some powder free latex gloves were found to have high allergenic protein content.[24] HCWs using these gloves

are exposed via direct dermal contact and are at risk for developing latex sensitisation and if exposure continues they can later develop latex allergy.

In South Africa the health and safety of workers is regulated by the Occupational Health and Safety Act No 85 of 1993 (OHSA).[25] The accompanying Hazardous Chemical Substances Regulations No?? (HCS) of OHSA has tasked the employer with ensuring health and safety in the workplace by applying the hierarchy of hygiene controls in addressing workplace hazardous chemicals.[25] In South African hospitals the procurement of latex gloves is based on the cost of gloves and the stock is obtained from various providers who meet the South African Bureau of Standards (SABS) specifications for latex gloves.

While it is important to diagnose and manage an individual worker with latex allergy, complete control of hazardous substance in the workplace is equally important. While a latex free work environment would be a preferred control strategy, substitution of powdered latex gloves with powder free gloves was shown to be cost effective and associated with improved clinical outcome.[21] As a result this was adopted as the most reasonable and practical approach in addressing the problem of latex allergy among HCWs both internationally and to some extent nationally.[26-28] This has proven to reduce latex induced clinical outcomes. Even with this intervention, studies in Western countries such as Germany and the UK have shown that the risk of latex sensitisation still exists and more needs to be done to protect HCWs.[29, 30]

The current study described the prevalence of latex sensitisation and allergy among healthcare workers who use hypoallergenic powder free and lightly powdered latex gloves.

METHODS

Study design and population

This was a cross sectional study conducted between July 2011 and January 2012. The study location was King Edward VIII hospital, the second largest hospital in the Southern hemisphere, providing regional and tertiary services to the whole of KwaZulu-Natal (KZN) and the Eastern Cape Province in South Africa. It has a bed status of 1300 and has a workforce of 2400. The hospital was chosen due to the large workforce with different departments, and the policy of using both powder free and low powdered latex gloves for approximately 10 years.

The study population was limited to HCWs currently employed at King Edward VIII Hospital for more than 12 months. HCWs were defined as all personnel employed in the hospital.

The prevalence of latex sensitization in HCWs using powdered latex gloves in the Western Cape Province was 11.9% in 2001.[16] We expected the prevalence at King Edward VIII hospital to be less than the 11.9% observed in the Western Cape Province due to the adoption of a hypoallergenic latex glove policy. Using EPI Info calculator version 3.04.04., it was assumed that 50% of sensitised workers have remained sensitive despite the introduction of hypoallergenic latex gloves 10 years prior. Using an expected latex sensitization prevalence of 6% for the exposed group and the prevalence among the general population being reported as less than 1% the required sample size was calculated to be 585 participants 2 exposed participants for every 1 non-exposed participant (exposed =390; unexposed =195). HCWs were considered to be exposed if they were likely to use gloves. Unexposed HCWs were drawn from the administrative staff of the hospital.

Questionnaire

We used an adaptation of the questionnaire used in an epidemiological study conducted at Groote Schuur in 2001[16] with permission from Professor Paul Potter, Allergology Unit, Medical School, University of Cape Town. The questionnaire containing open and closed ended questions was adapted to include items on exposure assessment. The questionnaire was administered by a trained research assistant (Honours degree in medical science) immediately prior to the skin prick test. The questionnaire collected data on the participants' demographics, personal risk factors, latex exposure assessment, clinical manifestations of latex sensitization (dermal and respiratory) and history of previous reactions suggestive of latex allergy.

Exposure Assessment

Individual Exposure

Individual latex exposure was determined by the type of gloves used, number of gloves used per day, and duration of glove use. The information was limited to 7 working shifts/days prior to the interview.

Departmental Exposure

Departmental exposure was defined as glove usage in the past 12 months (01 January 2011-31 December 2011). The overall departmental exposure was obtained by reviewing monthly glove usage by each department from the stock room register. This was used to estimate the annual exposure for employees who had rotated through different departments in the past 12 months. Non sterile latex gloves are distributed throughout the clinical departments while a high proportion of sterile gloves are distributed to labour ward, theatre, surgical wards and outpatient

departments. Glove type was defined as powdered and powder-free and latex free based on the previous literature.[24, 32]

Skin prick test (SPT)

The SPT was conducted using the Stallergenes kit.[32] It was performed in a room with access to emergency resuscitation services by a trained research assistant. The research assistant and principal investigator were trained by the Chief Pulmonary Technician at Inkosi Albert Luthuli Central hospital (A Quaternary Hospital in KwaZulu-Natal) on 2 separate occasions. The test was performed on the inner aspect of the participants' forearms, between the wrist and the elbow on normal skin. A positive and negative control were performed using histamine and buffered normal saline solution respectively on the same arm and they were 3 cm apart to prevent cross contamination. The protein concentration of the latex extract was 500µg/ml and the solution was applied as it was with no further dilutions. After 15-20 minutes subsequent to puncturing the skin, the SPT reaction wheal and flare was outlined by a black ink and clear tape was used to transfer the outline from skin to the results sheet by the trained research assistant or principal investigator.[33] A positive result was indicated by a mean wheal diameter measuring 3 mm or greater than the negative control. Results were recorded on a standardized result sheet. The research assistant's test performance was audited by the principal investigator at regular intervals to ensure correctness of technique and interpretation of the results.

Informed signed consent was obtained from all the participants prior to participation. They had the option of participating in the questionnaire interview and the SPT or refusing the SPT. The study protocol was approved by the Biomedical Research Ethics Committee of the University of

KwaZulu-Natal (BE048/11). Permission to conduct the study was also obtained from the KZN Provincial Department of Health and King Edward VIII hospital management.

Statistical analysis

Data was captured in Excel and analysed in Stata Version 11. Frequencies and medians with ranges were presented for categorical and continuous variables respectively. The Chi-square and the Kruskal-Wallis test was used to test for significant associations between categorical an continuous variables and the dependent variables under study on bivariate analysis respectively.

Binary logistic regression was used to test for significant associations between independent and dependent variables on multivariate analysis. The dependent variables used in the regression analysis were: Latex sensitisation, which was defined as having a SPT wheal of ≥3mm to latex extract; Latex allergy (LA) was defined as being SPT positive and a report of having any one or more of the listed work related clinical symptoms namely itchy eyes, red eyes, runny eyes, runny nose, itchy nose, sneezing, coughing, tight chest, wheezing, itchy skin, skin rash or dizziness. Independent variables that were considered for analysis were as follows: Age (yrs) and sex, duration of employment, job title, current department employed in, type of gloves used, number of pairs of gloves used per day, self reported and family history of atopy, food allergy and previous history of open surgery and number of surgical procedures. In the multivariate analysis, age was omitted due to collinearity with duration of employment. Departmental glove consumption was omitted and number of pair of gloves was used as an indicator of individual latex glove exposure. The variable number of pairs of gloves used and duration of employment were retained as continuous variables in the multivariate model.

RESULTS

Participant Demographics

Sixty five HCWs refused to participate in the study. Among the 520 HCWs who responded to the invitation there was an overall participation rate of 85.5 % (n=501) with 3.6% (n=19) refusing SPT. There was no significant difference between those refusing SPT and those who had the SPT with respect to latex exposure status, age, sex and duration of employment.

The median age of participants was 42.2 years (range: 22 years-65 years) with the greater proportion of them being females. The median duration of employment was 10.9 years (range: 1 year-42 years) with the majority of exposed participants having worked as a HCW for < 10 years. Most unexposed healthcare workers had been employed for > 20 years . Personal and family history of allergy were more prevalent among unexposed HCWs while exposed HCWS reported a higher prevalence of a fruit allergy and history of previous surgery (Table 1).

Prevalence of Latex Sensitisation and Allergy

The overall prevalence of latex sensitisation and latex allergy were 5.9% (n=29) and 4.6% (n=23) respectively. Although the difference was not significant, the prevalence of latex sensitisation was higher among the exposed group (7.1%) as compared to the unexposed group (3.1%). Latex allergy was significantly higher in the exposed group than unexposed group (5.9% vs 1.8%, p=0.04). There was a significant difference in the work related allergy symptoms between exposed and unexposed workers (40.9% *vs.* 31.7%, p=0.04) (Table 1). Symptoms that were significantly associated with latex sensitisation were skin rash (p< 0.000), itchy skin (p=0.001), runny nose (p=0.004), red eyes (p=0.01) and itchy eyes (p=0.01).

The prevalence of latex sensitization was higher among those who were exposed and those with employment duration of < 10yrs. Although the prevalence of latex sensitisation was lower among participants < 30 years of age, there was no significant variation with age or sex. There was a significant difference (p=0.04) in the prevalence of fruit allergy between those participants with latex sensitisation (17.2%) and unsensitised participants (6.9%) The exclusive use of powder free latex gloves was found to be significantly (p=0.003) higher among the participants who had latex sensitisation. There was equal distribution of powdered and powder free latex gloves among those who reported the use of mixed gloves. The prevalence of reporting previous open surgery and use of other non- occupational exposure latex containing material did not vary significantly between those who had latex sensitisation and those who were unsensitised. There was a significantly higher prevalence of reporting allergic reactions when handling other latex containing medical equipment among participants with latex allergy as compared to unsensitised participants (10.3% vs 1.7%, p=0.002) (Table 2).

Crude association of demographics, exposure status, medical and personal history and latex sensitisation, latex allergy

Latex exposure was significantly associated with latex allergy (OR: 3.4; 95% CI: 1.1-10.8). Working as a HCW for 5-9 yrs was significantly associated with latex sensitisation (OR: 2.6; 95% CI: 1.2-5.5) and latex allergy (OR: 3.3; 95% CI: 1.4-7.6), respectively. Employment duration as a HCW for >20 years was protective against latex allergy (OR: 0.2; 95% CI: 0.0-0.8). Working as an enrolled nurse was significantly associated with both latex sensitisation (OR: 2.5; 95% CI: 1.2-5.3) and latex allergy (OR: 2.4; 95% CI: 1.1-5.6). The exclusive use of powder free latex gloves was significantly associated with latex sensitisation (OR: 3.1; 95% CI: 1.4-6.8) and latex allergy (OR: 3.1; 95% CI: 1.7-9.1). Powdered and powder free latex gloves were equally

distributed among those who reported the use of mixed gloves. The annual consumption of pairs of gloves per HCW by department was ranked and grouped into tertiles. Although medical and surgical wards had low and moderate pairs of gloves consumption per HCW, these wards had the highest proportion of workers with latex sensitisation (n=6, 20.0% each). However the relation was only significant for those who reported the medical ward as being the current department in which they worked (p=0.01). The proportions for powdered latex glove use were 71% and 69% in medical and surgical wards, respectively and this was not statistically significant. Exposure to other latex containing medical devices was not significantly different from what was reported in other wards. There was no significant association between personal history, latex sensitisation and latex allergy. Fruit allergy was significantly associated with latex allergy (OR: 3.7; 95%: 1.4-10.4) (Table 3). Listed fruits were evaluated for their independent association with latex sensitisation. Avocado (p=0.01) and others (p=0.003) which included pineapple and orange showed significant associations with latex sensitisation (data not shown).

Multivariate analysis

While latex exposure had estimates above 2, there was no significant association with latex sensitisation and latex allergy. Duration of employment was found to be inversely associated with latex allergy in models I and II. The exclusive use of powder free latex gloves was significantly associated with latex sensitisation (OR: 4.2: 95% CI: 1.2-14.1) and latex allergy (OR: 5.1; 95%CI: 1.2-21.2) on multivariate analysis. This significant association disappeared when examining the number of pairs of powder free gloves used in the last 7 days. A weak association was observed for the number of pairs of powdered latex gloves used in the last 7 days with both latex sensitisation and latex allergy (model III and IV). There was a significant

association between fruit allergy and latex allergy in model I (OR: 3.1: 95% CI: 1.1-9.2) (Table 4).

DISCUSSION

This is an important study for South African HCWs as it examined the risk of latex sensitisation in a group of workers exposed to hypoallergenic latex gloves. As previously mentioned there has been no literature documenting the prevalence of latex sensitisation among South African HCWs using hypoallergenic lightly powered or powder-free latex gloves. The prevalence of latex sensitisation among exposed HCWs (7.1%) in this study is comparable to findings among HCWs in another South African hospital.[14] However it was considerably lower than the 11.9% prevalence reported by Potter in the same year.[16] While a substantial number of participants (37%) reported work related allergy symptoms, only 4.6% met our definition of latex allergy. The important symptoms associated with latex sensitisation were skin rash, itchy skin, runny nose, red and itchy eyes in keeping with previous studies.[4, 5] Elimination of powdered latex gloves has shown a reduction in the concentration of aeroallergens in the operating room with the low prevalence of latex allergy in our study population.

Although the relationship was weak, this study showed that the risk of latex sensitisation decreases with duration of employment. The explanation of our finding may be that new employees are only sensitised and have not yet manifested clinical symptoms and they continue using latex gloves. On the other hand senior HCWs may have been sensitised during their earlier years of employment and as a result they either moved to departments with less exposure to latex gloves or deliberately avoid latex containing products and therefore exhibit less latex related symptoms. Furthermore the introduction of hypoallergenic gloves 10 years prior to the study may explain the reduced sensitisation in senior HCWs as demonstrated in the study by smith et al

in 2007.[21] The published literature has been inconsistent in reporting the association between duration of employment and latex sensitisation. Jones and co-workers observed a high prevalence of latex sensitisation among junior dental students exposed to exclusive powder free latex gloves compared to dental staff and senior students.[34] Among Singaporean HCWs no significant difference was reported between duration of employment and latex sensitisation,[35] while among Italian nurses latex sensitisation was associated with an increasing duration of employment.[36]

In our study HCWs who exclusively used powdered free latex gloves had a 4 times greater odds of developing latex sensitisation. A possible explanation for this is that those who are sensitised and manifesting glove related symptoms preferentially used exclusive powder free latex gloves. Moreover the background prevalence of latex sensitisation in this study was relatively higher (3.5%) than previously reported prevalence in the general population by Bousquet et al.[13] Studies have shown that some of these "hypoallergenic" latex gloves actually contain high levels of allergens which can be release into the environment with aggressive manipulation.[24] Some of the sensitised HCWs may have been sensitised before the hospital implemented a hypoallergenic latex glove policy. Also Smith et al showed that complete avoidance of powdered latex glove can result in the reduction or no change in measurable IgE antibodies .[37] A study in Germany reported a high prevalence of 8% among 226 dental students who had only been exposed to exclusive powder free latex gloves.[29] Similarly in the UK despite a total ban on powdered latex gloves Clayton found a 10% prevalence of latex sensitisation in HCWs.[30] It is also not clear to what extent the aeroallergens released by colleagues using powdered latex gloves influence this finding. Furthermore the role of other latex containing medical devices during sensitisation period cannot be entirely ruled out.

In our study, frequency of exposure as measured by the number of gloves used in the last 7 working days showed a weak association between powdered latex gloves and latex sensitisation but no association could be demonstrated with powder free latex gloves. Airborne latex aeroallergens have been shown to increase with the number of powdered gloves used which subsequently increases the risk of latex sensitisation and clinical latex glove related allergy symptoms.[19]

The positive association between department with low glove consumption per HCW and latex sensitisation is in contrast with previous finding by Liss and co-workers.[9] They reported positive association with departments that had high glove consumption per HCWs. A possible reason for our observation is that HCWs with latex sensitisation may have been relocated to wards with low glove consumptions to minimise the exposure. In addition, the annual pair of gloves consumption per HCW by department does not provide an accurate indication of individual exposure; rather it gives us the annual distribution of gloves to different departments.

Several studies have reported atopy as a significant risk factor for latex sensitisation.[9, 10, 36] Similarly, the prevalence of reporting a history of personal atopy in this study was higher among latex sensitised participants although the association was not statistically significant. Watts and colleagues reported that the risk of latex sensitisation was increased by 14 times in the presence of personal atopy and 4 times in the presence of a family history atopy among 122 American HCWs studied.[10] Contrary to Watts and co-workers findings, the risk of latex sensitisation did not increase with a reporting of family history of atopy in our study population.[10]

Fruit latex allergy syndrome is a phenomenon seen where latex sensitised individuals demonstrate a cross reactivity with specific foods; particularly fruit. Studies have identified this

phenomenon among sensitised HCWs and the general population. This has been attributed to the similarity between fruit proteins and latex allergens.[38] Fruit allergy was significantly associated with latex sensitisation and latex allergy in our study. Our study was dependent on the self-reporting of fruit allergy and no objective tests were carried out. It is therefore possible that participants have independent simultaneous allergies to both fruit and latex without cross reactivity. Also, we were unable to determine whether latex sensitisation preceded the development of fruit allergy or vice versa.

Latex sensitised participants reported a high prevalence of a history of previous open surgery in our study. This has been reported to occur as a result of direct intraoperative exposure to latex containing medical devices such as catheters or tubes. Studies in children with congenital abnormalities have demonstrated that the risk for latex allergy increases with the number of open surgical procedures that they undergo.[39] Frequency of invasive procedures among adults was shown to increase the risk of latex sensitisation reporting while more than 10 procedures increased the risk of developing latex allergy.[40]

Strengths of this study include the high response rate (85.5%) and comparability to other studies.[8, 16] Access to the hospital employee database allowed us to better assess the representativeness of this study population by comparing demographic data of the non-participants and the participants. The participants were randomly selected minimising the potential of participant's bias that comes with a volunteer approach.

The presence of a control group provided a background prevalence of latex sensitisation in this population which allowed for a better estimation of associations attributable to work related factors. The use of Stallergenes latex specific SPT further strengthens the study. The SPT test is

regarded as the gold standard for the diagnosis of latex allergy and Stallergenes has been shown to have a diagnostic sensitivity and specificity of 93% and 100%, respectively.[32] The research assistant employed on this study was trained and initially shadowed and periodically supervised by the principal investigator to ensure appropriate administration of the questionnaire and the SPT thereby improving the reliability and validity of the study.

This study was limited by the cross sectional study design which was relatively low in cost and quick to conduct. It only allowed for the determination of prevalence of latex sensitisation at one point in time. Consequently the prevalence of latex sensitisation may have been underestimated as it is possible that HCWs who had already developed latex sensitisation have left the hospital before the study was conducted. Recall bias is another potential limitation in this study as workers were asked to recall the number of gloves used in the past 7 working days. HCWs may have overestimated or underestimated their individual exposures. Our study depended on self-reporting of personal and family atopic disorders and this may have resulted in the misclassification of atopy.

CONCLUSION

This study shows that even in the presence of powder free hypoallergenic glove use there is latex sensitisation and latex allergy, adding to previous findings that HCWs exposed to hypoallergenic latex gloves are still at risk for developing latex sensitisation and latex allergy. This indicates that latex sensitisation and allergy are still an important occupational hazard for HCWs. While it may be economically impractical to replace the latex gloves in our setting, reduction of allergen content in latex products is another strategy that can be implemented to address the problem and protect HCWs. A policy accompanied by clear implementation plans as well as sustainable education and training programmes to address latex sensitisation and allergy among HCWs

should be implemented.[41] In addition HCWs must be continuously monitored for the development of latex sensitisation and alternate latex free glove must be made available for them. More research is needed to identify the most cost effective way of implementing a latex free environment in resource limited countries, such as South Africa. In addition the current studies in South Africa have largely been cross-sectional in nature. More cohort analysis is required to better understand the chronicity of illness and disability associated with latex allergy.

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Contributorship

Dr Shumani Phaswana is the principal investigator who was involved from the conception of the idea, proposal writing, data collection, data management and interpretation of the results.

Dr Saloshni Naidoo contributed to the conception and design of the study, analysis and intepretation of the data, critical review of the intellectual conente of the article and final approval of the article.

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Competing interests

None

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Characteristic	Exposed N (%)	Unexposed N (%)
Number of participants	337 (67.3)	164 (32.7)
Demographics		

TABLES

Table 1: Demographics and associated risk factors amongst latex exposed and unexposed healthcare workers at King Edward VIII Hospital, KwaZulu-Natal South Africa, (n=501)

Characteristics	Latex SPT +ve[ǂ] (29) N (%)	Latex SPT -ve[ǂ] (472) N (%)
Demographics		
Age (years)		
≤30	30(8.9)	19(11.6)
>30-40	121(35.9)	40(24.4)
>40-50	101(29.9)	59(35.9)
>50	85(25.2)	46(28.1)
Duration of employment (years)		
≤5	34(10.1)	28(17.1)
>5-10**	135(40.1)	32(19.5)
>10-15	49(14.5)	17(10.4)
>15-20	24(7.1)	20(12.2)
>20*	90(26.7)	67(40.9)
Sex **		
Female	309(91.7)	95(57.9)
Male	28(8.3)	69(42.1)
Job Title (yes)		
Administrative		164(100.0)
Professional nurses	123(36.5)	
Enrolled nurses	141(41.8)	
Enrolled nursing assistants	73 (21.7)	
Medical and Personal History		
Personal history of Allergy Disease (yes)	147(43.6)	83(50.6)
Family history of Allergy Disease (yes)	197(58.5)	102(62.2)
Fruit allergy (yes)	29(8.6)	9(5.5)
Previous open surgery (yes)*	168(49.8)	61(37.2)
Work-related allergy symptoms(yes)*	138(40.9)	52(31.7)
Non-occupational latex exposure (yes)	161(47.8)	76(46.3)
Latex sensitisation (yes)	24(7.1)	5(3.1)
Current latex allergy (yes)*	20(5.9)	3(1.8)

Chi square, *p<0.05, **p<0.001

Table 2: Comparison of risk factors between latex sensitised (skin prick test positive) and non-sensitised (skin prick test negative) healthcare workers at King Edward VIII Hospital, KwaZulu-Natal South Africa (n=501)

Characteristics	N=29	Latex Sensitisation OR (95%CI)	N=233	LA[ǂ] OR (95%CI)
Demographics				
Age (years)				
≤30	1	0.5(0.0-1.9)	151(31.9)	0.4(0.0-2.4)
Age (years.)				
≤30		1 (3.5)	48(10.2)	
>30-40		13 (44.8)	148(31.4)	
>40-50		8 (27.6)	152(32.2)	
>50		7 (24.1)	124(26.3)	
Duration of employment				
≤5		3(10.3)	64(13.6)	
>5-10		16(55.2)	151(31.9)	
>10-15		3(10.3)	63(13.4)	
>15-20		1(3.5)	43(9.1)	
≥20		6(20.7)	151(31.9)	
Sex (yes)				
Male		5(17.2)	118(25.0)	
Female		24(82.8)	354(75.0)	
Job Title (yes)				
Administrative		5(17.2)	159(33.7)	
Professional nurses		5(17.2)	118(25.0)	
Enrolled nurses		14(48.3)	127(26.9)	
Enrolled nursing assistants		5(17.2)	68(14.4)	
Latex Exposure				
Exposure status(yes)		24 (82.8)	313(66.3)	
Type of gloves				
None		5(17.2)	165(34.6)	
Exclusive powdered latex glove (yes)		2(6.9)	36(7.6)	
Exclusive powder free latex glove (yes)*		11(37.9)	77(16.3)	
Mixed (yes)		11(37.9)	198(41.9)	
Medical and Personal History				
Personal history of Allergy Disease (yes)		16(55.2)	214(45.3)	
Family history of Allergy Disease (yes)		18(62.1)	281(59.5)	
Fruit allergy (yes) *		5(17.2)	33(6.9)	
Previous open surgery (yes)		18(62.1)	211(44.7)	
Non-occupational latex exposure (yes)		12(41.4)	225(47.7)	
Reaction to other latex medical devices (yes)*		3(10.3)	8(1.7)	

Chi Square, *p<0.05

[ǂ]Latex Skin Prick Test Positive

[ǂǂ]Latex Skin Prick Test Negative

Table 3: Crude Odds Ratios (OR) (95%CI) of demographics, exposure status, medical and personal history and latex sensitisation and latex allergy amongst healthcare workers at King Edward VIII Hospital, KwaZulu-Natal South Africa, (n=501)

>30-40	13	1.8(0.8-3.7)	11	2.0(0.9-4.6)
>40-50	8	0.8(0.4-1.8)	7	0.9(0.4-2.2)
>50	7	0.8(0.4-2.1)	4	0.6(0.2-1.7)
Duration of employment (years)				
<5	3	0.7(0.2-2.4)	3	0.9(0.3-3.2)
5-10	16	2.6(1.2-5.5)*	14	3.3(1.4-7.6)*
>10-15	3	0.7(0.2-2.4)	3	0.9(0.3-3.2)
>15-20	1	0.4(0.0-2.1)	1	0.5(0.0-2.8)
>20	6	0.5(0.2-1.4)	2	0.2(0.0-0.8)*
Sex (yes)				
Female	24	1.6(0.6-4.1)	20	2.2(0.7-7.2)
Job Title (yes)				
Administrative	5	0.4(0.2-1.1)	3	0.3(0.1-0.9)*
Professional nurses	5	0.6(0.2-1.6)	4	0.6(0.2-1.8)
Enrolled nurses	14	2.5(1.2-5.3)*	11	2.4(1.1-5.6)*
Enrolled nursing assistants	5	1.2(0.5-3.3)	5	1.7(0.6-4.5)
Latex Exposure				
Exposure status (yes)	24	2.4(0.9-6.3)	20	3.4(1.1-10.8)*
Type of gloves				
None	5	0.4(0.2-1.0)	3	0.3(0.1-0.9)*
Exclusive Powdered latex glove (yes)	2	0.9(0.0-3.6)	2	1.2(0.0-1.7)
Exclusive Powder free latex glove (yes)	11	3.1(1.4-6.8)*	10	3.1(1.7-9.1)*
Mixed gloves(yes)	11	0.8(0.4-1.8)	8	0.7(0.3-1.7)
Medical and Personal History				
Personal history of Allergy Disease (yes)	16	1.4(0.7-3.1)	12	1.3(0.5-2.9)
Family history of Allergy Disease (yes)	18	1.1(0.5-2.4)	14	1.1(0.5-2.4)
Fruit allergy (yes)	5	2.8(1.0-7.5)	5	3.7(1.4-10.4)*
Previous open surgery (yes)	18	1.1(0.5-2.4)	14	1.5(0.7-3.1)

Chi square, *p<0.05

†Latex Skin Prick Test Positive

‡‡Latex Skin Prick Test Positive and work related clinical symptoms of allergy

Table 4: Multivariate analysis of demographics, medical and personal history, exposure history and latex sensitisation (LS)ǂ and latex allergy (LA)ǂǂ amongst healthcare workers at King Edward III Hospital, KwaZulu-Natal South Africa, (n=501)

	MODEL I* (n=501)		MODEL II** (n=501)		MODEL III***(n=202)		MODEL IV****(n=252)	
Characteristics	LS OR (95%CI)	LA OR (95%CI)	LS OR (95%CI)	LA OR (95%CI)	LS OR (95%CI)	LA OR (95%CI)	LS OR (95%CI)	LA OR (95%CI)
Demographics								
Sex (female)	0.9(0.2-2.7)	1.1(0.3-4.4)	0.9(0.3-2.7)	1.1(0.3-4.5)	0.3(0.0-1.8)	0.3(0.0-3.1)	2.5(0.5-12.2)	2.5(0.5-12.2)
Duration of employment (years)	0.9(0.9-1.0)	0.9(0.8-0.9)	0.9(0.9-1.0)	0.9(0.8-0.8)	0.9(0.9-1.8)	0.7(0.5-1.0)	0.9(0.9-1.0)	0.9(0.9-1.0)
Latex Exposure								
Exposure status(yes)	2.2(0.7-6.7)	2.6(0.7-9.8)						
Type of gloves								
None			1	1				
Exclusive lightly powdered latex glove (yes)			1.6(0.3-9.8)	2.6(0.4-17.7)				
Exclusive Powder free latex glove (yes)			4.2(1.2-14.1)	5.1(1.2-21.2)				
Mixed gloves (yes)			1.7(0.5-5.6)	1.7(0.4-7.1)				

Pairs of Powdered latex Gloves in the last 7 days					1.1(1.0-1.2)	1.2(1.0-1.4)		
Pairs of Powder Free Latex Gloves in the last 7 days							1.0(0.9-1.1)	1.0(0.9-1.1)
Personal and Medical History								
Personal history of allergy disease (yes)	1.5(0.7-3.3)	1.4(0.6-3.2)	1.5(0.7-3.3)	1.3(0.6-3.2)	1.4(0.3-6.8)	1.6(0.2-11.6)	1.0(0.4-2.9)	0.9(0.3-2.8)
Family history of allergy disease (yes)	1.0(0.45-2.2)	0.9(0.4-2.2)	1.1(0.5-2.3)	0.9(0.4-2.3)	0.4(0.1-1.9)	0.5(0.1-3.6)	0.7(0.2-2.0)	0.8(0.3-2.7)
Fruit allergy (yes)	2.3(0.8-6.7)	3.1(1.1-9.2)	2.2(0.8-6.5)	3.0(0.9-9.1)	5.0(0.4-56.9)	9.7(0.6-163.0)	1.7(0.3-8.5)	2.0(0.4-10.4)
Previous open surgery (yes)	2.0(0.9-4.4)	1.9(0.8-4.6)	2.1(0.9-4.6)	1.9(0.8-4.7)	1.4(0.3-7.4)	1.2(0.1-11.1)	1.1(0.4-3.2)	1.2(0.4-3.8)

ǂLatex Skin Prick Test Positive

ǂǂLatex Skin Prick Test Positive and work related clinical symptoms of allergy
*Model included latex glove exposure status
**Model included type of gloves
***Model included number of pairs of powdered latex gloves
****Model included number of pairs of powder free latex gloves

STROBE Statement—Checklist of items that should be included in reports of ***cross-sectional studies***

	Item No	Recommendation
Title and abstract	1	(*a*) Indicate the study's design with a commonly used term in the title or the abstract
		(*b*) Provide in the abstract an informative and balanced summary of what was done and what was found
Introduction		
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported
Objectives	3	State specific objectives, including any prespecified hypotheses
Methods		
Study design	4	Present key elements of study design early in the paper
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection
Participants	6	(*a*) Give the eligibility criteria, and the sources and methods of selection of participants
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group
Bias	9	Describe any efforts to address potential sources of bias
Study size	10	Explain how the study size was arrived at
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why
Statistical methods	12	(*a*) Describe all statistical methods, including those used to control for confounding
		(*b*) Describe any methods used to examine subgroups and interactions
		(*c*) Explain how missing data were addressed
		(*d*) If applicable, describe analytical methods taking account of sampling strategy
		(*e*) Describe any sensitivity analyses
Results		
Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed
		(b) Give reasons for non-participation at each stage
		(c) Consider use of a flow diagram
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders
		(b) Indicate number of participants with missing data for each variable of interest
Outcome data	15*	Report numbers of outcome events or summary measures
Main results	16	(*a*) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included
		(*b*) Report category boundaries when continuous variables were categorized
		(*c*) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses

Discussion		
Key results	18	Summarise key results with reference to study objectives
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence
Generalisability	21	Discuss the generalisability (external validity) of the study results
Other information		
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based

*Give information separately for exposed and unexposed groups.

Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at http://www.plosmedicine.org/, Annals of Internal Medicine at http://www.annals.org/, and Epidemiology at http://www.epidem.com/). Information on the STROBE Initiative is available at www.strobe-statement.org.

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The prevalence of latex sensitisation and allergy and associated risk factors amongst health care workers using hypoallergenic latex gloves at King Edward VIII hospital, KwaZulu-Natal South Africa: A cross sectional study

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The prevalence of latex sensitisation and allergy and associated risk factors among healthcare workers using hypoallergenic latex gloves at King Edward VIII Hospital, KwaZulu-Natal South Africa: A cross sectional study

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ARTICLE SUMMARY

ARTICLE FOCUS

- The use of hypoallergenic latex gloves has been adopted as policy in different healthcare settings globally.
- However, information with regard to their use and the development of latex sensitisation and allergy among exposed healthcare workers is limited.
- We hypothesised that there is latex sensitization and allergy in healthcare workers using hypoallergenic latex gloves in a South African hospital.

KEY MESSAGE

- In the presence of powder free hypoallergenic gloves, latex sensitisation and latex allergy is still an important occupational health effect in healthcare workers.
- Healthcare workers should be continuously monitored for the development of latex sensitisation and allergy.
- There is a need for a national policy accompanied by clear implementation plans as well as sustainable education and training programmes to address latex sensitisation and allergy among HCWs.

STRENGTH AND LIMITATIONS

- Strength of the study included the presence of a control group providing a background prevalence of latex sensitisation in this population and random selection of participants which minimised the potential of participant bias that arises with a volunteer approach.
- This study was limited by the cross sectional study design as it only allowed for the determination of the prevalence of latex sensitisation; recall bias with regard to the number of gloves used in the past 7 working days and the self-reporting of personal and family atopic disorders may have resulted in the misclassification of exposure and atopy respectively.

What this paper adds

- In the presence of powder free hypoallergenic gloves, latex sensitisation and latex allergy is still an important occupational health hazard in healthcare workers

- Healthcare workers should be continuously monitored for the development of latex sensitisation and allergy

- There is a need for a national policy accompanied by clear implementation plans as well as sustainable education and training programmes to address latex sensitisation and allergy among HCWs

ABSTRACT

Objectives

The present study describes latex sensitisation and allergy prevalence and associated factors among healthcare workers using hypoallergenic latex gloves at King Edward VIII Hospital in KwaZulu-Natal South Africa.

Design

Cross sectional study

Setting

A tertiary hospital in eThekwini municipality, KwaZulu Natal, South Africa

Participants

600 healthcare workers were randomly selected and 501(337 exposed and 164 unexposed) participated. Participants who were pregnant, less than one year of work as healthcare worker and history of anaphylactic reaction were excluded from the study.

Primary and secondary outcome measures

Latex sensitisation and latex allergy were the outcome of interest and they were successfully measured

Results

Prevalence of latex sensitisation and allergy was observed among exposed workers (7.1% and 5.9%) and unexposed workers (3.1% and 1.8%). Work related allergy symptoms were significantly higher in exposed workers (40.9%, $p<0.05$). Duration of employment was inversely associated with latex allergy (OR: 0.9; 95% CI: 0.8-0.9). The risk of latex sensitisation (OR: 4.2; 95% CI: 1.2-14.1) and allergy (OR:

5.1; 95% CI: 1.2-21.2) increased with exclusive use of powder-free latex gloves. A dose –response relationship was observed for powdered latex gloves (OR: 1.1; 95% CI: 1.0-1.2). Atopy (OR: 1.5; 95% CI: 0.7-3.3 and OR: 1.4; 95% CI: 0.6-3.2) and fruit allergy (OR: 2.3; 95% CI: 0.8-6.7 and OR: 3.1; 95% CI: 1.1-9.2) also increased the risk of latex sensitisation and allergy.

Conclusion

This study adds to previous findings that healthcare workers exposed to hypoallergenic latex gloves are at risk for developing latex sensitisation highlighting its importance as an occupational hazard in healthcare. More research is needed to identify the most cost effective way of implementing a latex free environment in resource limited countries, such as South Africa. In addition more cohort analysis is required to better understand the chronicity of illness and disability associated with latex allergy.

INTRODUCTION

Latex allergy (LA) as an occupational disease among healthcare workers (HCWs) gained recognition after Nutter published a case report of contact urticaria in a HCW in 1979.[1] The increase in prevalence coincided with the emergence of the Human Immunodeficiency Virus/ Acquired immunodeficiency syndrome (HIV/AIDS) epidemic and the introduction of "universal precautions" in the healthcare industry which had resulted in the increased use of latex gloves among HCWs.[2]

Latex gloves are preferred due to their superior barrier and physical properties as compared to the non-latex gloves.[3] International epidemiological studies have reported the prevalence of latex allergy among HCWs to range between 2-22% depending on the population and diagnostic methods used.[4-11] The prevalence in the general population has been reported to range between 1-6%.[12, 13] In South Africa studies amongst HCWs reported a latex sensitisation prevalence of between 2.7 to 20.8%.[14-16] Latex allergy in HCWs is a compensable disease in South Africa in terms of the Compensation of Occupational Injuries and Diseases Act No. 130 of 1993.[17]

Powdered latex gloves were identified as an important risk factor for latex sensitisation and allergy in HCWs as they were found to contain high allergenic protein content.[18] Following these findings, hypoallergenic gloves with low allergen content namely, low powdered and powder free latex gloves were introduced. The European definition of powder free gloves is gloves with powder content not exceeding 2 mg per glove and leachable latex protein which is as low as is reasonably practical.[19]

Hypoallergenic gloves have been associated with reduced latex aeroallergen concentrations, reduced conversion rates and a subsequent decrease in clinic visits, and compensation claims for

latex induced occupational asthma and allergic contact dermatitis among HCWs.[18, 20] As much as the use of low or powder free gloves has been shown to reduce latex related symptoms, other studies have shown that exposed HCWs still exhibit symptoms at very low levels of measureable airborne latex allergens.[21] Most studies have reported on the airborne levels and inhalational route of exposure hence the recommendation on low powdered or powder free latex gloves. There is little consideration given to the dermal route of exposure despite the fact that exposure is as a result of direct contact in these instances.[22] Eliminating the cornstarch powder only removed the carrier and not the source of allergen which is in the latex itself. Therefore workers using powder free gloves are still exposed to the allergenic content of latex gloves. It has been shown that different brands from different suppliers contain differing levels of protein due to a lack of standards in latex glove manufacture.[23] A South African study reported that some powder free latex gloves were found to have high allergenic protein content.[23] HCWs using these gloves are exposed via direct dermal contact and are at risk for developing latex sensitization which maybe asymptomatic and if exposure continues they can later develop latex allergy which presents with clinical manifestations.

While it is important to diagnose and manage an individual worker with latex allergy in the early stages of the disease, complete control of hazardous substance in the workplace is equally if not more important. While a latex free work environment would be a preferred control strategy, substitution of powdered latex gloves with powder free gloves was shown to be cost effective and associated with improved clinical outcome.[20, 24-26] As a result this was adopted as the most reasonable and practical approach in addressing the problem of latex allergy among HCWs both internationally and to some extent nationally.[27-29] This has proven to reduce latex induced clinical outcomes. Even with this intervention, studies in Western countries such as Germany

and the UK have shown that the risk of latex sensitisation still exists and more needs to be done to protect HCWs.[30, 31]

The current study described the prevalence of latex sensitisation and allergy among healthcare workers who use hypoallergenic powder free and lightly powdered latex gloves.

METHODS

Study design and population

This was a cross sectional study conducted between July 2011 and January 2012. The study location was King Edward VIII hospital, the second largest hospital in the Southern hemisphere, providing regional and tertiary services to the whole of KwaZulu-Natal (KZN) and the Eastern Cape Province in South Africa. It has a bed status of 1300 and has a workforce of 2400. The hospital was chosen due to the large workforce with different departments, and the policy of using both powder free and low powdered latex gloves for approximately 10 years.

The study population was limited to HCWs currently employed at King Edward VIII Hospital for more than 12 months. HCWs were defined as all personnel employed in the hospital.

The prevalence of latex sensitization in HCWs using powdered latex gloves in the Western Cape Province was 11.9% in 2001.[16] We expected the prevalence at King Edward VIII hospital to be less than the 11.9% observed in the Western Cape Province due to the adoption of a hypoallergenic latex glove policy in 2001. Using EPI Info calculator version 3.04.04., it was assumed that 50% of sensitised workers have remained sensitised despite the introduction of hypoallergenic latex gloves 10 years prior. Using an expected latex sensitization prevalence of 6% for the exposed group and the prevalence among the general population being reported as

less than 1% the required sample size was calculated to be 585 participants 2 exposed participants for every 1 non-exposed participant (exposed =390; unexposed =195). HCWs were considered to be exposed if they were likely to use gloves. Unexposed HCWs were drawn from the administrative staff of the hospital.

Questionnaire

We used an adaptation of the questionnaire used in an epidemiological study conducted at Groote Schuur in 2001[16] with permission from Professor Paul Potter, Allergology Unit, Medical School, University of Cape Town. The questionnaire containing open and closed ended questions was adapted to include items on exposure assessment. The questionnaire was administered by a trained research assistant immediately prior to the skin prick test. The questionnaire collected data on the participants' demographics, personal risk factors, latex exposure assessment, clinical manifestations of latex sensitization (dermal and respiratory) and history of previous reactions suggestive of latex allergy.

Exposure Assessment

Individual Exposure

Individual latex exposure was determined by the type of gloves used, number of gloves used per day, and duration of glove use. The information was limited to 7 working shifts/days prior to the interview.

Departmental Exposure

Departmental exposure was defined as glove usage in the past 12 months (01 January 2011-31 December 2011). The overall departmental exposure was obtained by reviewing monthly glove usage by each department from the stock room register. This was used to estimate the annual exposure for employees who had rotated through different departments in the past 12 months. Non sterile latex gloves are distributed throughout the clinical departments while a high proportion of sterile gloves are distributed to labour ward, theatre, surgical wards and outpatient departments. Glove type was defined as powdered and powder-free and latex free based on the previous literature.[23, 32]

Skin prick test (SPT)

The SPT was conducted using the Stallergenes kit.[32] It was performed in a room with access to emergency resuscitation services by a trained research assistant. The research assistant and principal investigator were trained on 2 separate occasions. The test was performed on the inner aspect of the participants' forearms, between the wrist and the elbow on normal skin. A positive and negative control were performed using histamine (0.61% concentration of phenol) and buffered normal saline solution respectively on the same arm and they were 3 cm apart to prevent cross contamination. The protein concentration of the latex extract was 500µg/ml and the solution was applied as it was with no further dilutions. After 15-20 minutes subsequent to puncturing the skin, the SPT reaction wheal and flare was outlined by a black ink and clear tape was used to transfer the outline from skin to the results sheet by the trained research assistant or principal investigator.[33] A positive result was indicated by a mean wheal diameter measuring 3 mm or greater than the negative control. Results were recorded on a standardized result sheet. The research assistant's test performance was audited by the principal investigator at regular intervals to ensure correctness of technique and interpretation of the results.

Informed signed consent was obtained from all the participants prior to participation. They had the option of participating in the questionnaire interview and the SPT or refusing the SPT. The study protocol was approved by the Biomedical Research Ethics Committee of the University of KwaZulu-Natal (BE048/11). Permission to conduct the study was also obtained from the KZN Provincial Department of Health and King Edward VIII hospital management.

Statistical analysis

Data was captured in Excel and analysed in Stata Version 11. Frequencies and medians with ranges were presented for categorical and continuous variables respectively. The Chi-square and the Kruskal-Wallis test were used to test for significant associations between categorical and continuous variables and the dependent variables under study on bivariate analysis, respectively.

Binary logistic regression was used to test for significant associations between independent and dependent variables on multivariate analysis. The dependent variables used in the regression analysis were: Latex sensitisation, which was defined as having a SPT wheal of ≥3mm to latex extract; Latex allergy (LA) was defined as being SPT positive and a report of having any one or more of the listed work related clinical symptoms namely itchy eyes, red eyes, runny eyes, runny nose, itchy nose, sneezing, coughing, tight chest, wheezing, itchy skin, skin rash or dizziness. Independent variables that were considered for analysis were as follows: Age (yrs.) and sex, duration of employment, job title, current department employed in, type of gloves used, number of pairs of gloves used per day, self reported and family history of atopy, food allergy and previous history of open surgery and number of surgical procedures. In the multivariate analysis, age was omitted due to collinearity with duration of employment. Departmental glove consumption was omitted as this only indicated annual distribution of gloves per department and

not necessarily employees' exposure since enrolled nursing assistants and enrolled nurses are rotated through different departments in any given year. The number of pair of gloves was used as an indicator of individual latex glove exposure. The variable number of pairs of gloves used and duration of employment were retained as continuous variables in the multivariate model. Fractional polynomial and a fractional plot was used to visualise the dose-response relationship of these continuous exposure variables.

RESULTS

Participant Demographics

Sixty five HCWs refused to participate in the study. Among the 520 HCWs who responded to the invitation there was an overall participation rate of 85.5 % (n=501) with 3.6% (n=19) refusing SPT. There was no significant difference between those refusing SPT and those who had the SPT with respect to latex exposure status, age, sex and duration of employment.

The median age of participants was 42.2 years (range: 22 years-65 years) with the greater proportion of them being females. The median duration of employment was 10.9 years (range: 1 year-42 years) with the majority of exposed participants having worked as a HCW for < 10 years. Most unexposed healthcare workers had been employed for > 20 years. Personal and family history of allergy was more prevalent among unexposed HCWs while exposed HCWS reported a higher prevalence of a fruit allergy and history of previous surgery (Table 1).

Prevalence of Latex Sensitisation and Allergy

The overall prevalence of latex sensitisation and latex allergy were 5.9% (n=29) and 4.6% (n=23) respectively. Although the difference was not significant, the prevalence of latex

sensitisation was higher among the exposed group (7.1%) as compared to the unexposed group (3.1%). Latex allergy was significantly higher in the exposed group than unexposed group (5.9% vs 1.8%, p=0.04). There was a significant difference in the work related allergy symptoms between exposed and unexposed workers (40.9% *vs.* 31.7%, p=0.04) (Table 1). Symptoms that were significantly associated with latex sensitisation were skin rash (p< 0.000), itchy skin (p=0.001), runny nose (p=0.004), red eyes (p=0.01) and itchy eyes (p=0.01).

The prevalence of latex sensitization was higher among those who were exposed and those with employment duration of < 10yrs. Although the prevalence of latex sensitisation was lower among participants < 30 years of age, there was no significant variation with age or sex. There was a significant difference (p=0.04) in the prevalence of fruit allergy between those participants with latex sensitisation (17.2%) and unsensitised participants (6.9%) The exclusive use of powder free latex gloves was found to be significantly (p=0.003) higher among the participants who had latex sensitisation. There was equal distribution of powdered and powder free latex gloves among those who reported the use of mixed gloves. The prevalence of reporting previous open surgery and use of other non- occupational exposure latex containing material did not vary significantly between those who had latex sensitisation and those who were unsensitised. There was a significantly higher prevalence of reporting allergic reactions when handling other latex containing medical equipment among participants with latex allergy as compared to unsensitised participants (10.3% vs 1.7%, p=0.002) (Table 2).

Crude association of demographics, exposure status, medical and personal history and latex sensitisation, latex allergy

Latex exposure was significantly associated with latex allergy (OR: 3.4; 95% CI: 1.1-10.8). Working as a HCW for 5-9 years was significantly associated with latex sensitisation (OR: 2.6; 95% CI: 1.2-5.5) and latex allergy (OR: 3.3; 95% CI: 1.4-7.6), respectively. Employment duration as a HCW for >20 years was protective against latex allergy (OR: 0.2; 95% CI: 0.0-0.8). In comparison with unexposed workers, working as an enrolled nurse was significantly associated with both latex sensitisation (OR: 2.5; 95% CI: 1.2-5.3) and latex allergy (OR: 2.4; 95% CI: 1.1-5.6). The exclusive use of powder free latex gloves was significantly associated with latex sensitisation (OR: 3.1; 95% CI: 1.4-6.8) and latex allergy (OR: 3.1; 95% CI: 1.7-9.1). Powdered and powder free latex gloves were equally distributed among those who reported the use of mixed gloves. The annual consumption of pairs of gloves per HCW by department was ranked and grouped into tertiles. Although medical and surgical wards had low and moderate pairs of gloves consumption per HCW, these wards had the highest proportion of workers with latex sensitisation (n=6, 20.0% each). However the relation was only significant for those who reported the medical ward as being the current department in which they worked (p=0.01). The proportions for powdered latex glove use were 71% and 69% in medical and surgical wards, respectively and this was not statistically significant. Exposure to other latex containing medical devices was not significantly different from what was reported in other wards. There was no significant association between reported personal history of allergy disease, latex sensitisation and latex allergy. Fruit allergy was significantly associated with latex allergy (OR: 3.7; 95%: 1.4-10.4) (Table 3). Listed fruits were evaluated for their independent association with latex sensitisation. Avocado (OR: 12.3; 95% CI: 5.1-29.6) and others (OR: 5.1; 95% CI: 2.1-11.8) which included pineapple and orange showed significant associations with latex sensitisation (data not shown).

Multivariate analysis

While latex exposure had estimates of the OR above 2, there was no significant association with latex sensitisation and latex allergy. Duration of employment was found to be inversely associated with latex allergy in models I and II. The exclusive use of powder free latex gloves was significantly associated with latex sensitisation (OR: 4.2: 95% CI: 1.2-14.1) and latex allergy (OR: 5.1; 95%CI: 1.2-21.2) on multivariate analysis. This significant association disappeared when examining the number of pairs of powder free gloves used in the last 7 days. A weak association was observed for the number of pairs of powdered latex gloves used in the last 7 days with both latex sensitisation and latex allergy (model III and IV).Further analysis of duration of employment and number of pairs of gloves using fractional polynomial failed to demonstrate a dose-response relationship with either latex sensitisation or latex allergy. There was a significant association between fruit allergy and latex allergy in model I (OR: 3.1: 95% CI: 1.1-9.2) (Table 4).

DISCUSSION

This is an important study for South African HCWs as it examined the risk of latex sensitisation in a group of workers exposed to hypoallergenic latex gloves. As previously mentioned there has been no literature documenting the prevalence of latex sensitisation among South African HCWs using hypoallergenic lightly powered or powder-free latex gloves. The prevalence of latex sensitisation among exposed HCWs (7.1%) in this study is comparable to findings among HCWs in another South African hospital.[14] However it was considerably lower than the 11.9% prevalence reported by Potter in the same year.[16] While a substantial number of participants (37%) reported work related allergy symptoms, only 4.6% met our definition of latex allergy. The important symptoms associated with latex sensitisation were skin rash, itchy skin, runny

nose, red and itchy eyes in keeping with previous studies. Elimination of powdered latex gloves has shown a reduction in the concentration of aeroallergens in the operating room with the low prevalence of latex allergy in our study population.

Although the relationship was weak, this study showed that the risk of latex sensitisation decreases with duration of employment. The healthy worker effect is a possible explanation of this finding. Prior to availability of hypoallergenic latex gloves, workers who had developed latex allergy may have left employment or they may have changed their career path and moved into a more administrative or managerial role with no contact with latex gloves. Furthermore new employees are only sensitised and have not yet manifested clinical symptoms and they continue using latex gloves. On the other hand senior HCWs may have been sensitised during their earlier years of employment and as a result they either moved to departments with less exposure to latex gloves or deliberately avoid latex containing products and therefore exhibit less latex related symptoms. Moreover, the introduction of hypoallergenic gloves 10 years prior to the study may explain the reduced sensitisation in senior HCWs as demonstrated in the study by Smith et al in 2007. The published literature has been inconsistent in reporting the association between duration of employment and latex sensitisation. Although latex is one of the best studied allergens, no exposure response studies have been published with measured latex allergen levels. In addition, studies have demonstrated variation in allergen content of different gloves. These may lead to discrepancies in the literature with regard to the role of duration of employment as a surrogate measure of exposure.

In our study HCWs who exclusively used powdered free latex gloves had a 4 times greater odds of developing latex sensitisation. The fact that HCWs with latex sensitisation or allergy work more often with powder free latex gloves is indicative of reverse causality because of symptoms.

Moreover the background prevalence of latex sensitisation in this study was relatively higher (3.5%) than previously reported prevalence in the general population by Bousquet et al.[13] Studies have shown that some of these "hypoallergenic" latex gloves actually contain high levels of allergens which can be release into the environment with aggressive manipulation.[23] Some of the sensitised HCWs may have been sensitised before the hospital implemented a hypoallergenic latex glove policy. Also Smith et al showed that complete avoidance of powdered latex glove can result in the reduction or no change in measurable IgE antibodies.[34] A study in Germany reported a high prevalence of 8% among 226 dental students who had only been exposed to exclusive powder free latex gloves.[30] Similarly in the UK despite a total ban on powdered latex gloves Clayton found a 10% prevalence of latex sensitisation in HCWs.[31] It is also not clear to what extent the aeroallergens released by colleagues using powdered latex gloves influence this finding. Furthermore the role of other latex containing medical devices during sensitisation period cannot be entirely ruled out.

In our study, frequency of exposure as measured by the number of gloves used in the last 7 working days showed a weak association between powdered latex gloves and latex sensitisation but no association could be demonstrated with powder free latex gloves. Airborne latex aeroallergens have been shown to increase with the number of powdered gloves used which subsequently increases the risk of latex sensitisation and clinical latex glove related allergy symptoms.[18]

The positive association between department with low glove consumption per HCW and latex sensitisation is in contrast with previous finding by Liss and co-workers.[9] They reported positive association with departments that had high glove consumption per HCWs. Again, this could be as a result of reverse causality where HCWs with latex sensitisation may have been relocated to

wards with low glove consumption to minimise the exposure. In addition, the annual pair of gloves consumption per HCW by department does not provide an accurate indication of individual exposure; rather it gives us the annual distribution of gloves to different departments.

Several studies have reported atopy as a significant risk factor for latex sensitisation.[9, 10, 35] Similarly, the prevalence of reporting a history of personal atopy in this study was higher among latex sensitised participants although the association was not statistically significant. The role of atopy is complex because some individuals might also have become atopic after having been latex sensitised and cross sectional study is not suitable in establishing this association.

Fruit latex allergy syndrome is a phenomenon seen where latex sensitised individuals demonstrate a cross reactivity with specific foods; particularly fruit. Studies have identified this phenomenon among sensitised HCWs and the general population. This has been attributed to the similarity between fruit proteins and latex allergens.[36] Fruit allergy was significantly associated with latex sensitisation and latex allergy in our study. Our study was dependent on the self-reporting of fruit allergy and no objective tests were carried out. It is therefore possible that participants have independent simultaneous allergies to both fruit and latex without cross reactivity. Also, we were unable to determine whether latex sensitisation preceded the development of fruit allergy or vice versa. Fruit allergy prior to latex exposure could have contributed to the association observed in our study.

Latex sensitised participants reported a high prevalence of a history of previous open surgery in our study. This has been reported to occur as a result of direct intraoperative exposure to latex containing medical devices such as catheters or tubes. Studies in children with congenital abnormalities have demonstrated that the risk for latex allergy increases with the number of open

surgical procedures that they undergo.[37] Frequency of invasive procedures among adults was shown to increase the risk of latex sensitisation reporting while more than 10 procedures increased the risk of developing latex allergy.[38]

Strengths of this study include the high response rate (85.5%) and comparability to other studies.[8, 16] Access to the hospital employee database allowed us to better assess the representativeness of this study population by comparing demographic data of the non-participants and the participants. The participants were randomly selected minimising the potential of participant's bias that comes with a volunteer approach.

The presence of a control group provided a background prevalence of latex sensitisation in this population which allowed for a better estimation of associations attributable to work related factors. The use of Stallergenes latex specific SPT further strengthens the study. The SPT test is regarded as the gold standard for the diagnosis of latex allergy and Stallergenes has been shown to have a diagnostic sensitivity and specificity of 93% and 100%, respectively.[32] The research assistant employed on this study was trained and initially shadowed and periodically supervised by the principal investigator to ensure appropriate administration of the questionnaire and the SPT thereby improving the reliability and validity of the study.

This study was limited by the cross sectional study design which was relatively low in cost and quick to conduct. It only allowed for the determination of prevalence of latex sensitisation at one point in time. Consequently the prevalence of latex sensitisation may have been underestimated as it is possible that HCWs who had already developed latex sensitisation have left the hospital before the study was conducted. Some of the observed associations in the study may be as a result of a complex interplay between the healthy worker effect, reverse causality and exposure

reduction by the introduction of powder free latex gloves. These interactions can be better explored and understood in a longitudinal study. Recall bias is another potential limitation in this study as workers were asked to recall the number of gloves used in the past 7 working days. HCWs may have overestimated or underestimated their individual exposures. Our study depended on self-reporting of personal and family atopic disorders and this may have resulted in the misclassification of atopy. The role of atopy and cross-reactivity between allergens is a complex phenomenon which cannot be investigated in cross sectional study. Therefore, cohort studies are necessary to disentangle this phenomenon.

CONCLUSION

This study shows that even in the presence of powder free hypoallergenic glove use there is latex sensitisation and latex allergy, adding to previous findings that HCWs exposed to hypoallergenic latex gloves are still at risk for developing latex sensitisation and latex allergy. This indicates that latex sensitisation and allergy are still an important occupational hazard for HCWs. While it may be economically impractical to replace the latex gloves in our setting, reduction of allergen content in latex products is another strategy that can be implemented to address the problem and protect HCWs. A policy accompanied by clear implementation plans as well as sustainable education and training programmes to address latex sensitisation and allergy among HCWs should be implemented.[39] In addition HCWs must be continuously monitored for the development of latex sensitisation and alternate latex free glove must be made available for them. More research is needed to identify the most cost effective way of implementing a latex free environment in resource limited countries, such as South Africa. In addition the current studies in South Africa have largely been cross-sectional in nature. More cohort analysis is required to better understand the chronicity of illness and disability associated with latex allergy.

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Contributorship

Dr Shumani Phaswana is the principal investigator who was involved from the conception of the idea, proposal writing, data collection, data management and interpretation of the results.

Dr Saloshni Naidoo contributed to the conception and design of the study, analysis and interpretation of the data, critical review of the intellectual content of the article and final approval of the article.

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None

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TABLES

Table 1: Demographics and associated risk factors amongst latex exposed and unexposed healthcare workers at King Edward VIII Hospital, KwaZulu-Natal South Africa, (n=501)

Characteristic	Exposed N (%)	Unexposed N (%)
Number of participants	337 (67.3)	164 (32.7)
Demographics		
Age (years)		
≤30	30(8.9)	19(11.6)
>30-40	121(35.9)	40(24.4)
>40-50	101(29.9)	59(35.9)
>50	85(25.2)	46(28.1)
Duration of employment (years)		
≤5	39(11.6)	28(17.1)
>5-10**	135(40.1)	32(19.5)
>10-15	49(14.5)	17(10.4)
>15-20	24(7.1)	20(12.2)
>20*	90(26.7)	67(40.9)
Sex **		
Female	309(91.7)	95(57.9)
Male	28(8.3)	69(42.1)
Job Title (yes)		
Administrative		164(100.0)
Professional nurses	123(36.5)	
Enrolled nurses	141(41.8)	
Enrolled nursing assistants	73 (21.7)	
Medical and Personal History		
Personal history of Allergy Disease (yes)	147(43.6)	83(50.6)
Family history of Allergy Disease (yes)	197(58.5)	102(62.2)
Fruit allergy (yes)	29(8.6)	9(5.5)
Previous open surgery (yes)*	168(49.8)	61(37.2)
Work-related allergy symptoms(yes)*	138(40.9)	52(31.7)
Non-occupational latex exposure (yes)	161(47.8)	76(46.3)
Latex sensitisation (yes)	24(7.1)	5(3.1)
Current latex allergy (yes)*	20(5.9)	3(1.8)

Chi square, *p<0.05, **p<0.001

Table 2: Comparison of risk factors between latex sensitised (skin prick test positive) and non-sensitised (skin prick test negative) healthcare workers at King Edward VIII Hospital, KwaZulu-Natal South Africa (n=501)

Characteristics	Latex SPT +ve[ǂ] (29) N (%)	Latex SPT –ve[ǂǂ] (472) N (%)
Demographics		
Age (years.)		
≤30	1 (3.5)	48(10.2)
>30-40	13 (44.8)	148(31.4)
>40-50	8 (27.6)	152(32.2)
>50	7 (24.1)	124(26.3)
Duration of employment		
≤5	3(10.3)	64(13.6)
>5-10	16(55.2)	151(31.9)
>10-15	3(10.3)	63(13.4)
>15-20	1(3.5)	43(9.1)
>20	6(20.7)	151(31.9)
Sex (yes)		
Male	5(17.2)	118(25.0)
Female	24(82.8)	354(75.0)
Job Title (yes)		
Administrative	5(17.2)	159(33.7)
Professional nurses	5(17.2)	118(25.0)
Enrolled nurses	14(48.3)	127(26.9)
Enrolled nursing assistants	5(17.2)	68(14.4)
Latex Exposure		
Exposure status(yes)	24 (82.8)	313(66.3)
Type of gloves		
None	5(17.2)	165(34.6)
Exclusive powdered latex glove (yes)	2(6.9)	36(7.6)
Exclusive powder free latex glove (yes)*	11(37.9)	77(16.3)
Mixed (yes)	11(37.9)	198(41.9)
Medical and Personal History		
Personal history of Allergy Disease (yes)	16(55.2)	214(45.3)
Family history of Allergy Disease (yes)	18(62.1)	281(59.5)
Fruit allergy (yes) *	5(17.2)	33(6.9)
Previous open surgery (yes)	18(62.1)	211(44.7)
Non-occupational latex exposure (yes)	12(41.4)	225(47.7)
Reaction to other latex medical devices (yes)*	3(10.3)	8(1.7)

Chi Square, *p<0.05

[ǂ]Latex Skin Prick Test Positive

[ǂǂ]Latex Skin Prick Test Negative

Table 3: Crude Odds Ratios (OR) (95%CI) of demographics, exposure status, medical and personal history and latex sensitisation and latex allergy amongst healthcare workers at King Edward VIII Hospital, KwaZulu-Natal South Africa, (n=501)

Characteristics	N=29	Latex Sensitisation OR (95%CI)	N=23	LA[ǂǂ] OR (95%CI)
Demographics				
Age (years)				
≤30	1	0.3(0.0-1.9)	1	0.4(0.0-2.4)
>30-40	13	1.8(0.8-3.7)	11	2.0(0.9-4.6)
>40-50	8	0.8(0.4-1.8)	7	0.9(0.4-2.2)
>50	7	0.8(0.4-2.1)	4	0.6(0.2-1.7)
Duration of employment (years)				
<5	3	0.7(0.2-2.4)	3	0.9(0.3-3.2)
5-10	16	2.6(1.2-5.5)*	14	3.3(1.4-7.6)*
>10-15	3	0.7(0.2-2.4)	3	0.9(0.3-3.2)
>15-20	1	0.4(0.0-2.1)	1	0.5(0.0-2.8)
>20	6	0.5(0.2-1.4)	2	0.2(0.0-0.8)*
Sex (yes)				
Female	24	1.6(0.6-4.1)	20	2.2(0.7-7.2)
Job Title (yes)				
Administrative	5	0.4(0.2-1.1)	3	0.3(0.1-0.9)*
Professional nurses	5	0.6(0.2-1.6)	4	0.6(0.2-1.8)
Enrolled nurses	14	2.5(1.2-5.3)*	11	2.4(1.1-5.6)*
Enrolled nursing assistants	5	1.2(0.5-3.3)	5	1.7(0.6-4.5)
Latex Exposure				
Exposure status (yes)	24	2.4(0.9-6.3)	20	3.4(1.1-10.8)*
Type of gloves				
None	5	0.4(0.2-1.0)	3	0.3(0.1-0.9)*
Exclusive Powdered latex glove (yes)	2	0.9(0.0-3.6)	2	1.2(0.0-1.7)
Exclusive Powder free latex glove (yes)	11	3.1(1.4-6.8)*	10	3.1(1.7-9.1)*
Mixed gloves(yes)	11	0.8(0.4-1.8)	8	0.7(0.3-1.7)
Medical and Personal History				
Personal history of Allergy Disease (yes)	16	1.4(0.7-3.1)	12	1.3(0.5-2.9)
Family history of Allergy Disease (yes)	18	1.1(0.5-2.4)	14	1.1(0.5-2.4)
Fruit allergy (yes)	5	2.8(1.0-7.5)	5	3.7(1.4-10.0)*
Previous open surgery (yes)	18	1.1(0.5-2.4)	14	1.5(0.7-3.1)

Chi square, *p<0.05

[ǂ] Latex Skin Prick Test Positive

[ǂǂ] Latex Skin Prick Test Positive and work related clinical symptoms of allergy

Table 4: Multivariate analysis of demographics, medical and personal history, exposure history and latex sensitisation (LS)ǂ and latex allergy (LA)ǂǂ amongst healthcare workers at King Edward III Hospital, KwaZulu-Natal South Africa, (n=501)

	MODEL I* (n=501)		MODEL II** (n=501)		MODEL III***(n=202)		MODEL IV****(n=252)	
Characteristics	LS OR (95%CI)	LA OR (95%CI)	LS OR (95%CI)	LA OR (95%CI)	LS OR (95%CI)	LA OR (95%CI)	LS OR (95%CI)	LA OR (95%CI)
Demographics								
Sex (female)	0.9(0.2-2.7)	1.1(0.3-4.4)	0.9(0.3-2.7)	1.1(0.3-4.5)	0.3(0.0-1.8)	0.3(0.0-3.1)	2.5(0.5-12.2)	2.5(0.5-12.2)
Duration of employment (years)	0.9(0.9-1.0)	0.9(0.8-0.9)	0.9(0.9-1.0)	0.9(0.8-0.8)	0.9(0.9-1.8)	0.7(0.5-1.0)	0.9(0.9-1.0)	0.9(0.9-1.0)
Latex Exposure								
Exposure status(yes)	2.2(0.7-6.7)	2.6(0.7-9.8)						
Type of gloves								
None			1	1				
Exclusive lightly powdered latex glove (yes)			1.6(0.3-9.8)	2.6(0.4-17.7)				
Exclusive Powder free latex glove (yes)			4.2(1.2-14.1)	5.1(1.2-21.2)				
Mixed gloves (yes)			1.7(0.5-5.6)	1.7(0.4-7.1)				

Pairs of Powdered latex Gloves in the last 7 days					1.1(1.0-1.2)	1.2(1.0-1.4)		
Pairs of Powder Free Latex Gloves in the last 7 days							1.0(0.9-1.1)	1.0(0.9-1.1)
Personal and Medical History								
Personal history of allergy disease (yes)	1.5(0.7-3.3)	1.4(0.6-3.2)	1.5(0.7-3.3)	1.3(0.6-3.2)	1.4(0.3-6.8)	1.6(0.2-11.6)	1.0(0.4-2.9)	0.9(0.3-2.8)
Family history of allergy disease (yes)	1.0(0.45-2.2)	0.9(0.4-2.2)	1.1(0.5-2.3)	0.9(0.4-2.3)	0.4(0.1-1.9)	0.5(0.1-3.6)	0.7(0.2-2.0)	0.8(0.3-2.7)
Fruit allergy (yes)	2.3(0.8-6.7)	3.1(1.1-9.2)	2.2(0.8-6.5)	3.0(0.9-9.1)	5.0(0.4-56.9)	9.7(0.6-163.0)	1.7(0.3-8.5)	2.0(0.4-10.4)
Previous open surgery (yes)	2.0(0.9-4.4)	1.9(0.8-4.6)	2.1(0.9-4.6)	1.9(0.8-4.7)	1.4(0.3-7.4)	1.2(0.1-11.1)	1.1(0.4-3.2)	1.2(0.4-3.8)

ǂLatex Skin Prick Test Positive

ǂǂLatex Skin Prick Test Positive and work related clinical symptoms of allergy
*Model included latex glove exposure status
**Model included type of gloves
***Model included number of pairs of powdered latex gloves
****Model included number of pairs of powder free latex gloves

STROBE Statement—Checklist of items that should be included in reports of ***cross-sectional studies***

	Item No	Recommendation
Title and abstract	1	(*a*) Indicate the study's design with a commonly used term in the title or the abstract
		(*b*) Provide in the abstract an informative and balanced summary of what was done and what was found
Introduction		
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported
Objectives	3	State specific objectives, including any prespecified hypotheses
Methods		
Study design	4	Present key elements of study design early in the paper
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection
Participants	6	(*a*) Give the eligibility criteria, and the sources and methods of selection of participants
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group
Bias	9	Describe any efforts to address potential sources of bias
Study size	10	Explain how the study size was arrived at
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why
Statistical methods	12	(*a*) Describe all statistical methods, including those used to control for confounding
		(*b*) Describe any methods used to examine subgroups and interactions
		(*c*) Explain how missing data were addressed
		(*d*) If applicable, describe analytical methods taking account of sampling strategy
		(*e*) Describe any sensitivity analyses
Results		
Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed
		(b) Give reasons for non-participation at each stage
		(c) Consider use of a flow diagram
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders
		(b) Indicate number of participants with missing data for each variable of interest
Outcome data	15*	Report numbers of outcome events or summary measures
Main results	16	(*a*) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included
		(*b*) Report category boundaries when continuous variables were categorized
		(*c*) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses

Discussion		
Key results	18	Summarise key results with reference to study objectives
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence
Generalisability	21	Discuss the generalisability (external validity) of the study results
Other information		
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based

*Give information separately for exposed and unexposed groups.

Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at http://www.plosmedicine.org/, Annals of Internal Medicine at http://www.annals.org/, and Epidemiology at http://www.epidem.com/). Information on the STROBE Initiative is available at www.strobe-statement.org.

The prevalence of latex sensitisation and allergy and associated risk factors among healthcare workers using hypoallergenic latex gloves at King Edward VIII Hospital, KwaZulu-Natal South Africa: A cross sectional study

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ARTICLE SUMMARY

ARTICLE FOCUS

- The use of hypoallergenic latex gloves has been adopted as policy in different healthcare settings globally.
- However, information with regard to their use and the development of latex sensitisation and allergy among exposed healthcare workers is limited.
- We hypothesised that there is latex sensitization and allergy in healthcare workers using hypoallergenic latex gloves in a South African hospital.

KEY MESSAGE

- In the presence of powder free hypoallergenic gloves, latex sensitisation and latex allergy is still an important occupational health effect in healthcare workers.
- Healthcare workers should be continuously monitored for the development of latex sensitisation and allergy.
- There is a need for a national policy accompanied by clear implementation plans as well as sustainable education and training programmes to address latex sensitisation and allergy among HCWs.

STRENGTH AND LIMITATIONS

- Strength of the study included the presence of a control group providing a background prevalence of latex sensitisation in this population and random selection of participants which minimised the potential of participant bias that arises with a volunteer approach.
- This study was limited by the cross sectional study design as it only allowed for the determination of the prevalence of latex sensitisation; recall bias with regard to the number of gloves used in the past 7 working days and the self-reporting of personal and family atopic disorders may have resulted in the misclassification of exposure and atopy respectively.

What this paper adds

- In the presence of powder free hypoallergenic gloves, latex sensitisation and latex allergy is still an important occupational health hazard in healthcare workers

- Healthcare workers should be continuously monitored for the development of latex sensitisation and allergy

- There is a need for a national policy accompanied by clear implementation plans as well as sustainable education and training programmes to address latex sensitisation and allergy among HCWs

ABSTRACT

Objectives

The present study describes latex sensitisation and allergy prevalence and associated factors among healthcare workers using hypoallergenic latex gloves at King Edward VIII Hospital in KwaZulu-Natal South Africa.

Design

Cross sectional study

Setting

A tertiary hospital in eThekwini municipality, KwaZulu Natal, South Africa

Participants

600 healthcare workers were randomly selected and 501(337 exposed and 164 unexposed) participated. Participants who were pregnant, less than one year of work as healthcare worker and history of anaphylactic reaction were excluded from the study.

Primary and secondary outcome measures

Latex sensitisation and latex allergy were the outcome of interest and they were successfully measured

Results

Prevalence of latex sensitisation and allergy was observed among exposed workers (7.1% and 5.9%) and unexposed workers (3.1% and 1.8%). Work related allergy symptoms were significantly higher in exposed workers (40.9%, $p<0.05$). Duration of employment was inversely associated with latex allergy (OR: 0.9; 95% CI: 0.8-0.9). The risk of latex sensitisation (OR: 4.2; 95% CI: 1.2-14.1) and allergy (OR:

5.1; 95% CI: 1.2-21.2) increased with exclusive use of powder-free latex gloves. A dose –response relationship was observed for powdered latex gloves (OR: 1.1; 95% CI: 1.0-1.2). Atopy (OR: 1.5; 95% CI: 0.7-3.3 and OR: 1.4; 95% CI: 0.6-3.2) and fruit allergy (OR: 2.3; 95% CI: 0.8-6.7 and OR: 3.1; 95% CI: 1.1-9.2) also increased the risk of latex sensitisation and allergy.

Conclusion

This study adds to previous findings that healthcare workers exposed to hypoallergenic latex gloves are at risk for developing latex sensitisation highlighting its importance as an occupational hazard in healthcare. More research is needed to identify the most cost effective way of implementing a latex free environment in resource limited countries, such as South Africa. In addition more cohort analysis is required to better understand the chronicity of illness and disability associated with latex allergy.

INTRODUCTION

Latex allergy (LA) as an occupational disease among healthcare workers (HCWs) gained recognition after Nutter published a case report of contact urticaria in a HCW in 1979.[1] The increase in prevalence coincided with the emergence of the Human Immunodeficiency Virus/ Acquired immunodeficiency syndrome (HIV/AIDS) epidemic and the introduction of "universal precautions" in the healthcare industry which had resulted in the increased use of latex gloves among HCWs.[2]

Latex gloves are preferred due to their superior barrier and physical properties as compared to the non-latex gloves.[3] International epidemiological studies have reported the prevalence of latex allergy among HCWs to range between 2-22% depending on the population and diagnostic methods used.[4-11] The prevalence in the general population has been reported to range between 1-6%.[12, 13] In South Africa studies amongst HCWs reported a latex sensitisation prevalence of between 2.7 to 20.8%.[14-16] Latex allergy in HCWs is a compensable disease in South Africa in terms of the Compensation of Occupational Injuries and Diseases Act No. 130 of 1993.[17]

Powdered latex gloves were identified as an important risk factor for latex sensitisation and allergy in HCWs as they were found to contain high allergenic protein content.[18] Following these findings, hypoallergenic gloves with low allergen content namely, low powdered and powder free latex gloves were introduced. The European definition of powder free gloves is gloves with powder content not exceeding 2 mg per glove and leachable latex protein which is as low as is reasonably practical.[19]

Hypoallergenic gloves have been associated with reduced latex aeroallergen concentrations, reduced conversion rates and a subsequent decrease in clinic visits, and compensation claims for

latex induced occupational asthma and allergic contact dermatitis among HCWs.[18, 20] As much as the use of low or powder free gloves has been shown to reduce latex related symptoms, other studies have shown that exposed HCWs still exhibit symptoms at very low levels of measureable airborne latex allergens.[21] Most studies have reported on the airborne levels and inhalational route of exposure hence the recommendation on low powdered or powder free latex gloves. There is little consideration given to the dermal route of exposure despite the fact that exposure is as a result of direct contact in these instances.[22] Eliminating the cornstarch powder only removed the carrier and not the source of allergen which is in the latex itself. Therefore workers using powder free gloves are still exposed to the allergenic content of latex gloves. It has been shown that different brands from different suppliers contain differing levels of protein due to a lack of standards in latex glove manufacture.[23] A South African study reported that some powder free latex gloves were found to have high allergenic protein content.[23] HCWs using these gloves are exposed via direct dermal contact and are at risk for developing latex sensitization which maybe asymptomatic and if exposure continues they can later develop latex allergy which presents with clinical manifestations.

While it is important to diagnose and manage an individual worker with latex allergy in the early stages of the disease, complete control of hazardous substance in the workplace is equally if not more important. While a latex free work environment would be a preferred control strategy, substitution of powdered latex gloves with powder free gloves was shown to be cost effective and associated with improved clinical outcome.[20, 24-26] As a result this was adopted as the most reasonable and practical approach in addressing the problem of latex allergy among HCWs both internationally and to some extent nationally.[27-29] This has proven to reduce latex induced clinical outcomes. Even with this intervention, studies in Western countries such as Germany

and the UK have shown that the risk of latex sensitisation still exists and more needs to be done to protect HCWs.[30, 31]

The current study described the prevalence of latex sensitisation and allergy among healthcare workers who use hypoallergenic powder free and lightly powdered latex gloves.

METHODS

Study design and population

This was a cross sectional study conducted between July 2011 and January 2012. The study location was King Edward VIII hospital, the second largest hospital in the Southern hemisphere, providing regional and tertiary services to the whole of KwaZulu-Natal (KZN) and the Eastern Cape Province in South Africa. It has a bed status of 1300 and has a workforce of 2400. The hospital was chosen due to the large workforce with different departments, and the policy of using both powder free and low powdered latex gloves for approximately 10 years.

The study population was limited to HCWs currently employed at King Edward VIII Hospital for more than 12 months. HCWs were defined as all personnel employed in the hospital.

The prevalence of latex sensitization in HCWs using powdered latex gloves in the Western Cape Province was 11.9% in 2001.[16] We expected the prevalence at King Edward VIII hospital to be less than the 11.9% observed in the Western Cape Province due to the adoption of a hypoallergenic latex glove policy in 2001. Using EPI Info calculator version 3.04.04., it was assumed that 50% of sensitised workers have remained sensitised despite the introduction of hypoallergenic latex gloves 10 years prior. Using an expected latex sensitization prevalence of 6% for the exposed group and the prevalence among the general population being reported as

less than 1% the required sample size was calculated to be 585 participants 2 exposed participants for every 1 non-exposed participant (exposed =390; unexposed =195). HCWs were considered to be exposed if they were likely to use gloves. Unexposed HCWs were drawn from the administrative staff of the hospital.

Questionnaire

We used an adaptation of the questionnaire used in an epidemiological study conducted at Groote Schuur in 2001[16] with permission from Professor Paul Potter, Allergology Unit, Medical School, University of Cape Town. The questionnaire containing open and closed ended questions was adapted to include items on exposure assessment. The questionnaire was administered by a trained research assistant immediately prior to the skin prick test. The questionnaire collected data on the participants' demographics, personal risk factors, latex exposure assessment, clinical manifestations of latex sensitization (dermal and respiratory) and history of previous reactions suggestive of latex allergy.

Exposure Assessment

Individual Exposure

Individual latex exposure was determined by the type of gloves used, number of gloves used per day, and duration of glove use. The information was limited to 7 working shifts/days prior to the interview.

Departmental Exposure

Departmental exposure was defined as glove usage in the past 12 months (01 January 2011-31 December 2011). The overall departmental exposure was obtained by reviewing monthly glove usage by each department from the stock room register. This was used to estimate the annual exposure for employees who had rotated through different departments in the past 12 months. Non sterile latex gloves are distributed throughout the clinical departments while a high proportion of sterile gloves are distributed to labour ward, theatre, surgical wards and outpatient departments. Glove type was defined as powdered and powder-free and latex free based on the previous literature.[23, 32]

Skin prick test (SPT)

The SPT was conducted using the Stallergenes kit.[32] It was performed in a room with access to emergency resuscitation services by a trained research assistant. The research assistant and principal investigator were trained on 2 separate occasions. The test was performed on the inner aspect of the participants' forearms, between the wrist and the elbow on normal skin. A positive and negative control were performed using histamine (0.61% concentration of phenol) and buffered normal saline solution respectively on the same arm and they were 3 cm apart to prevent cross contamination. The protein concentration of the latex extract was 500µg/ml and the solution was applied as it was with no further dilutions. After 15-20 minutes subsequent to puncturing the skin, the SPT reaction wheal and flare was outlined by a black ink and clear tape was used to transfer the outline from skin to the results sheet by the trained research assistant or principal investigator.[33] A positive result was indicated by a mean wheal diameter measuring 3 mm or greater than the negative control. Results were recorded on a standardized result sheet. The research assistant's test performance was audited by the principal investigator at regular intervals to ensure correctness of technique and interpretation of the results.

Informed signed consent was obtained from all the participants prior to participation. They had the option of participating in the questionnaire interview and the SPT or refusing the SPT. The study protocol was approved by the Biomedical Research Ethics Committee of the University of KwaZulu-Natal (BE048/11). Permission to conduct the study was also obtained from the KZN Provincial Department of Health and King Edward VIII hospital management.

Statistical analysis

Data was captured in Excel and analysed in Stata Version 11. Frequencies and medians with ranges were presented for categorical and continuous variables respectively. The Chi-square and the Kruskal-Wallis test were used to test for significant associations between categorical and continuous variables and the dependent variables under study on bivariate analysis, respectively.

Binary logistic regression was used to test for significant associations between independent and dependent variables on multivariate analysis. The dependent variables used in the regression analysis were: Latex sensitisation, which was defined as having a SPT wheal of ≥3mm to latex extract; Latex allergy (LA) was defined as being SPT positive and a report of having any one or more of the listed work related clinical symptoms namely itchy eyes, red eyes, runny eyes, runny nose, itchy nose, sneezing, coughing, tight chest, wheezing, itchy skin, skin rash or dizziness. Independent variables that were considered for analysis were as follows: Age (yrs.) and sex, duration of employment, job title, current department employed in, type of gloves used, number of pairs of gloves used per day, self reported and family history of atopy, food allergy and previous history of open surgery and number of surgical procedures. In the multivariate analysis, age was omitted due to collinearity with duration of employment. Departmental glove consumption was omitted as this only indicated annual distribution of gloves per department and

not necessarily employees' exposure since enrolled nursing assistants and enrolled nurses are rotated through different departments in any given year. The number of pair of gloves was used as an indicator of individual latex glove exposure. The variable number of pairs of gloves used and duration of employment were retained as continuous variables in the multivariate model. Fractional polynomial and a fractional plot was used to visualise the dose-response relationship of these continuous exposure variables.

RESULTS

Participant Demographics

Sixty five HCWs refused to participate in the study. Among the 520 HCWs who responded to the invitation there was an overall participation rate of 85.5 % (n=501) with 3.6% (n=19) refusing SPT. There was no significant difference between those refusing SPT and those who had the SPT with respect to latex exposure status, age, sex and duration of employment.

The median age of participants was 42.2 years (range: 22 years-65 years) with the greater proportion of them being females. The median duration of employment was 10.9 years (range: 1 year-42 years) with the majority of exposed participants having worked as a HCW for < 10 years. Most unexposed healthcare workers had been employed for > 20 years. Personal and family history of allergy was more prevalent among unexposed HCWs while exposed HCWS reported a higher prevalence of a fruit allergy and history of previous surgery (Table 1).

Prevalence of Latex Sensitisation and Allergy

The overall prevalence of latex sensitisation and latex allergy were 5.9% (n=29) and 4.6% (n=23) respectively. Although the difference was not significant, the prevalence of latex

sensitisation was higher among the exposed group (7.1%) as compared to the unexposed group (3.1%). Latex allergy was significantly higher in the exposed group than unexposed group (5.9% vs 1.8%, p=0.04). There was a significant difference in the work related allergy symptoms between exposed and unexposed workers (40.9% *vs.* 31.7%, p=0.04) (Table 1). Symptoms that were significantly associated with latex sensitisation were skin rash (p< 0.000), itchy skin (p=0.001), runny nose (p=0.004), red eyes (p=0.01) and itchy eyes (p=0.01).

The prevalence of latex sensitization was higher among those who were exposed and those with employment duration of < 10yrs. Although the prevalence of latex sensitisation was lower among participants < 30 years of age, there was no significant variation with age or sex. There was a significant difference (p=0.04) in the prevalence of fruit allergy between those participants with latex sensitisation (17.2%) and unsensitised participants (6.9%) The exclusive use of powder free latex gloves was found to be significantly (p=0.003) higher among the participants who had latex sensitisation. There was equal distribution of powdered and powder free latex gloves among those who reported the use of mixed gloves. The prevalence of reporting previous open surgery and use of other non- occupational exposure latex containing material did not vary significantly between those who had latex sensitisation and those who were unsensitised. There was a significantly higher prevalence of reporting allergic reactions when handling other latex containing medical equipment among participants with latex allergy as compared to unsensitised participants (10.3% vs 1.7%, p=0.002) (Table 2).

Crude association of demographics, exposure status, medical and personal history and latex sensitisation, latex allergy

Latex exposure was significantly associated with latex allergy (OR: 3.4; 95% CI: 1.1-10.8). Working as a HCW for 5-9 years was significantly associated with latex sensitisation (OR: 2.6; 95% CI: 1.2-5.5) and latex allergy (OR: 3.3; 95% CI: 1.4-7.6), respectively. Employment duration as a HCW for >20 years was protective against latex allergy (OR: 0.2; 95% CI: 0.0-0.8). In comparison with unexposed workers, working as an enrolled nurse was significantly associated with both latex sensitisation (OR: 2.5; 95% CI: 1.2-5.3) and latex allergy (OR: 2.4; 95% CI: 1.1-5.6). The exclusive use of powder free latex gloves was significantly associated with latex sensitisation (OR: 3.1; 95% CI: 1.4-6.8) and latex allergy (OR: 3.1; 95% CI: 1.7-9.1). Powdered and powder free latex gloves were equally distributed among those who reported the use of mixed gloves. The annual consumption of pairs of gloves per HCW by department was ranked and grouped into tertiles. Although medical and surgical wards had low and moderate pairs of gloves consumption per HCW, these wards had the highest proportion of workers with latex sensitisation (n=6, 20.0% each). However the relation was only significant for those who reported the medical ward as being the current department in which they worked (p=0.01). The proportions for powdered latex glove use were 71% and 69% in medical and surgical wards, respectively and this was not statistically significant. Exposure to other latex containing medical devices was not significantly different from what was reported in other wards. There was no significant association between reported personal history of allergy disease, latex sensitisation and latex allergy. Fruit allergy was significantly associated with latex allergy (OR: 3.7; 95%: 1.4-10.4) (Table 3). Listed fruits were evaluated for their independent association with latex sensitisation. Avocado (OR: 12.3; 95% CI: 5.1-29.6) and others (OR: 5.1; 95% CI: 2.1-11.8) which included pineapple and orange showed significant associations with latex sensitisation (data not shown).

Multivariate analysis

While latex exposure had estimates of the OR above 2, there was no significant association with latex sensitisation and latex allergy. Duration of employment was found to be inversely associated with latex allergy in models I and II. The exclusive use of powder free latex gloves was significantly associated with latex sensitisation (OR: 4.2: 95% CI: 1.2-14.1) and latex allergy (OR: 5.1; 95%CI: 1.2-21.2) on multivariate analysis. This significant association disappeared when examining the number of pairs of powder free gloves used in the last 7 days. A weak association was observed for the number of pairs of powdered latex gloves used in the last 7 days with both latex sensitisation and latex allergy (model III and IV).Further analysis of duration of employment and number of pairs of gloves using fractional polynomial failed to demonstrate a dose-response relationship with either latex sensitisation or latex allergy. There was a significant association between fruit allergy and latex allergy in model I (OR: 3.1: 95% CI: 1.1-9.2) (Table 4).

DISCUSSION

This is an important study for South African HCWs as it examined the risk of latex sensitisation in a group of workers exposed to hypoallergenic latex gloves. As previously mentioned there has been no literature documenting the prevalence of latex sensitisation among South African HCWs using hypoallergenic lightly powered or powder-free latex gloves. The prevalence of latex sensitisation among exposed HCWs (7.1%) in this study is comparable to findings among HCWs in another South African hospital.[14] However it was considerably lower than the 11.9% prevalence reported by Potter in the same year.[16] While a substantial number of participants (37%) reported work related allergy symptoms, only 4.6% met our definition of latex allergy. The important symptoms associated with latex sensitisation were skin rash, itchy skin, runny

nose, red and itchy eyes in keeping with previous studies. Elimination of powdered latex gloves has shown a reduction in the concentration of aeroallergens in the operating room with the low prevalence of latex allergy in our study population.

Although the relationship was weak, this study showed that the risk of latex sensitisation decreases with duration of employment. The healthy worker effect is a possible explanation of this finding. Prior to availability of hypoallergenic latex gloves, workers who had developed latex allergy may have left employment or they may have changed their career path and moved into a more administrative or managerial role with no contact with latex gloves. Furthermore new employees are only sensitised and have not yet manifested clinical symptoms and they continue using latex gloves. On the other hand senior HCWs may have been sensitised during their earlier years of employment and as a result they either moved to departments with less exposure to latex gloves or deliberately avoid latex containing products and therefore exhibit less latex related symptoms. Moreover, the introduction of hypoallergenic gloves 10 years prior to the study may explain the reduced sensitisation in senior HCWs as demonstrated in the study by Smith et al in 2007. The published literature has been inconsistent in reporting the association between duration of employment and latex sensitisation. Although latex is one of the best studied allergens, no exposure response studies have been published with measured latex allergen levels. In addition, studies have demonstrated variation in allergen content of different gloves. These may lead to discrepancies in the literature with regard to the role of duration of employment as a surrogate measure of exposure.

In our study HCWs who exclusively used powdered free latex gloves had a 4 times greater odds of developing latex sensitisation. The fact that HCWs with latex sensitisation or allergy work more often with powder free latex gloves is indicative of reverse causality because of symptoms.

Moreover the background prevalence of latex sensitisation in this study was relatively higher (3.5%) than previously reported prevalence in the general population by Bousquet et al.[13] Studies have shown that some of these "hypoallergenic" latex gloves actually contain high levels of allergens which can be release into the environment with aggressive manipulation.[23] Some of the sensitised HCWs may have been sensitised before the hospital implemented a hypoallergenic latex glove policy. Also Smith et al showed that complete avoidance of powdered latex glove can result in the reduction or no change in measurable IgE antibodies.[34] A study in Germany reported a high prevalence of 8% among 226 dental students who had only been exposed to exclusive powder free latex gloves.[30] Similarly in the UK despite a total ban on powdered latex gloves Clayton found a 10% prevalence of latex sensitisation in HCWs.[31] It is also not clear to what extent the aeroallergens released by colleagues using powdered latex gloves influence this finding. Furthermore the role of other latex containing medical devices during sensitisation period cannot be entirely ruled out.

In our study, frequency of exposure as measured by the number of gloves used in the last 7 working days showed a weak association between powdered latex gloves and latex sensitisation but no association could be demonstrated with powder free latex gloves. Airborne latex aeroallergens have been shown to increase with the number of powdered gloves used which subsequently increases the risk of latex sensitisation and clinical latex glove related allergy symptoms.[18]

The positive association between department with low glove consumption per HCW and latex sensitisation is in contrast with previous finding by Liss and co-workers.[9] They reported positive association with departments that had high glove consumption per HCWs. Again, this could be as a result of reverse causality where HCWs with latex sensitisation may have been relocated to

wards with low glove consumption to minimise the exposure. In addition, the annual pair of gloves consumption per HCW by department does not provide an accurate indication of individual exposure; rather it gives us the annual distribution of gloves to different departments.

Several studies have reported atopy as a significant risk factor for latex sensitisation.[9, 10, 35] Similarly, the prevalence of reporting a history of personal atopy in this study was higher among latex sensitised participants although the association was not statistically significant. The role of atopy is complex because some individuals might also have become atopic after having been latex sensitised and cross sectional study is not suitable in establishing this association.

Fruit latex allergy syndrome is a phenomenon seen where latex sensitised individuals demonstrate a cross reactivity with specific foods; particularly fruit. Studies have identified this phenomenon among sensitised HCWs and the general population. This has been attributed to the similarity between fruit proteins and latex allergens.[36] Fruit allergy was significantly associated with latex sensitisation and latex allergy in our study. Our study was dependent on the self-reporting of fruit allergy and no objective tests were carried out. It is therefore possible that participants have independent simultaneous allergies to both fruit and latex without cross reactivity. Also, we were unable to determine whether latex sensitisation preceded the development of fruit allergy or vice versa. Fruit allergy prior to latex exposure could have contributed to the association observed in our study.

Latex sensitised participants reported a high prevalence of a history of previous open surgery in our study. This has been reported to occur as a result of direct intraoperative exposure to latex containing medical devices such as catheters or tubes. Studies in children with congenital abnormalities have demonstrated that the risk for latex allergy increases with the number of open

surgical procedures that they undergo.[37] Frequency of invasive procedures among adults was shown to increase the risk of latex sensitisation reporting while more than 10 procedures increased the risk of developing latex allergy.[38]

Strengths of this study include the high response rate (85.5%) and comparability to other studies.[8, 16] Access to the hospital employee database allowed us to better assess the representativeness of this study population by comparing demographic data of the non-participants and the participants. The participants were randomly selected minimising the potential of participant's bias that comes with a volunteer approach.

The presence of a control group provided a background prevalence of latex sensitisation in this population which allowed for a better estimation of associations attributable to work related factors. The use of Stallergenes latex specific SPT further strengthens the study. The SPT test is regarded as the gold standard for the diagnosis of latex allergy and Stallergenes has been shown to have a diagnostic sensitivity and specificity of 93% and 100%, respectively.[32] The research assistant employed on this study was trained and initially shadowed and periodically supervised by the principal investigator to ensure appropriate administration of the questionnaire and the SPT thereby improving the reliability and validity of the study.

This study was limited by the cross sectional study design which was relatively low in cost and quick to conduct. It only allowed for the determination of prevalence of latex sensitisation at one point in time. Consequently the prevalence of latex sensitisation may have been underestimated as it is possible that HCWs who had already developed latex sensitisation have left the hospital before the study was conducted. Some of the observed associations in the study may be as a result of a complex interplay between the healthy worker effect, reverse causality and exposure

reduction by the introduction of powder free latex gloves. These interactions can be better explored and understood in a longitudinal study. Recall bias is another potential limitation in this study as workers were asked to recall the number of gloves used in the past 7 working days. HCWs may have overestimated or underestimated their individual exposures. Our study depended on self-reporting of personal and family atopic disorders and this may have resulted in the misclassification of atopy. The role of atopy and cross-reactivity between allergens is a complex phenomenon which cannot be investigated in cross sectional study. Therefore, cohort studies are necessary to disentangle this phenomenon.

CONCLUSION

This study shows that even in the presence of powder free hypoallergenic glove use there is latex sensitisation and latex allergy, adding to previous findings that HCWs exposed to hypoallergenic latex gloves are still at risk for developing latex sensitisation and latex allergy. This indicates that latex sensitisation and allergy are still an important occupational hazard for HCWs. While it may be economically impractical to replace the latex gloves in our setting, reduction of allergen content in latex products is another strategy that can be implemented to address the problem and protect HCWs. A policy accompanied by clear implementation plans as well as sustainable education and training programmes to address latex sensitisation and allergy among HCWs should be implemented.[39] In addition HCWs must be continuously monitored for the development of latex sensitisation and alternate latex free glove must be made available for them. More research is needed to identify the most cost effective way of implementing a latex free environment in resource limited countries, such as South Africa. In addition the current studies in South Africa have largely been cross-sectional in nature. More cohort analysis is required to better understand the chronicity of illness and disability associated with latex allergy.

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Contributorship

Dr Shumani Phaswana is the principal investigator who was involved from the conception of the idea, proposal writing, data collection, data management and interpretation of the results.

Dr Saloshni Naidoo contributed to the conception and design of the study, analysis and interpretation of the data, critical review of the intellectual content of the article and final approval of the article.

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TABLES

Table 1: Demographics and associated risk factors amongst latex exposed and unexposed healthcare workers at King Edward VIII Hospital, KwaZulu-Natal South Africa, (n=501)

Characteristic	Exposed N (%)	Unexposed N (%)
Number of participants	337 (67.3)	164 (32.7)
Demographics		
Age (years)		
≤30	30(8.9)	19(11.6)
>30-40	121(35.9)	40(24.4)
>40-50	101(29.9)	59(35.9)
>50	85(25.2)	46(28.1)
Duration of employment (years)		
≤5	39(11.6)	28(17.1)
>5-10**	135(40.1)	32(19.5)
>10-15	49(14.5)	17(10.4)
>15-20	24(7.1)	20(12.2)
>20*	90(26.7)	67(40.9)
Sex **		
Female	309(91.7)	95(57.9)
Male	28(8.3)	69(42.1)
Job Title (yes)		
Administrative		164(100.0)
Professional nurses	123(36.5)	
Enrolled nurses	141(41.8)	
Enrolled nursing assistants	73 (21.7)	
Medical and Personal History		
Personal history of Allergy Disease (yes)	147(43.6)	83(50.6)
Family history of Allergy Disease (yes)	197(58.5)	102(62.2)
Fruit allergy (yes)	29(8.6)	9(5.5)
Previous open surgery (yes)*	168(49.8)	61(37.2)
Work-related allergy symptoms(yes)*	138(40.9)	52(31.7)
Non-occupational latex exposure (yes)	161(47.8)	76(46.3)
Latex sensitisation (yes)	24(7.1)	5(3.1)
Current latex allergy (yes)*	20(5.9)	3(1.8)

Chi square, *p<0.05, **p<0.001

Table 2: Comparison of risk factors between latex sensitised (skin prick test positive) and non-sensitised (skin prick test negative) healthcare workers at King Edward VIII Hospital, KwaZulu-Natal South Africa (n=501)

Characteristics	Latex SPT +ve[ǂ] (29) N (%)	Latex SPT –ve[ǂ ǂ] (472) N (%)
Demographics		
Age (years.)		
≤30	1 (3.5)	48(10.2)
>30-40	13 (44.8)	148(31.4)
>40-50	8 (27.6)	152(32.2)
>50	7 (24.1)	124(26.3)
Duration of employment		
≤5	3(10.3)	64(13.6)
>5-10	16(55.2)	151(31.9)
>10-15	3(10.3)	63(13.4)
>15-20	1(3.5)	43(9.1)
>20	6(20.7)	151(31.9)
Sex (yes)		
Male	5(17.2)	118(25.0)
Female	24(82.8)	354(75.0)
Job Title (yes)		
Administrative	5(17.2)	159(33.7)
Professional nurses	5(17.2)	118(25.0)
Enrolled nurses	14(48.3)	127(26.9)
Enrolled nursing assistants	5(17.2)	68(14.4)
Latex Exposure		
Exposure status(yes)	24 (82.8)	313(66.3)
Type of gloves		
None	5(17.2)	165(34.6)
Exclusive powdered latex glove (yes)	2(6.9)	36(7.6)
Exclusive powder free latex glove (yes)*	11(37.9)	77(16.3)
Mixed (yes)	11(37.9)	198(41.9)
Medical and Personal History		
Personal history of Allergy Disease (yes)	16(55.2)	214(45.3)
Family history of Allergy Disease (yes)	18(62.1)	281(59.5)
Fruit allergy (yes) *	5(17.2)	33(6.9)
Previous open surgery (yes)	18(62.1)	211(44.7)
Non-occupational latex exposure (yes)	12(41.4)	225(47.7)
Reaction to other latex medical devices (yes)*	3(10.3)	8(1.7)

Chi Square, *p<0.05

[ǂ]Latex Skin Prick Test Positive

[ǂ ǂ]Latex Skin Prick Test Negative

Table 3: Crude Odds Ratios (OR) (95%CI) of demographics, exposure status, medical and personal history and latex sensitisation and latex allergy amongst healthcare workers at King Edward VIII Hospital, KwaZulu-Natal South Africa, (n=501)

Characteristics	N=29	Latex Sensitisation OR (95%CI)	N=23	LA[ǂǂ] OR (95%CI)
Demographics				
Age (years)				
≤30	1	0.3(0.0-1.9)	1	0.4(0.0-2.4)
>30-40	13	1.8(0.8-3.7)	11	2.0(0.9-4.6)
>40-50	8	0.8(0.4-1.8)	7	0.9(0.4-2.2)
>50	7	0.8(0.4-2.1)	4	0.6(0.2-1.7)
Duration of employment (years)				
<5	3	0.7(0.2-2.4)	3	0.9(0.3-3.2)
5-10	16	2.6(1.2-5.5)*	14	3.3(1.4-7.6)*
>10-15	3	0.7(0.2-2.4)	3	0.9(0.3-3.2)
>15-20	1	0.4(0.0-2.1)	1	0.5(0.0-2.8)
>20	6	0.5(0.2-1.4)	2	0.2(0.0-0.8)*
Sex (yes)				
Female	24	1.6(0.6-4.1)	20	2.2(0.7-7.2)
Job Title (yes)				
Administrative	5	0.4(0.2-1.1)	3	0.3(0.1-0.9)*
Professional nurses	5	0.6(0.2-1.6)	4	0.6(0.2-1.8)
Enrolled nurses	14	2.5(1.2-5.3)*	11	2.4(1.1-5.6)*
Enrolled nursing assistants	5	1.2(0.5-3.3)	5	1.7(0.6-4.5)
Latex Exposure				
Exposure status (yes)	24	2.4(0.9-6.3)	20	3.4(1.1-10.8)*
Type of gloves				
None	5	0.4(0.2-1.0)	3	0.3(0.1-0.9)*
Exclusive Powdered latex glove (yes)	2	0.9(0.0-3.6)	2	1.2(0.0-1.7)
Exclusive Powder free latex glove (yes)	11	3.1(1.4-6.8)*	10	3.1(1.7-9.1)*
Mixed gloves(yes)	11	0.8(0.4-1.8)	8	0.7(0.3-1.7)
Medical and Personal History				
Personal history of Allergy Disease (yes)	16	1.4(0.7-3.1)	12	1.3(0.5-2.9)
Family history of Allergy Disease (yes)	18	1.1(0.5-2.4)	14	1.1(0.5-2.4)
Fruit allergy (yes)	5	2.8(1.0-7.5)	5	3.7(1.4-10.0)*
Previous open surgery (yes)	18	1.1(0.5-2.4)	14	1.5(0.7-3.1)

Chi square, *p<0.05

[ǂ] Latex Skin Prick Test Positive

[ǂǂ] Latex Skin Prick Test Positive and work related clinical symptoms of allergy

Table 4: Multivariate analysis of demographics, medical and personal history, exposure history and latex sensitisation (LS)ǂ and latex allergy (LA)ǂǂ amongst healthcare workers at King Edward III Hospital, KwaZulu-Natal South Africa, (n=501)

	MODEL I* (n=501)		MODEL II** (n=501)		MODEL III***(n=202)		MODEL IV****(n=252)	
Characteristics	LS OR (95%CI)	LA OR (95%CI)	LS OR (95%CI)	LA OR (95%CI)	LS OR (95%CI)	LA OR (95%CI)	LS OR (95%CI)	LA OR (95%CI)
Demographics								
Sex (female)	0.9(0.2-2.7)	1.1(0.3-4.4)	0.9(0.3-2.7)	1.1(0.3-4.5)	0.3(0.0-1.8)	0.3(0.0-3.1)	2.5(0.5-12.2)	2.5(0.5-12.2)
Duration of employment (years)	0.9(0.9-1.0)	0.9(0.8-0.9)	0.9(0.9-1.0)	0.9(0.8-0.8)	0.9(0.9-1.8)	0.7(0.5-1.0)	0.9(0.9-1.0)	0.9(0.9-1.0)
Latex Exposure								
Exposure status(yes)	2.2(0.7-6.7)	2.6(0.7-9.8)						
Type of gloves								
None			1	1				
Exclusive lightly powdered latex glove (yes)			1.6(0.3-9.8)	2.6(0.4-17.7)				
Exclusive Powder free latex glove (yes)			4.2(1.2-14.1)	5.1(1.2-21.2)				
Mixed gloves (yes)			1.7(0.5-5.6)	1.7(0.4-7.1)				

Pairs of Powdered latex Gloves in the last 7 days					1.1(1.0-1.2)	1.2(1.0-1.4)		
Pairs of Powder Free Latex Gloves in the last 7 days							1.0(0.9-1.1)	1.0(0.9-1.1)
Personal and Medical History								
Personal history of allergy disease (yes)	1.5(0.7-3.3)	1.4(0.6-3.2)	1.5(0.7-3.3)	1.3(0.6-3.2)	1.4(0.3-6.8)	1.6(0.2-11.6)	1.0(0.4-2.9)	0.9(0.3-2.8)
Family history of allergy disease (yes)	1.0(0.45-2.2)	0.9(0.4-2.2)	1.1(0.5-2.3)	0.9(0.4-2.3)	0.4(0.1-1.9)	0.5(0.1-3.6)	0.7(0.2-2.0)	0.8(0.3-2.7)
Fruit allergy (yes)	2.3(0.8-6.7)	3.1(1.1-9.2)	2.2(0.8-6.5)	3.0(0.9-9.1)	5.0(0.4-56.9)	9.7(0.6-163.0)	1.7(0.3-8.5)	2.0(0.4-10.4)
Previous open surgery (yes)	2.0(0.9-4.4)	1.9(0.8-4.6)	2.1(0.9-4.6)	1.9(0.8-4.7)	1.4(0.3-7.4)	1.2(0.1-11.1)	1.1(0.4-3.2)	1.2(0.4-3.8)

ǂLatex Skin Prick Test Positive

ǂǂLatex Skin Prick Test Positive and work related clinical symptoms of allergy
*Model included latex glove exposure status
**Model included type of gloves
***Model included number of pairs of powdered latex gloves
****Model included number of pairs of powder free latex gloves

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The prevalence of latex sensitisation and allergy and associated risk factors among healthcare workers using hypoallergenic latex gloves at King Edward VIII Hospital, KwaZulu-Natal South Africa: A cross sectional study

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ABSTRACT

Objectives

The present study describes latex sensitisation and allergy prevalence and associated factors among healthcare workers using hypoallergenic latex gloves at King Edward VIII Hospital in KwaZulu-Natal South Africa.

Design

Cross sectional study

Setting

A tertiary hospital in eThekwini municipality, KwaZulu Natal, South Africa

Participants

600 healthcare workers were randomly selected and 501(337 exposed and 164 unexposed) participated. Participants who were pregnant, less than one year of work as healthcare worker and history of anaphylactic reaction were excluded from the study.

Primary and secondary outcome measures

Latex sensitisation and latex allergy were the outcome of interest and they were successfully measured

Results

Prevalence of latex sensitisation and allergy was observed among exposed workers (7.1% and 5.9%) and unexposed workers (3.1% and 1.8%). Work related allergy symptoms were significantly higher in exposed workers (40.9%, $p<0.05$). Duration of employment was inversely associated with latex allergy (OR: 0.9; 95% CI: 0.8-0.9). The risk of latex sensitisation (OR: 4.2; 95% CI: 1.2-14.1) and allergy (OR: 5.1; 95% CI: 1.2-21.2) increased with exclusive use of powder-free latex gloves. A dose –response

relationship was observed for powdered latex gloves (OR: 1.1; 95% CI: 1.0-1.2). Atopy (OR: 1.5; 95% CI: 0.7-3.3 and OR: 1.4; 95% CI: 0.6-3.2) and fruit allergy (OR: 2.3; 95% CI: 0.8-6.7 and OR: 3.1; 95% CI: 1.1-9.2) also increased the risk of latex sensitisation and allergy.

Conclusion

This study adds to previous findings that healthcare workers exposed to hypoallergenic latex gloves are at risk for developing latex sensitisation highlighting its importance as an occupational hazard in healthcare. More research is needed to identify the most cost effective way of implementing a latex free environment in resource limited countries, such as South Africa. In addition more cohort analysis is required to better understand the chronicity of illness and disability associated with latex allergy.

ARTICLE SUMMARY

ARTICLE FOCUS

- The use of hypoallergenic latex gloves has been adopted as policy in different healthcare settings globally.
- However, information with regard to their use and the development of latex sensitisation and allergy among exposed healthcare workers is limited.
- We hypothesised that there is latex sensitization and allergy in healthcare workers using hypoallergenic latex gloves in a South African hospital.

KEY MESSAGE

- In the presence of powder free hypoallergenic gloves, latex sensitisation and latex allergy is still an important occupational health effect in healthcare workers.
- Healthcare workers should be continuously monitored for the development of latex sensitisation and allergy.
- There is a need for a national policy accompanied by clear implementation plans as well as sustainable education and training programmes to address latex sensitisation and allergy among HCWs.

STRENGTH AND LIMITATIONS

- Strength of the study included the presence of a control group providing a background prevalence of latex sensitisation in this population and random selection of participants which minimised the potential of participant bias that arises with a volunteer approach.
- This study was limited by the cross sectional study design as it only allowed for the determination of the prevalence of latex sensitisation; recall bias with regard to the number of gloves used in the past 7 working days and the self-reporting of personal and family atopic disorders may have resulted in the misclassification of exposure and atopy respectively.

What this paper adds

 In the presence of powder free hypoallergenic gloves, latex sensitisation and latex allergy is still an important occupational health hazard in healthcare workers

 Healthcare workers should be continuously monitored for the development of latex sensitisation and allergy

 There is a need for a national policy accompanied by clear implementation plans as well as sustainable education and training programmes to address latex sensitisation and allergy among HCWs

INTRODUCTION

Latex allergy (LA) as an occupational disease among healthcare workers (HCWs) gained recognition after Nutter published a case report of contact urticaria in a HCW in 1979.[1] The increase in prevalence coincided with the emergence of the Human Immunodeficiency Virus/ Acquired immunodeficiency syndrome (HIV/AIDS) epidemic and the introduction of "universal precautions" in the healthcare industry which had resulted in the increased use of latex gloves among HCWs.[2]

Latex gloves are preferred due to their superior barrier and physical properties as compared to the non-latex gloves.[3] International epidemiological studies have reported the prevalence of latex allergy among HCWs to range between 2-22% depending on the population and diagnostic methods used.[4-11] The prevalence in the general population has been reported to range between 1-6%.[12, 13] In South Africa studies amongst HCWs reported a latex sensitisation prevalence of between 2.7 to 20.8%.[14-16] Latex allergy in HCWs is a compensable disease in South Africa in terms of the Compensation of Occupational Injuries and Diseases Act No. 130 of 1993.[17]

Powdered latex gloves were identified as an important risk factor for latex sensitisation and allergy in HCWs as they were found to contain high allergenic protein content.[18] Following these findings, hypoallergenic gloves with low allergen content namely, low powdered and powder free latex gloves were introduced. The European definition of powder free gloves is gloves with powder content not exceeding 2 mg per glove and leachable latex protein which is as low as is reasonably practical.[19]

Hypoallergenic gloves have been associated with reduced latex aeroallergen concentrations, reduced conversion rates and a subsequent decrease in clinic visits, and compensation claims for

latex induced occupational asthma and allergic contact dermatitis among HCWs.[18, 20] As much as the use of low or powder free gloves has been shown to reduce latex related symptoms, other studies have shown that exposed HCWs still exhibit symptoms at very low levels of measureable airborne latex allergens.[21] Most studies have reported on the airborne levels and inhalational route of exposure hence the recommendation on low powdered or powder free latex gloves. There is little consideration given to the dermal route of exposure despite the fact that exposure is as a result of direct contact in these instances.[22] Eliminating the cornstarch powder only removed the carrier and not the source of allergen which is in the latex itself. Therefore workers using powder free gloves are still exposed to the allergenic content of latex gloves. It has been shown that different brands from different suppliers contain differing levels of protein due to a lack of standards in latex glove manufacture.[23] A South African study reported that some powder free latex gloves were found to have high allergenic protein content.[23] HCWs using these gloves are exposed via direct dermal contact and are at risk for developing latex sensitization which maybe asymptomatic and if exposure continues they can later develop latex allergy which presents with clinical manifestations.

While it is important to diagnose and manage an individual worker with latex allergy in the early stages of the disease, complete control of hazardous substance in the workplace is equally if not more important. While a latex free work environment would be a preferred control strategy, substitution of powdered latex gloves with powder free gloves was shown to be cost effective and associated with improved clinical outcome.[20, 24-26] As a result this was adopted as the most reasonable and practical approach in addressing the problem of latex allergy among HCWs both internationally and to some extent nationally.[27-29] This has proven to reduce latex induced clinical outcomes. Even with this intervention, studies in Western countries such as Germany

and the UK have shown that the risk of latex sensitisation still exists and more needs to be done to protect HCWs.[30, 31]

The current study described the prevalence of latex sensitisation and allergy among healthcare workers who use hypoallergenic powder free and lightly powdered latex gloves.

METHODS

Study design and population

This was a cross sectional study conducted between July 2011 and January 2012. The study location was King Edward VIII hospital, the second largest hospital in the Southern hemisphere, providing regional and tertiary services to the whole of KwaZulu-Natal (KZN) and the Eastern Cape Province in South Africa. It has a bed status of 1300 and has a workforce of 2400. The hospital was chosen due to the large workforce with different departments, and the policy of using both powder free and low powdered latex gloves for approximately 10 years.

The study population was limited to HCWs currently employed at King Edward VIII Hospital for more than 12 months. HCWs were defined as all personnel employed in the hospital.

The prevalence of latex sensitization in HCWs using powdered latex gloves in the Western Cape Province was 11.9% in 2001.[16] We expected the prevalence at King Edward VIII hospital to be less than the 11.9% observed in the Western Cape Province due to the adoption of a hypoallergenic latex glove policy in 2001. Using EPI Info calculator version 3.04.04., it was assumed that 50% of sensitised workers have remained sensitised despite the introduction of hypoallergenic latex gloves 10 years prior. Using an expected latex sensitization prevalence of 6% for the exposed group and the prevalence among the general population being reported as

less than 1% the required sample size was calculated to be 585 participants 2 exposed participants for every 1 non-exposed participant (exposed =390; unexposed =195). HCWs were considered to be exposed if they were likely to use gloves. Unexposed HCWs were drawn from the administrative staff of the hospital.

Questionnaire

We used an adaptation of the questionnaire used in an epidemiological study conducted at Groote Schuur in 2001[16] with permission from Professor Paul Potter, Allergology Unit, Medical School, University of Cape Town. The questionnaire containing open and closed ended questions was adapted to include items on exposure assessment. The questionnaire was administered by a trained research assistant immediately prior to the skin prick test. The questionnaire collected data on the participants' demographics, personal risk factors, latex exposure assessment, clinical manifestations of latex sensitization (dermal and respiratory) and history of previous reactions suggestive of latex allergy.

Exposure Assessment

Individual Exposure

Individual latex exposure was determined by the type of gloves used, number of gloves used per day, and duration of glove use. The information was limited to 7 working shifts/days prior to the interview.

Departmental Exposure

Departmental exposure was defined as glove usage in the past 12 months (01 January 2011-31 December 2011). The overall departmental exposure was obtained by reviewing monthly glove usage by each department from the stock room register. This was used to estimate the annual exposure for employees who had rotated through different departments in the past 12 months. Non sterile latex gloves are distributed throughout the clinical departments while a high proportion of sterile gloves are distributed to labour ward, theatre, surgical wards and outpatient departments. Glove type was defined as powdered and powder-free and latex free based on the previous literature.[23, 32]

Skin prick test (SPT)

The SPT was conducted using the Stallergenes kit.[32] It was performed in a room with access to emergency resuscitation services by a trained research assistant. The research assistant and principal investigator were trained on 2 separate occasions. The test was performed on the inner aspect of the participants' forearms, between the wrist and the elbow on normal skin. A positive and negative control were performed using histamine (0.61% concentration of phenol) and buffered normal saline solution respectively on the same arm and they were 3 cm apart to prevent cross contamination. The protein concentration of the latex extract was 500µg/ml and the solution was applied as it was with no further dilutions. After 15-20 minutes subsequent to puncturing the skin, the SPT reaction wheal and flare was outlined by a black ink and clear tape was used to transfer the outline from skin to the results sheet by the trained research assistant or principal investigator.[33] A positive result was indicated by a mean wheal diameter measuring 3 mm or greater than the negative control. Results were recorded on a standardized result sheet. The research assistant's test performance was audited by the principal investigator at regular intervals to ensure correctness of technique and interpretation of the results.

Informed signed consent was obtained from all the participants prior to participation. They had the option of participating in the questionnaire interview and the SPT or refusing the SPT. The study protocol was approved by the Biomedical Research Ethics Committee of the University of KwaZulu-Natal (BE048/11). Permission to conduct the study was also obtained from the KZN Provincial Department of Health and King Edward VIII hospital management.

Statistical analysis

Data was captured in Excel and analysed in Stata Version 11. Frequencies and medians with ranges were presented for categorical and continuous variables respectively. The Chi-square and the Kruskal-Wallis test were used to test for significant associations between categorical and continuous variables and the dependent variables under study on bivariate analysis, respectively.

Logistic regression was used to test for significant associations between independent and dependent variables on multivariate analysis. The dependent variables used in the regression analysis were: Latex sensitisation, which was defined as having a SPT wheal of ≥3mm to latex extract; Latex allergy (LA) was defined as being SPT positive and a report of having any one or more of the listed work related clinical symptoms namely itchy eyes, red eyes, runny eyes, runny nose, itchy nose, sneezing, coughing, tight chest, wheezing, itchy skin, skin rash or dizziness. Independent variables that were considered for analysis were as follows: Age (yrs.) and sex, duration of employment, job title, current department employed in, type of gloves used, number of pairs of gloves used per day, self reported and family history of atopy, food allergy and previous history of open surgery and number of surgical procedures. In the multivariate analysis, age was omitted due to collinearity with duration of employment. Departmental glove consumption was omitted as this only indicated annual distribution of gloves per department and

not necessarily employees' exposure since enrolled nursing assistants and enrolled nurses are rotated through different departments in any given year. The number of pair of gloves was used as an indicator of individual latex glove exposure. The variable number of pairs of gloves used and duration of employment were retained as continuous variables in the multivariate model. Fractional polynomial and a fractional plot was used to visualise the dose-response relationship of these continuous exposure variables.

RESULTS

Participant Demographics

Sixty five HCWs refused to participate in the study. Among the 520 HCWs who responded to the invitation there was an overall participation rate of 85.5 % (n=501) with 3.6% (n=19) refusing SPT. There was no significant difference between those refusing SPT and those who had the SPT with respect to latex exposure status, age, sex and duration of employment.

The median age of participants was 42.2 years (range: 22 years-65 years) with the greater proportion of them being females. The median duration of employment was 10.9 years (range: 1 year-42 years) with the majority of exposed participants having worked as a HCW for < 10 years. Most unexposed healthcare workers had been employed for > 20 years. Personal and family history of allergy was more prevalent among unexposed HCWs while exposed HCWS reported a higher prevalence of a fruit allergy and history of previous surgery (Table 1).

Prevalence of Latex Sensitisation and Allergy

The overall prevalence of latex sensitisation and latex allergy were 5.9% (n=29) and 4.6% (n=23) respectively. Although the difference was not significant, the prevalence of latex

sensitisation was higher among the exposed group (7.1%) as compared to the unexposed group (3.1%). Latex allergy was significantly higher in the exposed group than unexposed group (5.9% vs 1.8%, p=0.04). There was a significant difference in the work related allergy symptoms between exposed and unexposed workers (40.9% *vs.* 31.7%, p=0.04) (Table 1). Symptoms that were significantly associated with latex sensitisation were skin rash (p< 0.000), itchy skin (p=0.001), runny nose (p=0.004), red eyes (p=0.01) and itchy eyes (p=0.01).

The prevalence of latex sensitization was higher among those who were exposed and those with employment duration of < 10yrs. Although the prevalence of latex sensitisation was lower among participants < 30 years of age, there was no significant variation with age or sex. There was a significant difference (p=0.04) in the prevalence of fruit allergy between those participants with latex sensitisation (17.2%) and unsensitised participants (6.9%) The exclusive use of powder free latex gloves was found to be significantly (p=0.003) higher among the participants who had latex sensitisation. There was equal distribution of powdered and powder free latex gloves among those who reported the use of mixed gloves. The prevalence of reporting previous open surgery and use of other non- occupational exposure latex containing material did not vary significantly between those who had latex sensitisation and those who were unsensitised. There was a significantly higher prevalence of reporting allergic reactions when handling other latex containing medical equipment among participants with latex allergy as compared to unsensitised participants (10.3% vs 1.7%, p=0.002) (Table 2).

Crude association of demographics, exposure status, medical and personal history and latex sensitisation, latex allergy

Latex exposure was significantly associated with latex allergy (OR: 3.4; 95% CI: 1.1-10.8). Working as a HCW for 5-9 years was significantly associated with latex sensitisation (OR: 2.6; 95% CI: 1.2-5.5) and latex allergy (OR: 3.3; 95% CI: 1.4-7.6), respectively. Employment duration as a HCW for >20 years was protective against latex allergy (OR: 0.2; 95% CI: 0.0-0.8). In comparison with unexposed workers, working as an enrolled nurse was significantly associated with both latex sensitisation (OR: 2.5; 95% CI: 1.2-5.3) and latex allergy (OR: 2.4; 95% CI: 1.1-5.6). The exclusive use of powder free latex gloves was significantly associated with latex sensitisation (OR: 3.1; 95% CI: 1.4-6.8) and latex allergy (OR: 3.1; 95% CI: 1.7-9.1). Powdered and powder free latex gloves were equally distributed among those who reported the use of mixed gloves. The annual consumption of pairs of gloves per HCW by department was ranked and grouped into tertiles. Although medical and surgical wards had low and moderate pairs of gloves consumption per HCW, these wards had the highest proportion of workers with latex sensitisation (n=6, 20.0% each). However the relation was only significant for those who reported the medical ward as being the current department in which they worked (p=0.01). The proportions for powdered latex glove use were 71% and 69% in medical and surgical wards, respectively and this was not statistically significant. Exposure to other latex containing medical devices was not significantly different from what was reported in other wards. There was no significant association between reported personal history of allergy disease, latex sensitisation and latex allergy. Fruit allergy was significantly associated with latex allergy (OR: 3.7; 95%: 1.4-10.4) (Table 3). Listed fruits were evaluated for their independent association with latex sensitisation. Avocado (OR: 12.3; 95% CI: 5.1-29.6) and others (OR: 5.1; 95% CI: 2.1-11.8) which included pineapple and orange showed significant associations with latex sensitisation (data not shown).

Multivariate analysis

While latex exposure had estimates of the OR above 2, there was no significant association with latex sensitisation and latex allergy. Duration of employment was found to be inversely associated with latex allergy in models I and II. The exclusive use of powder free latex gloves was significantly associated with latex sensitisation (OR: 4.2: 95% CI: 1.2-14.1) and latex allergy (OR: 5.1; 95%CI: 1.2-21.2) on multivariate analysis. This significant association disappeared when examining the number of pairs of powder free gloves used in the last 7 days. A weak association was observed for the number of pairs of powdered latex gloves used in the last 7 days with both latex sensitisation and latex allergy (model III and IV).Further analysis of duration of employment and number of pairs of gloves using fractional polynomial failed to demonstrate significant dose-response relationship with either latex sensitisation or latex allergy. Duration of employment showed significant (p= 0.000) dose-response relationship when analysed using using penalised spline with degree of freedom =2 (Figure1). There was a significant association between fruit allergy and latex allergy in model I (OR: 3.1: 95% CI: 1.1-9.2) (Table 4).

DISCUSSION

This is an important study for South African HCWs as it examined the risk of latex sensitisation in a group of workers exposed to hypoallergenic latex gloves. As previously mentioned there has been no literature documenting the prevalence of latex sensitisation among South African HCWs using hypoallergenic lightly powered or powder-free latex gloves. The prevalence of latex sensitisation among exposed HCWs (7.1%) in this study is comparable to findings among HCWs in another South African hospital.[14] However it was considerably lower than the 11.9% prevalence reported by Potter in the same year.[16] While a substantial number of participants

(37%) reported work related allergy symptoms, only 4.6% met our definition of latex allergy. The important symptoms associated with latex sensitisation were skin rash, itchy skin, runny nose, red and itchy eyes in keeping with previous studies. Elimination of powdered latex gloves has shown a reduction in the concentration of aeroallergens in the operating room with the low prevalence of latex allergy in our study population.

Although the relationship was weak, this study showed that the risk of latex sensitisation decreases with duration of employment. The healthy worker effect is a likely explanation of this finding. Prior to availability of hypoallergenic latex gloves, workers who had developed latex allergy may have left employment or they may have changed their career path and moved into a more administrative or managerial role with no contact with latex gloves. Furthermore new employees are only sensitised and have not yet manifested clinical symptoms and they continue using latex gloves. On the other hand senior HCWs may have been sensitised during their earlier years of employment and as a result they either moved to departments with less exposure to latex gloves or deliberately avoid latex containing products and therefore exhibit less latex related symptoms. Moreover, the introduction of hypoallergenic gloves 10 years prior to the study may explain the reduced sensitisation in senior HCWs as demonstrated in the study by Smith et al in 2007. The published literature has been inconsistent in reporting the association between duration of employment and latex sensitisation. Although latex is one of the best studied allergens, no exposure response studies have been published with measured latex allergen levels. In addition, studies have demonstrated variation in allergen content of different gloves. These may lead to discrepancies in the literature with regard to the role of duration of employment as a surrogate measure of exposure.

In our study HCWs who exclusively used powdered free latex gloves had a 4 times greater odds of developing latex sensitisation. The fact that HCWs with latex sensitisation or allergy work more often with powder free latex gloves is indicative of reverse causality because of symptoms. Moreover the background prevalence of latex sensitisation in this study was relatively higher (3.5%) than previously reported prevalence in the general population by Bousquet et al.[13] Studies have shown that some of these "hypoallergenic" latex gloves actually contain high levels of allergens which can be release into the environment with aggressive manipulation.[23] Some of the sensitised HCWs may have been sensitised before the hospital implemented a hypoallergenic latex glove policy. Also Smith et al showed that complete avoidance of powdered latex glove can result in the reduction or no change in measurable IgE antibodies.[34] A study in Germany reported a high prevalence of 8% among 226 dental students who had only been exposed to exclusive powder free latex gloves.[30] Similarly in the UK despite a total ban on powdered latex gloves Clayton found a 10% prevalence of latex sensitisation in HCWs.[31] It is also not clear to what extent the aeroallergens released by colleagues using powdered latex gloves influence this finding. Furthermore the role of other latex containing medical devices during sensitisation period cannot be entirely ruled out.

In our study, frequency of exposure as measured by the number of gloves used in the last 7 working days showed a weak association between powdered latex gloves and latex sensitisation but no association could be demonstrated with powder free latex gloves. Airborne latex aeroallergens have been shown to increase with the number of powdered gloves used which subsequently increases the risk of latex sensitisation and clinical latex glove related allergy symptoms.[18]

The positive association between department with low glove consumption per HCW and latex sensitisation is in contrast with previous finding by Liss and co-workers.[9] They reported positive association with departments that had high glove consumption per HCWs. Again, this could be as a result of reverse causality where HCWs with latex sensitisation may have been relocated to wards with low glove consumption to minimise the exposure. In addition, the annual pair of gloves consumption per HCW by department does not provide an accurate indication of individual exposure; rather it gives us the annual distribution of gloves to different departments.

Several studies have reported atopy as a significant risk factor for latex sensitisation.[9, 10, 35] Similarly, the prevalence of reporting a history of personal atopy in this study was higher among latex sensitised participants although the association was not statistically significant. The role of atopy is complex because some individuals might also have become atopic after having been latex sensitised and cross sectional study is not suitable in establishing this association.

Fruit latex allergy syndrome is a phenomenon seen where latex sensitised individuals demonstrate a cross reactivity with specific foods; particularly fruit. Studies have identified this phenomenon among sensitised HCWs and the general population. This has been attributed to the similarity between fruit proteins and latex allergens.[36] Fruit allergy was significantly associated with latex sensitisation and latex allergy in our study. Our study was dependent on the self-reporting of fruit allergy and no objective tests were carried out. It is therefore possible that participants have independent simultaneous allergies to both fruit and latex without cross reactivity. Also, we were unable to determine whether latex sensitisation preceded the development of fruit allergy or vice versa. Fruit allergy prior to latex exposure could have contributed to the association observed in our study.

Latex sensitised participants reported a high prevalence of a history of previous open surgery in our study. This has been reported to occur as a result of direct intraoperative exposure to latex containing medical devices such as catheters or tubes. Studies in children with congenital abnormalities have demonstrated that the risk for latex allergy increases with the number of open surgical procedures that they undergo.[37] Frequency of invasive procedures among adults was shown to increase the risk of latex sensitisation reporting while more than 10 procedures increased the risk of developing latex allergy.[38]

Strengths of this study include the high response rate (85.5%) and comparability to other studies.[8, 16] Access to the hospital employee database allowed us to better assess the representativeness of this study population by comparing demographic data of the non-participants and the participants. The participants were randomly selected minimising the potential of participant's bias that comes with a volunteer approach.

The presence of a control group provided a background prevalence of latex sensitisation in this population which allowed for a better estimation of associations attributable to work related factors. The use of Stallergenes latex specific SPT further strengthens the study. The SPT test is regarded as the gold standard for the diagnosis of latex allergy and Stallergenes has been shown to have a diagnostic sensitivity and specificity of 93% and 100%, respectively.[32] The research assistant employed on this study was trained and initially shadowed and periodically supervised by the principal investigator to ensure appropriate administration of the questionnaire and the SPT thereby improving the reliability and validity of the study.

This study was limited by the cross sectional study design which was relatively low in cost and quick to conduct. It only allowed for the determination of prevalence of latex sensitisation at one

point in time. Consequently the prevalence of latex sensitisation may have been underestimated as it is possible that HCWs who had already developed latex sensitisation have left the hospital before the study was conducted. Some of the observed associations in the study may be as a result of a complex interplay between the healthy worker effect, reverse causality and exposure reduction by the introduction of powder free latex gloves. These interactions can be better explored and understood in a longitudinal study. Recall bias is another potential limitation in this study as workers were asked to recall the number of gloves used in the past 7 working days. HCWs may have overestimated or underestimated their individual exposures. Our study depended on self-reporting of personal and family atopic disorders and this may have resulted in the misclassification of atopy. The role of atopy and cross-reactivity between allergens is a complex phenomenon which cannot be investigated in cross sectional study. Therefore, cohort studies are necessary to disentangle this phenomenon.

CONCLUSION

This study shows that even in the presence of powder free hypoallergenic glove use there is latex sensitisation and latex allergy, adding to previous findings that HCWs exposed to hypoallergenic latex gloves are still at risk for developing latex sensitisation and latex allergy. This indicates that latex sensitisation and allergy are still an important occupational hazard for HCWs. While it may be economically impractical to replace the latex gloves in our setting, reduction of allergen content in latex products is another strategy that can be implemented to address the problem and protect HCWs. A policy accompanied by clear implementation plans as well as sustainable education and training programmes to address latex sensitisation and allergy among HCWs should be implemented.[39] In addition HCWs must be continuously monitored for the development of latex sensitisation and alternate latex free glove must be made available for

them. More research is needed to identify the most cost effective way of implementing a latex free environment in resource limited countries, such as South Africa. In addition the current studies in South Africa have largely been cross-sectional in nature. More cohort analysis is required to better understand the chronicity of illness and disability associated with latex allergy.

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Contributorship

Dr Shumani Phaswana is the principal investigator who was involved from the conception of the idea, proposal writing, data collection, data management and interpretation of the results.

Dr Saloshni Naidoo contributed to the conception and design of the study, analysis and interpretation of the data, critical review of the intellectual content of the article and final approval of the article.

Data sharing

No additional unpublished data

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None declared

Figure legend

Figure 1: Exposure-response relationship between duration of employment and latex sensitisation using penalised splines including a.) All particioants and b) Spt positive only

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TABLES

Table 1: Demographics and associated risk factors amongst latex exposed and unexposed healthcare workers at King Edward VIII Hospital, KwaZulu-Natal South Africa, (n=501)

Characteristic	Exposed N (%)	Unexposed N (%)
Number of participants	337 (67.3)	164 (32.7)
Demographics		
Age (years)		
≤30	30(8.9)	19(11.6)
>30-40	121(35.9)	40(24.4)
>40-50	101(29.9)	59(35.9)
>50	85(25.2)	46(28.1)
Duration of employment (years)		
≤5	39(11.6)	28(17.1)
>5-10**	135(40.1)	32(19.5)
>10-15	49(14.5)	17(10.4)
>15-20	24(7.1)	20(12.2)
>20*	90(26.7)	67(40.9)
Sex **		
Female	309(91.7)	95(57.9)
Male	28(8.3)	69(42.1)
Job Title (yes)		
Administrative		164(100.0)
Professional nurses	123(36.5)	
Enrolled nurses	141(41.8)	
Enrolled nursing assistants	73 (21.7)	
Medical and Personal History		
Personal history of Allergy Disease (yes)	147(43.6)	83(50.6)
Family history of Allergy Disease (yes)	197(58.5)	102(62.2)
Fruit allergy (yes)	29(8.6)	9(5.5)
Previous open surgery (yes)*	168(49.8)	61(37.2)
Work-related allergy symptoms(yes)*	138(40.9)	52(31.7)
Non-occupational latex exposure (yes)	161(47.8)	76(46.3)
Latex sensitisation (yes)	24(7.1)	5(3.1)
Current latex allergy (yes)*	20(5.9)	3(1.8)

Chi square, *p<0.05, **p<0.001

Table 2: Comparison of risk factors between latex sensitised (skin prick test positive) and non-sensitised (skin prick test negative) healthcare workers at King Edward VIII Hospital, KwaZulu-Natal South Africa (n=501)

Characteristics	Latex SPT +ve[ǂ] (29) N (%)	Latex SPT –ve[ǂǂ] (472) N (%)
Demographics		
Age (years.)		
≤30	1 (3.5)	48(10.2)
>30-40	13 (44.8)	148(31.4)
>40-50	8 (27.6)	152(32.2)
>50	7 (24.1)	124(26.3)
Duration of employment		
≤5	3(10.3)	64(13.6)
>5-10	16(55.2)	151(31.9)
>10-15	3(10.3)	63(13.4)
>15-20	1(3.5)	43(9.1)
>20	6(20.7)	151(31.9)
Sex (yes)		
Male	5(17.2)	118(25.0)
Female	24(82.8)	354(75.0)
Job Title (yes)		
Administrative	5(17.2)	159(33.7)
Professional nurses	5(17.2)	118(25.0)
Enrolled nurses	14(48.3)	127(26.9)
Enrolled nursing assistants	5(17.2)	68(14.4)
Latex Exposure		
Exposure status(yes)	24 (82.8)	313(66.3)
Type of gloves		
None	5(17.2)	165(34.6)
Exclusive powdered latex glove (yes)	2(6.9)	36(7.6)
Exclusive powder free latex glove (yes)*	11(37.9)	77(16.3)
Mixed (yes)	11(37.9)	198(41.9)
Medical and Personal History		
Personal history of Allergy Disease (yes)	16(55.2)	214(45.3)
Family history of Allergy Disease (yes)	18(62.1)	281(59.5)
Fruit allergy (yes) *	5(17.2)	33(6.9)
Previous open surgery (yes)	18(62.1)	211(44.7)
Non-occupational latex exposure (yes)	12(41.4)	225(47.7)
Reaction to other latex medical devices (yes)*	3(10.3)	8(1.7)

Chi Square, *p<0.05

[ǂ]Latex Skin Prick Test Positive

[ǂǂ]Latex Skin Prick Test Negative

Table 3: Crude Odds Ratios (OR) (95%CI) of demographics, exposure status, medical and personal history and latex sensitisation and latex allergy amongst healthcare workers at King Edward VIII Hospital, KwaZulu-Natal South Africa, (n=501)

Characteristics	N=29	Latex Sensitisation OR (95%CI)	N=23	LA[ǂǂ] OR (95%CI)
Demographics				
Age (years)				
≤30	1	0.3(0.0-1.9)	1	0.4(0.0-2.4)
>30-40	13	1.8(0.8-3.7)	11	2.0(0.9-4.6)
>40-50	8	0.8(0.4-1.8)	7	0.9(0.4-2.2)
>50	7	0.8(0.4-2.1)	4	0.6(0.2-1.7)
Duration of employment (years)				
<5	3	0.7(0.2-2.4)	3	0.9(0.3-3.2)
5-10	16	2.6(1.2-5.5)*	14	3.3(1.4-7.6)*
>10-15	3	0.7(0.2-2.4)	3	0.9(0.3-3.2)
>15-20	1	0.4(0.0-2.1)	1	0.5(0.0-2.8)
>20	6	0.5(0.2-1.4)	2	0.2(0.0-0.8)*
Sex (yes)				
Female	24	1.6(0.6-4.1)	20	2.2(0.7-7.2)
Job Title (yes)				
Administrative	5	0.4(0.2-1.1)	3	0.3(0.1-0.9)*
Professional nurses	5	0.6(0.2-1.6)	4	0.6(0.2-1.8)
Enrolled nurses	14	2.5(1.2-5.3)*	11	2.4(1.1-5.6)*
Enrolled nursing assistants	5	1.2(0.5-3.3)	5	1.7(0.6-4.5)
Latex Exposure				
Exposure status (yes)	24	2.4(0.9-6.3)	20	3.4(1.1-10.8)*
Type of gloves				
None	5	0.4(0.2-1.0)	3	0.3(0.1-0.9)*
Exclusive Powdered latex glove (yes)	2	0.9(0.0-3.6)	2	1.2(0.0-1.7)
Exclusive Powder free latex glove (yes)	11	3.1(1.4-6.8)*	10	3.1(1.7-9.1)*
Mixed gloves(yes)	11	0.8(0.4-1.8)	8	0.7(0.3-1.7)
Medical and Personal History				
Personal history of Allergy Disease (yes)	16	1.4(0.7-3.1)	12	1.3(0.5-2.9)
Family history of Allergy Disease (yes)	18	1.1(0.5-2.4)	14	1.1(0.5-2.4)
Fruit allergy (yes)	5	2.8(1.0-7.5)	5	3.7(1.4-10.0)*
Previous open surgery (yes)	18	1.1(0.5-2.4)	14	1.5(0.7-3.1)

Chi square, *p<0.05

[ǂ] Latex Skin Prick Test Positive

[ǂǂ] Latex Skin Prick Test Positive and work related clinical symptoms of allergy

Table 4: Multivariate analysis of demographics, medical and personal history, exposure history and latex sensitisation (LS)ǂ and latex allergy (LA)ǂǂ amongst healthcare workers at King Edward III Hospital, KwaZulu-Natal South Africa, (n=501)

	MODEL I* (n=501)		MODEL II** (n=501)		MODEL III***(n=202)		MODEL IV****(n=252)	
Characteristics	LS OR (95%CI)	LA OR (95%CI)	LS OR (95%CI)	LA OR (95%CI)	LS OR (95%CI)	LA OR (95%CI)	LS OR (95%CI)	LA OR (95%CI)
Demographics								
Sex (female)	0.9(0.2-2.7)	1.1(0.3-4.4)	0.9(0.3-2.7)	1.1(0.3-4.5)	0.3(0.0-1.8)	0.3(0.0-3.1)	2.5(0.5-12.2)	2.5(0.5-12.2)
Duration of employment (years)	0.9(0.9-1.0)	0.9(0.8-0.9)	0.9(0.9-1.0)	0.9(0.8-0.9)	0.9(0.9-1.8)	0.7(0.5-1.0)	0.9(0.9-1.0)	0.9(0.9-1.0)
Latex Exposure								
Exposure status(yes)	2.2(0.7-6.7)	2.6(0.7-9.8)						
Type of gloves								
None			1	1				
Exclusive lightly powdered latex glove (yes)			1.6(0.3-9.8)	2.6(0.4-17.7)				
Exclusive Powder free latex glove (yes)			4.2(1.2-14.1)	5.1(1.2-21.2)				
Mixed gloves (yes)			1.7(0.5-5.6)	1.7(0.4-7.1)				

Pairs of Powdered latex Gloves in the last 7 days					1.1(1.0-1.2)	1.2(1.0-1.4)		
Pairs of Powder Free Latex Gloves in the last 7 days							1.0(0.9-1.1)	1.0(0.9-1.1)
Personal and Medical History								
Personal history of allergy disease (yes)	1.5(0.7-3.3)	1.4(0.6-3.2)	1.5(0.7-3.3)	1.3(0.6-3.2)	1.4(0.3-6.8)	1.6(0.2-11.6)	1.0(0.4-2.9)	0.9(0.3-2.8)
Family history of allergy disease (yes)	1.0(0.45-2.2)	0.9(0.4-2.2)	1.1(0.5-2.3)	0.9(0.4-2.3)	0.4(0.1-1.9)	0.5(0.1-3.6)	0.7(0.2-2.0)	0.8(0.3-2.7)
Fruit allergy (yes)	2.3(0.8-6.7)	3.1(1.1-9.2)	2.2(0.8-6.5)	3.0(0.9-9.1)	5.0(0.4-56.9)	9.7(0.6-163.0)	1.7(0.3-8.5)	2.0(0.4-10.4)
Previous open surgery (yes)	2.0(0.9-4.4)	1.9(0.8-4.6)	2.1(0.9-4.6)	1.9(0.8-4.7)	1.4(0.3-7.4)	1.2(0.1-11.1)	1.1(0.4-3.2)	1.2(0.4-3.8)

ǂLatex Skin Prick Test Positive

ǂǂLatex Skin Prick Test Positive and work related clinical symptoms of allergy
*Model included latex glove exposure status
**Model included type of gloves
***Model included number of pairs of powdered latex gloves
****Model included number of pairs of powder free latex gloves

The prevalence of latex sensitisation and allergy and associated risk factors among healthcare workers using hypoallergenic latex gloves at King Edward VIII Hospital, KwaZulu-Natal South Africa: A cross sectional study

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ARTICLE SUMMARY

ARTICLE FOCUS

- The use of hypoallergenic latex gloves has been adopted as policy in different healthcare settings globally.
- However, information with regard to their use and the development of latex sensitisation and allergy among exposed healthcare workers is limited.
- We hypothesised that there is latex sensitization and allergy in healthcare workers using hypoallergenic latex gloves in a South African hospital.

KEY MESSAGE

- In the presence of powder free hypoallergenic gloves, latex sensitisation and latex allergy is still an important occupational health effect in healthcare workers.
- Healthcare workers should be continuously monitored for the development of latex sensitisation and allergy.
- There is a need for a national policy accompanied by clear implementation plans as well as sustainable education and training programmes to address latex sensitisation and allergy among HCWs.

STRENGTH AND LIMITATIONS

- Strength of the study included the presence of a control group providing a background prevalence of latex sensitisation in this population and random selection of participants which minimised the potential of participant bias that arises with a volunteer approach.
- This study was limited by the cross sectional study design as it only allowed for the determination of the prevalence of latex sensitisation; recall bias with regard to the number of gloves used in the past 7 working days and the self-reporting of personal and family atopic disorders may have resulted in the misclassification of exposure and atopy respectively.

What this paper adds

- In the presence of powder free hypoallergenic gloves, latex sensitisation and latex allergy is still an important occupational health hazard in healthcare workers

- Healthcare workers should be continuously monitored for the development of latex sensitisation and allergy

- There is a need for a national policy accompanied by clear implementation plans as well as sustainable education and training programmes to address latex sensitisation and allergy among HCWs

ABSTRACT

Objectives

The present study describes latex sensitisation and allergy prevalence and associated factors among healthcare workers using hypoallergenic latex gloves at King Edward VIII Hospital in KwaZulu-Natal South Africa.

Design

Cross sectional study

Setting

A tertiary hospital in eThekwini municipality, KwaZulu Natal, South Africa

Participants

600 healthcare workers were randomly selected and 501(337 exposed and 164 unexposed) participated. Participants who were pregnant, less than one year of work as healthcare worker and history of anaphylactic reaction were excluded from the study.

Primary and secondary outcome measures

Latex sensitisation and latex allergy were the outcome of interest and they were successfully measured

Results

Prevalence of latex sensitisation and allergy was observed among exposed workers (7.1% and 5.9%) and unexposed workers (3.1% and 1.8%). Work related allergy symptoms were significantly higher in exposed workers (40.9%, $p<0.05$). Duration of employment was inversely associated with latex allergy (OR: 0.9; 95% CI: 0.8-0.9). The risk of latex sensitisation (OR: 4.2; 95% CI: 1.2-14.1) and allergy (OR:

5.1; 95% CI: 1.2-21.2) increased with exclusive use of powder-free latex gloves. A dose –response relationship was observed for powdered latex gloves (OR: 1.1; 95% CI: 1.0-1.2). Atopy (OR: 1.5; 95% CI: 0.7-3.3 and OR: 1.4; 95% CI: 0.6-3.2) and fruit allergy (OR: 2.3; 95% CI: 0.8-6.7 and OR: 3.1; 95% CI: 1.1-9.2) also increased the risk of latex sensitisation and allergy.

Conclusion

This study adds to previous findings that healthcare workers exposed to hypoallergenic latex gloves are at risk for developing latex sensitisation highlighting its importance as an occupational hazard in healthcare. More research is needed to identify the most cost effective way of implementing a latex free environment in resource limited countries, such as South Africa. In addition more cohort analysis is required to better understand the chronicity of illness and disability associated with latex allergy.

INTRODUCTION

Latex allergy (LA) as an occupational disease among healthcare workers (HCWs) gained recognition after Nutter published a case report of contact urticaria in a HCW in 1979.[1] The increase in prevalence coincided with the emergence of the Human Immunodeficiency Virus/ Acquired immunodeficiency syndrome (HIV/AIDS) epidemic and the introduction of "universal precautions" in the healthcare industry which had resulted in the increased use of latex gloves among HCWs.[2]

Latex gloves are preferred due to their superior barrier and physical properties as compared to the non-latex gloves.[3] International epidemiological studies have reported the prevalence of latex allergy among HCWs to range between 2-22% depending on the population and diagnostic methods used.[4-11] The prevalence in the general population has been reported to range between 1-6%.[12, 13] In South Africa studies amongst HCWs reported a latex sensitisation prevalence of between 2.7 to 20.8%.[14-16] Latex allergy in HCWs is a compensable disease in South Africa in terms of the Compensation of Occupational Injuries and Diseases Act No. 130 of 1993.[17]

Powdered latex gloves were identified as an important risk factor for latex sensitisation and allergy in HCWs as they were found to contain high allergenic protein content.[18] Following these findings, hypoallergenic gloves with low allergen content namely, low powdered and powder free latex gloves were introduced. The European definition of powder free gloves is gloves with powder content not exceeding 2 mg per glove and leachable latex protein which is as low as is reasonably practical.[19]

Hypoallergenic gloves have been associated with reduced latex aeroallergen concentrations, reduced conversion rates and a subsequent decrease in clinic visits, and compensation claims for

latex induced occupational asthma and allergic contact dermatitis among HCWs.[18, 20] As much as the use of low or powder free gloves has been shown to reduce latex related symptoms, other studies have shown that exposed HCWs still exhibit symptoms at very low levels of measureable airborne latex allergens.[21] Most studies have reported on the airborne levels and inhalational route of exposure hence the recommendation on low powdered or powder free latex gloves. There is little consideration given to the dermal route of exposure despite the fact that exposure is as a result of direct contact in these instances.[22] Eliminating the cornstarch powder only removed the carrier and not the source of allergen which is in the latex itself. Therefore workers using powder free gloves are still exposed to the allergenic content of latex gloves. It has been shown that different brands from different suppliers contain differing levels of protein due to a lack of standards in latex glove manufacture.[23] A South African study reported that some powder free latex gloves were found to have high allergenic protein content.[23] HCWs using these gloves are exposed via direct dermal contact and are at risk for developing latex sensitization which maybe asymptomatic and if exposure continues they can later develop latex allergy which presents with clinical manifestations.

While it is important to diagnose and manage an individual worker with latex allergy in the early stages of the disease, complete control of hazardous substance in the workplace is equally if not more important. While a latex free work environment would be a preferred control strategy, substitution of powdered latex gloves with powder free gloves was shown to be cost effective and associated with improved clinical outcome.[20, 24-26] As a result this was adopted as the most reasonable and practical approach in addressing the problem of latex allergy among HCWs both internationally and to some extent nationally.[27-29] This has proven to reduce latex induced clinical outcomes. Even with this intervention, studies in Western countries such as Germany

and the UK have shown that the risk of latex sensitisation still exists and more needs to be done to protect HCWs.[30, 31]

The current study described the prevalence of latex sensitisation and allergy among healthcare workers who use hypoallergenic powder free and lightly powdered latex gloves.

METHODS

Study design and population

This was a cross sectional study conducted between July 2011 and January 2012. The study location was King Edward VIII hospital, the second largest hospital in the Southern hemisphere, providing regional and tertiary services to the whole of KwaZulu-Natal (KZN) and the Eastern Cape Province in South Africa. It has a bed status of 1300 and has a workforce of 2400. The hospital was chosen due to the large workforce with different departments, and the policy of using both powder free and low powdered latex gloves for approximately 10 years.

The study population was limited to HCWs currently employed at King Edward VIII Hospital for more than 12 months. HCWs were defined as all personnel employed in the hospital.

The prevalence of latex sensitization in HCWs using powdered latex gloves in the Western Cape Province was 11.9% in 2001.[16] We expected the prevalence at King Edward VIII hospital to be less than the 11.9% observed in the Western Cape Province due to the adoption of a hypoallergenic latex glove policy in 2001. Using EPI Info calculator version 3.04.04., it was assumed that 50% of sensitised workers have remained sensitised despite the introduction of hypoallergenic latex gloves 10 years prior. Using an expected latex sensitization prevalence of 6% for the exposed group and the prevalence among the general population being reported as

less than 1% the required sample size was calculated to be 585 participants 2 exposed participants for every 1 non-exposed participant (exposed =390; unexposed =195). HCWs were considered to be exposed if they were likely to use gloves. Unexposed HCWs were drawn from the administrative staff of the hospital.

Questionnaire

We used an adaptation of the questionnaire used in an epidemiological study conducted at Groote Schuur in 2001[16] with permission from Professor Paul Potter, Allergology Unit, Medical School, University of Cape Town. The questionnaire containing open and closed ended questions was adapted to include items on exposure assessment. The questionnaire was administered by a trained research assistant immediately prior to the skin prick test. The questionnaire collected data on the participants' demographics, personal risk factors, latex exposure assessment, clinical manifestations of latex sensitization (dermal and respiratory) and history of previous reactions suggestive of latex allergy.

Exposure Assessment

Individual Exposure

Individual latex exposure was determined by the type of gloves used, number of gloves used per day, and duration of glove use. The information was limited to 7 working shifts/days prior to the interview.

Departmental Exposure

Departmental exposure was defined as glove usage in the past 12 months (01 January 2011-31 December 2011). The overall departmental exposure was obtained by reviewing monthly glove usage by each department from the stock room register. This was used to estimate the annual exposure for employees who had rotated through different departments in the past 12 months. Non sterile latex gloves are distributed throughout the clinical departments while a high proportion of sterile gloves are distributed to labour ward, theatre, surgical wards and outpatient departments. Glove type was defined as powdered and powder-free and latex free based on the previous literature.[23, 32]

Skin prick test (SPT)

The SPT was conducted using the Stallergenes kit.[32] It was performed in a room with access to emergency resuscitation services by a trained research assistant. The research assistant and principal investigator were trained on 2 separate occasions. The test was performed on the inner aspect of the participants' forearms, between the wrist and the elbow on normal skin. A positive and negative control were performed using histamine (0.61% concentration of phenol) and buffered normal saline solution respectively on the same arm and they were 3 cm apart to prevent cross contamination. The protein concentration of the latex extract was 500µg/ml and the solution was applied as it was with no further dilutions. After 15-20 minutes subsequent to puncturing the skin, the SPT reaction wheal and flare was outlined by a black ink and clear tape was used to transfer the outline from skin to the results sheet by the trained research assistant or principal investigator.[33] A positive result was indicated by a mean wheal diameter measuring 3 mm or greater than the negative control. Results were recorded on a standardized result sheet. The research assistant's test performance was audited by the principal investigator at regular intervals to ensure correctness of technique and interpretation of the results.

Informed signed consent was obtained from all the participants prior to participation. They had the option of participating in the questionnaire interview and the SPT or refusing the SPT. The study protocol was approved by the Biomedical Research Ethics Committee of the University of KwaZulu-Natal (BE048/11). Permission to conduct the study was also obtained from the KZN Provincial Department of Health and King Edward VIII hospital management.

Statistical analysis

Data was captured in Excel and analysed in Stata Version 11. Frequencies and medians with ranges were presented for categorical and continuous variables respectively. The Chi-square and the Kruskal-Wallis test were used to test for significant associations between categorical and continuous variables and the dependent variables under study on bivariate analysis, respectively.

~~Binary~~ Logistic regression was used to test for significant associations between independent and dependent variables on multivariate analysis. The dependent variables used in the regression analysis were: Latex sensitisation, which was defined as having a SPT wheal of ≥3mm to latex extract; Latex allergy (LA) was defined as being SPT positive and a report of having any one or more of the listed work related clinical symptoms namely itchy eyes, red eyes, runny eyes, runny nose, itchy nose, sneezing, coughing, tight chest, wheezing, itchy skin, skin rash or dizziness. Independent variables that were considered for analysis were as follows: Age (yrs.) and sex, duration of employment, job title, current department employed in, type of gloves used, number of pairs of gloves used per day, self reported and family history of atopy, food allergy and previous history of open surgery and number of surgical procedures. In the multivariate analysis, age was omitted due to collinearity with duration of employment. Departmental glove consumption was omitted as this only indicated annual distribution of gloves per department and

not necessarily employees' exposure since enrolled nursing assistants and enrolled nurses are rotated through different departments in any given year. The number of pair of gloves was used as an indicator of individual latex glove exposure. The variable number of pairs of gloves used and duration of employment were retained as continuous variables in the multivariate model. Fractional polynomial and a fractional plot was used to visualise the dose-response relationship of these continuous exposure variables.

RESULTS

Participant Demographics

Sixty five HCWs refused to participate in the study. Among the 520 HCWs who responded to the invitation there was an overall participation rate of 85.5 % (n=501) with 3.6% (n=19) refusing SPT. There was no significant difference between those refusing SPT and those who had the SPT with respect to latex exposure status, age, sex and duration of employment.

The median age of participants was 42.2 years (range: 22 years-65 years) with the greater proportion of them being females. The median duration of employment was 10.9 years (range: 1 year-42 years) with the majority of exposed participants having worked as a HCW for < 10 years. Most unexposed healthcare workers had been employed for > 20 years. Personal and family history of allergy was more prevalent among unexposed HCWs while exposed HCWS reported a higher prevalence of a fruit allergy and history of previous surgery (Table 1).

Prevalence of Latex Sensitisation and Allergy

The overall prevalence of latex sensitisation and latex allergy were 5.9% (n=29) and 4.6% (n=23) respectively. Although the difference was not significant, the prevalence of latex

sensitisation was higher among the exposed group (7.1%) as compared to the unexposed group (3.1%). Latex allergy was significantly higher in the exposed group than unexposed group (5.9% vs 1.8%, p=0.04). There was a significant difference in the work related allergy symptoms between exposed and unexposed workers (40.9% *vs*. 31.7%, p=0.04) (Table 1). Symptoms that were significantly associated with latex sensitisation were skin rash (p< 0.000), itchy skin (p=0.001), runny nose (p=0.004), red eyes (p=0.01) and itchy eyes (p=0.01).

The prevalence of latex sensitization was higher among those who were exposed and those with employment duration of < 10yrs. Although the prevalence of latex sensitisation was lower among participants < 30 years of age, there was no significant variation with age or sex. There was a significant difference (p=0.04) in the prevalence of fruit allergy between those participants with latex sensitisation (17.2%) and unsensitised participants (6.9%) The exclusive use of powder free latex gloves was found to be significantly (p=0.003) higher among the participants who had latex sensitisation. There was equal distribution of powdered and powder free latex gloves among those who reported the use of mixed gloves. The prevalence of reporting previous open surgery and use of other non- occupational exposure latex containing material did not vary significantly between those who had latex sensitisation and those who were unsensitised. There was a significantly higher prevalence of reporting allergic reactions when handling other latex containing medical equipment among participants with latex allergy as compared to unsensitised participants (10.3% vs 1.7%, p=0.002) (Table 2).

Crude association of demographics, exposure status, medical and personal history and latex sensitisation, latex allergy

Latex exposure was significantly associated with latex allergy (OR: 3.4; 95% CI: 1.1-10.8). Working as a HCW for 5-9 years was significantly associated with latex sensitisation (OR: 2.6; 95% CI: 1.2-5.5) and latex allergy (OR: 3.3; 95% CI: 1.4-7.6), respectively. Employment duration as a HCW for >20 years was protective against latex allergy (OR: 0.2; 95% CI: 0.0-0.8). In comparison with unexposed workers, working as an enrolled nurse was significantly associated with both latex sensitisation (OR: 2.5; 95% CI: 1.2-5.3) and latex allergy (OR: 2.4; 95% CI: 1.1-5.6). The exclusive use of powder free latex gloves was significantly associated with latex sensitisation (OR: 3.1; 95% CI: 1.4-6.8) and latex allergy (OR: 3.1; 95% CI: 1.7-9.1). Powdered and powder free latex gloves were equally distributed among those who reported the use of mixed gloves. The annual consumption of pairs of gloves per HCW by department was ranked and grouped into tertiles. Although medical and surgical wards had low and moderate pairs of gloves consumption per HCW, these wards had the highest proportion of workers with latex sensitisation (n=6, 20.0% each). However the relation was only significant for those who reported the medical ward as being the current department in which they worked (p=0.01). The proportions for powdered latex glove use were 71% and 69% in medical and surgical wards, respectively and this was not statistically significant. Exposure to other latex containing medical devices was not significantly different from what was reported in other wards. There was no significant association between reported personal history of allergy disease, latex sensitisation and latex allergy. Fruit allergy was significantly associated with latex allergy (OR: 3.7; 95%: 1.4-10.4) (Table 3). Listed fruits were evaluated for their independent association with latex sensitisation. Avocado (OR: 12.3; 95% CI: 5.1-29.6) and others (OR: 5.1; 95% CI: 2.1-11.8) which included pineapple and orange showed significant associations with latex sensitisation (data not shown).

Multivariate analysis

While latex exposure had estimates of the OR above 2, there was no significant association with latex sensitisation and latex allergy. Duration of employment was found to be inversely associated with latex allergy in models I and II. The exclusive use of powder free latex gloves was significantly associated with latex sensitisation (OR: 4.2: 95% CI: 1.2-14.1) and latex allergy (OR: 5.1; 95%CI: 1.2-21.2) on multivariate analysis. This significant association disappeared when examining the number of pairs of powder free gloves used in the last 7 days. A weak association was observed for the number of pairs of powdered latex gloves used in the last 7 days with both latex sensitisation and latex allergy (model III and IV).Further analysis of duration of employment and number of pairs of gloves using fractional polynomial failed to demonstrate significant dose-response relationship with either latex sensitisation or latex allergy. Duration of employment showed significant (p= 0.000) dose-response relationship when analysed using using penalised spline with degree of freedom =2 (Figure1). There was a significant association between fruit allergy and latex allergy in model I (OR: 3.1: 95% CI: 1.1-9.2) (Table 4).

DISCUSSION

This is an important study for South African HCWs as it examined the risk of latex sensitisation in a group of workers exposed to hypoallergenic latex gloves. As previously mentioned there has been no literature documenting the prevalence of latex sensitisation among South African HCWs using hypoallergenic lightly powered or powder-free latex gloves. The prevalence of latex sensitisation among exposed HCWs (7.1%) in this study is comparable to findings among HCWs in another South African hospital.[14] However it was considerably lower than the 11.9% prevalence reported by Potter in the same year.[16] While a substantial number of participants

(37%) reported work related allergy symptoms, only 4.6% met our definition of latex allergy. The important symptoms associated with latex sensitisation were skin rash, itchy skin, runny nose, red and itchy eyes in keeping with previous studies. Elimination of powdered latex gloves has shown a reduction in the concentration of aeroallergens in the operating room with the low prevalence of latex allergy in our study population.

Although the relationship was weak, this study showed that the risk of latex sensitisation decreases with duration of employment. The healthy worker effect is a likely~~possible~~ explanation of this finding. Prior to availability of hypoallergenic latex gloves, workers who had developed latex allergy may have left employment or they may have changed their career path and moved into a more administrative or managerial role with no contact with latex gloves. Furthermore new employees are only sensitised and have not yet manifested clinical symptoms and they continue using latex gloves. On the other hand senior HCWs may have been sensitised during their earlier years of employment and as a result they either moved to departments with less exposure to latex gloves or deliberately avoid latex containing products and therefore exhibit less latex related symptoms. Moreover, the introduction of hypoallergenic gloves 10 years prior to the study may explain the reduced sensitisation in senior HCWs as demonstrated in the study by Smith et al in 2007. The published literature has been inconsistent in reporting the association between duration of employment and latex sensitisation. Although latex is one of the best studied allergens, no exposure response studies have been published with measured latex allergen levels. In addition, studies have demonstrated variation in allergen content of different gloves. These may lead to discrepancies in the literature with regard to the role of duration of employment as a surrogate measure of exposure.

In our study HCWs who exclusively used powdered free latex gloves had a 4 times greater odds of developing latex sensitisation. The fact that HCWs with latex sensitisation or allergy work more often with powder free latex gloves is indicative of reverse causality because of symptoms. Moreover the background prevalence of latex sensitisation in this study was relatively higher (3.5%) than previously reported prevalence in the general population by Bousquet et al.[13] Studies have shown that some of these "hypoallergenic" latex gloves actually contain high levels of allergens which can be release into the environment with aggressive manipulation.[23] Some of the sensitised HCWs may have been sensitised before the hospital implemented a hypoallergenic latex glove policy. Also Smith et al showed that complete avoidance of powdered latex glove can result in the reduction or no change in measurable IgE antibodies.[34] A study in Germany reported a high prevalence of 8% among 226 dental students who had only been exposed to exclusive powder free latex gloves.[30] Similarly in the UK despite a total ban on powdered latex gloves Clayton found a 10% prevalence of latex sensitisation in HCWs.[31] It is also not clear to what extent the aeroallergens released by colleagues using powdered latex gloves influence this finding. Furthermore the role of other latex containing medical devices during sensitisation period cannot be entirely ruled out.

In our study, frequency of exposure as measured by the number of gloves used in the last 7 working days showed a weak association between powdered latex gloves and latex sensitisation but no association could be demonstrated with powder free latex gloves. Airborne latex aeroallergens have been shown to increase with the number of powdered gloves used which subsequently increases the risk of latex sensitisation and clinical latex glove related allergy symptoms.[18]

The positive association between department with low glove consumption per HCW and latex sensitisation is in contrast with previous finding by Liss and co-workers.[9] They reported positive association with departments that had high glove consumption per HCWs. Again, this could be as a result of reverse causality where HCWs with latex sensitisation may have been relocated to wards with low glove consumption to minimise the exposure. In addition, the annual pair of gloves consumption per HCW by department does not provide an accurate indication of individual exposure; rather it gives us the annual distribution of gloves to different departments.

Several studies have reported atopy as a significant risk factor for latex sensitisation.[9, 10, 35] Similarly, the prevalence of reporting a history of personal atopy in this study was higher among latex sensitised participants although the association was not statistically significant. The role of atopy is complex because some individuals might also have become atopic after having been latex sensitised and cross sectional study is not suitable in establishing this association.

Fruit latex allergy syndrome is a phenomenon seen where latex sensitised individuals demonstrate a cross reactivity with specific foods; particularly fruit. Studies have identified this phenomenon among sensitised HCWs and the general population. This has been attributed to the similarity between fruit proteins and latex allergens.[36] Fruit allergy was significantly associated with latex sensitisation and latex allergy in our study. Our study was dependent on the self-reporting of fruit allergy and no objective tests were carried out. It is therefore possible that participants have independent simultaneous allergies to both fruit and latex without cross reactivity. Also, we were unable to determine whether latex sensitisation preceded the development of fruit allergy or vice versa. Fruit allergy prior to latex exposure could have contributed to the association observed in our study.

Latex sensitised participants reported a high prevalence of a history of previous open surgery in our study. This has been reported to occur as a result of direct intraoperative exposure to latex containing medical devices such as catheters or tubes. Studies in children with congenital abnormalities have demonstrated that the risk for latex allergy increases with the number of open surgical procedures that they undergo.[37] Frequency of invasive procedures among adults was shown to increase the risk of latex sensitisation reporting while more than 10 procedures increased the risk of developing latex allergy.[38]

Strengths of this study include the high response rate (85.5%) and comparability to other studies.[8, 16] Access to the hospital employee database allowed us to better assess the representativeness of this study population by comparing demographic data of the non-participants and the participants. The participants were randomly selected minimising the potential of participant's bias that comes with a volunteer approach.

The presence of a control group provided a background prevalence of latex sensitisation in this population which allowed for a better estimation of associations attributable to work related factors. The use of Stallergenes latex specific SPT further strengthens the study. The SPT test is regarded as the gold standard for the diagnosis of latex allergy and Stallergenes has been shown to have a diagnostic sensitivity and specificity of 93% and 100%, respectively.[32] The research assistant employed on this study was trained and initially shadowed and periodically supervised by the principal investigator to ensure appropriate administration of the questionnaire and the SPT thereby improving the reliability and validity of the study.

This study was limited by the cross sectional study design which was relatively low in cost and quick to conduct. It only allowed for the determination of prevalence of latex sensitisation at one

point in time. Consequently the prevalence of latex sensitisation may have been underestimated as it is possible that HCWs who had already developed latex sensitisation have left the hospital before the study was conducted. Some of the observed associations in the study may be as a result of a complex interplay between the healthy worker effect, reverse causality and exposure reduction by the introduction of powder free latex gloves. These interactions can be better explored and understood in a longitudinal study. Recall bias is another potential limitation in this study as workers were asked to recall the number of gloves used in the past 7 working days. HCWs may have overestimated or underestimated their individual exposures. Our study depended on self-reporting of personal and family atopic disorders and this may have resulted in the misclassification of atopy. The role of atopy and cross-reactivity between allergens is a complex phenomenon which cannot be investigated in cross sectional study. Therefore, cohort studies are necessary to disentangle this phenomenon.

CONCLUSION

This study shows that even in the presence of powder free hypoallergenic glove use there is latex sensitisation and latex allergy, adding to previous findings that HCWs exposed to hypoallergenic latex gloves are still at risk for developing latex sensitisation and latex allergy. This indicates that latex sensitisation and allergy are still an important occupational hazard for HCWs. While it may be economically impractical to replace the latex gloves in our setting, reduction of allergen content in latex products is another strategy that can be implemented to address the problem and protect HCWs. A policy accompanied by clear implementation plans as well as sustainable education and training programmes to address latex sensitisation and allergy among HCWs should be implemented.[39] In addition HCWs must be continuously monitored for the development of latex sensitisation and alternate latex free glove must be made available for

them. More research is needed to identify the most cost effective way of implementing a latex free environment in resource limited countries, such as South Africa. In addition the current studies in South Africa have largely been cross-sectional in nature. More cohort analysis is required to better understand the chronicity of illness and disability associated with latex allergy.

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Contributorship

Dr Shumani Phaswana is the principal investigator who was involved from the conception of the idea, proposal writing, data collection, data management and interpretation of the results.

Dr Saloshni Naidoo contributed to the conception and design of the study, analysis and interpretation of the data, critical review of the intellectual content of the article and final approval of the article.

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TABLES

Table 1: Demographics and associated risk factors amongst latex exposed and unexposed healthcare workers at King Edward VIII Hospital, KwaZulu-Natal South Africa, (n=501)

Characteristic	Exposed N (%)	Unexposed N (%)
Number of participants	337 (67.3)	164 (32.7)
Demographics		
Age (years)		
≤30	30(8.9)	19(11.6)
>30-40	121(35.9)	40(24.4)
>40-50	101(29.9)	59(35.9)
>50	85(25.2)	46(28.1)
Duration of employment (years)		
≤5	39(11.6)	28(17.1)
>5-10**	135(40.1)	32(19.5)
>10-15	49(14.5)	17(10.4)
>15-20	24(7.1)	20(12.2)
>20*	90(26.7)	67(40.9)
Sex **		
Female	309(91.7)	95(57.9)
Male	28(8.3)	69(42.1)
Job Title (yes)		
Administrative		164(100.0)
Professional nurses	123(36.5)	
Enrolled nurses	141(41.8)	
Enrolled nursing assistants	73 (21.7)	
Medical and Personal History		
Personal history of Allergy Disease (yes)	147(43.6)	83(50.6)
Family history of Allergy Disease (yes)	197(58.5)	102(62.2)
Fruit allergy (yes)	29(8.6)	9(5.5)
Previous open surgery (yes)*	168(49.8)	61(37.2)
Work-related allergy symptoms(yes)*	138(40.9)	52(31.7)
Non-occupational latex exposure (yes)	161(47.8)	76(46.3)
Latex sensitisation (yes)	24(7.1)	5(3.1)
Current latex allergy (yes)*	20(5.9)	3(1.8)

Chi square, *p<0.05, **p<0.001

Table 2: Comparison of risk factors between latex sensitised (skin prick test positive) and non-sensitised (skin prick test negative) healthcare workers at King Edward VIII Hospital, KwaZulu-Natal South Africa (n=501)

Characteristics	Latex SPT +ve[ǂ] (29) N (%)	Latex SPT –ve[ǂ ǂ] (472) N (%)
Demographics		
Age (years.)		
≤30	1 (3.5)	48(10.2)
>30-40	13 (44.8)	148(31.4)
>40-50	8 (27.6)	152(32.2)
>50	7 (24.1)	124(26.3)
Duration of employment		
≤5	3(10.3)	64(13.6)
>5-10	16(55.2)	151(31.9)
>10-15	3(10.3)	63(13.4)
>15-20	1(3.5)	43(9.1)
>20	6(20.7)	151(31.9)
Sex (yes)		
Male	5(17.2)	118(25.0)
Female	24(82.8)	354(75.0)
Job Title (yes)		
Administrative	5(17.2)	159(33.7)
Professional nurses	5(17.2)	118(25.0)
Enrolled nurses	14(48.3)	127(26.9)
Enrolled nursing assistants	5(17.2)	68(14.4)
Latex Exposure		
Exposure status(yes)	24 (82.8)	313(66.3)
Type of gloves		
None	5(17.2)	165(34.6)
Exclusive powdered latex glove (yes)	2(6.9)	36(7.6)
Exclusive powder free latex glove (yes)*	11(37.9)	77(16.3)
Mixed (yes)	11(37.9)	198(41.9)
Medical and Personal History		
Personal history of Allergy Disease (yes)	16(55.2)	214(45.3)
Family history of Allergy Disease (yes)	18(62.1)	281(59.5)
Fruit allergy (yes) *	5(17.2)	33(6.9)
Previous open surgery (yes)	18(62.1)	211(44.7)
Non-occupational latex exposure (yes)	12(41.4)	225(47.7)
Reaction to other latex medical devices (yes)*	3(10.3)	8(1.7)

Chi Square, *p<0.05

[ǂ]Latex Skin Prick Test Positive

[ǂ ǂ]Latex Skin Prick Test Negative

Table 3: Crude Odds Ratios (OR) (95%CI) of demographics, exposure status, medical and personal history and latex sensitisation and latex allergy amongst healthcare workers at King Edward VIII Hospital, KwaZulu-Natal South Africa, (n=501)

Characteristics	N=29	Latex Sensitisation OR (95%CI)	N=23	LA[ǂǂ] OR (95%CI)
Demographics				
Age (years)				
≤30	1	0.3(0.0-1.9)	1	0.4(0.0-2.4)
>30-40	13	1.8(0.8-3.7)	11	2.0(0.9-4.6)
>40-50	8	0.8(0.4-1.8)	7	0.9(0.4-2.2)
>50	7	0.8(0.4-2.1)	4	0.6(0.2-1.7)
Duration of employment (years)				
<5	3	0.7(0.2-2.4)	3	0.9(0.3-3.2)
5-10	16	2.6(1.2-5.5)*	14	3.3(1.4-7.6)*
>10-15	3	0.7(0.2-2.4)	3	0.9(0.3-3.2)
>15-20	1	0.4(0.0-2.1)	1	0.5(0.0-2.8)
>20	6	0.5(0.2-1.4)	2	0.2(0.0-0.8)
Sex (yes)				
Female	24	1.6(0.6-4.1)	20	2.2(0.7-7.2)
Job Title (yes)				
Administrative	5	0.4(0.2-1.1)	3	0.3(0.1-0.9)*
Professional nurses	5	0.6(0.2-1.6)	4	0.6(0.2-1.8)
Enrolled nurses	14	2.5(1.2-5.3)*	11	2.4(1.1-5.6)*
Enrolled nursing assistants	5	1.2(0.5-3.3)	5	1.7(0.6-4.5)
Latex Exposure				
Exposure status (yes)	24	2.4(0.9-6.3)	20	3.4(1.1-10.8)*
Type of gloves				
None	5	0.4(0.2-1.0)	3	0.3(0.1-0.9)*
Exclusive Powdered latex glove (yes)	2	0.9(0.0-3.6)	2	1.2(0.0-1.7)
Exclusive Powder free latex glove (yes)	11	3.1(1.4-6.8)*	10	3.1(1.7-9.1)*
Mixed gloves(yes)	11	0.8(0.4-1.8)	8	0.7(0.3-1.7)
Medical and Personal History				
Personal history of Allergy Disease (yes)	16	1.4(0.7-3.1)	12	1.3(0.5-2.9)
Family history of Allergy Disease (yes)	18	1.1(0.5-2.4)	14	1.1(0.5-2.4)
Fruit allergy (yes)	5	2.8(1.0-7.5)	5	3.7(1.4-10.0)*
Previous open surgery (yes)	18	1.1(0.5-2.4)	14	1.5(0.7-3.1)

Chi square, *p<0.05

ǂ Latex Skin Prick Test Positive

ǂǂLatex Skin Prick Test Positive and work related clinical symptoms of allergy

Table 4: Multivariate analysis of demographics, medical and personal history, exposure history and latex sensitisation (LS)ǂ and latex allergy (LA)ǂǂ amongst healthcare workers at King Edward III Hospital, KwaZulu-Natal South Africa, (n=501)

	MODEL I* (n=501)		MODEL II** (n=501)		MODEL III***(n=202)		MODEL IV****(n=252)	
Characteristics	LS OR (95%CI)	LA OR (95%CI)	LS OR (95%CI)	LA OR (95%CI)	LS OR (95%CI)	LA OR (95%CI)	LS OR (95%CI)	LA OR (95%CI)
Demographics								
Sex (female)	0.9(0.2-2.7)	1.1(0.3-4.4)	0.9(0.3-2.7)	1.1(0.3-4.5)	0.3(0.0-1.8)	0.3(0.0-3.1)	2.5(0.5-12.2)	2.5(0.5-12.2)
Duration of employment (years)	0.9(0.9-1.0)	0.9(0.8-0.9)	0.9(0.9-1.0)	0.9(0.8-0.9)	0.9(0.9-1.8)	0.7(0.5-1.0)	0.9(0.9-1.0)	0.9(0.9-1.0)
Latex Exposure								
Exposure status(yes)	2.2(0.7-6.7)	2.6(0.7-9.8)						
Type of gloves								
None			1	1				
Exclusive lightly powdered latex glove (yes)			1.6(0.3-9.8)	2.6(0.4-17.7)				
Exclusive Powder free latex glove (yes)			4.2(1.2-14.1)	5.1(1.2-21.2)				
Mixed gloves (yes)			1.7(0.5-5.6)	1.7(0.4-7.1)				

Pairs of Powdered latex Gloves in the last 7 days					1.1(1.0-1.2)	1.2(1.0-1.4)		
Pairs of Powder Free Latex Gloves in the last 7 days							1.0(0.9-1.1)	1.0(0.9-1.1)
Personal and Medical History								
Personal history of allergy disease (yes)	1.5(0.7-3.3)	1.4(0.6-3.2)	1.5(0.7-3.3)	1.3(0.6-3.2)	1.4(0.3-6.8)	1.6(0.2-11.6)	1.0(0.4-2.9)	0.9(0.3-2.8)
Family history of allergy disease (yes)	1.0(0.45-2.2)	0.9(0.4-2.2)	1.1(0.5-2.3)	0.9(0.4-2.3)	0.4(0.1-1.9)	0.5(0.1-3.6)	0.7(0.2-2.0)	0.8(0.3-2.7)
Fruit allergy (yes)	2.3(0.8-6.7)	3.1(1.1-9.2)	2.2(0.8-6.5)	3.0(0.9-9.1)	5.0(0.4-56.9)	9.7(0.6-163.0)	1.7(0.3-8.5)	2.0(0.4-10.4)
Previous open surgery (yes)	2.0(0.9-4.4)	1.9(0.8-4.6)	2.1(0.9-4.6)	1.9(0.8-4.7)	1.4(0.3-7.4)	1.2(0.1-11.1)	1.1(0.4-3.2)	1.2(0.4-3.8)

ǂLatex Skin Prick Test Positive

ǂǂLatex Skin Prick Test Positive and work related clinical symptoms of allergy
*Model included latex glove exposure status
**Model included type of gloves
***Model included number of pairs of powdered latex gloves
****Model included number of pairs of powder free latex gloves

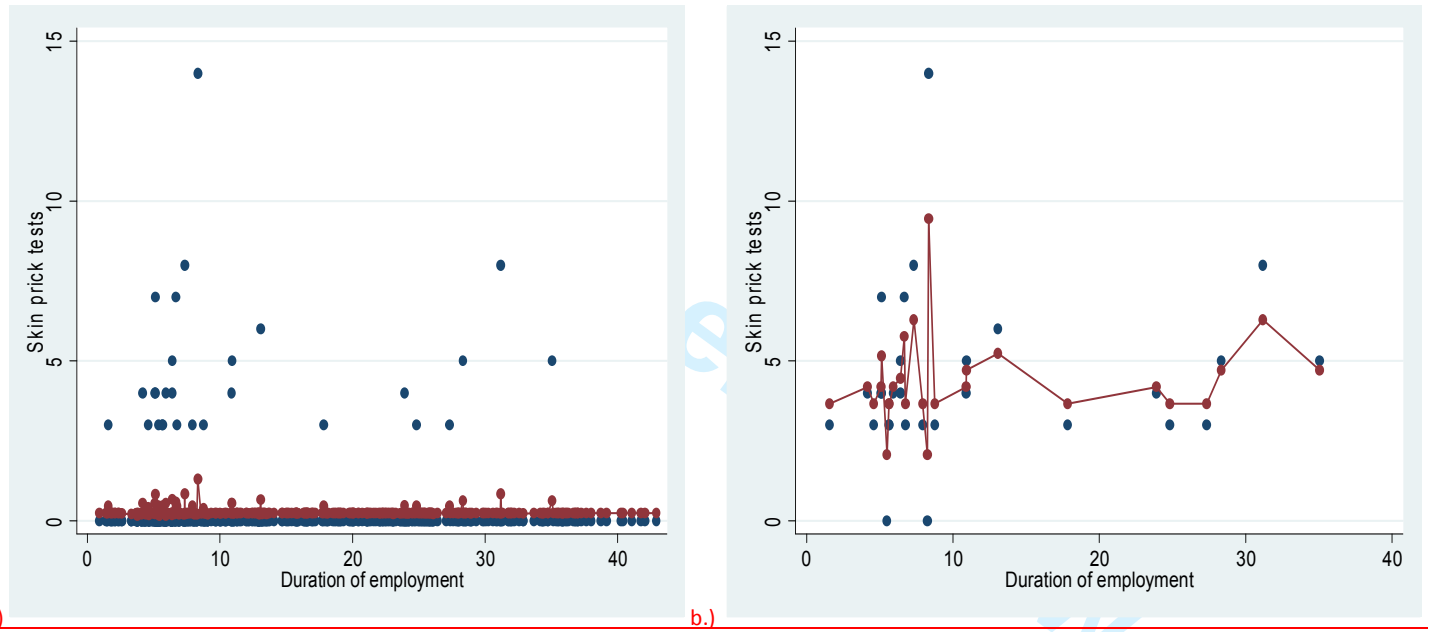


Figure 1: Exposure-response relationship between duration of employment and latex sensitisation using penalised splines including a.) All particioants and b) Spt positive only

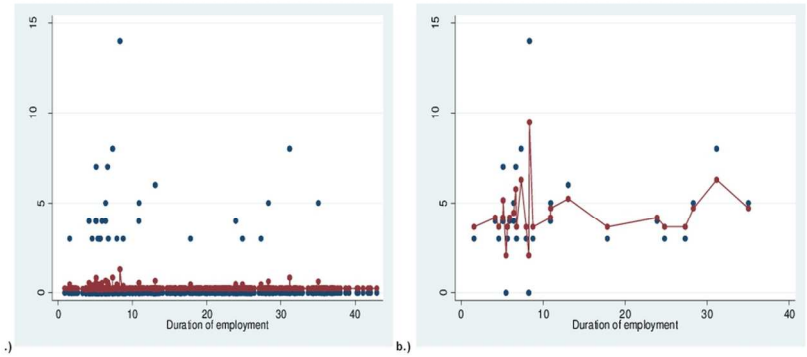
STROBE Statement—Checklist of items that should be included in reports of ***cross-sectional studies***

	Item No	Recommendation
Title and abstract	1	(*a*) Indicate the study's design with a commonly used term in the title or the abstract
		(*b*) Provide in the abstract an informative and balanced summary of what was done and what was found
Introduction		
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported
Objectives	3	State specific objectives, including any prespecified hypotheses
Methods		
Study design	4	Present key elements of study design early in the paper
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection
Participants	6	(*a*) Give the eligibility criteria, and the sources and methods of selection of participants
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group
Bias	9	Describe any efforts to address potential sources of bias
Study size	10	Explain how the study size was arrived at
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why
Statistical methods	12	(*a*) Describe all statistical methods, including those used to control for confounding
		(*b*) Describe any methods used to examine subgroups and interactions
		(*c*) Explain how missing data were addressed
		(*d*) If applicable, describe analytical methods taking account of sampling strategy
		(*e*) Describe any sensitivity analyses
Results		
Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed
		(b) Give reasons for non-participation at each stage
		(c) Consider use of a flow diagram
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders
		(b) Indicate number of participants with missing data for each variable of interest
Outcome data	15*	Report numbers of outcome events or summary measures
Main results	16	(*a*) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included
		(*b*) Report category boundaries when continuous variables were categorized
		(*c*) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses

Discussion		
Key results	18	Summarise key results with reference to study objectives
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence
Generalisability	21	Discuss the generalisability (external validity) of the study results
Other information		
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based

*Give information separately for exposed and unexposed groups.

Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at http://www.plosmedicine.org/, Annals of Internal Medicine at http://www.annals.org/, and Epidemiology at http://www.epidem.com/). Information on the STROBE Initiative is available at www.strobe-statement.org.



.) b.)

Figure 1: Exposure-response relationship between duration of employment and latex sensitisation using penalised splines including a.) All particioants and b) Spt positive only

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