



Original Article

Effect of Occupational Exposure on Allergic Diseases and Relationship with Serum IgE Levels in the Tannery Workers in Bangladesh

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ABSTRACT: The tannery workers in Hazaribagh, Dhaka, have been found to suffer from a wide range of allergic diseases. Serum IgE level plays a crucial role in the development of allergy. Occupational exposure to chromium compounds and other chemicals used in mineral tanning processes may elevate IgE levels and cause allergy. We evaluated serum IgE levels and investigated its relationship with allergic diseases in the tannery workers and control subjects. The tannery workers had a single or more than one type of allergic diseases including food allergy, allergic contact dermatitis, allergic rhinitis, eosinophilia, allergic urticaria, drug allergy, and non-specific allergy. IgE levels were significantly higher in the tannery workers (339.6 IU/mL) compared to that in the unexposed controls (207.5 IU/mL). Tannery workers without allergic diseases had significantly elevated levels of IgE (313.5 IU/mL) compared to the controls (90.4 IU/mL) without allergy. IgE levels were maximally elevated in the tanners with allergic urticaria (563.4 IU/mL) followed by non-specific allergy (390.1 IU/mL), and food allergy (346.3 IU/mL) whereas control subjects with eosinophilia had maximally elevated levels of IgE (737.1 IU/mL) followed by allergic contact dermatitis (479.1 IU/mL), and allergic urticaria (373.3 IU/mL). Allergy attacks were more frequent in the tanners during the hot season while the control subjects had frequent attacks during the cold season. These observations suggested that occupational exposure to chromium and other toxic chemicals and pollution in the working environment were associated with the development of allergic diseases and elevated levels of IgE in the tannery workers in Bangladesh.

KEYWORDS: Tannery workers, allergic diseases, serum IgE, Hazaribagh, Bangladesh.

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INTRODUCTION

In Bangladesh, nearly 10,000 people earn their livelihood from the tanneries of Hazaribagh¹, a very densely populated area in the capital city Dhaka, where around 300 tannery industries are located on 25 hectares of land. These industries use mineral tanning processes which discharge about 6000 cubic meters of liquid effluent and 10 tons of solid waste everyday² that cause devastating effects on the environment - water, soil, air, plants, human beings and all other ecological systems. According to a report titled, "The Top Ten Toxic Threats: Cleanup, Progress, and Ongoing Challenges" published by Zurich-based Green Cross Switzerland and New York-based Blacksmith Institute, at least 160,000 people of Dhaka city have become victims of pollution due to the presence of toxic chemicals, mainly chromium, in Hazaribagh. Chromium (III) sulphate is widely used in the leather industry as the basic tanning agent³. The tannery workers are under constant threat of adverse health effects due to excessive exposure to nitrosamines, chromate pigments, soft sodium sulfate, lime, ammonium sulphate, benzidine-based direct dyestuffs, formaldehyde, leather dust, and aromatic organic solvents⁴. Chromium may enter the body by breathing, eating and by direct cutaneous contact⁵; therefore, the tannery workers

are exposed to this element, mainly in the inorganic chromium (III) form, or in the protein bound form, such as leather dust.

The impact of chemical exposure can cause dizziness, headache, irritation of eyes, skin or lungs, and allergic diseases². The total chromium content in tannery air of Mexico had been reported 1–54 $\mu\text{g}/\text{m}^3$ and the evaluated additional element daily intake for workers was in the range of 150–325 μg , while the level for the unexposed population was < 30 μg ⁶. In Egypt, workers have potentially high exposure levels to chromium (VI) in the cement production and construction industry and to chromium (III) in the leather tanning industry. It had been found that about one third of these workers had severe skin and chest manifestations while severe nasal manifestations were observed in 22.7% and 20% of cement and tannery workers, respectively⁷. The prevalence of occupational allergy had been investigated in Indonesian tanneries and found only 3% of 472 workers had occupational allergic contact dermatitis; identification of the causative allergens showed potassium dichromate (9.2%), N,N-diphenylguanidine (5.3%), benzidine (3.9%) and sodium metabisulfite (2.6%) were the occupationally relevant sensitizers⁸. Another study conducted from 1991 to 1997

found that chromium was responsible for 5.6% of a total 2543 cases of occupational allergic contact dermatitis among the Finnish working population⁹.

Although chromium (III) compounds are not potential carcinogenic agents for humans¹⁰, however positive epidermal tests to high concentration of Cr (III) have been observed^{11,12}. Occupational exposure to Cr (III) increases the risk of dermatitis, ulcers and perforation of the nasal septum, and respiratory illnesses, as well as increased lung and nasal cancer¹³⁻¹⁵. Under certain conditions Cr (III) can be transformed to Cr (VI)¹⁶; this hexavalent chromium or chromate is extremely hazardous that cause lung cancer, tumor or kidney inflammation at very low concentration, whereas Cr (III) is an essential nutrient with a broad safety range and low toxicity¹⁷. Chromium exposed subjects show allergic reactions with severe redness and swelling of the skin. Allergic contact dermatitis may arise from exposure to either trivalent or hexavalent chromium. It has been shown that hexavalent chromium penetrates the undamaged skin, and subsequently reduces to Cr (III) that combines to proteins and other skin components to form a whole skin allergen¹⁶.

We have reported earlier that a significantly higher proportion of the tannery workers (67%) of Hazaribagh suffer from various types of allergic diseases including food allergy, allergic contact dermatitis, allergic bronchitis and multiple allergies¹⁸. A recent study conducted on 120 tannery workers of Sialkot, Pakistan, showed 13% of the tanners had skin rashes, 12% had chronic bronchitis, 8% had gastritis and 3% had conjunctivitis¹⁹. Also, the workers had hematological, hepatic and renal function impairment because of oxidative stress on their body systems. In another study on 418 laborers of 15 tanneries in Kanpur, India, reported incidences of asthma (38%), dermatitis (23%), and chronic bronchitis (14%)²⁰. Serum IgE has a direct, strong correlation with allergic diseases, but none of the previous studies evaluated the levels of IgE in the tannery workers who suffer from various allergies. Therefore, the present study was undertaken to investigate the relationship of serum IgE levels with occupational allergy among the tannery workers in Bangladesh.

MATERIALS AND METHODS

Study subjects and sample collection

This cross sectional study was carried out on 117 subjects of whom 73 were tannery workers from four tanneries of Hazaribagh, situated at the south-western part of the capital city Dhaka, Bangladesh, having work exposure at the tanneries for at least 2 years; and the remaining 44 were non-tannery workers who were self-employed in shops, salesmen, gardeners, day laborers and office staffs. All the study participants were men and subjects with known intestinal parasitic infestations were excluded from the study. The guidelines of the ethical review committee of the Biological Science Faculty, University of Dhaka, were followed during sample collection. Only full consenting persons were enrolled in this study by simple random sampling method. The occupational health information of each study subject was recorded on a preformed questionnaire. About 3 mL of peripheral blood was aseptically drawn from each of the study subjects with the

help of an expert and collected in anticoagulant containing vacutainer tubes. Serum was separated from these blood samples and stored at -20°C until analyzed.

Working environment at tannery

The working environment of the tanneries was heavily littered with raw hides and skins that might be contaminated with a variety of bacteria, molds and yeasts which could cause various diseases such as anthrax, leptospirosis, tetanus and brucellosis, as reported elsewhere²¹. The large quantities of dust produced in buffering operations would normally be contaminated with pathogenic microorganisms and putrefaction products. Tannery effluent often contained highly odorous wastes that were mostly dumped into the nearby river Buriganga while solid wastes from fleshing and shaving were dumped on the roadsides or in and around garbage bins^{1,22}, which might be potential health hazards. Quite often the tannery workers were seen eating, drinking or smoking in their work area without cleaning contaminated hands. Direct exposure to different chemicals caused temporary effects such as dizziness, headache, irritation of eyes, skin or lungs, allergic diseases and suffocation.

Classification of allergic diseases

A dermatologist of Bangladesh Medical College Hospital examined all the study participants carefully and classified the type of allergic diseases, as described elsewhere¹⁸. Briefly, allergic rhinitis was characterized by watery exudation of the conjunctivae, nasal mucosa and upper respiratory tract as well as sneezing and coughing. A food allergy was defined as an immediate hypersensitivity reaction involving itching, swelling in the throat, and difficulty in breathing caused by ingestion of foods. Other food allergy reactions were more delayed, causing gastrointestinal problems (constipation, diarrhea, gas formation, cramping, and bloating), rashes, and headaches. Allergic urticaria was characterized by hives or swollen skin with a kind of rash notable for pale red, raised, itchy bumps that sometimes caused a burning or stinging sensation on different parts of the body surface.

Allergic contact dermatitis was inflammation characterized by eczematous skin lesions usually observed following contact with certain chemicals. The symptoms included itching, erythematous rash, papulovesicular eruption, exudation, pustule, and lichenified rash. Dry, scaly skin was the most common morphological feature, followed by hyperpigmentation, exudation, vesicles, fissuring, and lichenification of allergic contact dermatitis. The predominant sites of allergic contact dermatitis were palms, followed by fingers, dorsum, and in some cases the entire hand and feet. Study subjects who have had more than one allergic disease had been included under multiple allergies whereas itchy skin from unknown causes was classified non-specific allergy. Drug allergy was erythematous rash and itchy skin after taking a specific drug.

Determination of Serum IgE

The quantitative test for IgE was based on a solid phase ELISA technique. The ELISA plate and the reagents were obtained from DRG Diagnostics, Germany. The test was performed according to the recommended protocol of the manufacturer. Briefly, the assay system utilized one anti-IgE antibody in the solid phase and another one was in the antibody-enzyme conjugate solution. The serum sample was added to the anti-IgE coated microtiter plates and the

content of IgE was determined by the standard procedure. The results were expressed in IU/mL.

Statistical analyses

Data analyses were carried out using the software Statistical Package for Social Science (version 17.0 for Windows, SPSS Inc., Chicago, USA). The programs used were simple statistics and Independent-Samples t test. Significance of differences in categorical variables was assessed by Chi-square test and Fisher exact test. A *p* value of ≤ 0.05 was the criterion for a statistically significant difference. The mean \pm SD values were calculated for each parameter.

RESULTS

Demographic and clinical characteristics of the subjects

In this study, the mean age of the tannery workers was 30.3 ± 11.4 yrs (range: 14 - 62 yrs) while that of the non-tannery workers was 32.0 ± 8.9 yrs (range: 17 - 62 yrs). About 66% of the tannery workers were below 30 yrs of age compared to about 50% of the non-tannery workers within this age group. The tannery workers had mean duration of work at tanneries for 5.8 ± 5.2 yrs. Their body mass index (BMI) was 21.4 ± 2.9 compared to 22.3 ± 2.6 of the non-

tannery workers, and the family history of allergy was about 23% and 18%, respectively. It was found that the BMI, age, and family history of allergy between the study groups did not vary significantly. A high proportion of the tannery workers (49 out of 73, 67%) were suffering from allergic diseases compared to the control subjects (17 out of 44, 39%) which differed significantly ($\chi^2 = 7.94, p < 0.01$), as reported elsewhere¹⁸.

Levels of IgE in the study populations

The normal serum concentration of IgE is 0-200 IU/mL in western countries whereas in the tropical countries this level may vary from 1000-2000 IU/mL. There is no established range of serum IgE for the healthy Bangladeshi population. In this study, the control subjects had a median value of serum IgE level of 86.8 IU/mL with a mean value of 207.5 ± 255.3 IU/mL, and the levels varied from 3.0-830.0 IU/mL. On the other hand, the tannery workers had a median value of serum IgE level of 280.0 IU/mL with a mean value of 339.6 ± 275.3 IU/mL, and the levels varied from 4.4-950.0 IU/mL. It was found that IgE level in the tannery workers was significantly higher than that in the control subjects ($p < 0.01$). Interestingly, the levels of IgE were significantly higher in the tannery workers without any complain of allergy compared to the control subjects, without allergy (Table 1).

Table 1. Evaluation of serum IgE levels and allergy in the tannery workers and control subjects.

Study group	Study subjects (No. of subjects)	Serum IgE (IU/mL) Mean \pm SD	Statistics: <i>p</i> -value between groups
(a)	Tannery workers (N=73)	339.6 \pm 275.3	(a) vs (b): <i>p</i> <0.005
(b)	Control subjects (N=44)	207.5 \pm 255.3	
(c)	Control subjects without allergy (N=27)	90.4 \pm 98.3	(c) vs (d): <i>p</i> =0.001
(d)	Control subjects with allergy (N=17)	393.5 \pm 315.6	(d) vs (e): <i>p</i> =0.596
(e)	Tannery workers with allergy (N=49)	352.4 \pm 258.4	(e) vs (f): <i>p</i> =0.574
(f)	Tannery workers without allergy (N=24)	313.5 \pm 311.2	(c) vs (f): <i>p</i> <0.01

IgE levels in different allergic diseases

The study subjects with allergy (tannery workers: N=49; control subjects: N=17) were grouped with respect to

different allergic diseases and their serum IgE levels were compared (Table 2). It was observed that IgE levels were highly variable both in the tannery workers and control

Table 2. Comparison of serum IgE levels in the tannery workers and control subjects in different allergic diseases.

Type of allergic diseases	Levels of serum IgE: Mean \pm SD (IU/mL)		<i>p</i> -value
	Tannery workers with allergy (N=49)	Control subjects with allergy (N=17)	
Food allergy	346.3 \pm 283.6 (N=12)	345.1 \pm 341.4 (N=5)	0.99
Allergic contact dermatitis	322.7 \pm 170.0 (N=9)	479.1 \pm 139.9 (N=3)	0.18
Allergic rhinitis	282.2 \pm 277.2 (N=5)	265.6 \pm 288.6 (N=5)	0.93
Eosinophilia	268.4 \pm 168.3 (N=9)	737.1 \pm 109.3 (N=3)	0.002
Allergic urticaria	563.4 \pm 247.4 (N=5)	373.3 (N=1)	—
Non-specific allergy	390.1 \pm 323.5 (N=6)	—	—
Drug allergy	217.1 \pm 106.7 (N=3)	—	—

IgE levels in allergic urticaria, non-specific allergy and drug allergy could not be compared between tannery workers and control subjects either because of very few or absence of cases.

subjects having similar allergic diseases; however, the mean values were higher in the tannery workers in case of allergic urticaria (TW: 563.4 IU/mL; CS: 373.3 IU/mL), food allergy (TW: 346.3 IU/mL; CS: 345.1 IU/mL) and allergic rhinitis (TW: 282.2 IU/mL; CS: 265.6 IU/mL). The mean IgE level in allergic contact dermatitis was higher in

the control subjects (479.1 IU/mL) than in the tannery workers (322.7 IU/mL); while in eosinophilia, IgE level in the control subjects (737.1 IU/mL) was significantly higher ($p=0.002$) than in the tannery workers (268.4 IU/mL). IgE levels in the tannery workers with allergic urticaria, non-specific allergy (390.1 IU/mL) and drug allergy (217.1

IU/mL) could not be compared to the corresponding levels in the control subjects either because of very few or absence of cases. Multiple allergy was not compared among the study populations, and the allergic subjects were grouped according to their main complain of the type of allergic diseases.

Seasonal incidence of allergic diseases

In order to determine the seasonal incidence of allergic diseases among the study populations, the seasons were divided into two categories: hot season (March to October) and cold season (November to February). It was found that

of the 49 tannery workers having allergy, 61.2% were attacked more frequently (more than 4 times) with allergic diseases during the hot season, and 16.3% during the cold season. On the other hand of the 17 subjects having allergy among the controls, 47.1% were attacked more frequently during the hot season, and 29.4% during the cold season. It was also found that 22.5% of the tannery workers and 23.5% of the control subjects were attacked with allergic diseases in both seasons. These results are presented in Table 3 that shows while similar percentages of the study populations suffer allergy attacks during both seasons;

Table 3. Seasonal incidence of allergy attack in tannery workers and control subjects.

Allergy in study group	No. of subjects (%) with seasonal incidence of allergy		
	Hot season	Cold season	Both seasons
Tannery worker, N=49	30 (61.2)	08 (16.3)	11 (22.5)
Control subjects, N=17	08 (47.1)	05 (29.4)	04 (23.5)
Statistics*	$p>0.05$	$p>0.05$	$p>0.05$

Hot season (March to October), Cold season (November to February). *Chi-square test.

a higher proportion of the tanners had allergy attacks during the hot season. High temperature may cause more emission of fumes, smoke or fine particles from different chemicals used in tanning of raw hides. These may cause severe skin and lung irritation, itch, rash and burning sensation on body surfaces leading to various allergic diseases. Also, hot weather may be favorable for rapid growth of a variety of bacteria, molds and yeasts in the tannery working area, which may be potential risk factors for various allergies.

DISCUSSION

The leather industry in Bangladesh is one of the most profitable and the fourth largest foreign exchange earner of the country contributing about 6% of the total export earnings. The benefit of the tannery industry to the economy as well to our society can be measured, but the damage made by this industry to the environment as well as to the society cannot be measured by any scale²³. The tanners suffer from different types of skin and respiratory diseases resulting from repeated exposure to hazardous chemicals when measuring and mixing those as part of the tanning process. Moreover, the houses of tannery workers in Hazaribagh are built next to contaminated streams, ponds, and canals. Due to exposure to toxic chemicals used to process and dye the leather, acid burns, rashes, aches, dizziness and nausea are also common health problems faced by the local residents. A previous study found that the incidence of illness among the residents of Hazaribagh was 16% higher than those living in other areas of Dhaka city¹. Since IgE is associated with intestinal parasitic infections (excluded from this study) and allergic diseases, levels of IgE have been assessed in the tannery workers who suffer from different types of allergy. The established levels of serum IgE in the normal healthy Bangladeshi population is not known although it is thought to be much higher than in people living in western countries; however, we have reported the value to be 186 ± 221 IU/mL in our previous work²⁴. It has been reported in a recent study conducted on the tannery workers in Sialkot, Pakistan that 54% of the workers had chromium levels in blood above the upper limit set by the Agency for Toxic Substance and Drug Registry¹⁹. These workers had significantly raised

chromium levels in their biological fluids that had adverse health effects due to enhanced oxidative stress and inflammatory changes. Another study on factory workers in tanneries of Kasur found the total chromium content in the blood of younger workers (under 20 years) was significantly higher (24%) when compared with the age-matched non-workers²⁵. In a group of Mexican tannery workers highly exposed to chromium from tanning and retanning departments, an inverse association was found between serum chromium and urine iron (-0.524), urine chromium and hemoglobin (-0.594) suggesting that chromium had an adverse effect on iron metabolism, which was possibly associated with excessive body chromium accumulation⁵. It has been found that occupational exposure to Cr (III) can lead to a detectable DNA damage of human peripheral lymphocytes, and the damage was associated with chromium levels in blood²⁶.

Serum IgE and associated cellular responses play crucial role in the development of allergic diseases. Sensitization to chromium, commonly used in leather tanneries, produce two types of hypersensitivity reactions: type I - an IgE-mediated immediate response, and type IV - a delayed, cell-mediated immune mechanism. Following an induction phase during which the individual becomes sensitized, subsequent exposures result in an allergic response, with symptoms typically presenting as dermatitis or asthma. It had been reported earlier that of the 73 tannery workers, 25% suffered from food allergy, 29% from allergic contact dermatitis, and 16% suffered from eosinophilia, among other allergies; the frequency of allergic contact dermatitis was significantly higher ($p=0.02$, Chi-square test) in the tannery workers compared to only 9% cases among the unexposed controls (N=44)¹⁸. In this study, the serum IgE levels both in the tannery workers and control subjects varied widely from 4.4-950 IU/mL and 3-830 IU/mL, respectively, although the relative incidences of allergic diseases were much lower in the control subjects. The mean IgE level in the tanners (339.6 ± 275.3 IU/mL) was significantly higher than that in the control subjects (207.5 ± 255.3 IU/mL). However, the maximally elevated IgE levels were found in the control subjects with eosinophilia, followed by tannery workers with allergic urticaria, control subjects with allergic contact dermatitis.

These differences could be due to variability of the types of allergic diseases or individual exposure pattern.

The working environment of the occupational populations may vary widely between high- and low-income countries, and epidemiological study on health complaints in tannery workers is among the few. One study examined the atmosphere of the working areas in the leather factories of Tuzla, Istanbul, and detected fungal genera *Penicillium* spp., followed by *Aspergillus*, *Alternaria*, *Scopulariopsis*, and *Cladosporium* spp. which were multiplying at differing rates and were found as risk factors for increasing respiratory obstruction among the tannery workers²⁷. Another study in Pakistan found the prevalence of asthma in leather tannery workers to be associated with educational status, ethnicity, smoking, perceived to have allergy and duration of work²⁸. A previous study in Egypt reported that IgE level and absolute eosinophil count were statistically higher among exposed tannery workers with contact dermatitis than among workers away from exposure to chromium²⁹. We reported earlier that the tannery workers had significantly higher eosinophil counts than the unexposed subjects¹⁸. In this study, IgE levels in the tannery workers without any complain or symptoms of allergy were found significantly higher compared to the control subjects without allergy. This observation supports that exposure to toxic chemicals, chromium, and pollution in the working environment elevates serum IgE.

The relationship between IgE levels and airway hyperresponsiveness in the presence or absence of asthma and other atopic diseases has been investigated in a birth cohort of 562 children (age: 11yrs) in New Zealand. The mean IgE levels in the boys and girls were 121 and 98 IU/mL, respectively. The prevalence of asthma was strongly related to serum IgE levels; no asthma was found in children with IgE level <30 IU/mL, and 36% of those with IgE levels >1000 IU/mL had asthma. These observations suggested that children who had been asymptomatic and had no history of atopic disease, airway hyperresponsiveness appeared to be closely linked to allergy, as reflected by serum IgE level³⁰. In order to find out the relationship between serum IgE levels and severity of asthma, a study conducted in India found the mean IgE levels was about 152 IU/mL in normal healthy subjects while the value was 1045 IU/mL in severe asthmatics. The authors found no statistically significant correlation between IgE levels with mild, moderate or severe asthma since the variability in each level of asthma was very large³¹.

From the above studies conducted in different populations of geographical locations and age groups, it has been revealed that serum IgE levels vary among the healthy control populations. It is not surprising that multiple genes have been found associated with asthma in different populations. A recent study also suggests that genetics of asthma and allergic diseases are multifactorial and are conditional on other factors such as environmental exposure and race/ethnicity³². Further, it has been shown that many genes have been linked to IgE production, but few have been linked to the developmental aspects of genetic association with IgE production³³, and the genetic association profiles of the IgE production among fetus, infancy and childhood are different. In the present study, exposure to high levels of chromium and other toxicants used in tannery processing and the working environment at

the leather industries of Hazaribagh might cause elevated levels of serum IgE in the tannery workers.

CONCLUSION

This study clearly showed the tannery workers of Hazaribagh, Dhaka, Bangladesh, have significantly elevated levels of serum IgE and suffer from different types of allergic diseases. IgE levels in the tannery workers without any symptoms of allergy were significantly higher. The health problems including allergic diseases may be reduced by decreased exposure to chromium and other toxic chemicals and improving the factory working-environment, control and elimination of allergens, control of humidity and reducing exposure to excessive heat or cold.

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