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Chromium-mediated hyperpigmentation of skin in male tannery workers in Bangladesh

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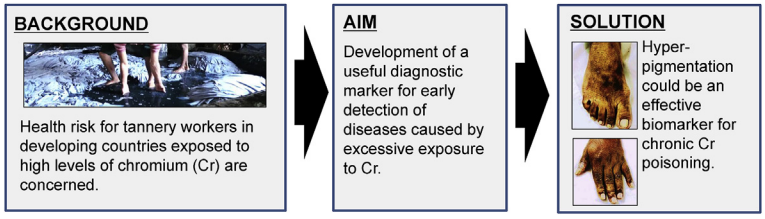
HIGHLIGHTS

- Cr level in both hair and toenails reflects chronic exposure to Cr in tannery workers.
- Excessive Cr exposure developed hyperpigmented skin in male tannery workers.
- Hyperpigmentation could be an effective biomarker for chronic Cr poisoning.
- Cr mediated hyperpigmentation could easily be digitalized by spectrophotometer.

GRAPHICAL ABSTRACT



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ABSTRACT

Since tannery workers in developing countries are chronically exposed to high levels of chromium (Cr), there are serious concerns about health problems. However, there has been limited study in which Cr levels were measured in tannery workers, who are chronically exposed to Cr. Our preliminary inspection showed that there was hyperpigmented skin in tannery workers. We therefore investigated the correlation between skin pigmentation levels digitally evaluated as L* values by using a reflectance spectrophotometer and Cr levels in skin appendages in 100 male tannery workers and in 49 male non-tannery workers in Bangladesh. Digitalized skin pigmentation levels of the face and feet in addition to Cr levels in hair and toenails in tannery workers were significantly higher than those in non-tannery workers in our univariate analysis. Spearman's rank correlation coefficient analysis showed significant correlation between duration of tannery work (years) and Cr levels in hair ($r = 0.62$) and toenails ($r = 0.61$). Our multivariate analysis also showed that Cr levels in hair and toenails were significantly correlated with digitalized skin pigmentation levels of the face and feet in addition to duration of tannery work in all participants. Thus, our results showed the development of hyperpigmented skin in tannery workers. Our results also suggested that hyperpigmented skin could be a useful diagnostic marker for chronic

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exposure to Cr. Furthermore, cutaneous L* value might be a convenient marker for detection of chronic Cr poisoning, since the digitalized values enable objective evaluation of skin pigmented levels by general people as well as dermatologists.

1. Introduction

Millions of people worldwide have occupational exposure to chromium (Cr) and it is an important issue (Earth and Cross, 2016). Chronic exposure to Cr has been reported to be involved in the development of various cancers including lung, pancreas and nasal carcinomas (Battista et al., 1995; Mikoczy et al., 1996). In fact, the International Agency for Research on Cancer (IARC, 2004) defined Cr compounds as potent occupational carcinogens (Beyersmann and Hartwig, 2008). Chronic exposure to Cr is also involved in the development of cutaneous and mucosal diseases including dermatitis, ulcerations and perforation of the nasal septum (Krishna, 2004; Lin et al., 1994; Rastogi et al., 2008). Since high levels of Cr are used in tanning processes in developing countries, there are serious concerns about health risks for tannery workers who are exposed to Cr via direct skin contact and inhalation (Hasan et al., 2016; Yoshinaga et al., 2018; Watch, 2012). To our knowledge, however, there has been no study showing Cr levels in both hair and toenails of tannery workers. Moreover, there has been limited study showing evidence of the effect of chronic exposure to Cr on heath in tannery workers.

Hyperpigmented skin is derived from various diseases including solar dermatitis and contact dermatitis (Khanna and Rasool, 2011). Hyperpigmented skin is also known as a useful diagnostic marker for various types of chemical poisoning including arsenicosis (Mazumder et al., 1998; Yu et al., 2006). We previously showed that a reflectance spectrophotometer is a useful device for digitalizing skin pigmentation level as an L* value in humans (Kato et al., 2011). Though diagnosis by dermatologists was essential to evaluate the level of skin pigmentation in previous studies, the L* value enables simple objective evaluation of skin pigmentation.

In the leather industry, there is now global segregation of duties for production of raw materials in developing countries and their processing in developed countries (Febriana et al., 2012). As a result of the segregation, the process from peeling raw hides to finished leather is handled at the tanneries in developing countries including Bangladesh. Previous studies showed that Cr levels inside and around tanneries exceeded the maximum permissible limits of workplaces (0.1 mg/L by WHO/FAO) and the environment (0.1 mg/L by WHO) at Hazaribagh, a built-up area of tanneries, in Dhaka City, Bangladesh (Asfaw et al., 2017; Yoshinaga et al., 2018).

In this study, we performed fieldwork study focusing on tannery workers at Hazaribagh in Dhaka City as well as non-tannery workers (office workers) at Kaliganj in Gazipur City in Bangladesh. We then measured Cr levels in cutaneous appendicular organs in the participants. We finally focused on the effect of Cr level in skin appendage samples on hyperpigmentation of skin in 100 male tannery workers because hyperpigmented skin was found in tannery workers in our preliminary inspection.

2. Materials and methods

2.1. Epidemiological study and ethics approval

This epidemiological study was approved by Nagoya University International Bioethics Committee following the regulations of the Japanese government (approval number: 2013−0070) and the Faculty of Biological Science, University of Dhaka (Ref. no. 5509/Bio.Sc). A letter with written permission from the Tannery Owners Association in Bangladesh to conduct fieldwork research involving their tannery workers and factories was received prior to the start of this study. Informed consent in written form with permission to publish the health findings including photos was obtained from all of the participants in this study. Ethical principles involved in research including human subjects was ensured all of the time (WMA, 2013).

A comparative cross-sectional study was conducted in randomly selected 100 male tannery workers aged from 19 to 65 years (mean ± SD age: 36.77 ± 11.58 years) who worked in tanneries in Hazaribagh, Dhaka City and in 49 male non-tannery workers aged from 20 to 70 years (mean ± SD age: 35.49 ± 10.37 years) who were mainly office workers in Kaliganj, Gazipur City in Bangladesh. Tannery workers used tap water for drinking and daily use that was supplied by the local government, whereas non-tannery workers used well water for drinking and daily use. Water samples were free from arsenic in both areas (Kinniburgh and Smedley, 2001). After obtaining informed written consent, data were collected using a self-reporting questionnaire that included questions on age, sex, body mass index (BMI) (weight in kg/height in m^2), working duration under sunlight in a day and duration of tannery work (in years). The mean ± SD value of BMI in the participants was 23.18 ± 3.5.

2.2. Measurements of skin pigmentation (L* value) and Cr level

A reflectance spectrophotometer (RGB-1002, Lutron Electronic Enterprise Co. Ltd) was used to estimate skin pigmentation levels as L* values on the face and foot. L* values in the L*a*b* system are indicators of skin pigmentation levels (Kato et al., 2011). A higher L* value indicates a lower skin pigmentation level and a lower L*value indicates a higher skin pigmentation. All of the participants washed their body parts including their face and feet with soap and water after work and before participating in this study. Hair and toenail samples were collected from the participants and Cr levels in both hair and toenail samples were measured by the method previously described (Kato et al., 2013; Yajima et al., 2018). Briefly, careful washing with detergent followed by ultra-sonication and treatment with acetone was performed for all the hair and toenail samples to remove any adherent substance from the surfaces of the samples. Then samples were treated with 61% HNO_3 (Grade: EL, Kanto Chemical Co., Inc.) at 80 °C for 3 h and then treated with 30% H_2O_2 (Grade: Atomic Absorption Spectrometry, Kanto Chemical Co., Inc.) at 80 °C for 3 h. Finally, Cr levels were measured by using an inductively coupled plasma mass spectrometer (ICP-MS, 7500cx, Agilent Technologies) after filtration by 45 μm filters. Arsenic (As) levels in hair and toenails were also measured at the same time.

2.3. Statistical analysis

Statistical analyses were performed according to a previously established method (Ohgami et al., 2016). The Mann-Whitney *U* test was conducted to compare Cr levels in hair and toenail samples

with the respective L* values of the faces and feet in tannery and non-tannery workers since Cr levels in hair and toenails did not show normal distributions and L* values of the faces and feet showed normal distributions. Spearman's rank correlation coefficient was used to correlate the duration of tannery work with Cr levels in hair and toenails. A receiver operating characteristics (ROC) curve was used to define the cut-off values of L* values. Means of duration of tannery work and Cr levels in hair and toenails were used to define the cut-off values since they were not normally distributed. Levene's and Bartlett's tests were used to evaluate equalities of variances. p values of < 0.05, < 0.01 and < 0.001 were considered statistically significant in all analyses. A binary logistic regression model [odds ratio (OR) at 95% CI] was used in multivariate and univariate analyses to evaluate correlations between Cr levels in hair and toenails and the respective L* values. Confounding factors including age, BMI and working duration under direct sunlight in a day and As levels in hair or toenails were used in multivariate analysis. McFadden's pseudo R^2 analyses was performed to evaluate the relative contributions (%) of the factors on skin pigmentation levels (L* values). The statistical software JMP Pro v. 11.0.0 was used to analyze the data.

3. Results

3.1. Preliminary inspection for tannery workers

Photographs were taken inside tanneries at Hazaribagh in Dhaka City, a built-up area of tanneries in Bangladesh (Fig. 1A and B). We noted that sunlight exposure for tannery workers was protected by built-up roofs in the tanneries (Fig. 1A). The feet and hands of tannery workers were directly exposed to water polluted with a high level of Cr in the tanning process (Fig. 1B). Hyperpigmented skin lesions on the forehead (Fig. 1C), foot (Fig. 1D) and hand (Fig. 1E) were found as typical skin lesions in tannery workers in a preliminary inspection conducted by our medical doctors.

Fig. 1. The tannery and the workers. Built-up area with a roof made of dark galvanized corrugated steel sheet in the tannery for sunlight protection during leather processing. The transparent texture of some parts of the roof is due to light reflection (A). Hands and feet of the tannery workers were exposed to water polluted with high level of Cr in the tanning process (B). Hyperpigmented skin lesions in the forehead (C), foot (D) and hand (E) were found in the tannery workers during a preliminary inspection by medical doctors.

3.2. Baseline characteristics of the participants

Baseline characteristics of the participants including non-tannery workers (n = 49) and tannery workers (n = 100) are shown in Table 1. Mean Cr levels in hair and toenails of the participants were 2.64 μg/g and 124.00 μg/g respectively. Thus, the mean Cr level in toenails was almost 50-fold higher than that in hair of all the participants ($p < 0.001$). Large numerical differences between the maximum and minimum levels of Cr in hair and toenails (e.g., 2770.1 μg/g vs. 0.13 μg/g in toenails) were obtained because the tannery workers were exposed to a high level of Cr in the tanning process, but the control subjects (non-tannery workers) never worked in tannery nor were exposed to Cr knowingly. The mean L* values of faces and feet in the participants were 63.5 and 86.83 respectively. The L* value of the face was significantly lower than that the foot ($p < 0.001$).

3.3. Comparison of Cr levels in hair and toenails

Cr levels in hair and toenails of tannery workers and those in hair and toenails of non-tannery workers were compared in our univariate analysis (Fig. 2). The mean Cr level of hair in tannery workers was more than 20-fold higher than that in non-tannery workers ($p < 0.001$). Similarly, the mean Cr level in toenails of tannery workers was more than 300-fold higher than that in non-tannery workers ($p < 0.001$).

Table 1
Baseline characteristics of participants.

Characteristics		Total participants (n = 149)
Age (years)	Mean	36.35
	SD	11.17
	Max	70
	Min	19
	Median	35
BMI	Mean	23.18
	SD	3.5
	Max	35.55
	Min	16.07
	Median	22.77
Occupation	Non-tannery Workers	49
	Tannery Workers	100
Duration of tannery work (years)	0– 10	94
	11– 38	55
Duration of working under sunlight in a day (hours)	1	16
	2	106
	3	16
	4	11
Cr level in hair (μg/g)	Mean[a]	2.64
	Max	53.82
	Min	0.05
	Median	1.06
Cr level in toenails (μg/g)	Mean[a]	124.00**
	Max	2770.1
	Min	0.13
	Median	6.94
L* values[b] of the face	Mean	63.5
	SD	14.71
	Max	112.03
	Min	33.69
	Median	62.36
L* values[b] of the feet	Mean	86.83##
	SD	19.53
	Max	136.09
	Min	30.09
	Median	84.73

Note: ** and ## are significantly different ($p < 0.001$ in both comparisons) as analyzed by the Mann-Whitney *U* test compared with Cr level in hair and L* values of the face, respectively.
[a] Mean Cr levels in hair and toenails are shown as geometric means.
[b] Higher L* values indicate lower levels of skin pigmentation.

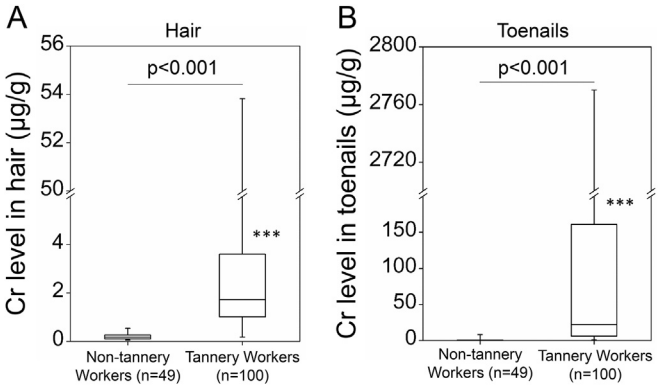

Fig. 2.. Effect of tannery work on Cr levels in hair and toenails of the participants. Levels (box plot) of Cr (μg/g) in hair (A) and toenails (B) of non-tannery workers (n = 49) and tannery workers (n = 100) in Bangladesh are presented. The boxes contain 50% of all values (observations between the 25th and 75th percentiles). The horizontal lines inside the boxes represent medians. The bars extend from the boxes to the highest and lowest values. Significantly different (***, $p < 0.001$) from Cr levels in non-tannery workers by the Mann-Whitney *U* test.

3.4. Comparison of L* values of faces and feet

Mean L* values of faces and feet measured by using a reflectance spectrophotometer were also compared between the tannery workers and non-tannery workers in univariate analysis (Fig. 3). The mean L* value of the faces in tannery workers was more than 1.1-fold lower than that in non-tannery workers ($p < 0.02$). Similarly, the mean L* value of feet in tannery workers was more than 1.2-fold lower than that in non-tannery workers ($p < 0.001$).

3.5. Correlations between duration of tannery work and Cr levels

Spearman's rank correlation coefficient was used to correlate the duration of tannery work (in years) with Cr levels in hair and toenails in all participants (n = 149) (Fig. 4). Strong correlations

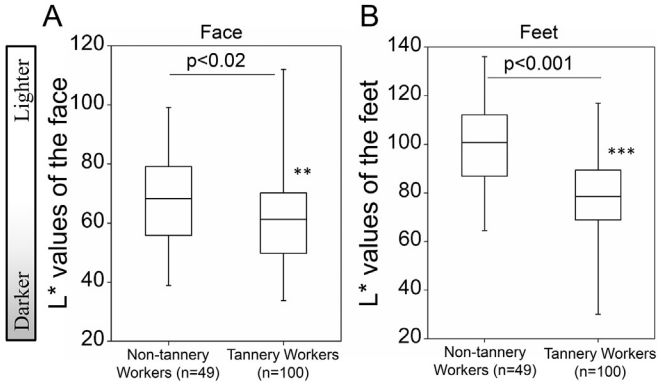

Fig. 3. Effect of tannery work on skin pigmentation levels of the face and feet of participants. Skin pigmentation levels (box plot) based on L* values of the faces (A) and feet (B) of non-tannery workers (n = 49) and tannery workers (n = 100) in Bangladesh are presented. The boxes contain 50% of all values (observations between the 25th and 75th percentiles). The horizontal lines inside the boxes represent medians. The bars extend from the boxes to the highest and lowest values. Significantly different (***, $p < 0.001$, **, $p < 0.02$) from L* values of non-tannery workers by the Mann-Whitney *U* test.

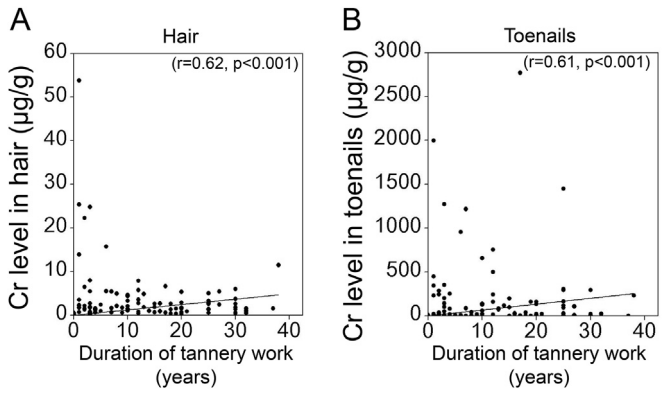

Fig. 4. Correlations of duration of tannery work (years) with Cr levels in hair and toenails of participants. Correlations of duration of tannery work (years) with Cr levels in hair (A) and toenails (B) of the participants are analyzed. Strong correlation ($r = 0.60–0.79$, $p < 0.001$) was obtained by Spearman's rank correlation coefficient.

were found between the duration of tannery work and Cr levels in hair ($r = 0.62$, $p < 0.001$) and toenails ($r = 0.61$, $p < 0.001$) in all participants. On the other hand, we do not know the reason why Cr levels in hair and toenails in some newcomers were high. Detailed personal records will be useful to further clarify the correlation between duration of tannery work and Cr levels in our future study.

3.6. Correlation between exposure to Cr and skin pigmentation

Multivariate analysis was conducted after adjusting confounders including age, BMI and duration of work under sunlight in a day (Table 2) in order to estimate correlations between variables related to Cr exposure and levels of skin pigmentation (L* values) of the faces and feet in all participants ($n = 149$). L* values of the faces and feet significantly correlated with duration of tannery work (long duration vs. short duration: OR = 2.68, 95% CI = 1.18–6.11, $p < 0.02$; OR = 4.75, 95% CI = 1.20–11.30, $p < 0.001$), Cr levels in hair (high level vs. low level: OR = 2.8, 95% CI = 1.18-6.64, $p < 0.05$; OR = 5.05, 95% CI = 2.21–11.56, $p = 0.001$) and Cr levels in toenails (high level vs. low level: OR = 6.86, 95% CI = 2.35–20.05, $p < 0.001$; OR = 2.79, 95% CI = 1.21–6.45, $p < 0.02$). Thus, for example a higher level of Cr in toenails (124.01–2770.10) caused higher levels of skin pigmentation of the face in all participants with an odds ratio of 6.86 compared to a lower level (0.13–124.00). Further univariate analysis also showed similar correlations between variables related to Cr exposure and levels of skin pigmentation in all participants (Table S1).

Table 2
Multivariate analysis for the associations between Cr exposure and L* values of the face (<67.03) and feet (<80.92).

	L* value[b]	
	Face	Feet
	OR (95% CI)[a]/*p value	OR (95% CI)[a]/*p value
Duration of tannery work (years)		
0–10	Reference	Reference
11–38	2.68 (1.18, 6.11) **	4.75 (1.20, 11.30) ***
Cr level in hair (μg/g)		
0.05–2.64	Reference	Reference
2.65–53.82	2.65 (1.14, 6.19) *	5.01 (2.22, 11.31) ***
Cr level in toenail (μg/g)		
0.13–124.00	Reference	Reference
124.01–2770.10	6.72 (2.32, 19.48) ***	2.81 (1.22, 6.49) **

Note: Multivariate analysis included age, BMI and duration of working under sunlight (hours/day) as confounding factors.

[a] OR = odds ratio, 95% CI = 95% confidence interval, ***$p < 0.001$, **$p < 0.01$ and *$p < 0.05$ are statistically significant.

[b] Higher L* values indicate lower levels of skin pigmentation. For example, a higher level of Cr in toenails (124.01–2770.10) resulted in the development of higher levels of skin pigmentation of the face in all participants with an odds ratio of 6.72 compared to a lower level of Cr in toenails (0.13–124.00).

3.7. McFadden's pseudo R^2 analysis to determine relative contributions

Finally, we conducted McFadden's pseudo R^2 analysis (Table 3) to determine the relative contributions (%) of the factors to development of skin pigmentation. Our results showed that the relative contribution (%) of Cr level in hair or toenails to skin pigmented levels of the face and feet was higher than the contribution of As level in different situations. For example, the relative contributions of known factors to skin pigmentation levels on the face (L* values) in all participants were 12.3% for Cr level in toenails, 6.5% for age, 4.7% for BMI, 1.4% for working duration under sunlight in a day and 0% for As level in hair (Table 3B).

4. Discussion

We showed Cr levels in both hair and toenails of tannery workers. Cr levels in hair and toenail samples of 100 male tannery

Table 3
Pigmentation levels (L* values) of the face and feet on McFadden's pseudo R^2 for each factor including As levels in hair or toenails as confounders.

	Relative contribution [Pseudo R^2 (%)][a] on L* values	
	Face	Feet
A		
Age	5.9*	0.0
BMI	2.7	0.4
Working under sunlight (hours/day)	0.9	2.0
Cr level in hair	4.6*	13.0***
As level in hair	0.1	2.2
Model redundancy[b]	85.8	82.4
B		
Age	6.5**	0.0
BMI	4.7*	0.7
Working under sunlight (hours/day)	1.4**	2.1
Cr level in toenails	12.3***	5.1*
As level in hair	0.0	2.8
Model redundancy[b]	75.1	89.3
C		
Age	6.1*	0.0
BMI	2.7	0.5
Working under sunlight (hours/day)	0.9	2.6
Cr level in hair	4.8*	13.3***
As level in toenails	0.4	0.0
Model redundancy[b]	85.1	82.4
D		
Age	6.6*	0.0
BMI	4.6*	0.8
Working under sunlight (hours/day)	1.3**	2.8
Cr level in hair	12.3***	5.0*
As level in hair	0.1	0.2
Model redundancy[b]	75.1	89.3

Note: ***, $p < 0.001$, **, $p < 0.01$ and *, < 0.05 are statistically significant. p values were calculated using the logistic ratio test for each factor.

[a] Relative contribution of each factor was calculated using the following formula: Relative contribution [Pseudo R^2 (%)] = (Pseudo R^2 of the final five-factor model − Pseudo R^2 of the nested four-factor model with the factor of interest removed)/ Pseudo R^2 of the five-factor model.

[b] The remaining contribution (model redundancy) was calculated as the difference between Pseudo R^2 of the final five-factor model and the sum of the relative contribution of each factor, which was an estimate of the model explained by more than one factor.

workers were ≥20-fold and ≥360-fold higher, respectively, than those in hair and toenail samples of 49 male non-tannery workers. Moreover, there were significant correlations between Cr levels in hair and toenails and the duration of tannery work (years). Thus, our results provide direct evidence of exposure to a high level of Cr in tannery workers.

As shown in previous studies (El-Hassan et al., 2014), a preliminary inspection by our medical doctors showed increased frequencies of various skin lesions including hyperpigmentation, erythema, scales and lichenification in tannery workers compared to those in non-tannery workers. We then focused on skin pigmentation level because it can be digitally evaluated as L* value by using a reflectance spectrophotometer. In addition, the participants in this study were all males, a condition that is suitable for analysis of skin pigmentation because the constitutive levels of skin pigmentation are different in males and females (Hernando et al., 2016). Our univariate and multivariate analyses both showed that skin pigmentation levels of the faces and feet were correlated with duration of tannery work as were Cr levels of hair and toenail. Our results suggest that chronic exposure to a high level of Cr results in the development of hyperpigmented skin in male tannery workers.

Hyperpigmented skin is a hallmark symptom for patients with arsenicosis (Yajima et al., 2017). Previous studies showed that there were millions of patients with arsenicosis derived from arsenic (As)-polluted well drinking water in Bangladesh (Li et al., 2018). The mean As level in hair (282 μg/kg) in tannery workers was 1.7-fold higher than that (0.16 μg/g) in non-tannery workers, while the mean As level in toenails (0.40 μg/g) in tannery workers was comparable to that (0.31 μg/g) in non-tannery workers (Fig. S1). Our previous study (Kato et al., 2013) showed that As levels in hair and toenails in the patients with arsenicosis in Bangladesh were 1.82 μg/g and 2.67 μg/g, respectively, which are 6.5–7.8-fold higher than those in tannery workers in this study. In multivariate analysis including As levels in hair and toenails as confounding factors, significant correlations between skin pigmentation levels in the faces and feet and Cr levels in hair and toenails were maintained (Tables S2 and S3). On the other hand, hyperpigmented skin is also a typical symptom of sunlight exposure (Jablonski and Chaplin, 2010). Our results indicated that chronic exposure to Cr increased levels of skin pigmentation of an area not exposed to sunlight (foot) as well as a sunlight-exposed area (face) in workers of tanneries that have roofs for protection against direct sunlight (Biswas and Rahman, 2013; Stupar et al., 1999). In multivariate analysis including duration of working under sunlight in a day as a confounding factor, significant correlations between skin pigmentation levels of both the faces and feet and Cr levels in hair and toenails were maintained. Multivariate analysis of McFadden's Pseudo R^2 values was carried out to determine the relative contributions (%) of Cr levels in hair and toenails and other confounding factors to face and foot pigmentation levels. The relative contributions of Cr levels in hair and toenails had the greatest contribution to skin pigmentation of the faces and feet in various conditions, though the relative contribution of age to pigmented levels of the face in analysis including As levels in hair and toenails as confounding factors was higher than that of Cr levels in hair (Gilchrest et al., 1979). Taken together the results of our univariate and multivariate analyses suggest that Cr levels in hair and toenails might generally be the greatest contributors to skin pigmentation in tannery workers.

Skin pigmentation levels were objectively digitized using a reflectance spectrophotometer in this study, though skin hyperpigmentation is usually diagnosed by dermatologists with special skill and knowledge. Our previous study showed that skin pigmentation levels digitalized by using a reflectance spectrophotometer were strongly correlated with As levels in hair and toenail samples from residents of rural areas of Bangladesh who were drinking As-polluted well water (Yajima et al., 2018). Since Cr-mediated skin hyperpigmentation levels could be objectively diagnosed with high reliability without special skill and knowledge, our results suggest that the digitalized level of hyperpigmentation can contribute to early detection and prevention of diseases caused by excessive exposure to Cr.

The reason why Cr exposure results in the development of skin hyperpigmentation of the faces and feet in tannery workers remains unclear. Since it was shown in this study that the feet of tannery workers have direct contact with Cr-polluted water, chronic damage and inflammation of foot skin by the previously reported corrosive effect of Cr (Estlander et al., 2000; Gammelgaard et al., 1992) may result in the development of hyperpigmented foot skin in tannery workers. However, hyperpigmented skin also develops in facial skin that is not in direct contact with Cr-polluted water in tannery workers. Previously reported percutaneous and *trans*-airway exposure to Cr in a tannery (Were et al., 2014) may be involved in the development of hyperpigmented skin of the face. Our previous studies showed that endothelin-1 might be one of key molecules for the development of As-mediated skin hyperpigmentation (Yajima et al., 2017, 2018). Further study is needed to determine whether the molecular mechanism of skin hyperpigmentation induced by Cr is similar to that induced by As.

There are some limitations in this pilot study. There is limited generalizability of our findings because this study focused on tannery workers in developing countries (Earth and Cross, 2010) who are daily exposed to a high level of Cr. It is also difficult to find a causal relationship between Cr levels in skin appendages and hyperpigmented skin, though our cross-sectional study was useful for finding their correlation. Cohort studies to elucidate the causality will be needed in the future. Furthermore, the number of participants in this study was small. Further studies with a larger number of participants are needed to clarify the correlation between Cr exposure and hyperpigmented skin.

5. Conclusions

A high level of Cr in both hair and toenails provided the direct evidence of chronic Cr poisoning in tannery workers through occupational exposure. Our study showed that chronic exposure to the high level of Cr results in the development of hyperpigmented skin in male tannery workers. Since Cr-mediated skin hyperpigmentation levels could be objectively diagnosed with high reliability without special skill and knowledge, the digitalized level of hyperpigmentation can be a useful diagnostic marker for early detection and prevention of diseases caused by excessive exposure to Cr.

Conflicts of interest

The authors declare that they have no actual or potential conflict of interest including any financial, personal or other relationships with other people or organizations.

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Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.chemosphere.2019.04.112.

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