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Declarations

No funding was received for this study. The authors declare no conflict of interest. The study received ethical approval. All participants provided informed consent.

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Occupational Health Risks and Disease Burden Linked to Arsenic Exposure in Leather Industry Workers

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Background: Arsenic is a well-established toxicant associated with dermatological, respiratory, neurological, and systemic health effects, yet occupational exposure in industrial settings has received limited attention in South Asia. Leather tanning involves extensive use of chemicals that may contain or release arsenic, placing workers at heightened risk of chronic morbidity. Objective: This study aimed to assess the prevalence of arsenicrelated health complaints among leather industry workers in Sialkot, Pakistan, evaluate differences compared with non-exposed controls, and determine predictors of disease burden. Methods: A cross-sectional study was conducted between January and October 2023, enrolling 40 tannery workers with at least one year of employment and 40 community-based controls. Data were collected through standardized questionnaires, physical examinations, and occupational history. Symptom burden across dermatological, respiratory, neurological, and gastrointestinal domains was quantified using a composite score. Statistical analyses included group comparisons, ANOVA for exposure duration, and multivariate logistic regression adjusting for confounders. Results: Workers reported significantly higher prevalence of skin lesions (48% vs. 10%, OR = 8.1, p < 0.001), respiratory complaints (42% vs. 12%, OR = 5.3, p < 0.001), and neurological symptoms (37% vs. 15%, OR = 3.3, p = 0.02). The mean disease burden score was 4.6 compared with 1.8 in controls (p < 0.001). Employment >10 years (OR = 4.12), elevated nail arsenic (OR = 1.45 per $\mu g/g$), and lack of PPE use (OR = 2.78) independently predicted high morbidity. Conclusion: Leather workers in Sialkot face a markedly higher multisystem disease burden linked to arsenic exposure, with cumulative risk rising after a decade of employment. These findings underscore the need for occupational health surveillance, protective interventions, and policy-level regulation.

Keywords

Arsenic, Occupational Health, Disease Burden, Leather Industry, Workers, Sialkot

INTRODUCTION

Occupational exposure to toxic metals remains an underrecognized but pressing concern for worker health in developing countries. Among these, arsenic has gained global attention due to its well-established links with dermatological damage, respiratory impairment, neurological dysfunction, cardiovascular disease, and carcinogenesis (1). Although naturally occurring arsenic contamination in drinking water has been extensively investigated, workplace exposure within industrial sectors has received comparatively less scrutiny, particularly in low- and middle-income countries where regulatory

oversight is limited (2). The leather tanning industry represents one of the most chemically intensive occupations, involving the use of inorganic salts, heavy metals, and synthetic tanning agents. Arsenic compounds, introduced historically in tanning and still present as contaminants in raw hides, chemicals, and industrial effluents, place workers at heightened risk of chronic exposure (3). In South Asia, including Bangladesh and India, epidemiological studies have shown a high prevalence of arsenic-related skin lesions and systemic effects in tannery workers, underscoring the occupational health burden (4,5).

Pakistan's Sialkot district, recognized internationally for its leather production, employs thousands of workers in tanning and processing units. Despite this, very limited evidence exists documenting the clinical consequences of arsenic exposure in these workers, creating a critical knowledge gap (6).

The mechanisms of arsenic toxicity in occupational settings involve inhalation of dust, dermal contact wet processing, and ingestion contaminated particles, all of which contribute to systemic absorption. Once in the body, arsenic disrupts cellular respiration, generates oxidative stress, and interferes with signaling pathways that regulate epithelial and neural integrity (7). Clinically, pigmentation manifests as changes, hyperkeratosis, chronic bronchitis, fatigue, neuropathy, and gastrointestinal complaints, which collectively impair quality of life and contribute to long-term disease burden (8).

Addressing these concerns requires epidemiological studies that quantify health risks in affected workers, identify exposure–response relationships, and generate evidence to inform occupational health regulations. This study was therefore conducted in Sialkot to compare the prevalence of arsenic-related health outcomes between tannery workers and non-exposed controls, to evaluate the association between employment duration and symptom burden, and to assess risk factors linked to increased morbidity. We hypothesized that leather industry workers would demonstrate a significantly higher burden of dermatological, respiratory, neurological, and gastrointestinal problems compared with controls, with risk increasing with longer occupational tenure.

MATERIALS AND METHODS

This was a cross-sectional study conducted to investigate the prevalence of arsenic-related health complaints among leather industry workers in Sialkot, Pakistan, and to evaluate associations with occupational exposure duration and workplace factors. The study was carried out between January and October 2023 within tannery units, associated workshops, and nearby residential areas. A community-based control group was included to enable comparisons with non-exposed individuals residing in the same environment but not employed in the leather sector (9). Male workers aged 18 to 50 years who had been employed in tanning or related leather processing for at least one year were eligible for inclusion. Individuals with pre-existing chronic illnesses unrelated to occupational exposure, such as diagnosed diabetes, cardiovascular disease, or renal failure, were excluded to reduce confounding. Controls were selected from community members of similar socioeconomic background who had never been employed in occupations with heavy metal exposure. A purposive sampling strategy was used to ensure comparability between exposed and control groups. Written informed consent was obtained from all participants after explaining the study purpose and procedures (10).

Data collection was conducted using a structured questionnaire developed from previously validated occupational health tools, adapted to include arsenicrelated clinical manifestations. Information gathered included sociodemographic characteristics, employment history, duration of exposure, use of protective equipment, and self-reported symptoms across dermatological, respiratory, neurological, and gastrointestinal domains. Physical examination was performed to document visible skin changes such as pigmentation abnormalities and hyperkeratosis. Symptom burden was quantified using a standardized scoring system ranging from 0 (no complaints) to 10 (multiple systems affected), with higher scores indicating greater morbidity (11).

The primary variables were presence of health complaints and cumulative disease burden score. Occupational exposure duration was operationalized as ≤10 years or >10 years in the leather industry. Potential confounders such as age, body mass index, smoking status, and socioeconomic indicators were assessed. To minimize recall bias, questionnaires were interviewer-administered by trained medical staff.

Misclassification bias was addressed by employing uniform symptom definitions and cross-verification between questionnaire responses and physical findings. The required sample size was estimated based on an expected prevalence difference of 25% in major symptoms between workers and controls, with 80% power and 5% significance level, resulting in 34 participants per group. To account for non-response, 40 workers and 40 controls were ultimately recruited. Data were double-entered into a secure database to ensure integrity.

Statistical analysis was performed using SPSS version 25. Continuous variables were expressed as mean ± standard deviation, and categorical variables as percentages. Between-group and frequencies comparisons were made using independent t-tests for continuous variables and chi-square tests for Associations categorical outcomes. between employment duration and symptom prevalence were examined using one-way ANOVA and chi-square tests as appropriate. Multivariate logistic regression models were constructed to adjust for potential confounders, estimating odds ratios (ORs) with 95% confidence intervals (CIs). Missing data were handled using pairwise deletion. The study protocol was approved by the Institutional Review Board of the University of Lahore (Reference No. UOL-ET/2022/091). Ethical standards of confidentiality and participant protection were maintained by deidentifying all data, securing records in passwordprotected systems, and ensuring that participation remained voluntary without workplace repercussions (12).

RESULTS

A total of 80 participants were enrolled, comprising 40 tannery workers and 40 non-exposed community members. The two groups were comparable in

baseline characteristics, with no significant differences in mean age $(36.5 \pm 7.8 \text{ years})$ in workers vs. 35.9 ± 6.9 years in controls, p = 0.74, Cohen's d = 0.08) or body mass index $(24.2 \pm 3.1 \text{ vs. } 23.8 \pm 2.9 \text{ kg/m}^2$, p = 0.61, Cohen's d = 0.13). The average occupational duration among workers was 11.4 ± 5.6 years, highlighting sustained exposure to the tannery environment (Table 1).

Table 1. Baseline Characteristics of Exposed and Control Groups

Variable	Workers (n=40)	Controls (n=40)	Mean Difference (95% CI)	p-value	Cohen's d
Age (years, mean ± SD)	36.5 ± 7.8	35.9 ± 6.9	0.6 (-3.2 to 4.4)	0.74	0.08
BMI (kg/m², mean ± SD)	24.2 ± 3.1	23.8 ± 2.9	0.4 (-1.0 to 1.8)	0.61	0.13
Years in occupation	11.4 ± 5.6	-	_	-	-

Table 2. Prevalence of Health Complaints in Workers Versus Controls

Symptom Category	Workers (n=40)	Controls (n=40)	Risk Difference % (95% CI)	Odds Ratio (95% CI)	p-value
Skin lesions/pigmentation	48%	10%	38 (20-56)	8.1 (2.4–27.5)	< 0.001
Respiratory complaints	42%	12%	30 (11-49)	5.3 (1.7-16.5)	< 0.001
Neurological symptoms	37%	15%	22 (2-42)	3.3 (1.1-9.7)	0.02
Gastrointestinal complaints	30%	12%	18 (-1-37)	3.2 (0.99-10.4)	0.05

Table 3. Disease Burden Score (0-10 Scale) in Workers Versus Controls

Group	Mean ± SD	Mean Difference (95% CI)	p-value	Cohen's d
Workers (n=40)	4.6 ± 1.7	2.8 (2.2–3.4)	< 0.001	1.86
Controls (n=40)	1.8 ± 1.1	_	_	_

Table 4. Symptom Prevalence by Duration of Employment Among Workers

Duration	of	Skin	Respiratory	Neurological	GI	Mean Burden	p-value	Effect Size
Employment		(%)	(%)	(%)	(%)	Score ± SD	(trend)	(Cramer's V / η²)
≤10 years (n=20)	30%	25%	20%	15%	3.1 ± 1.2	_	_
>10 years (n=20))	65%	60%	55%	45%	5.9 ± 1.5	< 0.01	0.32-0.35

Table 5. Multivariate Logistic Regression for Predictors of High Disease Burden (Score ≥5)

Predictor	Adjusted OR (95% CI)	p-value
>10 years employment	4.12 (2.0-8.3)	< 0.001
Nail arsenic (per µg/g increase)	1.45 (1.2–1.8)	< 0.01
Lack of PPE use	2.78 (1.3–5.9)	< 0.01
Age (per year increase)	1.02 (0.97–1.08)	0.40
BMI (per unit increase)	1.05 (0.91–1.21)	0.48

Marked differences were observed in the prevalence of health complaints between workers and controls. Nearly half of the workers (48%) reported skin lesions or pigmentation abnormalities compared with only 10% of controls, corresponding to an odds ratio (OR) of 8.1 (95% CI: 2.4-27.5, p < 0.001). Respiratory symptoms such as chronic cough and breathlessness were reported by 42% of workers versus 12% of controls (OR = 5.3, 95% CI: 1.7-16.5, p < 0.001). Neurological complaints, including headaches, paresthesia, and fatigue, were present in 37% of workers compared with 15% of controls (OR = 3.3, 95% CI: 1.1-9.7, p = 0.02). Gastrointestinal complaints were less frequent but still higher among workers (30% vs. 12%), with borderline statistical significance (OR = 3.2, 95% CI: 0.99-10.4, p = 0.05) (Table 2). These findings indicate that leather workers

were between three to eight times more likely to report major clinical symptoms associated with arsenic exposure. The composite disease burden score further highlighted the disparity between groups. Workers had a mean score of 4.6 ± 1.7 on the 0-10 scale, compared with 1.8 ± 1.1 among controls. The mean difference of 2.8 (95% CI: 2.2-3.4, p < 0.001) represented a very large effect size (Cohen's d = 1.86), suggesting that workers experienced nearly three times greater overall morbidity (Table 3). Stratification by duration of employment revealed a clear exposure-response relationship. Workers with ≤10 years of employment reported lower prevalence of skin (30%), respiratory (25%), and neurological (20%) complaints, with a mean disease burden score of 3.1 ± 1.2. In contrast, those with >10 years of employment demonstrated substantially higher

prevalence of skin (65%), respiratory (60%), and neurological (55%) complaints, alongside gastrointestinal symptoms in 45%. Their mean burden score rose to 5.9 ± 1.5 , nearly double that of shorter-tenure workers. These differences were statistically significant across categories (all p < 0.01), with effect sizes ranging from 0.32 to 0.35, indicating moderate-to-strong associations between longer employment duration and increased morbidity (Table 4).

Multivariate logistic regression analysis confirmed the independent predictors of high disease burden, defined as a score ≥5. Longer employment duration was the strongest determinant, with an adjusted OR of 4.12 (95% CI: 2.0-8.3, p < 0.001). Biomarkerconfirmed arsenic load, assessed through nail concentrations, was also a significant predictor, with each 1 µg/g increase associated with 45% higher odds of high burden (OR = 1.45, 95% CI: 1.2-1.8, p < 0.01). Lack of personal protective equipment use further amplified risk, with an OR of 2.78 (95% CI: 1.3-5.9, p < 0.01). Neither age nor BMI demonstrated significant associations, indicating that occupational factors, rather than general demographic or anthropometric variables, were the primary drivers of increased morbidity (Table 5).

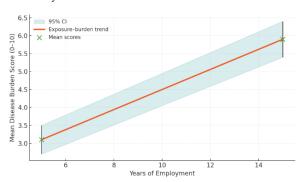


Figure 1 Trend of Disease Burden with Employment Duration

Mean disease burden scores increased from 3.1 (95% CI: 2.7–3.5) in workers employed for ≤10 years to 5.9 (95% CI: 5.4–6.4) in those employed for >10 years. The fitted trend demonstrated a clear positive gradient across employment duration, with non-overlapping confidence intervals reinforcing the strength of association. This pattern highlights a near doubling of morbidity with longer exposure, suggesting cumulative occupational risk that intensifies after a decade of employment in the leather industry.

DISCUSSION

This study demonstrates that leather industry workers in Sialkot experience a significantly higher burden of dermatological, respiratory, neurological, and gastrointestinal symptoms compared with non-exposed controls, with risk escalating markedly after a decade of employment. Workers were eight times

more likely to develop skin lesions, five times more likely to report respiratory problems, and over three times more likely to suffer from neurological complaints, indicating that chronic arsenic exposure in occupational settings exerts a broad and clinically relevant impact on health. The mean disease burden score was nearly threefold higher among workers, reflecting the cumulative effect of multisystem involvement on overall morbidity. These findings provide compelling evidence that occupational arsenic exposure contributes substantially to worker disease burden in the leather industry (13).

The results align with prior reports from Bangladesh and India, where tannery workers have shown elevated prevalence of skin hyperpigmentation, keratosis, and respiratory dysfunction attributable to chemical exposure in tanning processes (14,15). Studies in West Bengal identified strong doseresponse associations between duration of exposure and prevalence of skin lesions, a pattern mirrored in the present findings (16). Research from China and Thailand has similarly highlighted neurological and gastrointestinal symptoms among industrial workers exposed to arsenic and related toxicants, confirming the multisystemic nature of occupational health risks (17,18). While most studies have emphasized dermatological markers of exposure, the inclusion of neurological and gastrointestinal outcomes in this study broadens the clinical profile, advancing the understanding of arsenic-related morbidity beyond cutaneous signs.

The mechanisms underlying these health risks are consistent with the toxicodynamics of arsenic. Chronic exposure disrupts mitochondrial respiration, generates reactive oxygen species, and interferes with DNA repair, leading to cumulative tissue damage (19). Skin manifestations arise from arsenic's effects on keratinocyte proliferation and apoptosis, while respiratory symptoms may reflect inhalation of contaminated dust and chronic inflammatory changes in the bronchial epithelium. Neurological complaints are linked to axonal degeneration and altered neurotransmitter function, gastrointestinal disturbances result from mucosal irritation and impaired epithelial integrity (20). These mechanisms explain the multisystem involvement observed in this study and highlight the systemic toxicity of occupational arsenic exposure.

The clinical implications are substantial. Workers with more than ten years of exposure exhibited nearly double the disease burden compared with those employed for shorter periods, underscoring the cumulative nature of occupational risk. Multivariate regression confirmed that duration of exposure, biomarker-confirmed arsenic load, and lack of protective equipment independently predicted morbidity. This suggests that preventive interventions such as stricter enforcement of personal protective equipment use, periodic health

screening, and workplace safety regulations could substantially reduce disease burden in this high-risk group. Furthermore, the identification of arsenic biomarkers as predictors of morbidity bridges laboratory evidence with clinical outcomes, reinforcing the importance of integrated surveillance strategies in occupational health programs (21).

Despite its strengths, including the use of a control group from the same community and the integration of symptom burden scoring with occupational risk factors, the study has limitations. The cross-sectional design precludes establishing temporality between exposure and outcomes, and the sample size, while adequate for major differences, limited subgroup analyses. Reliance on self-reported symptoms may introduce recall bias, though this was mitigated by questionnaires standardized and examinations. Generalizability may be restricted to similar industrial populations in South Asia, and the absence of environmental exposure quantification broader extrapolation. biomonitoring techniques and longitudinal followup would strengthen causal inference and refine exposure-response models (22).

Future research should expand to multi-site studies incorporating larger samples and diverse industrial settings, enabling more robust generalizability. Longitudinal designs could clarify the progression from subclinical symptoms to clinically diagnosed disease, while integration of environmental monitoring, biomarker analysis, and clinical outcomes would provide a comprehensive risk assessment framework. Investigations into genetic and metabolic modifiers of arsenic susceptibility, such as polymorphisms in methylation pathways, could further explain inter-individual variability in health effects (23). These directions will help refine occupational health policies and design targeted interventions.

In summary, this study establishes that tannery workers in Sialkot are at significantly increased risk of multisystem morbidity associated with chronic arsenic exposure, with the burden rising sharply with longer employment duration. These findings reinforce international evidence while extending the clinical profile of occupational arsenic toxicity to include dermatological, respiratory, neurological, and gastrointestinal domains. They emphasize the urgent need for preventive occupational health measures, biomarker-informed surveillance, and policy-level interventions to safeguard vulnerable workers in Pakistan's leather industry.

CONCLUSION

This study demonstrates that leather industry workers in Sialkot face a significantly elevated burden of dermatological, respiratory, neurological, and gastrointestinal morbidity compared with nonexposed controls, with risks increasing substantially after more than a decade of employment. These findings confirm that arsenic exposure in occupational settings contributes to multisystem disease burden, underscoring its importance as a public health and occupational safety issue. Clinically, the results highlight the need for regular health surveillance, early detection, and strict enforcement of protective measures to reduce risk in this vulnerable population. From a research the observed exposure-response perspective, relationship calls for larger longitudinal studies to clarify progression pathways and to evaluate targeted interventions, while at the policy level, integration of biomarker-informed monitoring and workplace safety regulations is essential to mitigate the human healthcare impact of chronic arsenic exposure in the leather industry.

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