

ORIGINAL ARTICLE

Adverse respiratory effects associated with cadmium exposure in small-scale jewellery workshops in India

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ABSTRACT**Background** Cadmium (Cd) is an important metal with both common occupational and environmental sources of exposure. Although it is likely to cause adverse respiratory effects, relevant human data are relatively sparse.**Methods** A cross-sectional study of 133 workers in jewellery workshops using Cd under poor hygienic conditions and 54 referent jewellery sales staffs was performed. We assessed symptoms, performed spirometry, measured urinary Cd levels in all study subjects and quantified airborne total oxidant contents for 35 job areas in which the studied workforce was employed. We tested the association of symptoms with exposure relative to the unexposed referents using logistic regression analysis, and tested the association between urinary Cd levels and lung function using multiple regression analysis, adjusting for demographics, smoking and area-level airborne oxidants.**Results** Exposed workers had 10 times higher urinary Cd values than referents (geometric mean 5.8 vs 0.41 µg/dl; p<0.01). Of the exposed subjects, 75% reported respiratory tract symptoms compared with 33% of the referents (OR=3.1, 95% CI 1.4 to 7.3). Forced vital capacity (FVC) and forced expiratory volume in 1 s (FEV₁) were also lower among the exposed workers than the referents (>600 ml decrement for each, p<0.001). For every 1 µg increase in urinary Cd there was a 34 ml decrement in FVC and a 39 ml decrement in FEV₁ (p<0.01), taking into account other covariates including workplace airborne oxidant concentrations.**Conclusions** This cohort of heavily exposed jewellery workers experienced frequent respiratory symptoms and manifested a marked deficit in lung function, demonstrating a strong response to Cd exposure.**INTRODUCTION**

The process of making gold-containing ornamental metal jewellery and related objects comprises three stages: alloying metal for its intended use; fabricating the intended object, which can include soldering or brazing; and polishing or buffing the completed piece. Each of these stages of the production process can lead to various metallic (eg, cadmium (Cd)) and non-metallic (eg, fume) exposures of potential health concern.

Cd metal is one such exposure. Cd is a component of certain metal solders, including so-called 'gold carat' solders used in jewellery fabrication. In addition, Cd can be employed as a metal additive in jewellery alloying, combined with gold and silver to produce what is sometimes called 'green gold'. Cd is a well-established respiratory toxin.¹ Acute high-level**Key messages****What is the key question?**

- Is occupational cadmium exposure associated with pulmonary function impairment?

What is the bottom line?

- The poor hygienic conditions in Indian jewellery making workshops that entail cadmium overexposure linked to clinically relevant lung function deficits.

Why read on?

- Past data on this topic have been mixed; this study provides convincing support for the adverse target organ effects of chronic cadmium inhalation.

human inhalation exposure, typically through flame cutting or brazing Cd-containing materials, is associated with acute lung injury and diffuse alveolar damage.^{2,3} In experimental animal models, repeated Cd inhalation causes emphysema.^{4,5} There is also evidence that human exposure can have a similar adverse effect. Indeed, the natural Cd content of cigarettes or environmental Cd exposure interactions with cigarette smoking may be mechanisms underlying obstructive lung disease caused by smoking.^{6,7}Thus, delineating the respiratory effects of sub-acute and chronic inhalation of Cd is of both occupational and wider public health importance. To date, the seminal report of Davison and colleagues has best described a heavily Cd-exposed cohort,⁸ although there have been other limited investigations of this topic, some of which have shown an adverse respiratory effect⁹⁻¹² while other studies have not.¹³⁻¹⁵ We report our findings among a group of Cd-exposed jewellery workers in whom Cd levels and lung function data were systematically analysed.**METHODS****Overall study design and subject participation**

We performed a cross-sectional study among workers engaged in manufacturing gold jewellery that involved the use of Cd-containing solder, including persons with varying duties and a range of anticipated exposure levels. A total of 233 men were screened from 276 potential study participants randomly identified among a total workforce estimated to be 350 in 35 working areas. Women are not employed in this industry in the region studied. The

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Table 1 Baseline characteristics of the participants

Characteristic	Referent (n=54)	Exposed (n=133)	p Value
Age (years)	37.6 (5.6)	35.7 (4.7)	0.39
Body mass index (kg/m ²)	23.4 (3.2)	22.5 (2.8)	0.54
Height (m)	1.71 (0.14)	1.68 (0.12)	0.62
Ever smoker	14 (25.9%)	43 (32.3%)	0.49
Regular exposure to SHS	16 (29.6%)	49 (36.8%)	0.44
Parental asthma	3 (5.5%)	7 (5.3%)	0.94

Data are presented as mean (SD) or n (%).
SHS, second-hand smoke.

workshops were located within a 200 km radius of Kolkata, West Bengal. The study was carried out between late February and early April 2012.

Of the 276 workers screened for participation, we excluded subjects for the following reasons: current antibiotic therapy; being under the supervision of a healthcare provider for an active medical condition; or failing to perform spirometry successfully. After excluding 22 potential jewellery sales staffs and 67 exposed workers, 187 (80% of the recruited group) remained. The mean age was similar in the excluded participants and the included group (35.7±5.9 years vs 36.2±5.0 years; $p=0.38$). There were proportionally fewer ever smokers among the excluded group than among those included (16.9% vs 30.5%; $p<0.05$). Of the 187 participants included in the final analysis, 133 (71%) worked in active production and 54 (29%) were personnel associated with sales of the jewellery products that had been manufactured (the referent category in this analysis). The exposed group was further subcategorised by job type: metal melting/alloying ($n=32$); design and fabrication including flame cutting metal pieces and soldering/brazing ($n=61$); and jewellery buffing and polishing ($n=40$). Metal melting was generally carried out with charcoal burning in ceramic vessels. Flame cutting and brazing employed liquefied petroleum gas and a manual blow pipe. Buffing and polishing used predominantly manual tools with acid solutions for cleaning. The workers did not move among these three subcategories of employment.

Questionnaire assessment

We administered a structured questionnaire containing items on respiratory health, occupational exposure and lifestyle factors. This questionnaire was modified from the European Community Respiratory Health Survey¹⁶ and translated into Bengali. An English back-translation was used for validation.

Subjective respiratory complaints in the previous 12 months by questionnaire were categorised by symptom group. These included: (1) acute/current or chronic/prolonged cough; (2) acute or chronic wheezing or whistling of the chest; (3) production of phlegm; (4) breathing trouble; (5) nasal problems (irritation in nose, dryness or stuffy nose, sneezing, runny or blocked nose); (6) eye problems; (7) nasal problems with watery eyes; and (8) skin symptoms such as dryness, rashes, patchiness, irritation, dark spots, burns or swelling.

Lung function

We measured lung function using a computerised spirometer (Maestros Mediline Systems Ltd., India), consistent with American Thoracic Society guidelines,¹⁷ using the best of three values for forced vital capacity (FVC) and forced expiratory volume in 1 s (FEV₁). Predicted values used Indian population values.¹⁸ Spirometry was performed at sites removed from the workshops studied to avoid concomitant acute irritant exposures.

Measurement of urinary cadmium level

The first morning urine sample was collected by subjects in a standard glass container (Borosil, India) at home before coming to work. The concentration of Cd in the urine samples was quantified using atomic absorption spectroscopy (PerkinElmer, USA). Urine creatinine was not measured.

Measurement of total airborne oxidants in the workplace

We measured area-level total airborne oxidants (TAO) using a portable air monitor sampling pump employing impinger collection and a phenolphthalein-based colorimetric assay (LaMotte, USA), consistent with methods initially developed by Haagen-Smit and Brunelle to assess ambient air pollution.¹⁹ Concentrations are quantified in parts per million (ppm) total oxidant content. Air quality was monitored in the workshops as well as in the shops. Different workstations of the three different subcategories of tasks (melting, fabrication and polishing) were sampled. When more than one subcategory existed at a single employment site, the areas were not open to each other although some cross-contamination was possible. Sampling for referents was performed in their work offices. A minimum of four recordings of 10 min sampling duration at 1 litre flow rate was made at each work site studied and the mean value was calculated. The area-level measurement was assigned as the exposure level for all of the workers in that area. Measurements were made for the work areas of all the participants included in the analysis.

Table 2 Comparison of urinary cadmium levels between referents and exposed workers and among the exposure subcategories

Exposure group comparisons	Geometric mean±SD	Median	25th–75th percentile	Range
Referent vs exposed workers				
Referent (n=54)	0.41±0.11	0.43	0.29–0.54	0.18–0.78
Total exposed (n=133)	5.80±0.38	5.91	4.17–8.18	2.74–9.89
Across exposure subcategories				
Melting/alloying (n=32)	4.85±0.19	4.93	4.16–5.76	3.17–7.33
Fabricating (n=61)	8.31±0.10	8.32	7.83–8.99	6.22–9.89
Buffing/polishing (n=40)	3.87±0.15	3.91	3.52–4.37	2.74–5.90

All units are µg cadmium/dl urine.
 $p<0.01$ for all pairwise differences.

Table 3 Area-level total airborne oxidants by exposure category

Exposure category (sample n)	Median	Range
Referent vs exposed workers		
Referent workplaces (n=13)	85.3	68.1–92.4
Total exposed workplaces (n=22)	270.3	138.3–510.0
Across exposure subcategories		
Melting/alloying areas (n=10)	271.3	210.7–310.7
Fabricating areas (n=7)	150.0	138.3–175.3
Buffing/polishing areas (n=5)	450.0	420.0–510.0

All units are expressed in parts per million total oxidants in that area. Each measure represents the average value of at least four measurements made (see Methods section).

Data analysis

To graphically display urine Cd values, they were transformed into the natural logarithm of 1 plus the observed value (to avoid negative values for concentrations <1.0 µg/dl). To test differences between the exposed and referent groups we used the χ^2 or unpaired t test. Differences in spirometric data among groups were tested using one-way analysis of variance. To test differences between urinary Cd (expressed as the geometric mean) among the referents compared with all the exposed workers as a group, we used the Mann–Whitney U test. To test differences in pairwise comparisons of urinary Cd between the different exposure subgroups we used the Tukey modified t test.

Logistic regression analysis was used to test the association between exposure and respiratory symptom-based categorical outcomes expressed as ORs and 95% CIs. The models tested included the covariates of age (continuous), parental asthma/atopy (yes/no), smoking status (ever smoker=yes, never-smoker=no) and regular exposure to second-hand smoke (SHS) at home and/or at work (yes/no). The effect of exposure on lung function was analysed using multiple linear regression. Separate models were tested for each of five outcomes: FVC, FEV₁, FVC% predicted, FEV₁% predicted and FEV₁/FVC ratio. Models of FVC, FEV₁ and FEV₁/FVC were adjusted for age, height, smoking status, SHS exposure, parental atopy/asthma and TAO for the work area of each subject. Models for FVC% predicted and FEV₁% predicted included the variables other than age and height (already accounted for in the lung function prediction equation). All analyses were performed in SPSS V.20.

RESULTS

The baseline characteristics of the study participants are presented in table 1. Overall, the referent jewellery sales group was slightly older and had a higher mean body mass index than the exposed production workers, although these differences were not statistically significant ($p>0.20$). Cigarette smoking (32% vs 26%; $p>0.20$) and regular SHS exposure (37% vs 30%; $p=0.44$) were slightly more prevalent among the exposed workers, although these were present in a minority of participants in both groups and the differences were not statistically significant.

Urinary Cd levels are shown in table 2. The urinary Cd level among the exposed group overall was 10 times higher than in the referent group (geometric mean 5.8 ± 2.2 µg/dl vs 0.41 ± 0.15 µg/dl; $p<0.001$). Among the three exposure subcategories there was a twofold difference between the highest exposure group (fabricating) and the lowest exposure group (buffing/polishing) (geometric mean 8.3 ± 0.7 µg/dl vs 3.87 ± 0.72 µg/dl). All three exposed groups differed significantly from each other in pairwise comparisons ($p<0.01$).

We obtained 22 area-level averaged measures of TAO for clusters of exposed workers in the three job task subcategories ranging from 138 to 510 ppm, as well as 14 averaged measures of the workstations of the referents (range 68–92 ppm). The concentrations of TAO by overall exposure and by subcategory are presented in table 3. The median TAO level for the exposed group was nearly threefold greater than for the referents. Within the exposure subcategories, buffing and polishing tasks were associated with the highest median TAO levels and fabricating with the lowest.

The frequencies of respiratory symptoms by exposure categories are presented in table 4. Overall, being in the exposed group was associated with substantially increased odds of reporting any respiratory symptom (OR 3.1; 95% CI 1.4 to 7.3). The exposed workers reported a threefold higher prevalence of cough, wheezing and phlegm (18.8%, 17.3% and 23.3%, respectively) compared with the referent group (5.5%, 5.5% and 7.4%, respectively). Taking into account the covariates, the odds of each of the individual symptoms shown in table 4 were significantly elevated in the exposure group, except for eye irritation (in isolation from nasal symptoms).

Table 5 shows the spirometric findings for the referent and exposed groups. There were marked deficits in lung function associated with exposure. Overall, there was a 600 ml mean

Table 4 Occurrence of respiratory symptoms in the study population

Symptoms	Referents (n=54)	Exposed (n=133)	OR (95% CI)	p Value
Any respiratory tract symptom	18 (33.3)	99 (75.9)	3.13 (1.37 to 7.28)	0.019
Prolonged cough	3 (5.5)	25 (18.8)	4.93 (1.26 to 19.22)	0.021
Wheezing or whistling in chest	3 (5.5)	23 (17.3)	3.65 (1.05 to 12.74)	0.042
Phlegm in chest	4 (7.4)	31 (23.3)	3.92 (1.26 to 12.12)	0.017
Breathing trouble	5 (9.2)	30 (22.5)	2.90 (1.03 to 8.16)	0.043
Nasal allergy	10 (11.1)	56 (27.8)	3.49 (1.58 to 7.72)	0.002
Nasal problems with watery eyes	2 (3.7)	27 (20.3)	4.55 (1.30 to 15.92)	0.017
Other symptoms				
Eye problems	5 (9.2)	15 (11.3)	1.21 (0.41 to 3.54)	0.726
Skin problems	4 (7.4)	33 (24.8)	4.16 (1.38 to 12.58)	0.011

ORs (referent symptom prevalence=1.0) are adjusted for parental atopy or asthma, smoking and exposure to second-hand smoke at work and/or at home. Values for the respiratory symptoms do not add up to 100% due to multiple non-exclusive response categories.

Table 5 Lung function by exposure among 133 jewellery production workers and 54 referents

	Parameters				
	FVC	FVC (% predicted)	FEV ₁	FEV ₁ (% predicted)	FEV ₁ /FVC
Referent vs total exposed					
Referent (n=54)	3.49±0.29	92.7±4.6	3.04±0.24	92.2±2.8	0.87±0.03
Total exposed (n=133)	2.89±0.29	83.9±5.9	2.40±0.27	81.8±5.9	0.83±0.06
Within exposure subcategories					
Melting (n=32)	3.00±0.25	86.1±6.6	2.61±0.21	85.6±5.5	0.87±0.07
Fabricating (n=61)	2.99±0.22	84.9±4.2	2.47±0.20	82.4±4.5	0.83±0.05
Polishing/buffing (n=40)	2.64±0.27	80.5±6.5	2.12±0.18	77.6±5.7	0.81±0.06

Data are presented as mean±SD.

FVC, forced vital capacity in litres; FEV₁, forced expiratory volume in 1 s in litres.

Referent vs exposed group differences $p < 0.01$ for all lung function variables shown. Polishing vs melting and polishing vs fabricating differences in all lung function variables $p < 0.01$.

Melting vs fabricating differences in FEV₁ and FEV₁/FVC, $p < 0.01$ and FEV₁% predicted, $p < 0.05$; differences in FVC and FVC% predicted were not significant between the melting and fabricating groups.

exposure-associated difference in both FVC and FEV₁ (all differences were significant at $p < 0.01$). As a percentage of predicted values, the exposed group had lung function values 84% and 82% of predicted for FVC and FEV₁, respectively. Overall, 51 (38%) of the exposed workers had FEV₁ values less than 80% age and height predicted. The mean FEV₁/FVC ratio was also significantly lower among the exposed group than in the referents ($p < 0.01$). Within the subcategories of exposure, all the lung function variables were significantly ($p < 0.001$) lower among the polishing workers compared with those engaged in melting or fabrication. Compared with workers engaged in melting, the fabricators had lower mean FEV₁ and FEV₁/FVC values whereas the mean FVC values were similar between these two groups.

The relationship between urinary Cd concentrations and FEV₁ is shown in figure 1. This scatterplot shows that, although there is considerable variability, there is minimal overlap for both parameters between referents and the exposed group.

As shown in table 6, higher urinary Cd concentrations were associated with poorer lung function for each of the spirometric measures studied. Among the group as a whole (n=187), for each increase in Cd of 1 µg/dl we observed a 34 ml decrement in FVC and a 39 ml decrement in FEV₁, with a decline in the FEV₁/FVC ratio by 3% for the same unit increase in urinary

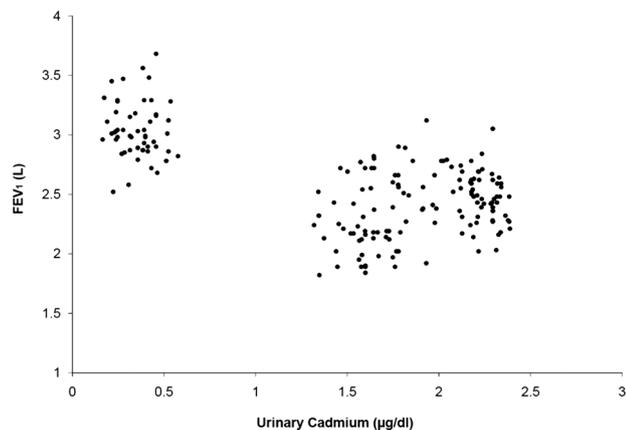


Figure 1 Forced expiratory volume in 1 s (FEV₁) in relation to urinary cadmium (Cd) levels among referents (cluster to upper left) and exposed workers (cluster to lower right). The urinary Cd values have been transformed, taking the natural logarithm of 1 plus the observed value.

Cd. The analyses within the exposed group alone (ie, excluding the referents) demonstrated a similar exposure response, albeit more pronounced (FVC deficit of 40 ml and FEV₁ deficit of 65 ml per 1 µg/dl urinary Cd).

DISCUSSION

We observed large and clinically relevant decrements in lung function associated with a Cd exposure response. This relationship takes into account airborne oxidant co-exposures, which were highest among the polishing workers, the group with a lower Cd exposure. The lung function decrement and symptom prevalence in this cohort underscores the clinical impact of the multifactorial poor hygienic conditions experienced by these jewellery workers.

The urinary Cd levels were highest among the fabricating workers, which is consistent with Cd-containing solder as the principal exposure source. A recent Indian press report highlighted the use of Cd-containing solder in gold jewellery.²⁰ Acute Cd inhalation toxicity from solder brazing has been documented in case reports from silver jewellery making in India.^{21 22} Subacute to chronic Cd exposure from 'silver solder' has been well-recognised in jewellery fabrication and in other industrial brazing applications.^{23 24} Cd overexposure from gold and silver alloying with Cd has also been reported.²⁵

Cd is toxic to various biological systems.²⁶⁻³¹ Among these, the respiratory tract is a key target organ with emphysema being a particularly important endpoint. An investigation of 101 Cd-exposed workers showing lung function decrements including lung carbon monoxide transfer factor (TLCO), a marker of emphysema, is especially noteworthy.⁸ Other occupational studies of respiratory effects due to Cd have yielded mixed results. Three studies (total exposed n=120) have shown Cd-associated adverse lung function deficits^{9 10 12} while another observed an increased risk of respiratory mortality.¹¹ In contrast, three other studies of Cd-exposed workers (total exposed n=205) did not observe lung function decrements.¹³⁻¹⁵ In the only study of jewellery workers using Cd-containing solder, only 8 of 25 workers with brazing fume exposure had detectable urine levels (> 0.4 µg/dl); pulmonary function was described as 'normal' in all but one worker with asthma.²³ The current study adds substantially to this pool of data and drives the balance of findings in support of Cd-associated adverse effects on lung function in humans.

Limitations of our study include its cross-sectional design and the possibility that acute and subacute effects were

Table 6 Effect (β) of occupational exposure on lung function

Parameters	β value (95% CI)	
	All subjects (n=187)	Exposed workers only (n=133)
FVC (l)	-0.034 (-0.044 to -0.023)	-0.04 (-0.07 to -0.009)
FVC % predicted	-0.84 (-1.08 to -0.60)	-1.53 (-2.31 to -0.76)
FEV ₁ (l)	-0.039 (-0.033 to -0.044)	-0.065 (-0.08 to -0.05)
FEV ₁ % predicted	-1.00 (-1.21 to -0.79)	-1.99 (-2.69 to -1.28)
FEV ₁ /FVC	-0.003 (-0.006 to -0.001)	-0.011 (-0.02 to -0.003)

All models included area-level TAO, parental atopy or asthma, smoking and exposure to second-hand smoke at work and/or at home. Models for FVC, FEV₁ and FEV₁/FVC also include height and age. All β values are statistically significant ($p < 0.01$).
FEV₁, forced expiratory volume in 1 s; FVC, forced vital capacity; TAO, total airborne oxidants.

superimposed on a cumulative impairment. One controlled study of toxic Cd exposure showed an acute decrement in FEV₁, FVC and TLCO 24 h after intentional exposure followed by at least partial recovery at 48 h.³² We did not measure TLCO in our study, although this is likely to be an important endpoint in Cd toxicity.⁸ Although our urinary measurements were not adjusted for creatinine concentration, such measurement imprecision is likely to have been non-systematic, although a recent study of child labourers manufacturing surgical instruments in Pakistan found that exposure-related differences in urine chromium levels were actually even greater with creatinine adjustment.³³ It is important, too, to emphasise that Cd was not the only relevant exposure in the jewellery workshops that we studied. We took airborne TAO into account but did not characterise this exposure further. One source may have been nitric acid (such exposure has been reported in the Indian jewellery industry³⁴), and other oxidants may have been produced by charcoal-fuelled metal alloying or flame torch-based brazing. An independent negative effect of concomitant TAO exposure on lung function is consistent with the greatest decrement in lung function occurring in polishers who had the highest TAO values yet relatively lower Cd levels (albeit substantially higher than the referents). Although we took this effect into account in our analysis, our study was not designed or powered to assess potential multiplicative interactions among combined risk factors. Furthermore, we did not measure area-level or personal airborne Cd or other particulates. Based on standard industrial hygiene principles, the working conditions were consistent with airborne Cd fume inhalation being the salient route of exposure, but we cannot exclude concomitant Cd exposure via ingestion. There were potential selection effects in that those excluded from the study were less likely to be ever smokers. Nonetheless, the proportion of ever smokers in the study group was not high and we took active smoking and SHS exposure into account in our multivariate analysis. There could have been other unmeasured confounders that we did not assess. Socioeconomic status probably differed between the referents and exposed groups, but there should not have been a gradient within the exposed subcategories, all of whom were drawn from multiple small worksites not typically recruited into occupational studies.

The adverse exposure effects we found underscore the deplorable conditions experienced by the jewellery workers that we studied. Clearly, there is a serious need for systematic surveillance of respiratory status in this population and enforcement of adequate protective measures.

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Contributors SM designed the study, collected and analysed data. PDB analysed and interpreted the data and wrote the manuscript. SS designed and supervised the study and took the final decision to submit the manuscript.

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Competing interests None.

Ethics approval Ethical approval was obtained from the Departmental Research Committee of the Department of Physiology, University of Kalyani and participants provided signed consent.

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