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Home-based and informal work exposes the families to high levels of potentially toxic elements

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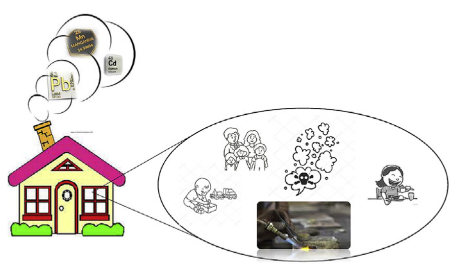
HIGHLIGHTS

- Potentially toxic elements concentrations found in the air analyzed raise concern.
- Workers relatives can have disturbances to their exposome due to the exposure scenario.
- Home-based and informal work present during childhood should be taken into account to study the children exposome.

GRAPHICAL ABSTRACT



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ABSTRACT

The city of Limeira presents a relevant productive chain of jewelry and fashion jewelry, including a scenario of outsourcing informal home practices. It is highly complex to understand the potentially toxic elements (PTE: Cr, Mn, Ni, Cu, Zn, As, Cd, Sn, Sb, Hg, and Pb) exposures of the workers because this productive chain encompasses households. This study aimed to investigate the associations between blood PTE levels and informal work in the home environment. Fifty-two families divided into Exposed group ($n = 112$) and Control group ($n = 53$) were included. Families' blood ($n = 165$) and welder's breathing zone air samples ($n = 9$) were collected and PTEs concentrations were determined by ICP-MS. Questionnaires were applied to collect sociodemographic information and workplace details. Principal component analysis, Mann-Whitney test, cluster and a logistic regression analysis based on environment-wide association studies (EWAS) were carried out. Ni, Cu, Zn, Cd and Pb concentrations in the air samples were higher than occupational guidelines. Eighty percent of the workers were female, and 43.5% of those females then worked as welder. A significant difference was found for Pb concentration between the exposed and control group ($p < 0.0001$) and between sexes ($p = 0.0046$). For Cu ($p < 0.0001$) and Sb ($p = 0.0434$), differences were found between the sexes. The receiver operating characteristic of the EWAS was 0.80, providing evidence of a potential model to associate exposure levels and occupational factors. PTEs concentrations in the air samples raised concerns, particularly for

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children, who were in the same exposure scenario. Inadequate work conditions were observed in the houses, revealing the need of public actions to protect these families.

1. Introduction

The human exposome englobes all exposures which a person may be underwent from conception onwards (Rappaport et al., 2014), and the occupational exposure is a highly relevant specific external exposure, once it may contribute substantially on the living conditions and health representing a huge portion of our lifetime (Harper et al., 2015). It has been estimated that around 8% of all cancers are caused by occupational exposures to carcinogens (Purdue et al., 2015) and that 7% of lung cancers in the general population are attributable to occupational exposures to carcinogens (Prüss-Ustün et al., 2016).

Home-based and informal jewelry-making processes in Limeira, São Paulo, Brazil, compose a scenario of outsourcing that is very peculiar. In this production process, it is complex to understand the exposures to potentially toxic elements (PTEs) such as chrome (Cr), manganese (Mn), nickel (Ni), copper (Cu), zinc (Zn), arsenic (As), cadmium (Cd), antimony (Sn), tin (Sb), mercury (Hg) and lead (Pb) of the workers, considering that all household is involved and potentially exposed, especially children. The jewelry and fashion jewelry production processes encompasse several steps which use products made up of chemical elements with high toxic potential (Antonini et al., 2003; Lacorte et al., 2013). Among these steps, we have the welding process, whose gases and particles could expose the workers. That chemical exposure is associated with damage to the immune system (Boshnakova et al., 1989; Tushl et al., 1997; Zeidler-Erdely et al., 2012) neurological development (Flynn and Susi, 2009; Olympio et al., 2009), pulmonary outcomes (Moulin, 1997; Antonini et al., 2004), and cardiovascular diseases (Ibfelt et al., 2010; Mocevic et al., 2015; Lanphear et al., 2018).

The outsourcing informal home-practices raises concerns once, besides children are potentially exposed to occupational levels of exposure, the households workers do not have access to training to adequately handle chemical components and do not operate in an environment with adequate occupational hygiene, so compliance with legislation to protect workers against chemical exposures tends not to occur. Furthermore, data about the concentration of PTEs in the air associated with biological concentration in welders are scarce (Ellingsen et al., 2017). Taking into account this complex exposure scenario, we intended to address the following questions: a) are there associations between blood elements levels and informal work in the home environment? and b) do breathing zone air elements levels of home-based welders cause risk to their health?.

2. Material and methods

2.1. Study population

The study protocol was reviewed and approved by the institutional review board of the School of Public Health of the University of Sao Paulo (Protocol N° 41965115.0.0000.5421). All participants signed an informed written consent to take part in the study.

A total of 165 participants from 52 families were invited to participate in this study. This population was divided into two groups: an exposed group (n = 112) and a control group (n = 53). The exposed group was made up of 112 workers from 29 families who had at least one outsourced worker who produced jewelry inside of the house. The processes performed by the workers were mainly welding and setting jewelry and fashion jewelry. The control group was composed of 23 people. From the Exposed group, families were selected, living nearby, but not neighboring and that should meet the criterion that they had no resident who worked with jewelry and fashion jewelry at home or in a private company. In order to select these families, from the working families, the researcher walked, clockwise always facing the street, from a sequence of 4 houses to the 4th was selected, initially to check if someone was working in the production of jewelry and jewelry. If not, this family was invited to participate in the study. Table 1 shows the demographic characteristics of the participants, and Fig. 1 illustrates the studied area and the distribution of the families in the city. The samples and data collection (that is, the blood and air samples and the questionnaires) were obtained between July and August 2017 on Tuesdays, Wednesdays, or Thursdays during the day for the control group and after 4:00 p.m. for the exposed group.

2.2. Blood collection, sample preparation and chemical analysis

The blood collection was performed by a trained nurse after the work shifts for the exposed group and during the day for the control group. Six milliliters of whole blood were collected for determination of PTEs (Cr, Mn, Ni, Cu, Zn, As, Cd, Sn, Sb, Hg and Pb) in heparinized tubes that were free of trace elements (Vacutainer®). After the collection, the blood samples were stored at −80 °C until the chemical analysis.

The determination of trace elements was carried out with an inductively coupled plasma mass spectrometer (ICP-MS) equipped with a reaction cell (ICP-MS 7900, Hachioji, Japan) and operated with high-purity argon (99.999%, White, Brazil) and helium (99.999%, White, Brazil) as the reaction gas. The sample introduction system was composed for a quartz double-pass spray chamber and a Burgener® nebulizer connected by Tygon® tubes to the peristaltic pump on the ICP-MS (set at 20 rpm). The blood samples were diluted 1:50 into a 15 mL polypropylene Falcon® tube (Becton Dickinson) with a solution containing 0.01% (v v^{-1}) Triton® X-100, 0.5% (v v^{-1}) nitric acid and 10 $\mu g\,L^{-1}$ of each one of the internal standard Yttrium. High purity de-ionized water (resistivity 18.2 $M\Omega\,cm^{-1}$) was used for the preparation of the samples and solutions (Batista et al., 2009). As a quality control, the method was validated by analyzing certified reference material (CRM) in every batch of samples (Seronorm® TE Whole Blood Level II - Stasjonsveien). The limits of detection (LOD) were 0.1597 $\mu g\,L^{-1}$, 0.036 $\mu g\,L^{-1}$, 0.164 $\mu g\,L^{-1}$, 0.534 $\mu g\,L^{-1}$, 1.060 $\mu g\,L^{-1}$, 0.096 $\mu g\,L^{-1}$, 0.001 $\mu g\,L^{-1}$, 0.017 $\mu g\,L^{-1}$, 0.005 $\mu g\,L^{-1}$, 0.1507 $\mu g\,L^{-1}$, and 0.002 $\mu g\,L^{-1}$ for Cr, Mn, Ni, Cu, Zn, As, Cd, Sn, Sb, Hg, and Pb, respectively. The LOQ were 1 $\mu g\,L^{-1}$ for the elements Cr, Mn, Ni, As, Cd, Sn, Sb, Hg and Pb, 50 $\mu g\,L^{-1}$ for Cu and Zn. The CRM recovery for all elements was between 80 and 120%.

2.3. Exposure assessment

An exposure assessment questionnaire was administered for all workers, and air samples were collected from nine welders. The

Table 1
Absolute frequency of demographic characteristics of the participants, by exposure group and sex. Limeira, São Paulo, 2017.

Variable	Overall		Exposed group		Control group	
	Males	Females	Males	Females	Males	Females
Subjects	66	99	51	61	15	38
Current Smokers	4	14	2	9	2	5
Age						
1 – 5 years	7	6	5	4	2	2
6 – 11 years	8	6	8	2	0	4
12 – 19 years	21	10	19	7	2	3
> 20 years	30	77	19	48	11	29
Educational level						
Illiterate	1	5	1	3	0	2
Basic school complete	57	69	48	44	9	25
Secondary school complete	3	24	0	13	3	11
University	2	1	0	1	2	0
Jewelry workers						
Assemblers	2	26	2	26	0	0
Welders	9	20	9	20	0	0

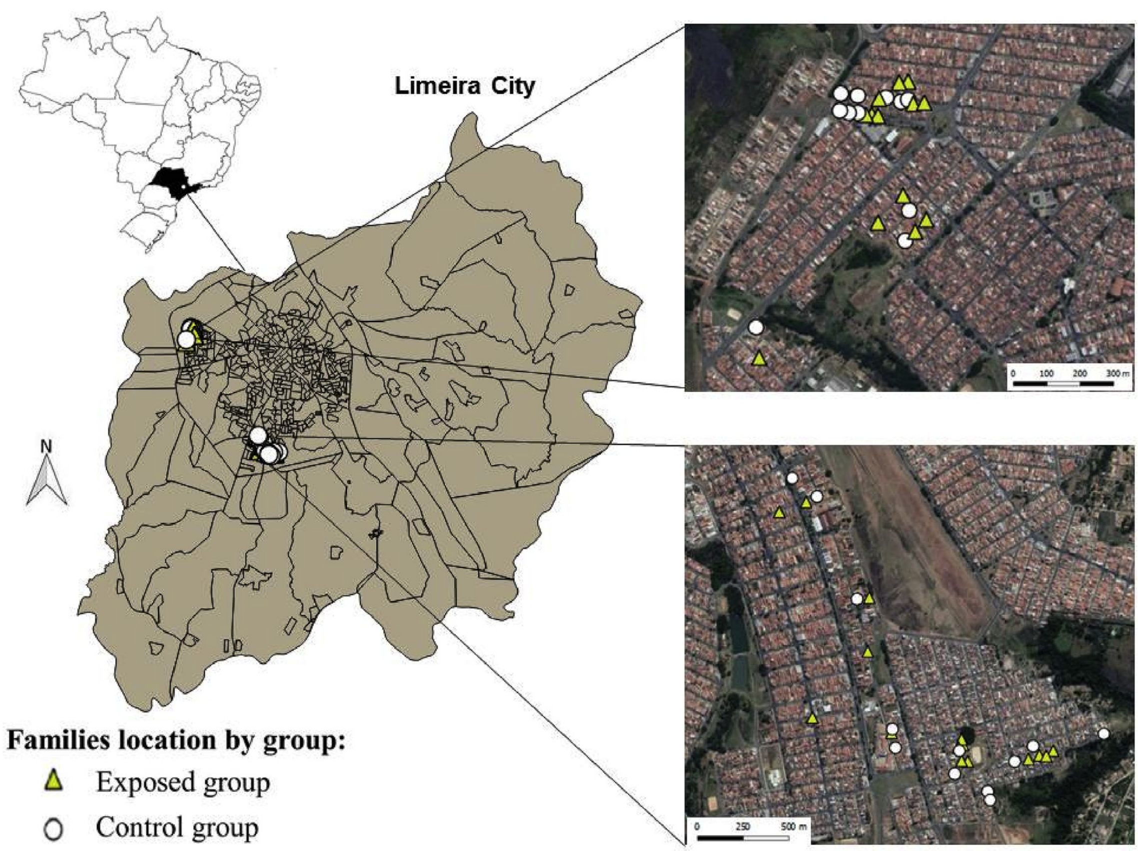

Fig. 1. Map of the city of Limeira and the distribution of the families by group (exposed or control).

collection of the welding fumes was performed using a filter media (mixed cellulose ester, 0.8 μm pore sizes, 37 mm) with a sampling pump (SKC AirChek XR5000®), set up with a 2 L min^{-1} flow rate, for four hours (OSHA, 2018). The pump was calibrated before sampling, using a calibrator (Gilian – Gilibrator 2), and the flow rate was rechecked after sampling. The welding fumes were collected by locating the sampling head within the welders' breathing zone. The filters were digested in a 15 mL polypropylene Falcon® tube (Becton Dickinson) with a solution containing 1 mL of 65% HNO_3, for 24 h at room temperature, and then diluted to 15 mL with high-purity deionized water (resistivity 18.2 MΩ cm^{-1}). The determination of the PTEs (Mn, Ni, Cd, Sb, Sn, Cu, Zn and Pb) was carried out with an ICP-MS equipped with a reaction cell (ICP-MS 7900, Hachioji, Japan) operating with high-purity argon (99.999%, White Martins, Brazil) and helium as the reaction gas (99.999%, White Martins, Brazil). Blanks were run before the analysis of air samples.

The exposure assessment questionnaire was administered during the air sample collection, and details about the location of work, the processes that the workers were performing, their job tasks, the use of protective equipment, and the working lifetime of each individual were collected. An emphasis was placed on collecting information about welding, other jobs associated with welding exposures, and materials and solvents that were manipulated (AIHA, 2015).

2.4. Data processing and statistical approach

The statistical analyses were conducted using Python programming language and STATA 13.1 software (STATA Corporation, TX, USA). Element concentrations in blood that were below the limit of quantification (LOQ) were assigned a value of LOQ/2. The proportion of <LOQ values were 8% for Sn and less than 3% for the other elements in the blood samples determination. The descriptive statistics of data relating to the 165 participants included the geometric mean (GM), the corresponding 95% confidence interval (95% CI) and the 95th percentiles. Differences in the concentration of PTEs in blood among the subgroups based on the different variables were tested by the Mann-Whitney *U* test. A principal component analysis (PCA) (Tipping and Bishop, 1999) was applied to investigate the relationships in the data, to reduce the actual data dimensions, and to assess the main sources of variation. Before applying PCA, the dataset was standardized by removing the mean and scaling to unit variance (Chan et al., 1983). PCA is an unsupervised learning technique that produces a series of new variables. These variables are linear combinations of the original variables and they can provide the variance by any projection of the data. In addition, PCA score plots reveal the strong influences in the principal components of the exposure factors, which are, in this case, age, sex, and smoking status. Additionally, a cluster analysis (Ball and Hall, 1967) was performed to identify any linkages between the data. Finally, EWAS approach (Patel et al., 2010) using a logistic regression analysis was carried out to gain further insight into a group of observations. EWAS is an approach that has been introduced in exposure science and provides the ability to seek emerging relationships between environmental factors and observed effects or variables (Pino et al., 2017). A logistic regression model was applied to EWAS trying to estimate the probability of being in one of these two groups based on the exposure factors and the concentration of PTE in blood. The logistic regression model was adjusted to age, gender as well as smoker and non-smoker participants.

Moreover, in this study a sensitivity analysis was performed in the applied model trying to assess the stability of the associations. The analysis consisted of a three-fold cross-validation procedure based on the independent subsampling of discovery and replication of data sets. Logistic model was performed for each 80:20 discovery and replication split.

For air samples, the GM and the corresponding 95% confidence interval (95% CI), as well as the minimum and maximum elements concentrations were presented.

The participants were also stratified by the following characteristics including age (1–5, 6–11, 12–19 and ≥ 20 years), sex (male or female), smoking status (yes or no), and by group (exposed or control). The exposed group was also stratified by welder and non-welder.

3. Results

The blood concentrations of eleven elements in blood were measured in 165 participants by ICP-MS. In addition, the exposure assessment was composed by applying specific questionnaire for all workers and the collection of air samples from nine welders, in the breath zone, to determine the elemental concentrations by ICP-MS of eight PTEs.

The distribution of data for the exposed and control groups, according to sex, age group, educational categories, and tobacco smoking status, are shown in Table 1. The percentage of current smokers was higher in the control group (13.2%). The median for age was 23 years in the exposed group and 33 years in the control group. Eighty percent of the workers were female, and 43.5% of those females then worked as welder. None of the workers reported the use of respiratory protection equipment, and only two workers reported the use of protection glasses during the welding process. None of the working environments, which were all located within houses, had mechanical ventilation systems or local exhaust ventilation.

The blood levels found for the elements As, Cr and Hg for all observations were below the LOD. Therefore, the values for these elements were not considered in any statistical test or descriptive analyses.

The GM and the 95th percentiles for the PTEs determined in blood, by sex and exposure group, are shown in Table 2. In the present study, it was not possible to calculate the GM for the elements Cd (for either groups) or Sn (for the control group) because of the number of values below the LOQ. The female participants from the exposed group had the highest GM for the tested elements; the only exception was Pb, for which the males in the exposed group had the highest GM ($Pb = 15.01\ \mu g\ L^{-1}$). A significant statistical difference was found for Pb concentrations between the exposed and control groups ($p < 0.0001$) and between males and females ($p = 0.0046$). For Cu ($p < 0.0001$) and Sb ($p = 0.0434$) were also found significant statistical differences between males and females.

Table 1S, supplementary material, presents the GM and 95th percentile values of PTEs, by age group, for the following datasets: studies performed in Brazil (Olympio et al., 2018; Takeda et al., 2017; Kira et al., 2016; Freire et al., 2015), cycle 2 (Canada, 2013) and cycle 3 (Canada, 2015) of the biomonitoring campaign for the general population of Canada, and the 2011 and 2012 biomonitoring campaign for the general population in the United States (CDC, 2015). In the present study, it was not possible to calculate the GM for the elements Cd and Sn for any of the age ranges or the 95th percentile for Cd for the 1–5, 6–11, and 12–19 age ranges because of the number of values below the LOQ. The exposed group presented the highest 95th percentile for all elements when the exposed and control groups were compared, except for Ni concentrations in the age range of 1–5 years (Ni in the 1–5 year age range = $7.50\ \mu g\ L^{-1}$ vs $9.64\ \mu g\ L^{-1}$).

Table 3 shows the GM, minimum and maximum values of the PTEs in the air, the permissible exposure limits (PEL) as the time-weighted average (TWA) exposure limits established by the Occupational Safety and Health Administration (OSHA, 2018), and the National Institute for Occupational Safety and Health (NIOSH, 2018), the Minimal Risk Level (MRL) for chronic exposure and the Environment level established by ATSDR. Brazilian occupational legislation established occupational exposure limit in the air only for the element Mn ($1\ mg\ m^{-3}$) (Brazil, 1978). The measured concentrations of Cu, Zn, Cd, and Pb exceeded the OSHA and NIOSH PEL-TWA limits. Values were also found be above the MRL for the elements Mn, Ni and Cd and Environment Levels for Mn, Ni, Zn, Cd, and Pb.

Fig. 2 shows the PCA scores plots for three different examined groups: the workers, relatives of the workers, and the control group.

Although the PCA is one of the most applied tool in the world of data analysis, when it is used features with low variance have high predictive relevance (Jolliffe, 1982). Therefore, the variance of the variables was also calculated. The PCA feature variance is presented in the supplementary material. The Fig. 1S shows that the first feature explains 20% of the variance within our data set while the first four explain more than 50% of the variance. Using ten features in the model, it is captured the 96% of the variance within the dataset. Hence, the additional importing of features eventually provides low information to the selected model.

A hierarchical clustering analysis was used to display the subclusters and the relationships in the dataset. Fig. 3 illustrates that

Table 2
Geometric means (GM) and their 95% confidence interval (CI 95%), and 95th percentiles (95th) for the potentially toxic elements levels (PTE) determined in the blood of study participants (μg L^{-1}), by exposure group and sex.

PTE	Exposed group						Control group					
	Male (n = 51)		Female (n = 61)		Overall		Male (n = 15)		Female (n = 38)		Overall	
	95^{th}	GM (CI 95%)	95^{th}	GM (CI 95%)	95^{th}	GM (CI 95%)	95^{th}	GM (CI 95%)	95^{th}	GM (CI 95%)	95^{th}	GM (CI 95%)
Mn	17.56	9.33 (8.51–10.23)	16.81	10.05 (9.24–10.93)	17.34	9.71 (9.13–10.33)	11.33	8.62 (7.74–9.59)	14.65	9.70 (8.81–10.68)	13.87	9.38 (8.70–10.11)
Ni	9.18	5.62 (5.16–6.12)	11.38	5.73 (5.12–6.42)	11.27	5.68 (5.29–6.10)	7.41	5.28 (4.71–5.93)	9.64	5.55 (4.84–6.37)	8.79	5.47 (4.95–6.06)
Cu	1,45	939 (884–998)	1,75	1,15 (1,08–1,23)	1,73	1,05 (1,00–1,10)	1,22	887 (788–998)	1,42	1,03 (970–1,09)	1,33	986 (934–1,04)
Zn	4,98	3,21 (2,99–3,45)	4,93	3,31 (3,10–3,54)	4,98	3,27 (3,11–3,43)	4,59	3,45 (3,16–3,75)	4,29	3,20 (3,01–3,41)	4,47	3,27 (3,11–3,44)
Cd	[a]	[a]	3.48	[a]	3.05	[a]	[a]	[a]	[a]	[a]	[a]	[a]
Sn	3.00	0.99 (0.82–1.19)	3.69	1.32 (1.10–1.59)	3.54	1.88 (1.72–2.05)	[a]	[a]	[a]	[a]	[a]	[a]
Sb	3.44	1.57 (1.36–1.84)	3.40	1.75 (1.53–2.00)	3.44	1.90 (1.75–2.05)	4.74	1.36 (0.96–1.95)	3.04	1.70 (1.51–1.93)	3.04	1.76 (1.60–1.94)
Pb	39.17	15.01 (12.73–17.71)	36.62	13.25 (11.40–15.40)	38.59	14.02 (12.56–15.66)	29.40	11.85 (8.68–16.19)	15.90	8.04 (6.93–9.33)	22.50	8.97 (7.79–10.33)

[a] Not calculated: proportion of results below limit of quantification was too high to provide a valid result.

Table 3
Geometric means (GM) and their 95% confidence interval (CI 95%), minimum and maximum values of the air elements concentrations (mg.m^{-3}) of the welders, Minimal Risk Levels (MRL, in mg m^{-3}) and Environment Levels (mg m^{-3}).

Element	GM (n = 9) (CI 95%)	Minimum - Maximum	OSHA[a] TWA[c] Limit	NIOSH[b] TWA[c] Limit	MRL[d]	Environment Level[e]
Mn	0.21 (0.15–0.30)	0.11–0.42	[f]	1 .00	3.10^{-4}	4.10^{-5}
Ni	0.21 (0.09–0.47)	0.03–0.54	1.0	0.015	9.10^{-5}	2.10^{-4}
Cu	1.46 (0.65–3.24)	0.00–4.68	0.1	0.10	[f]	[f]
Zn	27.31 (7.90–94.47)	2.73–551.42	5.0	5.00	[f]	2.10^{-3} - 1.6 10^{-2}
Cd	2.06 (0.27–15.81)	0.02–52.12	0.005	[f]	1.10^{-5}	2.10^{-6} – 1.5 10^{-5}
Sn	0.28 (0.06–1.35)	0.03–12.35	2.00	2.00	[f]	[f]
Sb	0.01 (0.01–0.01)	0.00–0.02	0.50	0.50	[f]	[f]
Pb	0.25 (0.07–0.90)	0.03–6.59	0.05	0.05	[f]	$<5.10^{-3}$

[a] OSHA - Occupational Safety and Health Administration.
[b] NIOSH - National Institute for Occupational Safety and Health.
[c] TWA - Time-weighted average.
[d] MRL – Minimal Risk Level for chronic inhalation (ATSDR).
[e] Environment Level (ATSDR).
[f] Not available/not calculated.

the distances between Sb and Pb as well as between Mn and Ni are the smaller among those in the dendrogram declaring a high similarity among the examined individuals.

The results of the model were evaluated using receiver operating characteristic (ROC) curve analysis (Fig. 4S). It has to be noted that in the present study, a permutation-based EWAS analysis was used for further evaluation and validation of the analysis of the model. The outcome of the analysis was that the occupational status randomly shuffled across the observations for 10,000 times and the workflow was carried out again. The false discovery rate was calculated for estimating the expected proportion of falsely rejected null hypotheses (Benjamini and Hochberg, 1995), control for type I error due to multiple hypotheses testing in associating the factors to occupational status. The followed workflow is presented in the supplementary material (Fig. 2S).

In the present study, the ROC model was used as a classifier to explore for exposure levels and factors associated with occupational exposures. The ROC index of the model rises the 0.80. The results of the permutation show the accuracy of the model for the permutated decrease the prediction accuracy of the model. This implies that the created null distribution permutating the outcome labels has a significant difference with the examined population allowing for further investigation of the model. The results of the permutation are presented in Fig. 3S.

4. Discussion

To the best of our knowledge, this study is the first to investigate the occupational exposures to PTE of informal and household workers and their families in the production of jewelry and fashion jewelry in Brazil. The jewelry workers are exposed to a wide range of PTEs, particularly the welders. We evaluated the air in the breathing zone of the welders and the blood element levels of the workers and their relatives in the same household. We also evaluated the blood element levels of a control group. We found concerning concentrations of the PTEs in the air, especially for the elements Ni and Cd, and all observations were above the tolerable limits.

Blood manganese levels found in the present study, for both groups, were similar to the levels reported in Canada (2013) and the United States (CDC, 2015), and they are lower than the values reported by Freire et al. (2015), whose study was performed using samples the general population in Brazil. Slightly higher blood concentration for Mn values were found in studies that were performed in welders (Wang et al., 2006; Pesch et al., 2012; Lee et al., 2016). Even though manganese intake, in low levels, is necessary for human health, exposures to high manganese levels are toxic (ATSDR, 2012a).

Ni blood levels for the exposed and control groups were higher than values reported by studies performed in Brazilian and other general populations (Table 1S). Nunes et al. (2010) found a mean concentration of Ni of 2.1 μg L^{-1} in samples from five different Brazilian states, including São Paulo. The GM values found for the Canadian biomonitoring campaign were very low, for all age ranges, compared to the values reported in the present study. Alimonti et al. (2011) found that the upper limit of the 95th percentile confidence interval was 2.62 μg L^{-1} for the general population in Italy who were aged 18–65 years, which was more than 50% lower than our findings (GM for ≥20 years: 5.90 μg L^{-1}). Blood Ni concentrations found in the present study (Table 2) was also higher

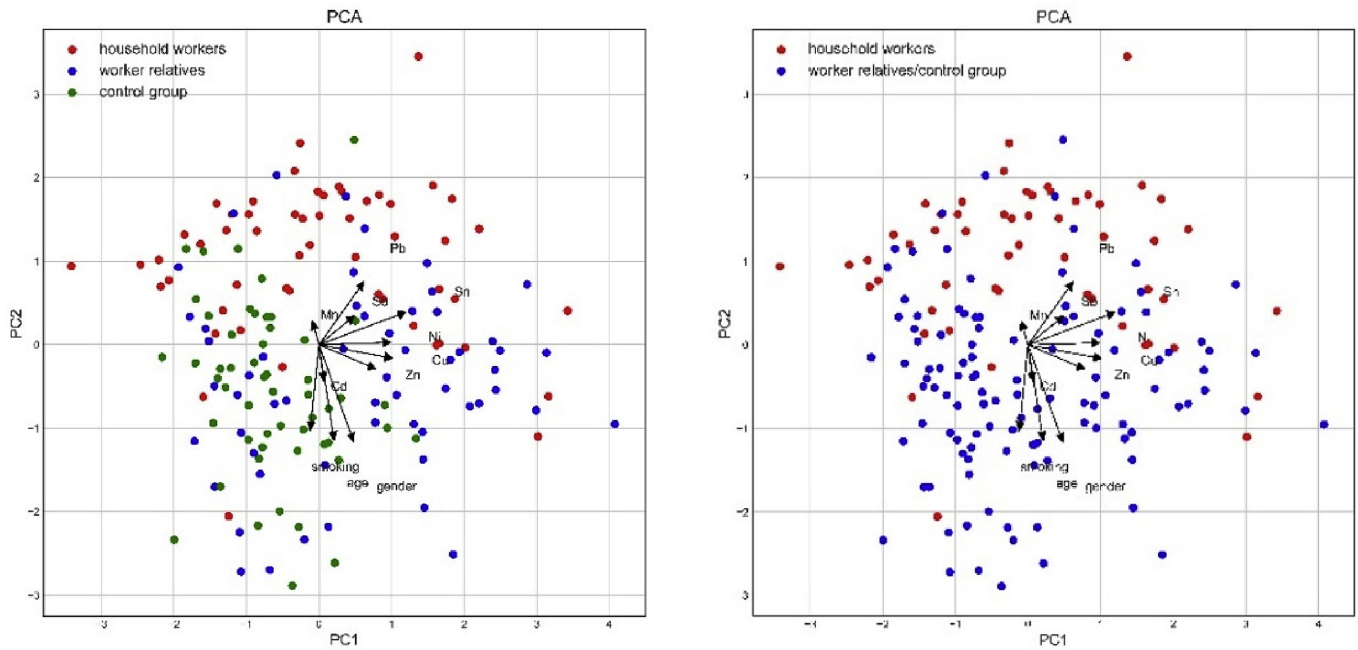

Fig. 2. Principal components analysis (PCA) scores plots of Limeira city participants blood elements levels evaluating variation among different exposure groups. In the left, PCA illustrates the scores plots (PC1 and PC2) for workers (red), relatives (blue) and control group (green). In the right, workers (red) as well as relatives and control group (blue) after merging them in one group in the right. (For interpretation of the references to color in this figure legend, the reader is referred to the Web version of this article.)

than the values found by a study that evaluated the blood concentrations of Ni in welders (Werfel et al., 1998). Mixtures that include nickel compounds and nickel metals are considered carcinogenic to humans, and may cause lung and nasal cavity cancers (IARC, 2017). Positive correlations between blood concentrations of Al, Co, Ni, and Pb and the levels of DNA damage were found by Botta et al. (2006). The authors studied French welders employed in different facilities related to the building industries. Werfel et al. (1998) measured the DNA damage and sister chromatid exchange (SCE) frequencies in lymphocytes of welders ($n = 39$) and controls ($n = 39$). A significantly higher rate of DNA single-strand breakages and significantly elevated SCE values were found for the welders.

Cu is an essential nutrient for human health; however, high doses can be harmful (ATSDR, 2004). Blood concentrations of Cu that were measured in samples in a Canadian population (Canada, 2013) were lower than the values found in the present study for both groups and for all age ranges (Table 1S). Lower concentrations of Cu in blood samples were also found in a study performed in workers from Pennsylvania who had welded at any point in their lifetime (Lee et al., 2016); the workers in Pennsylvania were not exposed at the time that the bio-evaluation was done, as was performed in the present study.

Zn is also an essential nutrient for human health, and certain levels of zinc intake are recommended based on sex and age (ATSDR, 2005). Concentrations of Zn in blood were lower for both groups in the present study compared to values found in the Canadian campaign for all age ranges (Canada, 2013).

For the element Cd, the proportion of results below the limit of quantification was too high to calculate the GM. However, it was possible to calculate the 95th percentile for the exposed group in the age range of ≥20 years, which was higher than a Brazilian study (Kira et al., 2016) and biomonitoring campaigns in Canada and the United States (Canada, 2015; CDC, 2015). Cd is classified as carcinogenic to humans (IARC, 2012). A significantly higher concentration of Cd was found in whole blood samples from welders ($GM = 3.54\ \mu g\ L^{-1}$; range $= 0.2–12.5\ \mu g\ L^{-1}$) compared to controls ($GM = 0.79\ \mu g\ L^{-1}$; range $= 0.1–4.8\ \mu g\ L^{-1}$) in a study performed in Hefei, China (Wang et al., 2006). This study also presented evidence that the welders had a higher prevalence of nervous system symptoms and lower standard scores on an eight-item questionnaire, such as depression–dejection, compared to controls (Wang et al., 2006).

A study performed in Benin, Africa, which included 70 male volunteers aged 18–65 years with no historical record of occupational exposure to metals, had 29 trace elements present in whole blood samples, including Sn and Sb. For Sn, the GM and 95th percentile results were lower than our findings ($GM = 0.21\ \mu g\ L^{-1}$; 95th percentile $= 0.48\ \mu g\ L^{-1}$). For Sb values, the values were higher than results found in the present study ($GM = 7.50\ \mu g\ L^{-1}$; 95th percentile $= 8.94\ \mu g\ L^{-1}$) (Yedomon et al., 2017). Although Sn is present in human tissue, there is no evidence that it is an essential element for human health (ATSDR, 2005).

The concentrations of Pb in blood for all age ranges were higher than the values found in the campaigns in Canada and the United States (Canada, 2015; CDC, 2015). Pb exposure is a major concern, especially for children. Inorganic Pb compounds are probably carcinogenic to humans (IARC, 2006). The GM and 95th percentile results for Pb in the 1–5 year age range ($GM = 18.09\ \mu g\ L^{-1}$; 95th percentile $= 29.21\ \mu g\ dL^{-1}$) were lower than findings from another Brazilian study ($GM = 21.60\ \mu g\ L^{-1}$; 95th percentile $= 69.00\ \mu g\ dL^{-1}$) (Olympio et al., 2017). Nevertheless, low-level exposures of Pb during childhood, that is exposures above $3\ \mu g\ dL^{-1}$, were associated with neurobehavioral deficits (Chiodo et al., 2004; Olympio et al., 2009).

In the cluster evaluation, the three groups were not clearly discriminated in PC1 and PC2. However, by merging the group of worker relatives with the control group into one group (Fig. 2), the two new groups could be discriminated into two clusters. Furthermore, the subcluster HCA model (Fig. 3) illustrated that smoking was an exposure factor that had a strong influence in the cluster analysis. Also, concentrations of Mn and Ni in the blood concentration were highly correlated with concentrations of Pb and

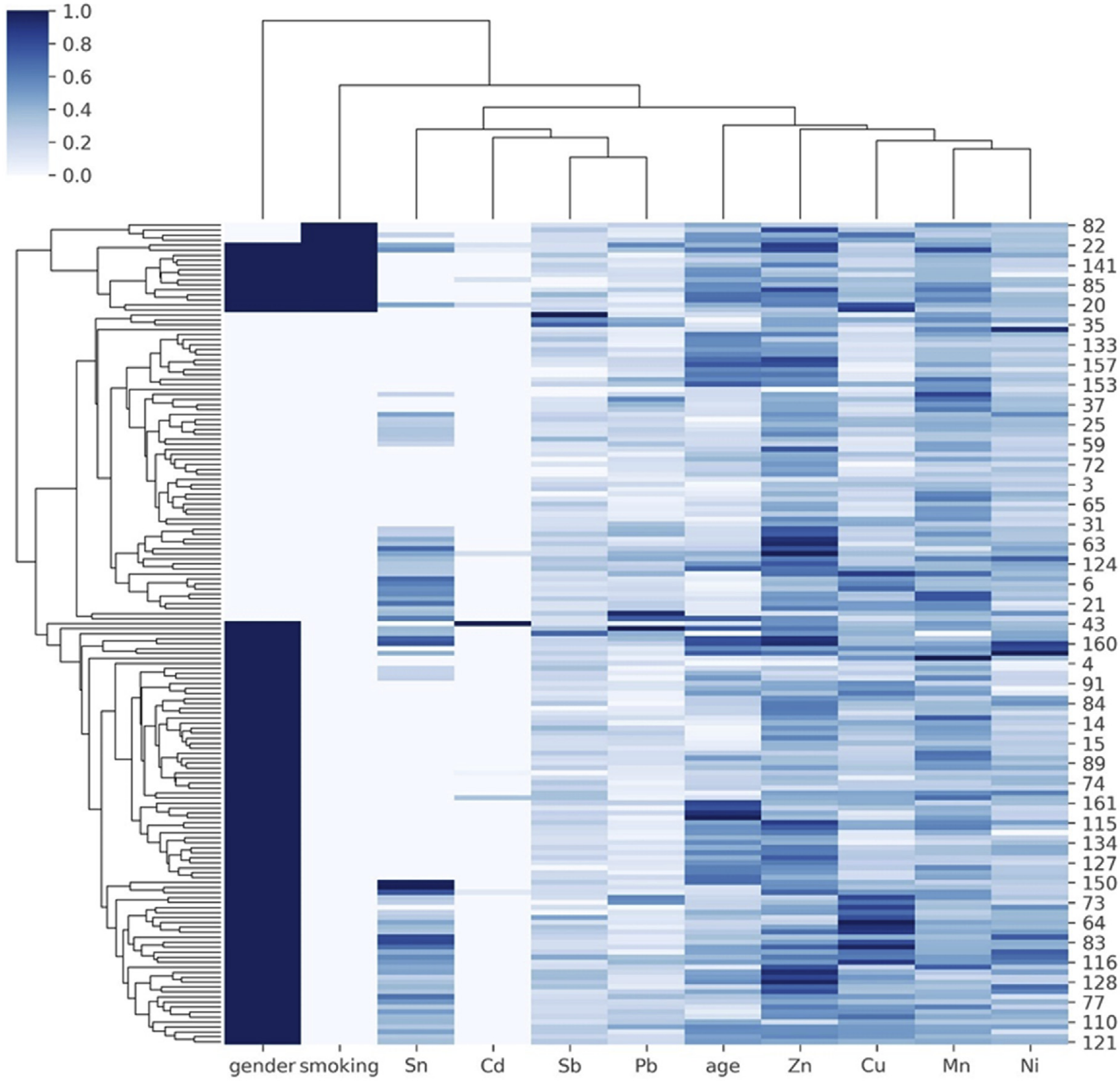

Fig. 3. Hierarchical cluster analysis based on the Euclidean distance. On the top axis of figure, the dendrogram depicts the distance among the exposure factors. The exposure factors can be found on the bottom axis. Additionally, on left axis depicts dendrogram among the participants. The right axis provides the id number of the individuals. However, because of the presentation reasons, not all the individuals' id numbers are illustrated to the right axis. The distance is scaled and the values range between 0 (white color) and 1(dark blue color). (For interpretation of the references to color in this figure legend, the reader is referred to the Web version of this article.)

Sb. The ROC curve of the applied EWAS approach revealed that the combination of age, smoking, sex, and blood concentrations of Mn, Ni, Cu, Cd, Sb, Sn, and Pb increased the odds of the outcome, which, in this case, was the odds of being a worker (Fig. 4S).

The type of welding process and the materials used during this step may affect the composition, morphology, and size of the particles present in the welding fumes (Antonini et al., 1997, 2004; Zimmer and Biswas, 2001). Therefore, the exposure assessment, as well as the worker exposure studies, are complex to understand and compare (Antonini et al., 2003, 2004; Pesch et al., 2015) because of the different exposure settings. The GMs calculated from the air samples of the welders are presented in Table 3, and they show that Cu, Zn, Cd, and Pb were measured at concentrations above the NIOSH and OSHA limits. The GM of the air concentration of Cd (2.06 mg m^{-3}) was higher than the OSHA PEL–TWA limit (OSHA PEL–TWA of Cd = 0.005 mg m^{-3}). The main route of Cd exposure in occupational environments is via the respiratory tract (ATSDR, 2012b). The GM for Pb was also five-fold higher than the OSHA and NIOSH limits. The main source of Pb exposure is ingestion of contaminated food and drinking water, and the absorption varies between children (40–50%) and adults (3–10%); however, about 95% of inorganic lead that is inhaled is absorbed (ATSDR, 2007). The GM concentrations of Zn and Cu in the present study were also higher than the PEL–TWA limits.

The use of individual and collective protective equipment plays an import role in occupational health and exposure scenarios. Controlling an exposure to the lowest feasible concentration is important for achieving occupational limits and guaranteeing the protection of the workers (Weiss et al., 2013; Lehnert et al., 2014). However, in the present study, no worker reported the use of respiratory protection equipment, and only 3.5% reported the use of protective glasses during the welding process. Furthermore, the workplaces in the houses did not have mechanical ventilation equipment and the workers shared the workplace with their relatives, even children were under the same exposure scenario. In previous studies, exposures have been noticeably reduced by using ventilation systems and individual protective equipment during the welding process (Weiss et al., 2013; Lehnert et al., 2014).

The personal measurements of PTEs in the breathing zone of welders, together with measurements of PTE concentrations in blood, were strengths of our study. However, there were some limitations that should be considered. It is important to bear in mind that this was a cross-sectional study. Information regarding various characteristics of the participants was collected to consider possible confounders, besides a control group to equalize the environmental exposure has been evaluated. However, in order to deepen our understanding of the exposure scenario, it is necessary to investigate other sources of exposures, such as water and food; to increase the number of samples analyzed in the cohort design; and to follow workers and non-workers. Intra-individual variations and diverse compositions of the material that the workers manipulated might impact the blood element levels and air element levels.

Even though we evaluated workers from the same field who were generally performing the same steps to produce jewelry, the exposure scenarios were different for each household. Furthermore, relatives who were under the same exposure scenarios, including children, could experience disturbances to their exposome. Due to the importance of exposures during childhood, this singular exposure should be taken into account for their exposure history. Those differences were also identified through the evaluation of sanitary sewers in the city of Limeira (Salles et al., 2018). Salles et al. (2018) evaluated the impact of informal work on the concentrations of PTEs (that was, As, Cd, Cr total, Cr-VI, Cu, Hg, Ni, Pb, Sn, and Zn) in the Limeira sewage network. It was concluded that the heterogeneity of the results indicated that the disposal of the evaluated PTEs was sporadic in nature. Moreover, carrying out occupational activities in the home could potentially affect the living conditions of other family members living in the house, especially children (Pereira et al., 2018) and women of childbearing age (Vieira et al., 2018), which could additionally affect study, leisure, and sleep time. That evidence, combined with the present study, provide an important basis for the assessment of the exposome of workers and their relatives.

5. Conclusion

The PTE concentrations found in the air analyzed in the present study raise concerns once the families, especially children, are in the same exposure scenario. The air elements levels were found to be higher than environmental limits for manganese, nickel, zinc, cadmium, and lead. Cadmium, zinc, and copper air levels surpassed even occupational limits. The elements concentration found in blood samples showed that the relatives of the workers have a higher exposure comparing to the Control group indicating an influence of exposure level by the shared workplace inside the workers' house. Inadequate work conditions were observed in the houses, revealing the urgent need to implement public actions to protect those workers and their families.

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Conflicts of interest

The authors declare that they have no competing financial interests.

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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.2018.11.083.

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