



Current trends of blood lead levels, distribution patterns and exposure variations among household members in Kabwe, Zambia



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HIGHLIGHTS

- We measured blood lead in household members in Kabwe, which has a history of Pb–Zn mining.
- Blood Lead Levels (BLL) ranged from 1.65 to 162 µg/dL and were highest in children compared to parents.
- LeadCare II analyser provided prompt diagnosis to identify children needing chelation therapy.
- Age, distance from the mine and direction were the main factors influencing Pb exposure.
- Children living near the Pb–Zn mine are at serious risks of Pb and Cd poisoning.

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ABSTRACT

Childhood lead (Pb) poisoning has devastating effects on neurodevelopment and causes overt clinical signs including convulsions and coma. Health effects including hypertension and various reproductive problems have been reported in adults. Historical Pb mining in Zambia's Kabwe town left a legacy of environmental pollution and childhood Pb poisoning. The current study aimed at establishing the extent of Pb poisoning and exposure differences among family members in Kabwe as well as determining populations at risk and identify children eligible for chelation therapy. Blood samples were collected in July and August 2017 from 1190 household members and Pb was measured using a portable LeadCare-II analyser. Participants included 291 younger children (3-months to 3-years-old), 271 older children (4-9-years-old), 412 mothers and 216 fathers from 13 townships with diverse levels of Pb contamination. The Blood Lead Levels (BLL) ranged from 1.65 to 162 µg/dL, with residents from Kasanda (mean 45.7 µg/dL) recording the highest BLL while Hamududu residents recorded the lowest (mean 3.3 µg/dL). Of the total number of children sampled (n = 562), 23% exceeded the 45 µg/dL, the threshold required for chelation therapy. A few children (5) exceeded the 100 µg/dL whereas none of the parents exceeded the 100 µg/dL value. Children had higher BLL than parents, with peak BLL-recorded at the age of 2-years-old. Lead exposure differences in Kabwe were attributed to distance and direction from the mine, with younger children at highest risk. Exposure levels in parents were equally alarming. For prompt diagnosis and treatment, a portable point-of-care device such as a LeadCare-II would be preferable in Kabwe.

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1. Introduction

Lead (Pb) poisoning accounts for about 0.6% of the global burden of disease (WHO, 2010), posing a serious public health concern worldwide. While acute toxicity is related to occupational exposure and is quite uncommon, low level chronic toxicity due to environmental pollution is much more common (ATSDR, 2017). Lead poisoning has devastating effects on neurodevelopment such as mental retardation and lowering of intelligence quotient (IQ) in children, which may further result in poor school performance, lower tertiary education attainment, behavioural disorders and poor lifetime earnings (WHO, 2018; Dapul and Laraque, 2014; Miranda et al., 2007; Canfield et al., 2003; Lidsky and Schneider, 2003). If not treated, Pb poisoning is characterized by persistent vomiting, anaemia, encephalopathy, lethargy, delirium, convulsions, coma and death (WHO, 2018; Flora et al., 2012; Pearce, 2007). The Institute for Health Metrics and Evaluation (IHME, 2017) estimated that in 2016 Pb exposure accounted for 540,000 deaths worldwide. In chronically exposed adults, significant health effects including renal dysfunction, hypertension and various reproductive problems have been shown even at low Pb exposures (Kumar, 2018; Wani et al., 2015). Cases of reduced fertility following chronic exposure have been reported in males (Benoff et al. 2000, 2003; Telisman et al., 2000) as well as miscarriages in pregnant women (Wani et al., 2015). Moreover, childhood Pb exposure poses significant economic losses in affected countries, especially in low- and middle-income countries (Attina and Trasande, 2013).

Clinical presentations of Pb poisoning vary widely depending upon the age, the amount and the duration of exposure, with some individuals seeming well at a blood lead levels (BLLs) that in others results in overt clinical signs (Bellinger, 2004). Given that detrimental effects of chronic Pb exposure are usually subclinical (Yabe et al., 2015, 2018), it may result in a delay in the appropriate diagnosis and chelation therapy, which has been recommended to be initiated at levels $\geq 45 \mu\text{g/dL}$ (CDC 2002; Needleman, 2004). Early diagnosis and chelation therapy are crucial as it has been reported that high BLLs exceeding $100 \mu\text{g/dL}$ in children can cause encephalopathy, convulsions, coma and death (CDC 2002). Therefore, measurement of BLLs plays a pivotal role in the diagnosis and management of patients as described in Pb poisoned children in Nigeria (Thurtle, 2014). Traditionally, BLLs have been measured using atomic absorption spectrophotometer (AAS), inductively coupled plasma mass spectrometry (ICP-MS), etc. Although highly sensitive to Pb measurement, these equipment are laboratory-based and require trained laboratory technologists. Moreover, they are expensive and would be time-consuming to ship samples to appropriate laboratories.

In a set-up like Kabwe town in Zambia, where historical Pb mining has resulted in alarming Pb poisoning, especially in children from townships in the vicinity of the closed mine and its tailing wastes (Yabe et al., 2018; Bose-O'Reilly et al., 2018; Yabe et al., 2015), prompt diagnosis and immediate chelation therapy would be required. Therefore, a portable point-of-care device such as a LeadCare II analyser, which can be used on-site in remote medical facilities like Kabwe would be appropriate and preferable. Given that BLL results are read within 3 min, Pb poisoning would be diagnosed and chelation therapy initiated promptly. Therefore, the current study investigated trends of BLL using a LeadCare II Analyser in Kabwe to identify children that required medical management to minimize the toxic effects of Pb. In addition, factors influencing Pb exposure in Kabwe were analyzed and exposure patterns among household members including fathers, mothers and children were evaluated.

2. Materials and methods

2.1. Sampling sites

Kabwe town, with a population of about 230,000 inhabitants and area size of $1,547 \text{ km}^2$, is the fourth largest town in Zambia. It is the provincial capital of Zambia's Central Province and is located at about $28^\circ 26' \text{E}$ and $14^\circ 27' \text{S}$. Kabwe has a long history of open-pit Pb–Zn mining, from 1902 to 1994. As observed by the Blacksmith Institute (2013), despite closure of the mine, scavenging of metal scraps from the abandoned tailings and wastes stored on the mine has continued to serve as a source of metal pollution, especially dusts emanating from the mine dumps (Fig. 1).

Moreover, some households were within 500 m of the tailings. As shown in Fig. 2, soils in townships in the vicinity of the mine and homes downwind from the tailings were highly polluted with Pb exceeding acceptable levels for residential areas (Bose-O'Reilly et al., 2018). In the current study, blood samples were collected from family members including fathers, mothers and children at health centres around the town of Kabwe, in July and August of 2017. More details about the study site and descriptions of townships that are within the vicinity of the mine can be obtained from the previous study (Yabe et al., 2015).

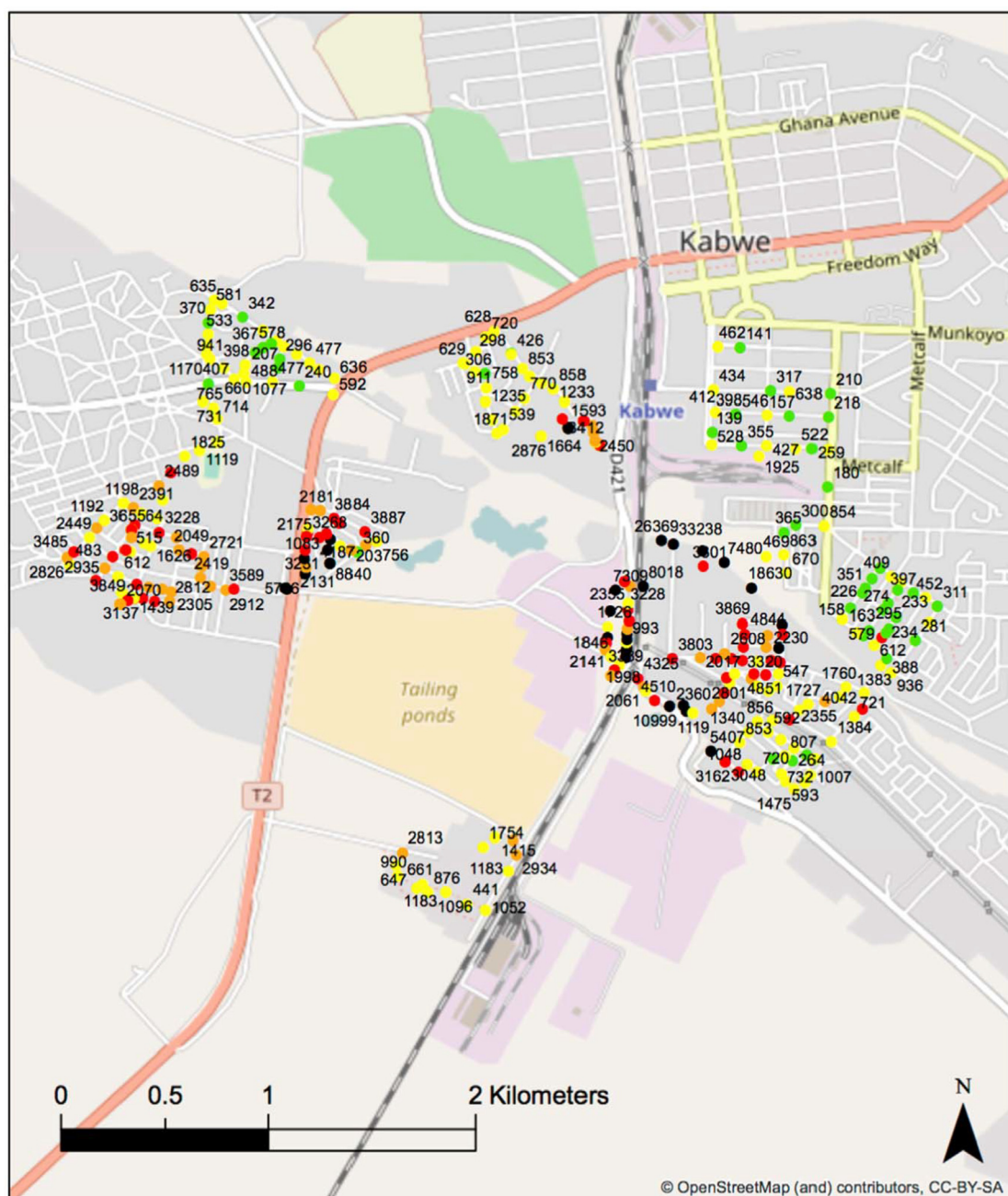
2.2. Sample collection

The study was approved by the University of Zambia Research Ethics Committee (UNZAREC; REF. No. 012-04-16). Further approvals were granted by the Ministry of Health through the Zambia National Health Research Ethics Board and the Kabwe District Medical Office. The study targeted households from areas diverse in the levels of Pb contamination based on the sample design in a parallel socioeconomic survey under the KAMPAL project (Hiwatari et al., 2018). 1000 target households were randomly chosen in two steps. In the first step, following the sampling frame of Central Statistical Office (CSO), which conducts official census in Zambia and has divided Kabwe town into 384 Standard Enumeration Areas (SEAs). Forty SEAs falling within the catchment area of health facilities were randomly selected (Fig. 3) while 25 households from each SEA were randomly selected in the second stage.

To conduct blood sampling, up to four household members (father, mother, and two children) were invited to local health centres. Younger non-school-going children up to 3 years old and older school-aged children older than 4 years were selected in the study. The age criterion was according to Yabe et al. (2015) who found significant differences BLL in children of the two age groups. Thirteen health centres with catchments areas covering the 40 SEAs were included. These included Kasanda, Chowa, Makululu, Katondo, Railway, Pollen, Mahatma Gandhi, Bwacha, Ngungu, Natuseko, Mpima Prison, Kang'omba and Hamududu with distances between the mine and the health centres ranging from 1.5 to 30 km (Fig. 3). After informed and written consent were obtained



Fig. 1. Figure showing men scavenging for scrape metals at the Kabwe Pb–Zn mine tailings (left) and houses located within 500 m to the tailings (right).



Lead (Pb) in Surface Soil (mg/kg)
Kabwe, Zambia
August 2014

Lead (mg/kg)

- <401
- 401-2,000
- 2,001-3,000
- 3,001-5,000
- 5,001 - 62,142

Fig. 2. Map of Kabwe showing distribution of Pb (mg/kg) in township soils around the Pb–Zn mining complex (Bose-O'Reilly et al., 2018).

from household heads, blood samples were collected as described earlier by Yabe et al. (2015). For each of the four family members included in the study, data on the age and sex were recorded. Sample collection and questionnaire administration were done by certified local nurses. In accordance with ethical requirements,

confidentiality was upheld in the study.

To avoid sample contamination, all sample collection supplies were kept in plastic ziploc storage bags before sample collection. Moreover, the blood collection site on the arm was thoroughly cleaned and wiped with alcohol swabs before needle pricking to

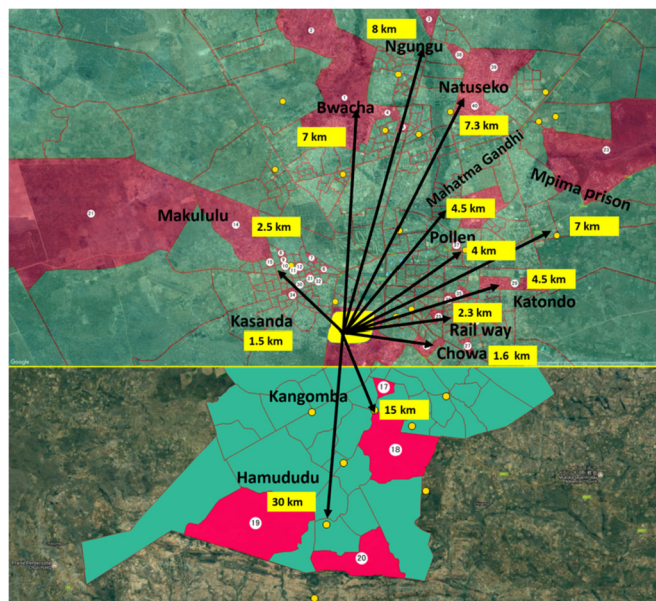


Fig. 3. Map of Kabwe showing the 40 selected SEAs (numbers 1–40 in white circles) widely distributed across the whole Kabwe town and the 13 health centres (yellow blocks) that were included in the study.

minimize contamination from dust. For infants, blood was collected by fingerstick after cleaning the finger with an alcohol swab. A new sterile lancet was used for each infant to penetrate a fingertip. The first drop of blood was wiped off with a clean and dry swab and 50 μ L blood sample was collected with a pre-supplied LeadCare II capillary tube and transferred into the LeadCare II reagent vial. After collection, blood samples were immediately analyzed for Pb using a LeadCare[®] II analyser. The remaining samples were immediately stored at -20°C at the health centres before being transported in cooler boxes on dry ice to the laboratory of the Kabwe District Health Offices where they were again stored at -20°C .

2.3. Blood Pb analysis

Lead metal analysis in whole blood samples was done on-site immediately after blood sample collection using a point-of-care blood Pb testing analyser, LeadCare[®] II (Magellan Diagnostics, USA) according to the manufacturer's instructions. The analyser uses an electrochemical technique called Anodic Stripping Voltammetry (ASV) to determine the amount of Pb in a blood sample (Magellan Industries Inc, 2013). The analyser has been evaluated by several researchers including (Stanton and Fritsch, 2007; Sobin et al., 2011; Neria et al., 2014). Briefly, individual heparinized venous blood samples were drawn using the manufacturer-supplied LeadCare II capillary tubes (approximately 50 μ L) and dispensed into labeled vials containing LeadCare II treatment reagent (250 μ L of 0.1% of HCl). These were thoroughly mixed by tipping the bottle ten times to enhance red blood cell lysis, which released the bound Pb. About 50 μ L of the blood/reagent mixture was then transferred to a sensor using the provided transfer dropper and analyzed for blood Pb concentration. Single analyses were performed with results reflected within 3 min in $\mu\text{g}/\text{dL}$ on the analyser's screen. For quality assurance, the instrument was calibrated using a probe before each new lot of test supplies (every 48 tests). Standard controls, one high and one low blood-based controls supplied by the manufacturer were analyzed to assess accuracy, these fell within the manufacturer-specified acceptability

limits of 6.9–13.7 $\mu\text{g}/\text{dL}$ for the low control and 21.8–32.6 $\mu\text{g}/\text{dL}$ for the high control. Since limits of quantitation were 3.3–65 $\mu\text{g}/\text{dL}$ as the LeadCare II Analyser can only detect BLL above 3.3 $\mu\text{g}/\text{dL}$. The precise values of BLLs below the 3.3 $\mu\text{g}/\text{dL}$ detection limit could not be determined. These BLLs below instrument detection limit were therefore treated as 1.65 $\mu\text{g}/\text{dL}$, the mean of 0 and 3.3 as suggested in other environmental studies (Wood et al., 2011; Ogden, 2010).

For samples above 65 $\mu\text{g}/\text{dL}$, a 3 times dilution was done using 0.1% HCl. Briefly, 50 μ L of collected blood was added into 100 μ L of 0.1% HCl. Then 50 μ L of diluted blood was pipetted into the LeadCare II reagent. This was mixed thoroughly and analyzed in the same way as for undiluted blood. The blood specimens and blood/reagent mixtures were maintained at room temperature throughout the analytical process.

2.4. Statistical analysis

All data were combined into a single electronic database and checked for accuracy and outliers. Statistical analysis was performed using JMP version 10 (SAS Institute, USA). The data are presented as mean, geometric mean (GM), median and minimum-maximum values in $\mu\text{g}/\text{dL}$. Tukey Kramer test was used to analyse BLL differences among family members (younger child, older child, father and mother) as well as area difference. Different letters indicated significant difference. Principal component analysis (PCA) was used to evaluate the relatedness between BLL with age, wind direction and distance from the mine. The data of BLLs ($\mu\text{g}/\text{dL}$) were log-transformed before PCA analysis to stabilize variances.

3. Results

3.1. Subjects and BLL

The current study focused on blood samples that were collected from a total number of 1190 household members including 291 younger children (3 months–3 years old) with an average age of 1.9 years; 271 older children (4–9 years old) with an average age of 6.5 years; 412 mothers with an average age of 39 years and 216 fathers with an average age of 46 years. Participants were drawn from 13 health centres servicing Kasanda, Chowa, Makululu, Katondo, Railway, Pollen, Mahatma Ghandi, Bwacha, Ngungu, Natuseko, Mpima Prison, Kang'omba and Hamududu townships. The recorded BLL ranged from 1.65 to 162 $\mu\text{g}/\text{dL}$ (Table 1).

3.2. Critical BLL values among household members

As shown in Table 2, of the 1,190 participants, 30% had BLL below 5 $\mu\text{g}/\text{dL}$, which is the level of concern. These comprised 57 younger children, 59 older children, 151 mothers and 85 fathers. Of the total number of children sampled ($n = 562$), a total of 130 (23%) exceeded the 45 $\mu\text{g}/\text{dL}$, the threshold required for chelation therapy. A few children (total of 5) exceeded the 100 $\mu\text{g}/\text{dL}$ whereas none of the parents exceeded the 100 $\mu\text{g}/\text{dL}$ value.

3.3. Pb exposure patterns among household members

Tukey test was performed to analyse age differences in BLL accumulation among family members. Children had significantly higher BLL than parents. However, there was no accumulation difference in BLL between younger children between the ages of 3 months to 3 years and older children aged 4–9 years. Moreover, BLL between fathers and mothers were not different. Similarly, there was no sex difference in blood Pb concentrations as the BLL between boys and girls were not different (data not shown). A positive correlation was seen in the BLL of mothers and their infants (data

Table 1BLL ($\mu\text{g/dL}$) exposure characteristics among household members in Kabwe, Zambia.

Category	All <i>n</i> = 1190	Younger child <i>n</i> = 291	Older child <i>n</i> = 271	Mother <i>n</i> = 412	Father <i>n</i> = 216
Mean	20.8	29.9	24.3	14.8	15.7
Geo. Mean	11.1	17.0	14.2	8.2	8.1
Standard Error	0.62	1.59	1.32	0.74	1.20
Median	13.0	22.0	17.3	10.8	8.6
Standard Deviation	21.4	27.1	21.7	15.0	17.7
Minimum	1.65	1.65	1.65	1.65	1.65
Maximum	162	162	103	86.7	88.2

Table 2BLL ($\mu\text{g/dL}$) exposure characteristics among household members in Kabwe, Zambia.

Category	All Number (%)	Young child Number (%)	Child Number (%)	Mother Number (%)	Father Number (%)
BLL ranges					
BLL < 5 $\mu\text{g/dL}$	352 (30)	57 (20)	59 (22)	151 (37)	85 (39)
BLL 5–44 $\mu\text{g/dL}$	666 (56)	154 (53)	162 (60)	239 (58)	111 (51)
BLL 45–99 $\mu\text{g/dL}$	167 (14)	76 (26)	49 (18)	22 (5.3)	20 (9.3)
BLL > 100 $\mu\text{g/dL}$	5 (0.4)	4 (1.4)	1 (0.4)	0 (0.0)	0 (0.0)

not shown).

3.4. Relationship between BLL and age

A combined dot plot and box-whisker plot was performed to evaluate the relationship between BLL and age (Fig. 4). In terms of the median BLL, a general trend indicated a high peak in children around the age of 2 years and lower BLL in older children, albeit with fluctuations. Very high BLLs are also more frequently observed among young children although BLL above 45 $\mu\text{g/dL}$ is observed in any age group.

3.5. Pb exposure differences among townships

In order to fully understand the Pb exposure patterns in Kabwe, differences in blood Pb accumulations in residents from the 13 townships were compared. Descriptive statistics of the BLL in residents enrolled at the 13 health centres are shown in Table 3.

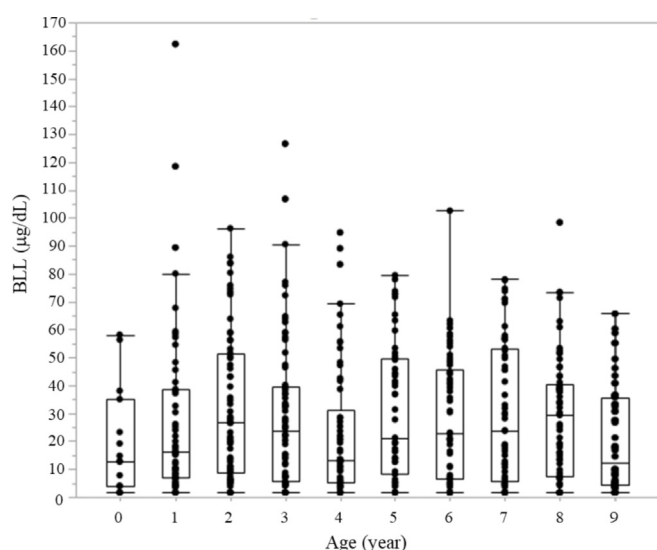


Fig. 4. Figure of combined dot plot and box-whisker plot showing relationship between BLL and age, with peak BLL recorded at 2 years old.

Residents in Kasanda Township, with mean BLL of 45.7 $\mu\text{g/dL}$ accumulated higher BLL than residents in the other 12 locations. Makululu Township had second highest mean BLL (29.3 $\mu\text{g/dL}$) followed by Chowa and Railway townships. Similar but lower BLL were recorded in residents from Natuseko, Kang'omba, Ngungu, Mpima Prison, Katondo and Mahatma Ghandi followed by Bwacha and Pollen townships. Residents in Hamududu community had the lowest BLL, with a mean value of 3.3 $\mu\text{g/dL}$.

3.6. Factors contributing to Pb exposure patterns in Kabwe

Principle component analysis (PCA) was performed on log-transformed data to evaluate the relationships among BLL, age, direction and distance from the mine to the township health centres. As shown in Fig. 5, the results of PCA accounted for 44.3% of the variation by the first principal component (PC1) and 26.4% by the second principal component (PC2). Whereas PC1 was positively determined by distance as well as a slight positive influence by age and direction, it was negatively influenced by BLL. On the other hand, PC2 had a strongly positive relationship with age, but rarely with distance and BLL. It was indicated that distance from the mine had a strong and bigger negative relationship with BLL while direction and age had lower negative relationship with BLL.

4. Discussion

A portable LeadCare© II analyser was used and proved to be an effective point of care blood Pb analyser in Kabwe, where alarming childhood Pb poisoning was previously reported (Yabe et al., 2015). Moreover, the LeadCare II analyser is less invasive and suitable for infants as it requires a smaller finger stick blood sample. In an environment like Kabwe where non-specific clinical symptoms of cumulative Pb poisoning can easily be confused with other diseases like malaria, a rapid and appropriate diagnosis of Pb poisoning cannot be overemphasized. The current study analyzed Pb exposure patterns among family members in Kabwe, where household members shared similar risk factors such as area, direction and living conditions. The study revealed that not only children were at risk of the toxic effects of Pb in Kabwe town but women and men as well. Young age was a significant risk factor given that BLL were highest in children, with peak levels recorded at the age of two, in agreement with similar trends in earlier studies (Yabe et al., 2015;

Table 3
Area differences in BLL ($\mu\text{g}/\text{dL}$) among Kabwe residents from 13 health centres.

	Kasanda	Makululu	Chowa	Railway	Natuseko	Bwacha	Ngungu	Pollen	Mahatma Ghandi	Mpima Prison	Katondo	Kang'omba	Hamududu
Mean	45.7	29.3	16.5	11.4	8.58	6.78	5.38	4.70	4.51	5.41	6.51	8.48	3.31
St'd Error	1.64	1.01	1.02	1.97	0.98	1.10	0.59	0.98	0.63	0.59	1.09	1.01	0.41
Median	44.9	24.3	16.6	10.5	6.95	3.90	4.80	1.65	4.60	4.90	3.80	5.40	1.65
Standard Deviation	23.5	19.0	10.5	6.81	6.92	11.1	3.50	4.69	2.36	4.13	7.17	9.94	4.08
Minimum	1.65	1.65	1.65	3.30	1.65	1.65	1.65	1.65	1.65	1.65	1.65	1.65	1.65
Maximum	162	119	48.3	26.2	34.3	94.8	14.2	16.8	9.00	23.3	38.7	63.5	35.6
Count	204	355	105	12	50	103	35	23	14	49	43	96	101

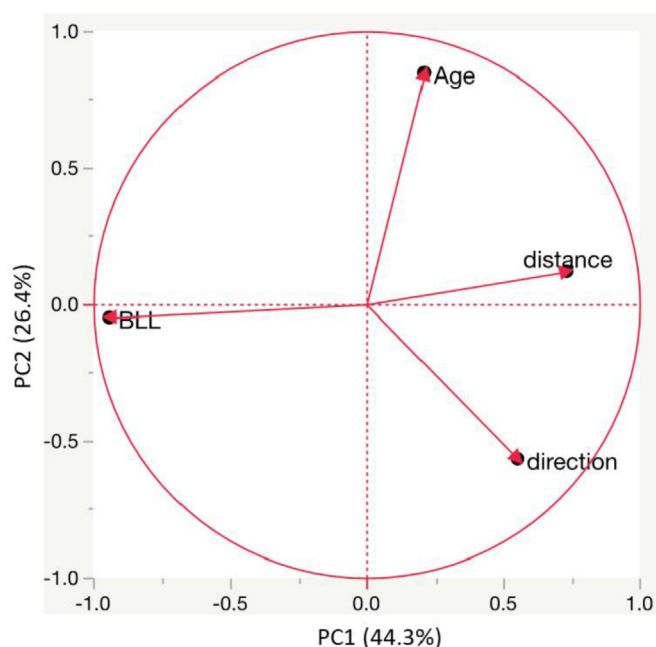


Fig. 5. Principal component analysis on log transformed data showing the influence of age, distance and wind direction on BLL among Kabwe residents.

Koller et al., 2004). This trend could be attributed to the hand-to-mouth or object-to-mouth (pica) behavior of children as they explore their environment after their onset of independent ambulation. In addition to increased exposure, children absorb a greater proportion of ingested Pb from the gastrointestinal tract than adults (Wani et al., 2015). Acute Pb poisoning exceeding $100 \mu\text{g}/\text{dL}$ can be fatal as seen in the Pb poisoning disaster in Nigeria, where more than 400 children died leaving numerous others with long-term neurological impairment (Dooyema et al., 2012; Lo et al., 2012). To minimize the pernicious effects of Pb toxicity in children, chelation therapy is recommended at levels $\geq 45 \mu\text{g}/\text{dL}$ as clinical symptoms such as abdominal pain, encephalopathy, convulsions, coma and death have been observed in BLLs > 60 (CDC, 2002; Needleman, 2004). The current study revealed that of the 556 children, 29% had BLL that exceeded $45 \mu\text{g}/\text{dL}$ and were recommended for chelation therapy. Moreover, the children were followed up for further assessment including neurodevelopmental impairment assessment (data not provided).

For the first time, the current study revealed high BLL in women in some areas in Kabwe, with concentrations up to $86 \mu\text{g}/\text{dL}$. These findings were similar to BLLs reported in women of child-bearing age in Sub-Saharan Africa where the overall weighted mean BLLs of $24.73 \mu\text{g}/\text{dL}$ was recorded, with the highest mean of $99 \mu\text{g}/\text{dL}$ being recorded in women from Nigeria (Bede-Ojimadu et al., 2018). Most of the mothers that participated in current the study (58%) had BLL ranging between 5 and $44 \mu\text{g}/\text{dL}$, a few (5%) were above

$45 \mu\text{g}/\text{dL}$ with none exceeded $100 \mu\text{g}/\text{dL}$. Exposure to Pb in the women could be attributed to multiple sources including dust inhalation, ingestion via diet or soil (pica), a habit that is common among pregnant women in Zambia, including Kabwe. Although most studies are focused on childhood Pb exposure, the findings in the current study should be considered carefully as increased BLLs in women of child-bearing age in Sub-Saharan Africa were associated with incidences of preeclampsia and hypertension (Bede-Ojimadu et al., 2018). Delayed puberty due to Pb exposure has also been observed in girls (Schoeters et al., 2008). With a half-life of many years to decades in adults, endogenous exposure to Pb due to increased bone resorption as seen in women during pregnancy and lactation (Rothenberg et al., 2000; Téllez-Rojo et al., 2002; Gulson et al., 2003; Manton et al., 2003) could also not be ruled out in the exposed mothers in Kabwe. When pregnant, blood Pb accumulation in women could pose a threat to the developing fetus given that maternal-fetal transfer is a major source of early life exposure to Pb (Chen et al., 2006; Gardella, 2001; Li et al., 2000; Lin et al., 1998). Additional Pb exposure to the infant can occur via breast milk as breastfeeding is a recognized source of postnatal Pb exposure (Counter et al., 2014). These exposure pathways could explain the alarmingly high BLL in infants in the current study, even before their ambulatory stage. This is critical as pediatric Pb poisoning during a vulnerable period of development can lead to negative neurodevelopmental impacts such as low IQ and cognitive impairments (Lanphear et al., 2005).

Similarly, increased Pb exposure in men from some Kabwe townships was recorded in the current study, with median BLLs of $8.60 \mu\text{g}/\text{dL}$ and maximum levels of $88.2 \mu\text{g}/\text{dL}$. This is also the first time that Pb exposure is being investigated in men in Kabwe and the sources of exposure could be similar to those of women, with the exception of pica, a practice common especially among expectant mothers. Findings in the current study were similar to reports in Iran where mean BLL of $41.41 \mu\text{g}/\text{dL}$ were reported in male workers at a battery manufacturing plant (Sadeghniai haghghi et al., 2013). Given that chronic low level Pb exposure has been associated with health complications including reduced sperm quality (Wu et al., 2012; Apostoli et al., 1998), the findings of the current study highlight the reproductive health risks that men in Kabwe could be exposed to through chronic Pb exposure. Moreover, Pb exposure has an interactive relationship with socio-economic factors. While socioeconomic conditions have been established as important predictors of exposure to Pb (Elias et al., 2007; Sargent et al., 1995), health effects of Pb exposure can be the sources of economic losses that can impact families negatively (UMRSC and MNCEH, 2014; Attina and Trasande, 2013; Gould, 2009; Ogunseitan and Smith, 2007). While many studies may place emphasis only on health effects of Pb exposure, the impact of Pb exposure and poisoning in Kabwe could be broad and include healthcare, social, and behavioural costs.

Area differences in BLL exposure patterns among Kabwe residents were established in the current study, where residents from Kasanda Mine Township had the highest BLL followed by Makululu

and Chowa Townships. BLLs in Railway, Natuseko, Katondo, Pollen, Mahatma Ghandi, Bwacha, Ngungu, Mpima Prison, Kang'omba were similar, with residents from Hamududu recording the lowest. These results reveal that severity to Pb poisoning risks among residents of Kabwe was different depending on area of residence. These differences could be attributed to distance from the mine and direction, with distance from the mine exerting the majority influence as seen on PCA analysis. It was shown that townships closest to the mine and lying in the western direction of the mine were affected the most, especially Kasanda, followed by Makululu. Since the wind direction is from east to west in Kabwe, more Pb contaminated dusts emanating from the mine tailings are likely to settle in Kasanda and Makululu than the other townships. Of interest was Natuseko Township, which is located in similar direction with similar distance from the mine as Bwacha and Ngungu Townships but recorded slightly higher BLLs than these two townships. Although not established, this could be attributed to transportation and piling of contaminated soils and stones from the mine in Natuseko Township many years ago (verbal communication from community members).

5. Conclusions

This is the first study that has revealed the true extent of Pb exposure in the whole Kabwe town, which poses a serious public hazard and should be given urgent attention. Exposure to Pb does not only affect children but their parents as well. Factors contributing to Pb exposure included age, distance and direction, with distance playing the major role. Therefore, younger children in townships closer to the mine and lying on the western side of the mine were the most vulnerable. To avert overt Pb toxicity, children with BLL exceeding 45 µg/dL would require chelation therapy. These children were referred to the office of the District Medical Director. Regular BLL monitoring using a portable analyser such as the LeadCare II should be considered for prompt diagnosis and initiation of treatment to avoid the irreversible Pb-induced neurological dysfunction in children. A thorough clinical evaluation of Pb poisoning among the affected children, including neurodevelopmental and cognitive impairments, would reveal the true extent of Pb poisoning in Kabwe. Measuring blood Pb in pregnant women and breast milk will be significant to clarify the exposure pathway from mother to child and recommend appropriate medical management and advice for the mother. Socio-economic factors contributing to Pb exposure and socio-economic impacts of Pb exposure also need to be thoroughly investigated to fully understand the Pb exposure-effect cycle. Moreover, urgent environmental remediation is required to reduce Pb exposure in Kabwe.

Declaration of competing interest

The authors declare no conflicts of interest.

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References

- Agency for Toxic Substances and Disease Registry (ATSDR), 2017. Lead Toxicity. What are possible health effects from lead exposure? Available: https://www.atsdr.cdc.gov/csem/lead/docs/csem-lead_toxicity_508.pdf. (Accessed 21 January 2019).
- Apostoli, P., Kiss, P., Porru, S., Bonde, J.P., Vanhoorne, M., 1998. Male reproductive toxicity of lead in animals and humans. *Occup. Environ. Med.* 55, 364–374.
- Attina, T.M., Trasande, L., 2013. Economic costs of childhood Pb exposure in low- and middle-income countries. *Environ. Health Perspect.* 121, 1097–1102.
- Bede-Ojimadu, O., Amadi, C.N., Orisakwe, O.E., 2018. Blood lead levels in women of child-bearing age in sub-Saharan Africa: a systematic review. *Front. Public Health* 6, 367.
- Bellinger, D.C., 2004. Lead. *Pediatrics* 113, 1016–1022.
- Benoff, S., Centola, G.M., Millan, C., Napolitano, B., Marmar, J.L., Hurley, I.R., 2003. Increased seminal plasma lead levels adversely affect the fertility potential of sperm in IVF. *Hum. Reprod.* 18, 374–383.
- Benoff, S., Jacob, A., Hurley, I.R., 2000. Male infertility and environmental exposure to lead and cadmium. *Hum. Reprod. Update* 6, 107–121.
- Blacksmith Institute (PureEarth), 2013. The world's worst 2013: the top ten toxic threats. Available: <https://www.worstopolluted.org>. (Accessed 29 October 2019).
- Bose-O'Reilly, S., Yabe, J., Makumba, J., Schutzmeier, P., Ericson, B., Caravanas, J., 2018. Lead intoxicated children in Kabwe, Zambia. *Environ. Res.* 168, 420–424.
- Canfield, R.L., Henderson Jr., C.R., Cory-Slechta, D.A., Cox, C., Jusko, T.A., Lanphear, B.P., 2003. Intellectual impairment in children with blood lead concentrations below 10 µg per deciliter. *N. Engl. J. Med.* 348, 1517–1526.
- Centers for Disease Control and Prevention (CDC), 2002. Managing elevated blood lead levels among young children: recommendations from the Advisory Committee on Childhood Lead Poisoning prevention. Available: <https://stacks.cdc.gov/view/cdc/26980>. (Accessed 29 December 2018).
- Chen, P.C., Pan, I.J., Wang, J.D., 2006. Parental exposure to lead and small for gestational age births. *Am. J. Ind. Med.* 49, 417–422.
- Counter, S.A., Buchanan, L.H., Ortega, F., Chiriboga, R., Correa, R., Collaguaso, M.A., 2014. Lead levels in the breast milk of nursing Andean mothers living in a lead-contaminated environment. *J. Toxicol. Environ. Health A* 77, 993–1003.
- Dapul, H., Laraque, D., 2014. Lead poisoning in children. *Adv. Pediatr.* 61, 313–333.
- Dooyema, C.A., Neri, A., Lo, Y.C., Durant, J., Dargan, P.I., Swarthout, T., Biya, O., Gidado, S.O., Haladu, S., Sani-Gwarzo, N., Nguku, P.M., Akpan, H., Idris, S., Bashir, A.M., Brown, M.J., 2012. Outbreak of fatal childhood lead poisoning related to artisanal gold mining in northwestern Nigeria. *Environ. Health Perspect.* 120, 601–607, 2010.
- Elias, S.M., Hashim, Z., Marjan, Z.M., Abdullah, A.S., Hashim, J.H., 2007. Relationship between blood Pb concentration and nutritional status among Malay primary school children in Kuala Lumpur, Malaysia. *Asia. Pac. J. Public Health* 19, 29–37.
- Flora, G., Gupta, D., Tiwari, A., 2012. Toxicity of lead: a review with recent updates. *Interdiscip. Toxicol.* 5, 47–58.
- Gardella, C., 2001. Lead exposure in pregnancy: a review of the literature and argument for routine prenatal screening. *Obstet. Gynecol. Surv.* 56, 231–238.
- Gould, E., 2009. Childhood lead poisoning: conservative estimates of the social and economic benefits of lead hazard control. *Environ. Health Perspect.* 117, 1162–1167.
- Gulson, B.L., Mizon, K.J., Korsch, M.J., Palmer, J.M., Donnelly, J.B., 2003. Mobilization of lead from human bone tissue during pregnancy and lactation - a summary of long-term research. *Sci. Total Environ.* 303, 79–104.
- Hiwatari, M., Yamada, D., Hangoma, P., Narita, D., Mphuka, C., Chitah, B., 2018. Kabwe Household Socioeconomic Survey (KHSS) 2017 Report. Kabwe Mine Pollution Amelioration Initiative (KAMPAI), pp. 1–91 (ISBN978-4-909032-02-7), available at: <http://satreps-kampai.vetmed.hokudai.ac.jp/publications/>.
- Institute for Health Metrics and Evaluation (IHME), 2017. Global Burden of Disease (GBD) Compare. IHME, University of Washington, Seattle, WA. Available: <https://vizhub.healthdata.org/gbd-compare/>. (Accessed 10 February 2019).
- Koller, K., Brown, T., Spurgeon, A., Levy, L., 2004. Recent developments in low-level lead exposure and intellectual impairment in children. *Environ. Health Perspect.* 112, 987–994.
- Kumar, S., 2018. Occupational and environmental exposure to lead and reproductive health impairment: an overview. *Indian J. Occup. Environ. Med.* 22, 128–137.
- Lanphear, B.P., Hornung, R., Khoury, J., Yolton, K., Baghurst, P., Bellinger, D.C., Canfield, R.L., Dietrich, K.N., Bornschein, R., Greene, T., Rothenberg, S.J.,

- Needleman, H.L., Schnaas, L., Wasserman, G., Graziano, J., Roberts, R., 2005. Low-level environmental lead exposure and children's intellectual function: an international pooled analysis. *Environ. Health Perspect.* 113, 894–899.
- Li, P.J., Sheng, Y.Z., Wang, Q.Y., Gu, L.Y., Wang, Y.L., 2000. Transfer of lead via placenta and breast milk in human. *Biomed. Environ. Sci.* 13, 85–89.
- Lidsky, T.L., Schneider, J.S., 2003. Lead neurotoxicity in children: basic mechanisms and clinical correlates. *Brain* 126, 5–19.
- Lin, S., Hwang, S.A., Marshall, E.G., Marion, D., 1998. Does paternal occupational lead exposure increase the risks of low birth weight or prematurity? *Am. J. Epidemiol.* 148, 173–181.
- Lo, Y.C., Dooyema, C.A., Neri, A., Durant, J., Jefferies, T., Medina-Marino, A., de Ravello, L., Thoroughman, D., Davis, L., Dankoli, R.S., Samson, M.Y., Ibrahim, L.M., Okechukwu, O., Umar-Tsafe, N.T., Dama, A.H., Brown, M.J., 2012. Childhood lead poisoning associated with gold ore processing: a village-level investigation-Zamfara State, Nigeria. *Environ. Health Perspect.* 120, 1450–1455. October–November 2010.
- Manton, W.I., Angle, C.R., Stanek, K.L., Kuntzelman, D., Reese, Y.R., Kuehnemann, T.J., 2003. Release of lead from bone in pregnancy and lactation. *Environ. Res.* 92, 139–151.
- Magellan Industries Inc, 2013. LeadCare II Blood Lead Analyzer User's Guide (V 1.09, Rev 04). Magellan Industries Inc, North Billerica, Mass, USA. <http://www.leadcare2.com/Product-Support/Product-Literature-Downloads>. (Accessed 20 February 2019).
- Miranda, M.L., Kim, D., Galeano, M.A., Paul, C.J., Hull, A.P., Morgan, S.P., 2007. The relationship between early childhood blood lead levels and performance on end-of-grade tests. *Environ. Health Perspect.* 115, 1242–1247.
- Needleman, H., 2004. Lead poisoning. *Annu. Rev. Med.* 55, 209–222.
- Neria, A.J., Royb, J., Jarrett, J., Panc, Y., Dooyemaa, C., Caldwell, K., Umar-Tsafed, N.T., Olubiyoe, R., Brown, M.J., 2014. Analysis of a novel field dilution method for testing samples that exceed the analytic range of point-of-care blood lead analyzers. *Int. J. Environ. Health Res.* 24, 418–428.
- Ogden, T.L., 2010. Handling results below the level of detection. *Ann. Occup. Hyg.* 54, 255–256.
- Ogunseitan, O.A., Smith, T.R., 2007. The Cost of environmental lead (Pb) poisoning in Nigeria. *Afr. J. Environ. Sci. Technol.* 1, 27–36.
- Pearce, J.M., 2007. Burton's line in lead poisoning. *Eur. Neurol.* 57, 118–119.
- Rothenberg, S.J., Khan, F., Manalo, M., Jiang, J., Cuellar, R., Reyes, S., Acosta, S., Jauregui, M., Diaz, M., Sanchez, M., Todd, A.C., Johnson, C., 2000. Maternal bone lead contribution to blood lead during and after pregnancy. *Environ. Res.* 82, 81–90.
- Sadeghniat haghghi, K., Aminian, O., Chavoshi, F., Sadat, B.L., Soltani, S., Rahmati, N.F., 2013. Relationship between blood lead level and male reproductive hormones in male lead exposed workers of a battery factory: a cross-sectional study. *Iran. J. Reproductive Med.* 11, 673–676.
- Sargent, J.D., Brown, M.J., Freeman, J.L., Bailey, A., Goodman, D., Freeman Jr., D.H., 1995. Childhood Pb Poisoning in Massachusetts Communities: it's association with sociodemographic and housing characteristics. *Am. J. Public Health* 85, 528–534.
- Schoeters, G., Den Hond, E., Dhooge, W., van Larebeke, N., Leijts, M., 2008. Endocrine disruptors and abnormalities of pubertal development. *Basic Clin. Pharmacol. Toxicol.* 102, 168–175.
- Sobin, C., Parisi, N., Schaub, T., de la Riva, E., 2011. A Bland-Altman comparison of the lead Care® System and Inductively Coupled Plasma Mass Spectrometry for detecting low-level lead in child whole blood samples. *J. Med. Toxicol.* 7, 24–32.
- Stanton, N.V., Fritsch, T.B.S., 2007. Evaluation of a second-generation portable blood lead analyzer in an occupational setting. *Am. J. Ind. Med.* 50, 1018–1024.
- Téllez-Rojo, M.M., Hernández-Avila, M., González-Cossío, T., Romieu, I., Aro, A., Palazuelos, E., Schwartz, J., Hu, H., 2002. Impact of breast-feeding on the mobilization of lead from bone. *Am. J. Epidemiol.* 155, 420–428.
- Telisman, S., Cvitkovic, P., Jurašovic, J., Pizent, A., Gavella, M., Rocic, B., 2000. Semen quality and reproductive endocrine function in relation to biomarkers of lead, cadmium, zinc and copper in men. *Environ. Health Perspect.* 108, 45–53.
- Thurtle, N., 2014. Description of 3,180 courses of Chelation with Dimercaptosuccinic Acid in Children ≤ 5 y with severe lead poisoning in Zamfara, Northern Nigeria: A Retrospective Analysis of Programme Data. *PLoS Med* 10, 11.
- University of Michigan Risk Science Center (UMRSC) and Michigan Network for Children's Environmental Health (MNCEH), 2014. Economic impacts of lead exposure and remediation in Michigan. http://www.mnceh.org/sites/www.mnceh.org/files/mnceh/press-releases/Lead_Cost_Report_MI_2014_smaller.pdf. (Accessed 11 April 2019).
- Wani, A.L., Ara, A., Usmani, J.A.H., 2015. Lead toxicity: a review. *Interdiscip. Toxicol.* 8, 55–64.
- Wood, M.D., Beresford, N.A., Copplestone, D., 2011. Limit of detection values in data analysis: do they matter? *Radioprotection* 46, S85–S90.
- World Health Organization, 2010. Childhood Lead Poisoning. WHO Press. <http://www.who.int/ceh/publications/leadguidance.pdf>. (Accessed 12 February 2019).
- World Health Organization, 2018. Lead poisoning and health. <https://www.who.int/news-room/fact-sheets/detail/lead-poisoning-and-health>. (Accessed 12 February 2019).
- Wu, H.M., Lin-Tan, D.T., Wang, M.L., Huang, H.Y., Lee, C.L., Wang, H.S., Soong, Y.K., Lin, J.L., 2012. Lead level in seminal plasma may affect semen quality for men without occupational exposure to lead. *Reprod. Biol. Endocrinol.* 10, 91.
- Yabe, J., Nakayama, S.M.M., Ikenaka, Y., Yohannes, Y.B., Bortey-Sam, N., Oroszlany, B., Muzandu, K., Choongo, K., Kabalo, A.N., Ntapisha, J., Mweene, A., Umemura, T., Ishizuka, M., 2015. Lead poisoning in children from townships in the vicinity of a lead-zinc mine in Kabwe, Zambia. *Chemosphere* 119, 941–947.
- Yabe, J., Nakayama, S.M.M., Ikenaka, Y., Yohannes, Y.B., Bortey-Sam Kabalo, A.N., Ntapisha, J., Mizukawa, H., Umemura, T., Ishizuka, M., 2018. Lead and cadmium excretion in feces and urine of children from polluted townships near a lead-zinc mine in Kabwe, Zambia. *Chemosphere* 202, 48–55.