Lead poisoning in children from townships in the vicinity of a lead–zinc mine in Kabwe, Zambia ☆

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HIGHLIGHTS

- We measured blood lead levels in children near a Pb–Zn mine in Zambia.
- 100% of the sampled children under 7 years had BLLs > 5 μg dL^{-1}.
- Highest BLLs were seen in children around the age of 2 years.
- BLLs > 150 μg dL^{-1} were recorded 8 children with a maximum of 427.8 μg dL^{-1}.
- The children living around the Pb–Zn mine are at serious risks of Pb poisoning.

ARTICLE INFO

ABSTRACT

Childhood lead poisoning is a serious public health concern worldwide. Blood lead levels exceeding 5 μg dL^{-1} are considered elevated. In Kabwe, the capital of Zambia's Central Province, extensive Pb contamination of township soils in the vicinity of a Pb–Zn mine and posing serious health risk to children has been reported. We investigated BLLs in children under the age of 7 years in townships around the mine; where blood samples were collected and analyzed using an ICP-MS. All of the sampled children had BLLs exceeding 5 μg dL^{-1}. Children in these areas could be at serious risk of Pb toxicity as 18% of the sampled children in Chowa, 57% (Kasanda) and 25% (Makululu) had BLLs exceeding 65 μg dL^{-1}. Eight children had BLLs exceeding 150 μg dL^{-1} with the maximum being 427.8 μg dL^{-1}. We recommend that medical intervention be commenced in the children with BLL exceeding 45 μg dL^{-1}.

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1. Introduction

Childhood lead (Pb) poisoning is a serious public health concern worldwide (Tong et al., 2000). Exposure to Pb affects multiple organ systems resulting in numerous morphological, biochemical and physiological changes that include hematological disorders, nervous system disturbances and impairment of liver and kidney functions (Lockitch, 1993; Al-Saleh, 1994; Canfield et al., 2003; Needleman, 2004). Young children are particularly vulnerable to Pb exposure and poisoning. This is because young children frequently explore their environment via hand-to-mouth and object-to-mouth activities; behaviors that are likely to increase Pb intake in children from polluted environments such as house dust or yard soils (Calabrese et al., 1997; Manton et al., 2000). Biological factors also play a significant role in increased Pb uptake in children as the average fractional gastrointestinal absorption of Pb is much greater in infants and young children than in adults (Ziegler et al., 1978). Moreover, Pb absorption is increased in the presence of nutritional deficiencies such as iron and calcium, which are more common in children than in adults (Bradman

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et al., 2001). Children are also more vulnerable to Pb poisoning compared with adults as the central nervous system is most sensitive to Pb toxicity during developmental stages (Lidsky and Schneider, 2003; Bellinger, 2004). Although the effects of Pb on the nervous system in adults tend to reverse after cessation of exposure (Baker et al., 1985), effects in children tend to persist (Needleman et al., 1990).

Lead concentration in whole blood (BLL) is the main biomarker used to monitor exposure and has been widely used in epidemiological studies (CDC, 2009). The Centers for Disease Control and Prevention (CDC, 2012) recently revised the blood lead "level of concern" from 10 to $5\,\mu g\,dL^{-1}$ in response to reports that BLLs < $10\,\mu g\,dL^{-1}$ can cause neurological abnormalities such as decreased intelligence quotient (IQ) in children (Canfield et al., 2003). Therefore, a threshold below which Pb does not result in neurological deficits has not been determined (Needleman, 2004). However, individuals differ widely in the BLL at which signs of Pb toxicity appear, with some individuals seeming well at a BLL that in others results in encephalopathy or even death (Bellinger, 2004). The detrimental effects of elevated BLLs in the range of $10–45\,\mu g\,dL^{-1}$ are usually subclinical and may include neurodevelopmental impairment (CDC, 2002). Generally, BLLs > $10\,\mu g\,dL^{-1}$ in children are considered elevated and it has been recommended that chelation therapy be initiated at levels $\geqslant 45\,\mu g\,dL^{-1}$ (CDC, 2002; Needleman, 2004). At higher BLLs > $60\,\mu g\,dL^{-1}$, clinical symptoms such as abdominal pain and arthralgia become visible in children (Needleman, 2004). Moreover, it has been reported that high BLLs exceeding $100\,\mu g\,dL^{-1}$ can cause encephalopathy, convulsions, coma and death, especially in children (CDC, 2002; TNO, 2001).

In the last decade, BLLs in children have reduced significantly in a number of developed countries following the phasing out of leaded gasoline (Wilhelm et al., 2006). However, childhood Pb toxicity continues to be a major public health problem in most developing countries. In Africa, major sources of childhood Pb poisoning include Pb mining and smelting, paint and battery recycling (Nriagu et al., 1996; Mathee et al., 2007). The recent Pb poisoning disaster in Nigeria, where more than 400 children died leaving numerous others with long-term neurological impairment including blindness and deafness, was attributed to gold ore-mining and processing, especially that metals were processed in their dwellings (Blacksmith Institute, 2011; Dooyema et al., 2012; Lo et al., 2012). In Kabwe Town, the capital of Zambia's Central Province, extensive Pb contamination of township soils in the vicinity of a Pb–Zn mine has been reported and poses a serious health risk to children in these townships (Tembo et al., 2006; Nakayama et al., 2011). In an earlier study, Pb poisoning and cases of encephalopathy were recorded in children from a township in the vicinity of the Pb–Zn mine in Kabwe (Clark APL, unpublished data).

Despite extensive Pb pollution in Kabwe, comprehensive studies of Pb exposure and poisoning in children in the vicinity of the mine are rare. In animal studies however, high concentrations of Pb were reported in wild rats (Nakayama et al., 2011, 2013) as well as blood and edible organs of cattle (Yabe et al., 2011; Ikenaka et al., 2012) and chickens (Yabe et al., 2013) reared in the vicinity of the mine in Kabwe. Therefore, the objectives of the current study were to investigate BLLs in children under the age of 7 years in townships around the Pb–Zn mine in Kabwe and to identify children with BLLs that require medical intervention.

2. Materials and methods

2.1. Sampling sites

Kabwe town, the provincial capital of Zambia's Central Province, is located at about 28°26′E and 14°27′S. Kabwe has a long history of Pb–Zn mining. The mine operated almost continuously from 1902 to 1994 without addressing the potential risks of metal pollution. Dense fumes rich in Pb and other metals were emitted from smelters and they polluted the environment in the surrounding communities extensively (Tembo et al., 2006). 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.

In the current study, blood samples were collected from children at health centers located in Chowa, Kasanda and Makukulu townships, in May–June of 2012. Kasanda Township lies west to the mine and its center is about 2.2 km from the smelter (Fig. 1). However, some households in Kasanda are within 1 km of the mine. Makululu Township is a large squatter compound that lies adjacent and to the west of Kasanda Township. These two townships are affected by dust emanating from the mine as the prevailing winds most of the time blow from the east to the west. Most houses in Makululu are made of mud brick walls, mud floors and thatched roofs. Moreover, lots of dust is emitted by vehicles as roads in the township are not tarred. Many households in the township use well water in addition to communal water taps and there are high levels of poverty in the community. Chowa Township is equally close to the mine as Kasanda but is least affected by dust as it lies on the windward side of the mine. In contrast to Makululu, houses in Kasanda and Chowa are made of concrete bricks and use indoor tap water. Children from these townships were selected because soil samples in these townships are highly polluted with Pb ($9–51188\,mg\,kg^{-1}$) and other metals (Nakayama et al., 2011).

2.2. Blood collection

The study was approved by the University of Zambia Research Ethics Committee (UNZAREC) and the Ministry of Health, Zambia. After informed and written consent was obtained from the children's parents or guardians, blood samples were collected by qualified laboratory technicians at Chowa, Kasanda and Makululu clinics. Before sampling commenced, an awareness campaign about the research activities was conducted by community health workers in each township to encourage parents/guardians to take their children under the age of 7 to the health centers for sample collection. To avoid sample contamination, all blood collection supplies were kept in plastic ziploc storage bags before sample collection. For each child, data on the age, sex and residential area were recorded. Blood up to 10 mL was collected from the cubital vein of each child, after careful cleaning and sanitization of the venipuncture site with an ethanol swab to avoid contamination, into plain blood collection tubes for Pb analysis. The blood samples were immediately stored in freezers at −20 °C after sampling and then transported in cooler boxes on dry ice to the laboratories of the Kabwe District Health Offices and Kabwe Provincial Veterinary Offices where they were again stored at −20 °C. After obtaining the material transfer agreement (MTA) clearance from the Zambia National Health Research Ethics Committee (NHREC), the blood samples were transported to Japan in cooler boxes on dry ice and analyzed for metal concentrations in Laboratory of Toxicology, Graduate School of Veterinary Medicine, Hokkaido University.

2.3. Sample preparation and metal extraction

All laboratory materials and instruments used in metal extraction were washed in 2% nitric acid (HNO_3) and oven dried. The metal was extracted in blood samples using microwave digestion system (Speedwave MWS-2; Berghof) according to the manufacture's instruction. Metal extraction was done as recommended by
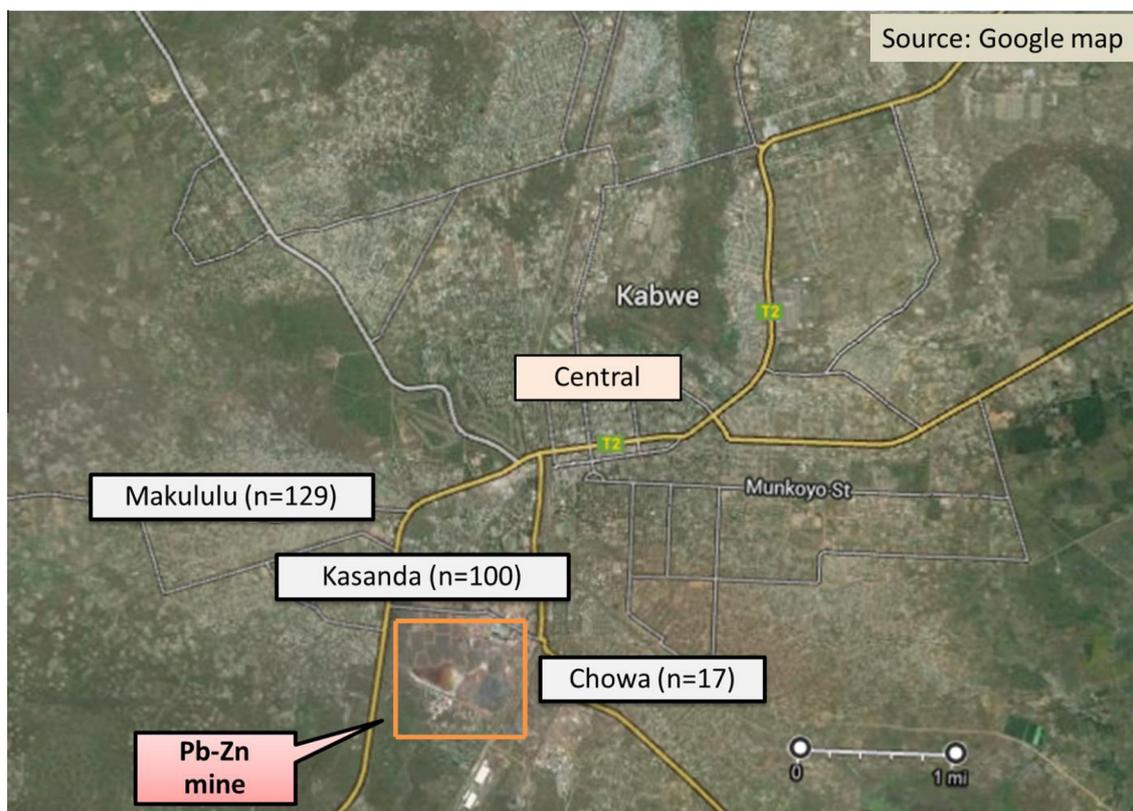
Fig. 1. A map of Kabwe showing different geographic areas and sampling sites.

Schweitzer and Cornett (2008). Briefly, 1 mL of each blood sample was placed in prewashed digestion flasks, and 5 mL of 60% nitric acid (Kanto Chemical) and 1 mL of 30% hydrogen peroxide (Kanto Chemical) were added. After digestion in the microwave for 52 min and temperatures of up to 190 °C, the digested samples were transferred into plastic tubes. The volume was then made up to 10 mL with bi-distilled and de-ionized water (Milli-Q).

2.4. Metal analysis

Blood Pb concentrations were analyzed by Inductively Coupled Plasma-Mass Spectrometer (ICP-MS; 7700 series, Agilent technologies, Tokyo, Japan). The precision and accuracy of the applied analytical method was evaluated by analyzing the recovery rate using digested blood samples and spiking Pb standard solutions. Using this method, a good recovery of 97% was obtained. Certified Reference Materials, DORM-3 (Fish protein, National Research Council of Canada, Ottawa, Canada) and DOLT-4 (Dogfish liver, National Research Council of Canada, Ottawa, Canada) were used to evaluate recoveries. Replicate analysis of these reference materials also showed good recoveries (95–105%). Instrument detection limit was $0.001\ \mu g\ L^{-1}$.

2.5. Statistical analysis

The data of BLLs were log transformed to stabilize variances. Statistical analysis was performed using JMP version 9 (SAS Institute, USA). The data are presented as mean, median and minimum-maximum values in $\mu g\ dL^{-1}$, wet weight. A stacked histogram was used to analyzed blood Pb accumulation trends in Kasanda and Makululu as well as in boys and girls. Stepwise multiple linear regression analyses on log-transformed data were used

to estimate the influence of area, sex and age (0–3 years and 4–7 years old) on BLLs. Correlations between age and BLL were analyzed by both linear and quadratic regression analysis. Samples from Chowa were not included in the comparisons due to smaller sample size compared to Kasanda and Makululu. A p-value of less than 0.05 was considered to indicate statistical significance.

3. Results

3.1. Blood lead levels (BLLs)

A total of 246 blood samples were collected from children, up to 7 years old, at Chowa ($n = 17$ samples), Kasanda ($n = 100$) and Makululu ($n = 129$) health centers. Concentrations of Pb in blood samples are shown in Table 1.

As shown in Table 2, all of the sampled children had BLLs exceeding the guideline value that raise 'health concerns' ($5\ \mu g\ dL^{-1}$). Numbers of children exceeding guideline values for initiating chelation therapy ($45\ \mu g\ dL^{-1}$), toxicity level ($65–149\ \mu g\ dL^{-1}$) and levels associated with encephalopathy and death ($>150\ \mu g\ dL^{-1}$) are also shown.

3.2. Blood Pb accumulation patterns

Using a stacked histogram, blood Pb accumulation patterns in children from Kasanda and Makululu as well as concentration differences between boys and girls in the two townships were analyzed (Fig. 2). Blood accumulation differences were highlighted as the highest BLLs were seen in younger children (0–3 years) than children aged 4–7 years (Fig. 3).

Table 1
Mean age (year) and BLLs (µg dL^{-1}) of children from Chowa, Kasanda and Makululu townships in vicinity of the Pb–Zn mine in Kabwe, Zambia.

Township	Mean age	Sample size	Arithmetic mean BLL	Median	Minimum	Maximum
Chowa	5.76	n = 17	39.0	39.3	15.6	79.7
Kasanda	3.65	n = 100	82.2	74.9	5.40	427.8
Makululu	4.51	n = 129	57.1	51.1	9.40	388.7

n = Number of samples.

Table 2
Numbers of children (under the age of 7 years) with elevated BLLs from the sampled townships in Kabwe.

Reference limits	Chowa (n = 17)	Kasanda (n = 100)	Makululu (n = 129)
<5 µg dL^{-1}	0	0	0
5–44 µg dL^{-1} – elevated levels	8	27	50
45–64 µg dL^{-1} – initiate treatment	7	15	44
65–149 µg dL^{-1} – toxicity level	2	50	33
>150 µg dL^{-1} – encephalopathy, death	0	8	2

n = Number of children sampled.
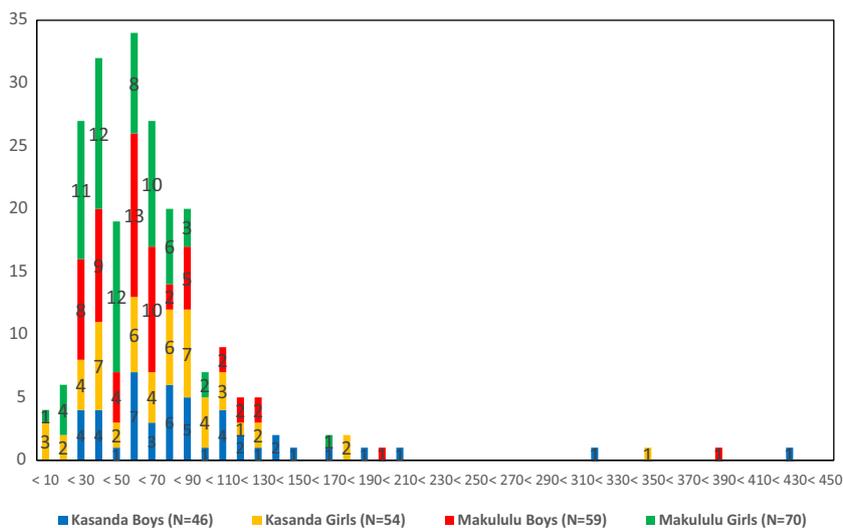
Fig. 2. Stacked histogram showing blood lead accumulation trends in children from Kasanda (46 boys and 54 girls) and Makululu (59 boys and 70 girls) townships of Kabwe, Zambia.
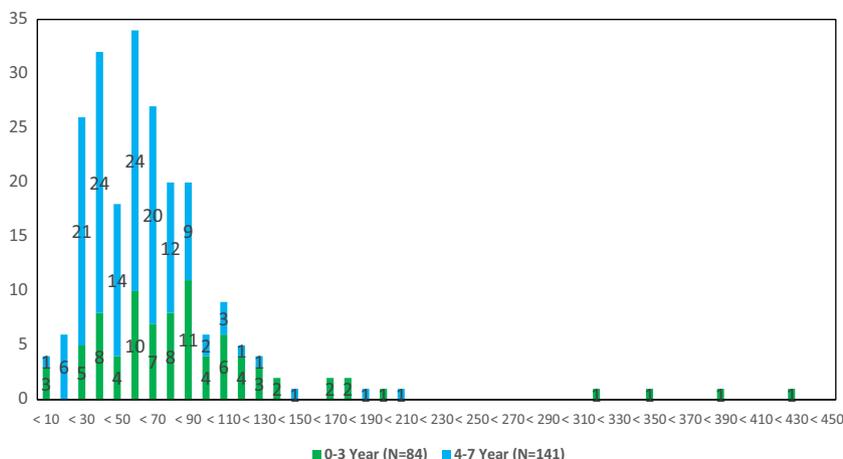
Fig. 3. Histogram showing blood lead accumulation trends in younger (0–3 years) and older (4–7 years) children from Kasanda and Makululu townships of Kabwe (Zambia).

3.3. Age and sex differences

Stepwise multiple linear regression analyses were performed on log-transformed data to estimate the influence of independent variables (age as continuous variable, sex represented as 0 for girls and 1 for boys, location (area) represented as 0 for Makululu and 1 for Kasanda) on BLLs (Table 3). Concentrations in children from Kasanda were higher than levels in children from Makululu ($p < 0.05$). There was no difference in the BLLs between boys and girls from Kasanda whereas in children from Makululu, BLLs were higher ($p < 0.05$) in boys than girls. Younger children aged 0–3 years accumulated higher concentrations of Pb in blood than children aged 4–7 years in both Kasanda and Makululu ($p < 0.05$).

Combining the data of Kasanda and Makululu, significant negative correlations between age and BLL were observed by both linear and quadratic regression analysis. Peak BLLs were observed around the age of 2 years (data not shown).

4. Discussion

The current study has demonstrated alarming childhood Pb poisoning in Zambia's Kabwe town, revealing serious Pb exposure in the children under the age of 7 years in townships surrounding the closed Pb–Zn mine. The study analyzed BLLs in children because it is well established that children are more vulnerable to Pb poisoning and sensitive to its neurotoxic effects than adults (Lidsky and Schneider, 2003). All of the sampled children in the current study had indications of Pb poisoning, with BLLs exceeding the 5 µg dL^{-1} "level of concern" set by CDC (2012). Moreover, the current study revealed that children in these townships could be at serious risk of Pb toxicity as 18% of the sampled children in Chowa, 57% (Kasanda) and 25% (Makululu) had BLLs exceeding 65 µg dL^{-1}; the threshold widely considered to result in Pb toxicity (CDC, 2002; Needleman, 2004). Of the 246 children in the current study, 8 had BLLs exceeding 150 µg dL^{-1}, up to 427 µg dL^{-1}.

These findings agreed with reports in an earlier study before closure of the mine, where mean BLLs of 37–107 µg dL^{-1} were recorded in children from Kasanda Township (Clark APL, unpublished data). Of the 91 children between the ages of 1–2 years that were attended to at Kasanda clinic in the earlier study, 89% were reported to have accumulated BLLs > 60 µg dL^{-1} (Clark APL, unpublished data) compared to 61% of the sampled children from the same clinic in the current study. Therefore, there could be no difference between the severity of Pb poisoning during active mining period and almost 20 years after closure of the mine. Higher BLLs than the current study were recorded in children under the age of 5 years in Zamfara State in Nigeria, where the affected families processed metals in their dwellings (Blacksmith Institute,

2011; Dooyema et al., 2012; Lo et al., 2012). In the study by Dooyema et al. (2012), BLLs exceeding 10 µg dL^{-1} were reported in all the 204 sampled children in Nigeria. In children from Nigeria, mean BLLs (107.5–153.3 µg dL^{-1}) were higher than mean BLLs in the current study (39–82.2 µg dL^{-1}). However, the maximum BLL of 445 µg dL^{-1} recorded in children from Nigeria was comparable to that of the current study (427.8 µg dL^{-1}). Although data on mortalities due to Pb poisoning in Kabwe are scarce, clinical signs consistent with Pb poisoning such as anemia, small stature and weakness were observed in children from the sampled areas during the current study. In Nigeria, over 400 children were reported to have died of Pb poisoning (Blacksmith Institute, 2011; Dooyema et al., 2012; Lo et al., 2012). Findings in the current study were higher than BLLs in children from an urban population in Kinshasa, Democratic Republic of Congo, where mean BLLs of 9.9 µg dL^{-1} and maximum concentrations of 49.3 µg dL^{-1} were recorded (Tuakuila et al., 2013). Moreover, BLLs in the current study were higher than mean BLLs (16.38 µg dL^{-1}) in children in the vicinity of Pb mines and sheltering plants in China (Lin et al., 2011). When compared to most European countries where the median BLL in the general population is below 5 µg dL^{-1} (Taylor et al., 2007), it is evident from the current study that levels of Pb poisoning in Kabwe, Zambia are alarming.

When the severity of Pb poisoning among the townships was compared in the current study, the mean BLL in children from Kasanda (82.2 µg dL^{-1}) was higher ($p < 0.05$) than Makululu (57.1 µg dL^{-1}). Kasanda and Makululu were subjected to atmospheric Pb pollution emanating from the neighboring mine as they are located on the western side of the mine, which is in the direction of the prevailing winds. However, the difference in BLLs in children from the two townships could be attributed to distance from the mines. Although all these townships were close to the mine, some households in Kasanda (even Chowa) were within 1 km of the mine and the abandoned mine dumps hence most of the polluted dust settles in Kasanda Township. Despite being further away from the mine compared to Kasanda, Makululu Township, the largest shanty compound in Zambia equally poses a serious threat as roads, dwellings and house floors are dusty. Therefore, more children in Makululu Township could be at risk of Pb poisoning due to poverty and poor living conditions.

There was no gender difference in BLLs between boys and girls in Kasanda Township. This finding was in agreement with observations in the Democratic Republic of Congo (Tuakuila et al., 2013). However, trends in blood Pb accumulations between boys and girls were observed in the current study as boys in Makululu Township accumulated higher BLLs ($p < 0.05$) than girls in the same township. The same was observed when data of both Kasanda and Makululu were combined. Different behaviors between boys and girls could

Table 3
Blood lead accumulation differences (age, sex and site) by stepwise multiple linear regression analyses in children from Kasanda and Makululu townships in Kabwe.

Parameter	Estimate	nDF	SS	F ratio	p value (Prob > F)
Kasanda and Makululu					
Intercept	1.898	1	0.00	0.00	1.0
Age	−0.035	1	1.05	15.84	**9.35E−05**
Sex{F–M}	−0.050	1	0.56	8.44	**0.004**
Area{Makululu–Kasanda}	−0.048	1	0.48	7.25	**0.008**
Kasanda					
Intercept	1.936	1	0.00	0.00	1.0
Age	−0.033	1	0.41	4.36	**0.039**
Sex{F–M}	−0.060	1	0.35	3.77	0.055
Makululu					
Intercept	1.861	1	0.00	0.00	1.0
Age	−0.038	1	0.66	14.3	**0.0002**
Sex{F–M}	−0.043	1	0.22	4.79	**0.030**

Bold indicate significant ($p < 0.05$), nDF: number of degrees of freedom for a term, SS: Sequential Sum of Squares.

be one of the factors contributing to this difference as boys are likely to cover more distance away from home and play near the mine dumps than girls. When children in the current study were grouped according to age, it was observed that younger children between the ages of 0–3 years accumulated higher BLLs than their older counterparts (4–7 years). Significant negative correlation between age and BLL supported this finding. Similarly, younger children (1–2 years) in the Democratic Republic of Congo accumulated higher BLLs than older children (Tuakuila et al., 2013). Therefore, findings in the current study emphasized the increased susceptibility of younger children to the health risks of Pb pollution.

Earlier studies also observed that BLLs tend to peak at around 2 years of age (Koller et al., 2004). This observation is not unexpected as this period encompasses both the onset of independent ambulation and the time when a child's oral exploration of the environment including hand-to-mouth or object-to-mouth behavior (pica) is greatest. This exposure pathway of children has been well documented in other studies (Lanphear and Roghmann, 1997; Lanphear et al., 2002). It has been established that children typically ingest an average of 50 mg d^{-1} of soil (Stanek and Calabrese, 1995). However, this amount can exceed 5 g a day in the case of pica (Mielke and Reagan, 1998), with some children having been reported to ingest 25–60 g during a single day (Calabrese et al., 1997). Given that maximum Pb concentration in soils in the vicinity of the mine in Kabwe is about $50\,000 \text{ µg g}^{-1}$ or 50 mg g^{-1} (Nakayama et al., 2011), it means that children who ingest about 5–60 g of soil d^{-1} in the vicinity of the mine in Kabwe would ingest 250–3000 mg of Pb d^{-1}. Since the permissible tolerable weekly intake (PTWI) of Pb is 25 µg kg^{-1} of body weight per week (WHO, 1987), concentrations of Pb ingested by children through pica in Kabwe mining area could be high.

The current study has demonstrated that childhood Pb poisoning in Zambia's Kabwe mining town is among the highest in the world, especially in children under the age of 3 years. Lead exposure among children is associated with developmental abnormalities including impaired cognitive function, reduced intelligence, impaired hearing and reduced stature (Canfield et al., 2003; Jusko et al., 2008). Although reports of clinical cases and deaths due to Pb poisoning among children in Kabwe are rare, the findings of the current study indicate that more studies need to be done in order to clearly establish the health effects of Pb poisoning in children exposed to Pb pollution in the townships around the mine in Kabwe. This is important because BLLs in all of the sampled children in the current study exceeded 5 µg dL^{-1}. In children, it has been established that neurobehavioral effects such as decrease in IQ may occur at BLLs $< 10 \text{ µg dL}^{-1}$ (Canfield et al., 2003). Moreover, BLLs of $40–60 \text{ µg dL}^{-1}$ are considered to be markedly elevated, resulting in distinct neurobehavioral effects (TNO, 2001). Since 18% of the sampled children from Chowa, 57% (Kasanda) and 25% (Makululu) in the current study had markedly elevated BLLs exceeding 65 µg dL^{-1}, it would not be surprising to observe neurological effects of Pb poisoning in the exposed children. Although this is the first published study evaluating Pb poisoning in Kabwe, it was earlier reported that during the mining period between 1971 and 1973, cases of suspected Pb poisoning with encephalopathy occurred among children aged 10–30 months living in the township of Kasanda (Clark APL, unpublished data). Therefore, the children in Chowa, Kasanda and Makululu townships should be closely monitored to enable early detection of clinical signs related to Pb toxicity and medical intervention.

5. Conclusions

Given that Pb poisoning among children in Kabwe was extensive, it is recommended that chelation therapy be commenced in the children with BLL exceeding 45 µg dL^{-1} prior to the onset of symptoms to reduce morbidity and prevent mortality in the affected children. This can be achieved for each child by devising and implementing an individualized plan of follow-up, especially for those children with extremely high BLLs. Interrupting the process of Pb poisoning through early detection and intervention can prevent children from dying or suffering severe permanent effects of Pb toxicity such as persistent seizures and mental retardation. Moreover, urgent interventions are required to reduce Pb exposure in the affected townships. This can be done through community-based programs to educate the affected communities about the health effects of Pb, sources of Pb and practical ways of reducing Pb exposure in their homes and communities.

References

Al-Saleh, I., 1994. Biochemical and clinical consequences of lead poisoning. Med. Res. Rev. 14, 415–486.

Baker, E.L., White, R.F., Pothier, L.J., Berkey, C.S., Dinse, G.E., Travers, P.H., et al., 1985. Occupational lead neurotoxicity: improvement in behavioral effects after reduction of exposure. Br. J. Ind. Med. 42, 507–516.

Bellinger, D.C., 2004. Lead. Pediatrics 113, 1016–1022.

Blacksmith Institute, 2011. Project Completion Report: Nigeria Lead Poisoning Crisis <http://www.blacksmithinstitute.org/nigerian-lead-poisoning-crisisblacksmith-report.html>.

Bradman, A., Eskenazi, B., Sutton, P., Athanasoulis, M., Goldman, L.R., 2001. Iron deficiency associated with higher blood lead in children living in contaminated environments. Environ. Health Perspect. 109, 1079–1084.

Calabrese, E.J., Stanek, E.J., James, R.C., Roberts, S.M., 1997. Soil ingestion: a concern for acute toxicity in children. Environ. Health Perspect. 105, 1354–1358.

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.

Centers for Disease Control and Prevention (CDC), 2009. Fourth National Report on Human Exposure to Environmental Chemicals <http://www.cdc.gov/exposurereport/pdf/FourthReport.pdf>.

Centers for Disease Control and Prevention (CDC), 2012. Low level lead exposure harms children: a renewed call for primary prevention. Report of the Advisory Committee on Childhood Lead Poisoning Prevention of the Centers for Disease Control and Prevention. Atlanta, Ga <www.cdc.gov/nceh/lead/acclpp/final_document_030712.pdf>.

Dooyema, C.A., Neri, A., Lo, Y.C., Durant, J., Dargan, P.I., Swarthout, T., et al., 2012. Outbreak of fatal childhood lead poisoning related to artisanal gold mining in northwestern Nigeria, 2010. Environ. Health Perspect. 120, 601–607.

Ikenaka, Y., Nakayama, S.M.M., Muroya, T., Yabe, J., Konnai, S., Darwish, W.S., et al., 2012. Effects of environmental lead contamination on cattle in a lead/zinc mining area: changes in cattle immune systems on exposure to lead in vivo and in vitro. Environ. Toxicol. Chem. 31, 2300–2305.

Jusko, T.A., Henderson Jr., C.R., Lanphear, B.P., Cory-Slechta, D.A., Parsons, P.J., Canfield, R.L., 2008. Blood lead concentrations <10 µg/dL and child intelligence at 6 years of age. Environ. Health Perspect. 116, 243–248.

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.

Lanphear, B.P., Roghmann, K.J., 1997. Pathways of lead exposure in urban children. Environ. Res. 74, 67–73.

Lanphear, B.P., Hornung, R., Ho, M., Howard, C.R., Eberly, S., Knauf, K., 2002. Environmental lead exposure during early childhood. J. Pediatr. 140, 40–47.

Lidsky, T.L., Schneider, J.S., 2003. Lead neurotoxicity in children: basic mechanisms and clinical correlates. Brain 126, 5–19.

Lin, S., Wang, X., Tak Sun Yu, I., Tang, W., Miao, J., Li, J., et al., 2011. Environmental lead pollution and elevated blood lead levels among children in a rural area of China. Am. J. Public Health 101, 834–841.

Lo, Y.C., Dooyema, C.A., Neri, A., Durant, J., Jefferies, T., Medina-Marino, A., et al., 2012. Childhood lead poisoning associated with gold ore processing: a village-level investigation – Zamfara State, Nigeria, October–November 2010. Environ. Health Perspect. 120, 1450–1455.

Lockitch, G., 1993. Perspectives on lead toxicity. Clin. Biochem. 26, 371–381.

Manton, W.I., Angle, C.R., Stanek, K.L., Reese, Y.R., Kuehnemann, T.J., 2000. Acquisition and retention of lead by young children. Environ. Res. 82, 60–80.

Mathee, A., Rollin, H., Levin, J., Naik, I., 2007. Lead in paint: three decades later and still a hazard for African children? Environ. Health Perspect. 115, 321–322.

Mielke, H.W., Reagan, P.L., 1998. Soil is an important pathway of human lead exposure. Environ. Health Perspect. 106 (Suppl. 1), 217–229.

Nakayama, S.M.M., Ikenaka, Y., Hamada, K., Muzandu, K., Choongo, K., Teraoka, H., et al., 2011. Metal and metalloid contamination in roadside soil and wild rats around a Pb–Zn mine in Kabwe, Zambia. Environ. Pollut. 159, 175–181.

Nakayama, S.M.M., Ikenaka, Y., Hamada, K., Muzandu, K., Choongo, K., Yabe, J., et al., 2013. Accumulation and biological effects of metals in wild rats in mining areas of Zambia. Environ. Monit. Assess. 185, 4907–4918.

Needleman, H.L., Schell, A., Bellinger, D., Leviton, A., Allred, E., 1990. The long-term effects of exposure to low doses of lead in childhood: an 11-year follow-up report. N. Engl. J. Med. 322, 83–88.

Needleman, H., 2004. Lead poisoning. Annu. Rev. Med. 55, 209–222.

Nriagu, J.O., Blankson, M.L., Ocran, K., 1996. Childhood lead poisoning in Africa: a growing public health problem. Sci. Total Environ. 181, 93–100.

Schweitzer, L., Cornett, C., 2008. Determination of heavy metals in whole blood using inductively-coupled plasma mass spectrometry: a comparison of microwave and dilution techniques. The Big M 4, 75–83.

Stanek, E.J., Calabrese, E.J., 1995. Daily estimates of soil ingestion in children. Environ. Health Perspect. 103, 276–285.

Taylor, A., Angerer, J., Arnaud, J., Claeys, F., Kristiansen, J., Mazarrasa, O., et al., 2007. Differences in national legislation for the implementation of lead regulations included in the European directive for the protection of the health and safety of workers with occupational exposure to chemical agents (98/24/EC). Int. Arch. Occup. Environ. Health 80, 254–264.

Tembo, B.D., Sichilongo, K., Cernak, J., 2006. Distribution of copper, lead, cadmium and zinc concentrations in soils around Kabwe town in Zambia. Chemosphere 63, 497–501.

The Netherlands Organization for Applied Scientific Research (TNO), 2001. Risks to Health and the Environment Related to the Use of Lead in Products. Report STB-01-39; TNO-MEP, Apeldoorn, The Netherlands.

Tong, S., Von Schirnding, Y.E., Prapamontol, T., 2000. Environmental lead exposure: a public health problem of global dimensions. Bull. World Health Org. 78, 1068–1077.

Tuakuila, J., Lison, D., Mbuyi, F., Haufroid, V., Hoet, P., 2013. Elevated blood lead levels and sources of exposure in the population of Kinshasa, the capital of the Democratic Republic of Congo. J. Expo. Sci. Environ. Epid. 23, 81–87.

Wilhelm, M., Schulz, D., Schwenk, M., 2006. Revised and new reference values for arsenic, cadmium, lead, and mercury in blood or urine of children: basis for validation of human biomonitoring data in environmental medicine. Int. J. Hyg. Environ. Health 209, 301–305.

World Health Organization, B., 1987. Toxicology Evaluation of Certain Food Additives and Contaminants (WHO Food Additives Series, No. 21). Cambridge University Press. pp. 223–255.

Yabe, J., Nakayama, S.M.M., Ikenaka, Y., Muzandu, K., Ishizuka, M., Umemura, T., 2011. Uptake of lead, cadmium, and other metals in the liver and kidneys of cattle near a lead–zinc mine in Kabwe, Zambia. Environ. Toxicol. Chem. 30, 1892–1897.

Yabe, J., Nakayama, S.M.M., Ikenaka, Y., Muzandu, K., Choongo, K., Mainda, G., et al., 2013. Metal distribution in tissues of free-range chickens near a lead–zinc mine in Kabwe, Zambia. Environ. Toxicol. Chem. 32, 189–192.

Ziegler, E.E., Edwards, B.B., Jensen, R.L., Mahaffey, K.R., Fomon, S.J., 1978. Absorption and retention of lead by infants. Pediatr. Res. 12, 29–34.