 doi:10.20944/preprints202208.0256.v1

Article

Lead exposure in infancy and subsequent childhood growth

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Abstract: Studies suggest that elevated postnatal blood lead levels (BLLs) are negatively associated with child growth. This study aimed to investigate associations of childhood BLLs at age one-year and growth outcomes at age six years (n=661) in a cohort of children in Allada, Benin. The growth outcomes studied are weight-for-age Z-score (WAZ), height-for-age Z-score (HAZ) and BMI-for-age Z-score (BMIZ), head circumference (HC), underweight, stunting and wasting. Multivariable regression models examined associations between blood lead levels, and growth outcomes with adjustment for potential confounders. The geometric mean BLLs was 59.3 µg/L and 82% of children had BLLs >35 µg/L at one year. After adjusting for confounding factors, no association was found between BLLs quartiles and HAZ, WAZ, BMIZ, and height and weight growth velocities. However, boys in the highest quartile had 1.02 cm lower HC (95% CI: [-1.81, -0. 24]) as compared to those in the lowest quartile with a dose-response trend across quartiles (Ptrend =0.02). Furthermore, an increased risk of being stunted was observed in children in the highest quartile of exposure compared to the first (OR: 2.43; 95% CI: [1.11 – 5.33]) with a dose-response trend (Ptrend =0.03). Blood lead was found to be associated with an increased risk of childhood stunting and lower head circumference in a resource-limited setting.

Keywords: Heavy metals; lead exposure; growth outcomes; cohort study

1. Introduction

Lead poisoning is a major problem that affects children worldwide, particularly in developing countries [1]. Lead exposure has been associated with adverse health effects including poor neurocognitive development, behavioural problems and with the risk of cardiovascular diseases in adult life [2-5]. The Centers for Disease Control and Prevention (CDC) have set a reference value of 35 µg/L to identify children with blood lead levels (BLLs) higher than most children's levels to recommend the initiation of public health actions [6]. Although these reference values are important in identifying children with higher BLLs, there are no identified BLLs considered as safe as there is a growing body of evidence that lower BLLs are associated with adverse health outcomes [2, 7].

Lead exposure, in 2016, was estimated to account for 63.2% of the global burden of developmental intellectual disability, 10.3% of the global burden of hypertensive heart disease, 5.6% of the global burden of ischemic heart disease and 6.2% of the global burden

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of stroke [8, 9]. Furthermore, estimates indicate that in 2017 lead exposure was responsible for 1.06 million deaths and 24.4 million years of disability-adjusted life years (DALYs) worldwide due to long-term effects on health [8].

Children can be exposed to lead from multiple sources including occupation, contaminated food and drinking water [10-12]. Ancient sources such as leaded gasoline - which was used globally before it was banned - were one of the significant contributors to lead poisoning. Residual emissions from leaded gasoline remain a source of lead exposure, via contamination of soils, dust and foodstuff. Furthermore, the use of old lead pipes or lead-soldered joints in either the distribution system or individual houses is known to contaminate water [12-15]. BLLs have been widely used as a biomarker of lead exposure largely because of their feasibility [16]. Therefore, most of the information on human exposure to, and the health effects of, lead are based on BLLs. Blood concentration of Pb remains the most commonly used biomarker in a general medical setting and public health surveillance [17].

Growth effects associated with lead are decreased birth weight and size and decreased anthropometric measures in children [15]. Some epidemiological studies have investigated the adverse effects of lead exposure during early periods of development on child growth. Some studies reported a negative association [18-22] between lead and child growth outcomes, while other studies found no associations [23-27]. Existing evidence come from studies that have been carried out in well-resourced countries where regulations to control and eliminate lead are in place. In the contrast, there is scarce evidence from low-and middle-income countries [28, 29] where the prevalence of lead exposure and poor child growth is comparatively high.

Within a birth cohort in south Benin, a high prevalence of BLLs >50 μg/L was observed in one-year-old infants from 2011-13 [12]. BLLs remained elevated when children were six years old [11]. Given the elevated BLLs and the fact that the effect of postnatal lead exposure on child growth is not well studied, particularly in low- and middle-income countries, this study aimed to investigate associations between childhood BLLs and subsequent growth in this Beninese cohort of children.

2. Materials and Methods

2.1. Study design and population

The current analysis is based on the data from the Allada cohort study. This study was carried out in three health centres (Allada, Attogon, and Sekou) in the district of Allada, a semi-rural district located in the South of Benin. Children were born to women enrolled in a randomized clinical trial (Malaria in Pregnancy Preventive Alternative Drugs, MiPPAD, NCT00811421) [30]. The original population comprised 961 children for whom detailed information is provided elsewhere [31]. The biomonitoring data on BLLs at age 1 year were not available for 300 children, leaving for the present investigation 661 children with available BLLs measured at age 1. In addition to height and weight growth data, head circumference measurements were also available at age 6 years for a subset of 370 children, which was included in the present investigation.

2.2. Study design and population

2.2.1. Exposure and relevant data collection

Blood lead levels were measured in whole blood collected from children aged 1-2 years old. BLLs were analyzed at the Centre de Toxicologie, Institut National de Santé Publique du Québec (INSPQ, Québec, Canada). All BLLs were analyzed by inductively coupled plasma mass spectrometry (ICP-MS) after dilution of blood samples with a detection limit of 0.2 μg/L. The analytical methods are described elsewhere (Bodeau-Livinec et al., 2016).

Parent characteristics studied were economic status (measured by family wealth score), maternal education, estimated preconception body mass index (BMI) [32], gestational age assessed by Ballard score, and gravidity. Information on family wealth at age 1 year was assessed through a checklist of material possession (such as a car, motorbike,

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bike, television, cow, and radio) which was later transformed into a wealth scale with scores ranging from 1 to 15 [12].

Children's characteristics assessed were child sex, birth weight, and iron deficiency at 1 year. Iron deficiency was defined as serum ferritin concentrations <12 µg/l in the absence of inflammatory conditions assessed by C-reactive protein (CRP) levels within range (<5 mg/L). Serum ferritin concentrations between 12- 70 µg/L in the presence of elevated CRP levels (>5 mg/L) were used as a threshold for iron deficiency.

2.2.2. Outcomes

Weight and height were measured between birth and age 6 years at the maternity clinic by trained staff, with children wearing light clothes only and no shoes. Detailed measurement procedures are described elsewhere **[31]**. Head circumference (HC) was measured with a measuring tape at age 6 years only.

The Jenss-Bayley growth model, which previously presented the best goodness-of-fit on the weight and height of these children **[31]**, allowed to predict weight, height, and momentaneous weight and height velocities at the same ages (between 1 and 6 years) for all children. Growth velocities were predicted using the first derivative of the individual equation [33]. For this research, model-predicted height/weight, growth velocities, and observed HC at ages 4 and 6 years are used in the analysis. Based on the predictions, height-for-age Z-score (HAZ), weight-for-age Z-score (WAZ), and BMI-for-age Z-score (BMIZ) (hereafter termed as growth dimensions) of children were calculated, using the updated 2007 WHO Child Growth Standards as a reference. Children with HAZ <-2, WAZ <-2 and WHZ <-2 were categorized as underweight, stunted and wasted, respectively [34].

2.2.3. Statistical analysis

Mean (HAZ, WAZ, BMIZ, WHZ, and HC) are presented with the proportion of children stunted, wasted and underweight at ages four and six. Child BLL at age one is described in terms of geometric mean and proportion of children with BLL beyond 35 µg/L.

Crude and multivariable regression models evaluated associations between blood lead levels, as the exposure variable, and growth dimensions (HAZ, WAZ, BMIZ, HC), as the continuous outcomes. Analyses were conducted using quartiles of BLL to account for non-linear associations and repeated using log-transformed continuous BLL to study linear trends. Multivariable models were adjusted for potential confounders based on crude associations (data not shown) and a priori variable selection. The selection of potential confounders, based on crude associations, was done in two steps. Firstly, variables were selected if associated with growth dimensions in the crude associations with a $p < 0.20$. Variables tested were maternal age at delivery (<22, 22-25, 26-30 and >31years), gravidity (nulliparous primigravida, and multigravida), maternal education (no education, primary education or more), family wealth score (1, 2 and 3), estimated pre-pregnancy BMI (<18.5, 18.5 – 24.9, 25-29.9 and > 30), gestational age (<37, >37 weeks), and birth weight (<25, >25 kg). In the second step, all the potential covariates with $p<0.2$ were included in the regression model: family wealth score estimated pre-pregnancy BMI, underweight, maternal age at delivery, and maternal education. Using a backward stepwise selection procedure, the least significant variable of the model was eliminated based on the Wald test and repeated the process with one less variable. The final models contained variables significantly associated with the growth outcomes ($p < 0.05$).

Models were adjusted, based on literature, for maternal characteristics (education, material possession/wealth score, estimated pre-conceptional BMI) and child characteristics (sex, low birth weight, and iron deficiency at age 1) [35-37]. Because iron deficiency may increase susceptibility to elevated BLLs [38] and is also known to be associated with food insecurity [39], iron deficiency (yes, no) was additionally adjusted in the final models.

Associations are presented with 95% confidence intervals (CI). Breastfeeding was not adjusted in the models as almost all children were breastfed

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Multiple linear regressions were run to assess associations between growth outcomes at age 4 and 6 years and BLLs. We included children with complete data on BLL at one year of age. We tested for effect modification by sex by calculating the p-value of product term between child sex and BLLs.

In additional analyses, multiple logistic regression models were run to assess the independent relationship between three forms of undernutrition (stunting, wasting and underweight) and different levels of BLLs. Models were further adjusted for child weight (only for stunting), and height (only for underweight) but not both variables in the same model to avoid multi-collinearity [29]. BLLs were compared between children with undernutrition and those without undernutrition using the Wilcoxon rank-sum test.

All statistical analyses were performed using STATA 14.1 (StataCorp. 2015. Stata Statistical Software: Release 14. College Station, TX: StataCorp LP). The statistical significance level was set at $p<0.05$.

3. Results

This section may be divided by subheadings. It should provide a concise and precise description of the experimental results, their interpretation, as well as the experimental conclusions that can be drawn.

3.1. Study population characteristics

The final study sample comprised 661 children with an almost equal proportion of boys (50.5%) and girls (49.5%). Table 1 describes the demographic and clinical characteristics of the study population. The mean maternal age at delivery was 25.6 years and 85.6% of mothers could not read or write at the age 1 year of the index child. 16.2% of mothers were underweight before pregnancy. At birth, children weighed on average 3.04 kg (SD, 0.40) with an average length of 49.1 cm (SD, 2.20¬). Most children (93.1%) were born full-term and almost all of them were exclusively breastfed till 6 months. The proportion of stunted children were 6.1% (n=40), 27.8% (n=182), 27.6% (n=181) and 1.85% (n= 12) at age 1, 2, 4 and 6 years, respectively. The proportion of wasted children were 4.1% (n=27), 1.5% (n=10), 5.0% (n=33) and 32.7% (n= 211) at age 1, 2, 4 and 6 years, respectively. The proportion of children underweight at age 4 and 6 years were 24.4% (=159) and 16.6% (n=108). Mean WAZ and HAZ in children at the age of 6 years were -1.24 (+ 0.78) and -0.31 (+ 0.83), respectively.

The average age for BLL assessment was 12 months (range: 12 to 18 months). The geometric mean BLLs at age one was 59.3 µg/L (median, 10th – 90th centile: 55.7, 30.5-129) and 82% of children presented with BLLs > 35 µg/L.

Table 1. Study population characteristics (N=661).

Characteristics	Category	n (%) or mean/median (SD)
Parental characteristics		
Gravidity		
	0	116 (17.6)
	1	129 (19.5)
	2	416 (62.9)
Maternal Education		
	Primary education or more	94 (14.4)
	No education	560 (85.6)
Maternal age at delivery (years)	<22	173 (26. 2)
	22-25	178 (26.9)
	26-30	191 (28.9)
	>31	119 (18.0)
Pre-pregnancy BMI (kg/m^2)		

 doi:10.20944/preprints202208.0256.v1

	Underweight (<18.5)	107 (16.2)
	Normal (18.5 – 24.9)	481 (72.8)
	Overweight (25-29.9) or obese (> 30)	73 (11.0)
		21 (3.2)
Gestational age (weeks)		
	<37	45 (6.9)
	>37	606 (93.1)
Family wealth score at age 1 (tertiles)		
	Lowest	268 (41.0)
	Medium	195 (29.8)
	Highest	191 (29.2)
Child characteristics		
Sex		
	Male	333 (50.5)
	Female	326 (49.5)
Low birth weight		
	Yes	54 (8.5)
	No	579 (91.5)
Birth length		49.1 (2.2)
Age of child at lead assessment (median, months)		12.0 (1.87)
Low birth weight (<2.5 kg)		
	Yes	54 (8.5)
	No	579 (91.5)
Blood lead level (median, µg/L)		55.7 (61.7)
Exclusive breastfeeding for 6 months		
	Yes	646 (97.7)
	No	12 (1.8)
Anaemia at age 1 year Hb<110 g/L		
	Yes	450 (71.5)
	No	179 (28.5)
Iron deficiency at 1 year (ferritin<12 µg/L or 12–70 µg/L if CRP>5mg/L)		
	Yes	293 (44.33)
	No	368 (55.67)
Malaria at age 1 year		
	Yes	65 (10.4)
	No	561 (89.6)
Weight-for-age Z-score (6 years)		-1.24 (0.78)

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Height-for-age Z-score (6 years)		-0.31 (0.83)
BMI-for-age Z-score (6 years)		-1.65 (0.87)
Head circumference (6 years) (n=370)		49.93 (1.79)
Medical centre location		
	Sekou	399 (60.6)
	Attogon/Allada	259 (39.4)

BMI: body mass index; SD: standard deviation. All values are reported as mean/median (SD) or n (percentage).

3.1. Association between BLLs at age 1 and WAZ, HAZ, BMI-Z and HC at age 6

No statistically significant inverse association was found between BLLs quartiles and HAZ, WAZ or BMIZ after adjusting for confounding factors (Table 2). Unadjusted associations between log-BLLs (continuous variable) at age one and head circumference (continuous variable) at age 6 suggested a difference by sex (p for interaction term, 0.048). However, the p for interaction term was 0.12 in the adjusted analyses. Unadjusted association between log-BLLs and head circumference at age 6 was found to be negative in boys (β = -0.43; 95% CI: [-0.84, -0.02]) compared to girls (β = 0.19; [-0.27, 0.64]). In the adjusted analyses when stratified by child sex boys in the highest quartile (median BLLs = 113 μg/L) had 1.02 cm lower HC (95% CI: [-1.81, -0. 24]) as compared to those in the lowest quartile (median BLLs = 32 μg/L) with a dose-response trend across quartiles (Ptrend =0.02).

 doi:10.20944/preprints202208.0256.v1

Table 2. Linear regression coefficients (95% confidence intervals) for the associations between blood lead levels at age 1 year and growth at age 4 and 6 years in Beninese children (Allada cohort).

Age (year)	BLLs quartile*	WAZ		HAZ		BMI-Z		WHZ		HC	
		unadjusted β coeff. [95% CI]	**adjusted β coeff. [95% CI]** [a]	**unadjusted β coeff. [95% CI]**	adjusted β coeff. [95% CI] [b]	unadjusted β coeff. [95% CI]	adjusted β coeff. [95% CI][c]	unadjusted β coeff. [95% CI]	adjusted β coeff. [95% CI][d]	unadjusted β coeff. [95% CI]	adjusted β coeff. [95% CI][e]
4	2nd	-0.01 (-0.16, 0.14)	-0.02 (-0.17, 0.13)	-0.06 (-0.21, 10)	-0.04 (-0.19, 0.11)	0.05 (-0.11, 0.21)	0.01 (-0.15, 0.18)	0.02 (-0.14, 0.19)	0.002 (0.98, -0.16)	-	-
	3rd	-0.07 (-0.22, 0.09)	-0.08 (-0.24, 0.07)	-0.08 (-0.24, 0.07)	-0.07 (-0.23, 0.08)	-0.01 (-0.17, 0.15)	-0.03 (-0.19, 0.13)	-0.02 (-0.19, 0.14)	-0.03 (-0.19, 0.14)	-	-
	4th	-0.17 (-0.33, -0.02)	-0.14 (-0.29, 0.01)	-0.17 (-0.32, -0.01)	-0.11 (0.26, 0.04)	-0.08 (-0.24, 0.08)	-0.05 (-0.21, 0.12)	-0.11 (-0.27, 0.05)	-0.07 (-0.23, 0.10)	-	-
	P-trend [†]	0.02	0.13	0.03	0.14	0.25	0.48	0.16	0.88		
6	2nd	0.01 (-0.16, 0.18)	-0.01 (-0.18, 0.16)	-0.07 (-0.25, 0.11)	-0.05 (-0.23, 0.13)	0.08 (-0.11, 0.27)	0.05 (-0.14, 0.23)	0.08 (-0.09, 0.25)	0.05 (-0.13, 0.22)	0.22 (-0.29, 0.72)	0.09 (-0.41, 0.59)
	3rd	-0.07 (-0.23, 0.10)	-0.07 (-0.24, 0.10)	-0.11 (-0.29, 0.07)	-0.10 (-0.28, 0.08)	0.02 (-0.17, 0.21)	-0.00 (-0.19, 0.18)	-0.01 (-0.19, 0.16)	-0.01 (-0.19, 0.17)	0.11 (-0.41, 0.62)	0.12 (-0.39, 0.64)
	4th	-0.16 (-0.33, 0.01)	-0.09 (-0.26, 0.08)	-0.19 (-0.37, -0.01)	-0.13 (-0.31, 0.05)	-0.04 (-0.23, 0.15)	0.00 (-0.19, 0.20)	-0.05 (-0.22, 0.12)	0.00 (-0.18, 0.18)	-0.37 (-0.90, 0.16)	-0.30 (-0.84, 0.23)
	P-trend [†]	0.05	0.21	0.04	0.13	0.58	0.89	0.40	0.56	0.16	0.33

BLLs: Blood lead levels. *1st quartile (not shown) is the reference category. [a,b,c,d] adjusted for maternal characteristics (education, material possession/wealth score, estimated pre-conceptional BMI) and child characteristics (sex, low birth weight, and iron deficiency at age 1). [†] *P* trends across quartiles of Pb were obtained by inserting its quartile as a continuous variable in the regression model.

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A statistically significant increased risk of being stunted was observed in children in the highest quartile of exposure (vs. 1st quartile; OR: 2.24 (1.08 – 4.66)) (Table 3). Furthermore, a modest dose-response relationship between BLLs quartiles and stunting was observed (Ptrend = 0.04). In stratified analyses by sex, a possible effect modification by sex was observed with a dose-response trend across quartiles observed only in girls (Ptrend =0.02) (Table 4).

In contrast, no significant association was observed with wasting at any age. BLLs were also not statistically different between children with and without underweight at any age.

 doi:10.20944/preprints202208.0256.v1

Table 3. Odds Ratio (OR) and 95% confidence intervals for the associations between blood lead levels at age 1-year and stunting, wasting and underweight at age4 and 6 years in Beninese children (Allada cohort).

Age (year)	**BLLs quartile***	**Stunting (HAZ < -2)**		**Wasting (WHZ < -2)**		**Underweight (WAZ < -2)**	
		unadjusted OR	adjusted OR [a]	unadjusted OR	Adjusted OR [b]	unadjusted OR	Adjusted OR [c]
4	2nd	1.52 (0.92-2.53)	1.44 (0.67 – 3.11)	0.45 (0.17-1.21)	0.42 (0.15 – 1.20)	1.01 (0.59-1.71)	1.13 (0.52-2.47)
	3rd	1.68 (1.02-2.78)	1.70 (0.76 – 3.80)	0.53 (0.21-1.37)	0.48 (0.18 – 1.28)	1.44 (0.87-2.38)	1.19 (0.54-2.63)
	4th	1.83 (1.11-3.02)	2.43 (1.11 – 5.33)	0.53 (0.21-1.36)	0.40 (0.15 – 1.09)	1.33 (0.80-2.22)	1.33 (0.60-2.97)
	p-trend †	0.02	0.03	0.20	0.09	0.14	0.49
6	2nd	0.75 (0.17-3.43)	0.98 (0.13 – 7.59)	0.68 (0.42-1.08)	0.70 (0.43 – 1.15)	0.88 (0.48-1.61)	0.85 (0.34-2.10)
	3rd	0.75 (0.17-3.43)	0.89 (0.09 – 9.01)	0.90 (0.57-1.42)	0.92 (0.57 – 1.49)	1.36 (0.77-2.39)	1.15 (0.48-2.77)
	4th	0.52 (0.09-2.86)	0.44 (0.04 – 5.07)	0.90 (0.57-1.42)	0.80 (0.49 – 1.29)	1.05 (0.58-1.91)	1.01 (0.40-2.55)
	p-trend †	0.47	0.51	0.93	0.58	0.52	0.81

BLLs: Blood lead levels. a adjusted ¬for maternal characteristics (education, material possession/wealth score, estimated pre-conceptional BMI) and child characteristics (sex, low birth weight, weight, and iron deficiency at age 1). b adjusted ¬for maternal characteristics (education, material possession/wealth score, estimated pre-conceptional BMI) and child characteristics (sex, low birth weight, and iron deficiency at age 1). c adjusted ¬for maternal characteristics (education, material possession/wealth score, estimated pre-conceptional BMI) and child characteristics (sex, low birth weight, height, and iron deficiency at age 1). † P trends across quartiles of Pb were obtained by inserting its quartile as a continuous variable in the regression model.

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Table 4. Odds Ratio (OR) and 95% confidence intervals for the associations between blood lead levels at age 1 year and stunting at age 4 years in Beninese children (Allada cohort) stratified by child sex.

Age (year)	BLLs quartile*	Stunting (HAZ < -2) adjusted OR [a]	
		Boys (n=218)	Girls (n=200)
4	2nd	0.90 (0.31 – 2.61)	3.36 (0.95-11.88)
	3rd	1.06 (0.33 – 3.45)	3.95 (1.11-14.09)
	4th	1.74 (0.57 – 5.32)	4.25 (1.27-14.21)
	p-trend †	0.27	0.02

BLLs: Blood lead levels. Analyses of growth height and weight growth velocities showed no significant association between BLL and velocities. However, a statistically insignificant trend was observed across the quartiles of exposure (Table 5).

Table 5. Regression coefficients (95% confidence intervals) for the associations between log-transformed blood lead levels at age 1 year and growth velocities at age 4 and 6 years in Beninese children (Allada cohort).

Age (year)	BLLs quartile*	Height velocities (mm/mo)		Weight velocities (g/mo)	
		unadjusted β coeff. [95% CI]	adjusted β coeff. [95% CI][a]	unadjusted β coeff. [95% CI]	adjusted β coeff. [95% CI][b]
4	2nd	-0.06 (-0.21, 0.10)	-0.11 (-0.44, 0.22)	0.03 (-0.13, 0.20)	0.00 (-0.16, 0.17)
	3rd	-0.08 (-0.24, 0.07)	-0.20 (-0.53, 0.14)	-0.01 (-0.17, 0.15)	-0.01 (-0.18, 0.15)
	4th	-0.17 (-0.32, -0.01)	-0.19 (0.52, 0.14)	-0.08 (-0.24, 0.08)	-0.03 (-0.20, 0.13)
	P-trend †	0.09	0.22	0.26	0.67
6	2nd	-0.13 (-0.46, 0.19)	-0.11 (-0.44, 0.22)	0.05 (-0.12, 0.21)	0.01 (-0.51, 0.18)
	3rd	-0.19 (0.52, 0.14)	-0.20 (-0.53, 0.14)	-0.01 (-0.18, 0.16)	-0.01 (-0.18, 0.16)
	4th	-0.29 (-0.61, 0.04)	-0.19 (-0.52, 0.14)	-0.08 (-0.24, 0.09)	-0.03 (-0.19, 0.14)
	P-trend †	0.08	0.22	0.29	0.71

*1st quartile (not shown) is the reference category. [a,b] adjusted for maternal characteristics (education, material possession/wealth score, estimated pre-conceptional BMI) and child characteristics (sex, low birth weight, and iron deficiency at age 1).† *P* trends across quartiles of Pb were obtained by inserting its quartile as a continuous variable in the regression model.

4. Discussion

Cross-sectional prevalence of stunting was low during the first year, peaked at 2-4 years, and recovered thereafter. Overall, no significant association was observed between BLLs at age one and child growth dimensions (HAZ, WAZ, BMIZ and HC) at age 6. However, when analyses were stratified by child sex, boys in the highest quartile had 1.02 cm lower HC (95% CI: [-1.81, -0. 24]) as compared to those in the lowest quartile with a dose-response trend across quartiles. Furthermore, the analyses of BLLs by its quartiles showed that children who belonged to the higher exposure quartiles had relatively higher odds of being stunted at the age of 4 years as compared to the first quartile of exposure OR 2.24 (95% CI: [1.08 – 4.66]). This association remained significant and stronger only in girls when analyses were stratified by sex. An earlier study among breastfed children in the Gambia also reported significant increases in stunting around 3 years with declining prevalence thereafter [40] corroborating the current evidence.

 doi:10.20944/preprints202208.0256.v1

This study expands the limited body of evidence on exposure to lead the during early years of development and child growth and is the first to examine the effect of lead exposure on linear growth in this population in Benin. Previous studies that investigated lead exposure and child growth reported inconsistent findings. A community-based cross-sectional study [21] conducted among children aged 6–59 months in Kampala, Uganda reported a negative association between concurrent blood lead and HAZ. However, this study was based on a small pilot sample of 100 children and evaluated only one growth dimension (HAZ). In addition, maternal BLLs assessed during pregnancy have been reported to be negatively associated with height for age and weight for age in children aged 4-6 years in Mexico [19]. Another cross-sectional study observed no associations between hair concentrations of lead and the growth dimension of children (N= 324) from homeless families aged < 6 years living in shelters for people without housing in France [25]. The population of this cross-sectional study had a higher proportion of children with BMI-Z < 2 standard deviations (90.6%) with more than half of the children suffering from food insecurity [25].

The current study observed a statistically significant association between BLLs quartiles and stunting at age four with the significant exposure-response relationship. A study of 729 slum-dweller children aged < 2 years with high a prevalence of stunting and elevated BLLs i.e., > 50 μg/L (39% and 86.6%, respectively) reported elevated BLLs as a significant predictor of stunting but not wasting [29], which corroborates our findings. One of the proposed mechanisms underlying poor physical growth is impairment of bone growth [15] and disruption of growth hormone secretion [41].

Inconsistencies between the current study results and those from prior studies are likely due to several factors including differences in study design and study populations. Previous studies from less developed countries that reported negative associations between Pb exposure and child growth outcomes differed in the prevalence of undernutrition and exposure levels. Exposure levels of Pb and the proportion of children stunted were generally lower in the current study than those reported in prior studies possible leading to lower power and thus thresholds may not have been reached for the previously reported growth outcome effects related to Pb in the current study. Indeed, the association between BLLs at age 1 and HAZ at later ages (2 and 4 years where more children were stunted as compared to age 1 and 6 years) shifted towards modest significance (data not shown). Similarly, the study population in an urban settlement in Uganda had a high prevalence of stunting at 22.7% [21], compared to our semi-rural population in Benin (6%), and a higher prevalence of elevated BLLs at 65% vs. 58.1% in our study.

5. Conclusions

This study did not find any strong evidence of an association between early childhood lead exposure and HAZ, WAZ, BMIZ and HC. However, high exposure quartiles were associated with stunting in a resource-limited setting.

Author Contributions: Conceptualization, F.B.-L; methodology, S.A, J.B. and F.B.-L; software, S.A. and J.B.; formal analysis, S.A.; investigation, R.Z. and F.B.-L.; resources, N.F, P.G., M.C., A.M. and J.M.A.; data curation, S.A., and R.Z.; writing—original draft preparation, S.A.; writing—review and editing, S.A, J.B., P.A., P.G., M.C., and F.B.-L.; visualization, S.A.; supervision, J.B. and F.B.-L.; project administration, F.B.-L. and R.Z.; funding acquisition, F.B.-L. All authors have read and agreed to the published version of the manuscript.

Funding: The Malaria in Pregnancy Preventive Alternative Drugs (MiPPAD) study was co-funded by the European and Developing Countries Clinical Trials Partnership (EDCTP; IP.2007.31080.002), the Malaria in Pregnancy Consortium and the following national agencies: Instituto de Salud Carlos III (PI08/0564), Spain; Federal Ministry of Education and Research (BMBF FKZ: da01KA0803), Germany; Institut de Recherche pour le Developpement (IRD), France. The 'Anaemia in Pregnancy: Etiologies and Consequences' (APEC) study received funding from a grant from the Bill & Melinda Gates Foundation. The TOLIMMUNPAL project was funded by Agence Nationale de la Recherche (ANR). The Eunice Kennedy Shriver National Institute of Child Health & Human Development (NIH/NICHD) funded The TOVI study (grant no. R21-HD060524). The EXPLORE study was funded

by Fondation de France. Shukrullah Ahmadi received funding from a grant from Fondation de France (reference 00079816).

Institutional Review Board Statement: The MiPPAD trial was approved by the institutional review board of the University of Abomey-Calavi, Benin. The APEC study was approved by the Ethics Committee of the Faculty of Medicine of Cotonou, Benin. The TOLIMMUNPAL study was approved by the Comité Consultatif de Déontologie et d'Éthique (CCDE) of the Institut de Recherche pour le Développement (IRD, France) and the Ethics Committee of the Faculté des Sciences de la Santé, Université d'Abomey Calavi, Benin (approval number: 43/11/2010/CE/FSS/UAC). The EXPLORE study was approved by the Research Ethics Committee of Institute of Applied Biomedical Sciences, Benin (Comité d'Ethique de la Recherche, Institut des Sciences Biomédicales Appliquées, CER-ISBA, Benin) (approval number: 87 du 17/05/2016). The TOVI study was approved by the institutional review boards of the University of Abomey-Calavi in Benin and New York University in the United States (IRB#09-1253)

Informed Consent Statement: Informed consent was obtained from all subjects involved in the study.

Data Availability Statement: The data presented in this study are available on request from the corresponding author.

Acknowledgments: The authors gratefully acknowledge families enrolled in the above-mentioned studies and the contributors of the research team and staff.

Conflicts of Interest: The authors declare no conflict of interest. The funders had no role in the design of the study; in the collection, analyses, or interpretation of data; in the writing of the manuscript; or in the decision to publish the results.

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