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Breastfeeding Duration and Cardiometabolic Health during Adolescence: A Longitudinal Analysis

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Conflict of Interest:

All authors declared no conflicts of interest. Funding bodies had no role in designing the current research questions, analyzing data for the study, interpreting the results, writing the manuscript, or the decision to submit the manuscript for publication.

Disclose prior presentation of study data as an abstract or poster:

There are no prior publications or submissions with any overlapping information, including studies and patients. However, we declare a poster presentation at the American Society of Nutrition Conference in 2019, titled "The Association Between Breastfeeding and Body Composition During Adolescence," which investigated the sex-specific associations between breastfeeding duration and body composition only at one time point during adolescence using linear regression models.

(https://www.sciencedirect.com/science/article/pii/S2475299123156976?via%3Dihub).

Data Statement:

The datasets supporting the conclusions of this article are not publicly available due to human subjects' protections. The de-identified data are available upon reasonable request to corresponding author, Karen E. Peterson (karenep@umich.edu) following review and approval by the ELEMENT Executive Committee.

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Keywords:

Breastfeeding, cardiometabolic health, body composition, Mexican, children and adolescents, longitudinal analysis, repeated measures study design

List of Abbreviations:

RCT: Randomized controlled trial

WC: Waist circumference.

SBP: Systolic blood pressure.

DBP: Diastolic blood pressure

TG: Triglycerides

HDL-C: High density lipoprotein cholesterol

LDL-C: Low density lipoprotein cholesterol.

TC: Total cholesterol

HOMA-IR: Homeostatic model assessment for insulin resistance

Abstract

Objective To investigate the longitudinal association between breastfeeding duration and cardiometabolic health, using repeated measures study design among children and adolescents.

Study design This study included 635 offspring aged 10 to 21 years (52% female) from the Early Life Exposure in Mexico to Environmental Toxicants (**ELEMENT**) birth cohort followed up to four time points during adolescence. Breastfeeding duration was prospectively quantified using questionnaires during early childhood. Cardiometabolic risk factors, body composition, and weight-related biomarkers were assessed as outcomes during adolescent follow-up visits. Sex-stratified linear mixed-effects models were used to model the association between quartiles of breastfeeding duration and outcomes, adjusting for age and additional covariates.

Results Median breastfeeding duration was 7 months (mo) (min=0, max=36). Boys in the 2nd quartile (median breastfeeding= 5 mo) had lower total fat mass % (β (SE) -3.2 (1.5) p= 0.037), and higher lean mass % (3.1 (1.6) *p*= 0.049) and skeletal muscle mass % (1.8 (0.8) *p*= 0.031) compared with the reference group (median breastfeeding= 2 mo). A positive linear trend between breastfeeding duration and trunk lean mass % (0.1 (0.04) *p*= 0.035) was found among girls. No association was found with other cardiometabolic indicators.

Conclusion Despite sex-specific associations of breastfeeding duration with body composition, there was a lack of substantial evidence for the protective effects of breastfeeding against impaired cardiometabolic health during adolescence among Mexican youth. Further longitudinal studies with a robust assessment of breastfeeding are recommended.

Keywords: breastfeeding, cardiometabolic health, body composition, Mexican, children and adolescents, longitudinal analysis, repeated measures study design

Breastfeeding is a gold clinical standard for infant feeding and nutrition [1-4]. Breastfeeding not only has favorable short-term outcomes for the infants and their mothers [5], but also infancy is a crucial period for preventing obesity and its consequences [6]. Obesity is associated with the risk and prevalence of impaired cardiometabolic health [7-10], which have been documented among children [11-17] and shown to track to adulthood [16,18-22]. Therefore, identifying the early determinants of cardiometabolic abnormalities is a fundamental step for risk reduction and prevention [9, 23], and targeting childhood obesity is one proposed preventive measure [10].

Breastfeeding has been shown to be a protective factor against childhood obesity [6, 24-28], and it has potential protective effects against coronary heart disease incidence and mortality [29]. Yet, studies examining the association between breastfeeding and youth cardiometabolic health reported conflicting results, ranging from protective effects for a few youth cardiometabolic health indicators [30-53] or null findings [39, 41, 54-72]. Thus, limited evidence is available on breastfeeding and youth cardiometabolic health [40, 53]. Moreover, most studies conducted were cross-sectional or retrospective cohort studies [53], which hindered drawing a conclusive statement [40], and only standard cardiometabolic risk factors were assessed.

The present study aimed to assess the longitudinal associations between breastfeeding duration and repeated measures of cardiometabolic health among Mexican children and adolescents. We assessed multiple cardiometabolic health indicators, including: waist circumference (WC), systolic and diastolic blood pressure (SBP), (DBP), triglycerides (TG), high- and low- density lipoprotein cholesterol (HDL-C), (LDL-C), total cholesterol (TC), fasting glucose, insulin, insulin resistance, body composition (total fat, lean, skeletal muscle, fat-free, trunk fat and lean mass), and weight-related biomarkers (C-peptide, leptin, IGF-1, adiponectin).

Methods

Study sample

A well-characterized birth cohort, the Early Life Exposure in Mexico to Environmental Toxicants (**ELEMENT)** project in Mexico City, Mexico, is the basis of the children and adolescents' sample in the current study [73, 74]. A description of the **ELEMENT** project was published elsewhere [75]. In short, between 1994 -2004, mother/child dyads (N=1,643) from prenatal clinics in low- to moderate-income populations were recruited [76]. A self-reported sociodemographic questionnaire was collected from mothers during childbirth. The **ELEMENT** project consists of three birth cohorts. Recruited mothers for two of the birth cohorts were enrolled in a randomized controlled trial (RCT) examining the role of calcium supplementation (1200 mg/day) in mitigating the effect of lead exposure on the offspring's neurobehavioral and physical developmental outcomes during lactation (Cohort 1) and pregnancy (Cohort 3). Cohort 2, on the other hand, was a cross-sectional study of pregnant women in their first trimesters and mothers at childbirth, who were recruited to assess the impact of lead exposure on offspring's neurocognitive outcomes [75]. Offspring were followed until four (Cohort 1) or five years of age (Cohort 2 and Cohort 3). Specifically, follow-up visits were conducted for Cohort 1 at 1, 4, 7, 12, 18, 24, 30, 36, 42, and 48 months post-partum, and for Cohort 2 and Cohort 3 at 3, 6, 7, 12, 18, 24, 30, 36, 48, and 60 months post-partum. Information about breastfeeding duration and feeding practices was collected at each of these follow-up visits.

Moreover, research staff followed the offspring multiple study visits during their childhood and adolescence and gathered data about growth, nutrition, health, and other factors. The available funds and aims of each follow-up study were the major determining factors for the sample size for each follow-up study visit. Additionally, the research team prioritized younger

children and children who had an available birth biospecimens at some of the follow-up visits. In 2008, the first childhood follow-up visit (known for the purposes of this secondary analysis as study visit 1) was conducted with a sample size of 828 children recruited from the original three cohorts. The second follow-up visit (study visit 2) was conducted in 2011, and the sample size was 250 children from Cohort 2 and Cohort 3; these children were given priority due to their available prenatal biological samples [75]. In 2015, the third follow-up visit (study visit 3), 554 children were recruited, prioritizing the 250 subjects recruited in study visit 2 (~90% returned) and additional children from the original Cohort 2 and Cohort 3. The last follow-up visit (study visit 4) was conducted in 2018, where ~ 94% of the participants enrolled in study visit 3 returned. In this study, data were used from four utilized follow-up study visits. **Figure 1 (Online)** illustrates the study design, sample size, and the time for assessing each outcome.

The current analysis included singleton and full-term infants (≥ 37 weeks of gestation) [46, 78, 79], who have information about breastfeeding duration, and at least one of the outcomes of interest at any of the four follow-up visits. Therefore, our sample included 309 boys and 325 girls who had either cardiometabolic risk factors (WC, SBP, DBP, TG, HDL-C, LDL-C, TC, glucose, insulin, Homeostatic Model Assessment of Insulin Resistance (HOMA-IR)), body composition (total fat, lean, skeletal muscle, fat-free, trunk fat and lean mass), or body weight related biomarkers (C-peptide, leptin, IGF-1, adiponectin). The **ELEMENT** project was conducted according to the guidelines of the Declaration of Helsinki and approved by the Institutional Review Boards of the University of Michigan (IRB # HUM00034344) and the National Institute of Public Health of Mexico (IRB# CI599207112010, CI599915102014). Informed consent was obtained from all subjects involved in the study. The research team

collected written informed consent and assent from mothers and adolescents, respectively, upon their enrollment.

Outcomes

Anthropometry and body composition: Trained research staff collected duplicate measurements for body weight (kilograms [kg]) to the nearest 0.1 kg and height (centimeter [cm]) to the nearest 0.5 cm in study visit 1 and study visit 2 using a digital scale (BAME Model 420; Catálogo Médico/Tanita Co. Tokyo, Japan with height rod (model WB-3000m [80]). Body weight and body composition were measured at study visit 3 and study visit 4 using the body composition device Inbody (model 230, Gangnam-gu, Seoul 135-960 KOREA). For waist circumference (cm) duplicate measurements were also performed to the nearest 0.1 cm using a non-stretchable measuring tape (SECA (model 201, Hamburg, Germany [80])). The average of the two measurements was used for the analysis [81]. *Cardiometabolic biomarkers:* Duplicate readings for SBP and DBP were recorded with participants in a seated position using a mercury sphygmomanometer (TXJ - 10 MD 3000 model, Homecare, China). The average of the two measurements was used for the analysis. Fasting blood samples for ≥ 8 hours were used to analyze serum glucose via automated chemiluminescence immunoassay (Immulite 1000; Siemens Medical Solutions) [82], and TG and HDL-C using a biochemical analyzer (Cobas Mira Plus; Roche Diagnostics) [82]. LDL-C was calculated as follows (TC - (TG/ 5) – HDL-c) [83]. Levels of insulin were quantified via enzyme-linked immunosorbent assay chemiluminescence method with IMMULITE® 1000, Erlangen, Germany equipment [84]. HOMA-IR was calculated as [fasting plasma glucose (mmol/l)*fasting serum insulin (mU/l))/ 22.5[85]; higher values represent low insulin sensitivity/insulin resistance [85]. *Other biomarkers:* IGF-1 was analyzed via Chemiluminescent Immunoassay (CLIA) (Siemens Healthcare Diagnostics Inc., SHD), leptin via

leptin radioimmunoassay kit (RIA) (Millipore Corporation, Billerica, MA 01821 USA, adiponectin using the Adiponectin radioimmunoassay kit (RIA) (EMD Millipore Corporation, Billerica, MA 01821 USA), and C-peptide vis an automated chemiluminescence immunoassay (Immulite 1000; Siemens Medical Solutions).

Breastfeeding Duration

Breastfeeding duration was the primary exposure, and it was calculated using mothers' self-reported information collected during infancy and early childhood follow-up visits. Information about breastfeeding duration was reported in months at each of the follow-up visits by asking mothers "*Are you breastfeeding now?*", and if no, mothers were asked "*When did you stop?*" at each of the follow-up visits [77]. The duration of breastfeeding was estimated in months from the first visit the mother reported not breastfeeding her infant [77].

Potential confounders:

Based on prior knowledge, potential confounders assessed for this research were classified as 1) childbirth and early life characteristics, which included gestational age**,** mode of delivery, birth weight, and mothers' age, marital status, parity, years of education, and enrollment in any of the **ELEMENT** RCTs (Cohort 1, Cohort 3), and 2) follow-up characteristics for the children, which were age and pubertal onset.

After childbirth, mothers reported information, including their ages, marital status (married, or others – includes free union, single, separated, and divorced), parity status, including the current pregnancy (1, 2, or ≥ 3), and years of education (years) (<12, 12, or >12), and mode of delivery (vaginal, or cesarean section). Gestational age (weeks) was estimated by a registered nurse. Because some of the recruited mothers for the **ELEMENT** project were enrolled in two RCTs of calcium supplementation either during the first trimester of pregnancy until 1-year

postpartum (Cohort 3) or during lactation (Cohort 1), we assessed if the enrollment in the RCT (none or control group, during pregnancy, or lactation) was a significant covariate in our models [74, 75].

During the first year of life, mothers were asked about the age of introducing infant formula and a limited list of foods and drink to their infants' diet. The list of foods and drinks were 1) tea with or without sugar, 2) fruit juice, 3) broth, 4) atole prepared with milk (a corn-based beverage prepared with milk), 5) boiled water with or without sugar, and 6) other foods. Age at introducing foods and drinks (months) was calculated by the earliest time when any of these foods or drinks were given to the infant. Age at introducing foods, drinks, or infant formula (months) was calculated by the earliest time any of these items were given. During the four follow-up visits, puberty was assessed through self-reported Tanner staging for breast and pubic hair (for girls), or genitalia and pubic hair (for boys) to assess pubertal status [86-88]. Following the same approach as previous **ELEMENT** publications, pubertal onset was classified as a binary indicator, by the earliest visit when children demonstrated Tanner Stage > 1 for pubic hair or genital development (boys), or pubic hair and breast development (girls) [89-91].

Statistical Analysis

Demographic characteristics of the study participants were presented as mean (standard deviation (SD)) for continuous variables and frequency (proportions) for categorical variables. All subjects with available data in each model were included; thus, we have a various number of repeated measures for each subject. Linear mixed effects models with compound symmetry error structure were conducted to examine the relationship between breastfeeding duration and the outcomes while accounting for the study design. Breastfeeding duration was categorized into quartiles to examine non-linear associations. The median breastfeeding duration (mo.) at each

quartile was assigned to the quartiles. Additionally, we assessed the *p* for trend across quartiles by modeling the categorized quartiles as a continuous exposure. We log-transformed a few outcomes (i.e., TG, glucose, insulin, HOMA-IR, C-peptide for boys and girls, and leptin for boys only) as their residuals from the linear mixed effects models indicated skewness. Residuals of the final models were assessed for the model assumptions. Findings are presented as a beta estimate (standard error) (β (SE)), and *p*.

We conducted a sex-stratified analysis due to the plausible differences in cardiometabolic health and body composition during the pubertal transition. The crude model included quartiles of the breastfeeding duration, and fully adjusted models include the child's age at each follow-up visit and pubertal onset and any covariates that were considered potential confounders among our study sample. Selection of potential confounders was guided by prior knowledge and their association with the sex-specific median of breastfeeding duration (< 7 months, or ≥ 7 months). The associations were assessed either via the independent sample T test or Mann Whitney U test for continuous variables that were normally and non-normally distributed, respectively, and the chi-squared test for categorical variables. A *p* of < 0.20 was used as a cut-off for including confounders in our models. Crude and adjusted models have the same number of participants because we excluded subjects who had missing information for any covariates included in the fully adjusted model. As a sensitivity analysis, we adjusted for age at introducing foods, drinks, or milk formula because of their potential to influence the outcomes [92, 93], which had no notable change in either magnitude or significance of the associations (data not shown). SAS statistical software package, version 9.4, was used for analyses (SAS Corp, NC, USA), and *p* of < 0.05 was considered as indicative of statistically significant associations.

Results

The present study included 634 children and adolescents; of whom 307 (48%) and 327 (52%) were boys and girls, respectively. **Table I** shows the descriptive information around the time of childbirth for mothers and their children. More than half of the mothers enrolled in our study had less than 12 years of education. Mother's mean age at childbirth was 26 years, and approximately 40% of them had no previous live births. Vaginal delivery was the common type of childbirth reported in our study (approx. 2/3 of births) (**Table 1)**. Median breastfeeding duration was 7 months (min=0, max=36), and a mean (SD) duration of follow-up was approximately 3 years (2.39) ranged from 0 – 8 years (Data not shown).

Table II presents the cardiometabolic health outcomes assessed in the study. Cardiometabolic risk factors were collected at the four follow-up visits in adolescence, except for TC and LDL-C which were collected at study visit 2 onward. For body weight-related biomarkers, study visit 2 was the starting point for collection, except for adiponectin, which was collected at study visit 3 and study visit 4 only. Body composition was assessed at study visit 3, and study visit 4 (**Table II**). Mean (SD) age in years at follow up study visits (each with different sample sizes) were 13 (3), 10 (2), 15 (2), and 16 (2).

Table I shows the selection of the covariates included in adjusted models. Among boys and girls, the mother's marital status was associated with breastfeeding duration; married women had a higher tendency of breastfeeding for 7 months or more. Among boys, gestational age was marginally higher among those had above median breastfeeding duration (p=0.0594). Among girls, mothers who underwent Cesarean section childbirth or were a first-time mother were likely to have shorter breastfeeding duration. Therefore, the mother's marital status and gestational age were included in the fully adjusted model for boys, and the mother's marital status, mode of

childbirth, and parity status were included in the fully adjusted model for girls. In addition to these covariates, we adjusted for child's age at each follow-up visit and pubertal onset (**Table I**).

Tables III and IV illustrate the longitudinal associations between breastfeeding duration and cardiometabolic health among boys and girls, respectively. A few significant associations with small effect sizes were detected for body composition parameters. Boys in the 2nd quartile of breastfeeding (median breastfeeding duration= 5 mo) had lower total fat % (β (SE)) (-3.22 (1.54) (*p* 0.0372), but higher lean % (3.09 (1.56) (*p* 0.0486) and skeletal muscle mass % (1.79 (0.82) (*p* 0.0486) compared with boys in the reference group (median breastfeeding duration = 2 mo). No associations were significant at higher quartiles **(Table III)**. Moreover, girls in the 4th quartile (median breastfeeding duration= 14 months) had higher trunk lean % (1.09 (0.52) (*p* 0.0370) compared with girls in the reference group (median breastfeeding duration= 2 mo). A positive linear trend between breastfeeding duration and trunk lean % (0.08 (0.04) *p*= 0.0350, was detected comparing the 4th to 1st quartile among girls **(Table IV)**. No significant associations, including linear trends, were found between breastfeeding duration and other cardiometabolic risk factors **(Table III and Table IV)**.

Discussion

In the current analysis using a longitudinal repeated measures study design of 623 Mexican youths aged 10 to 21 years, we examined the sex-stratified relationship between quartiles of breastfeeding duration and multiple measure of cardiometabolic health. Weak favorable evidence for breastfeeding duration was detected for total fat, lean and skeletal mass among boys and for lean truck mass among girls. Nevertheless, both crude and fully adjusted models showed a lack of any favorable long-term effect of breastfeeding duration on other cardiometabolic outcomes. To the best of the authors' knowledge, this study is the first

prospective study investigating the long-term effects of breastfeeding duration on holistic cardiometabolic health indicators using repeated measure design among Mexican youth.

Our primarily null associations between breastfeeding duration and youth cardiometabolic health indicators corroborate prior conclusions derived from multiple studies on different populations [39, 41, 54-72]. However, our null conclusions are in conflict with those who reported beneficial associations for some indicators of cardiometabolic health [30-53]. It is worth noting that contrasting between studies is a crude comparison due to the heterogeneities across studies in study design, age of assessing the outcomes, characteristics of the studied population, and assessment of the exposure and outcomes. Nevertheless, our null conclusion reinforces a lack of strong evidence for the long-term benefits for breastfeeding on youth cardiometabolic health distilled from systemic reviews [40, 53].

Our data showed a few significant associations with small effect sizes were detected for the association between breastfeeding duration and body composition parameters in boys and girls. We acknowledge the small effect size is consistent with the small effect size in other studies showed favorable impact of breastfeeding on cardiometabolic health [38, 46]. However, we propose the possibility of a false positive result for the body composition parameters due to the multiple comparisons, and because the protective effect on body composition is not supported by any of the biomarkers. Further studies are warranted to examine the effect of breastfeeding on body composition during adolescence.

Among our sample, 7 months of breastfeeding was the median duration, which is similar to the breastfeeding duration reported by other studies [38, 94-96]. However, the mean age for introducing foods, drinks, or infant formula was approximately 2 months, counter to public health recommendations. Other researchers also observed the early introduction of solid food

before 6 months of age [66, 92, 97]. These findings collectively raise a flag about the low adherence to the World Health Organization (WHO), the United Nations Children's Fund (UNICEF), and the American Academy of Pediatrics recommendations of at least six months of exclusive breastfeeding, defined as breastmilk as the only complete source of nutrition and hydration with no need for any other foods, liquids, or water. After then, complementary foods are recommended to be introduced with the continuation of breastfeeding for two years and beyond [98, 99]. Moreover, the early introduction of solid foods might attenuate any potentially favorable effect for breastfeeding because it has been positively associated with the risk for obesity [92]. Therefore, we encourage educating parents on the importance of exclusive breastfeeding practices during the first 6 months of age and addressing any concerns about the incompleteness of breast milk. Future studies are needed to explore and understand the mothers' attitudes toward the completeness of breast milk to help plan culturally-sensitive intervention programs to promote exclusive breastfeeding in the first 6 months. Such public health initiatives would help in meeting the global target set by the World Health Assembly Resolution of raising exclusive breastfeeding to 50% or more by 2025 [100].

We showed that breastfeeding duration was associated with several maternal characteristics during childbirth. Longer breastfeeding duration was reported among married mothers, which agrees with findings reported among different populations [101, 102]. Also, we showed that having multiple children was associated with longer breastfeeding duration, which was seen among Australian women [79]. We propose that having a previous child/children might increase the likelihood that mothers would be exposed to knowledge and skills about infant feeding practices because a higher rate of breastfeeding was positively associated with breastfeeding knowledge [103]. Lastly, the mode of delivery was associated with breastfeeding,

where cesarean section correlated with shorter duration. Other researchers reported similar findings [104-106], and they recommended educating mothers who went through cesarean section delivery with skills and support to facilitate breastfeeding [104].

The current study has several strengths. Using a well-characterized birth cohort, **ELEMENT**, allowed for adjusting for multiple characteristics measured at offspring birth. Furthermore, our repeated assessments of the outcomes overcome the limitations in prior prospective studies that examined the outcome at one single point of time [31, 32, 34, 37, 39, 45, 47, 48, 54, 58-65, 67, 68]. Another strength is the prospective collection of breastfeeding information during early childhood, which reduces the likelihood of recall bias in estimating the breastfeeding duration. Having said that, we acknowledge that the time lag between the follow-up visits was not consistent across the three cohorts, and the timing for the follow-up study was not designed primarily to capture the infant feeding practices. Despite these limitations, our breastfeeding duration was associated with some of the maternal characteristics [79, 101-106], and our conclusions were consistent with the majority of the studies conducted on this topic [39, 41, 54-72]. Moreover, our analysis was not limited to cardiometabolic risk factors, but we also included an assessment of body composition and body weight-related biomarkers to expand on the potential underlying mechanisms for cardiometabolic abnormalities at a young age. Lastly, sex-stratified analysis was conducted to acknowledge the sex differences in cardiometabolic health during the pubertal transition.

Despite these strengths, the study has several limitations. Our breastfeeding duration could not infer any information about the exclusiveness of breastfeeding. However, we investigated the role of introducing a few foods, drinks, or infant formula as sensitivity analyses, and we showed the introduction of solid foods did not alter our findings. Another limitation is

that our assessment of breastfeeding duration does not entail assessing the mode of feeding (i.e., actual breastfeeding vs. bottle, cup, or syringe feeding of human milk), which might influence the growth trajectory. Given these limitations, we acknowledge the possibility of misclassification in assessing breastfeeding duration, and higher breastfeeding duration cannot necessarily be interpreted as higher breastfeeding intensity because we did not assess the proportion of breastfeeding out of that total feedings given. To lessen the impact of exposure misclassification, we examined the linear trend across non-parametric quartiles of breastfeeding duration. Furthermore, the possibility of residual confounding could not be ruled out due to crude assessment of covariates or unmeasured confounding for cardiometabolic health, such as a family history of chronic diseases, and maternal pre-pregnancy weight and lifestyle practices, or adolescent behaviors such as smoking or alcohol use. Furthermore, while premature birth may be a confounder in the association between breastfeeding and later cardiometabolic, a very small number of infants born before 37 weeks of gestation limited our capacity to consider this covariate. Also, the possibility of reverse causation in our conclusion is valid because of the bi-directional relationship between infant feeding and weight gain, and growth pattern [63]. Lastly, our conclusions might not be generalized to all Mexican youth or youths with Mexican heritage who live outside of Mexico City due to the influence of the population's confounding structure on the association between breastfeeding and cardiometabolic health [42].

In conclusion, we report some evidence for sex-specific associations of breastfeeding duration with body composition, but overall, a largely null relationship between breastfeeding duration and cardiometabolic health in a sample of Mexican youth using a longitudinal design with repeated measures. Our findings supplement the existing knowledge on the long-term benefits of breastfeeding on Mexican youth cardiometabolic health using a population from a

low-to-middle-income country that is susceptible to cardiometabolic abnormalities, especially given that they have been shown to have insulin resistance while having a normal weight [107]. Further investigations are needed to expand on the knowledge using well-designed prospective studies among different pediatric populations. Moreover, we recommend future studies employ robust assessment methods for breastfeeding and other feeding practices [40, 53] to overcome the misclassifications in our crude breastfeeding assessment.

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Figure legends:

Figure 1 title: Figure 1(Online): Flowchart Summary of Analytical Samples of Early Life Exposures in Mexico to ENvironmental Toxicants (ELEMENT) Cohort:

Figure 1 abbrevations: Abbreviations: WC= waist circumference; SBP= systolic blood pressure; DBP= diastolic blood pressure; TG= triglycerides; HDL-C =high density lipoprotein cholesterol; HOMA-IR= Homeostatic Model Assessment for Insulin Resistance; BMI= body mass index; TC= total cholesterol; LDL-C= low density lipoprotein cholesterol; IGF-1= Insulin-like Growth Factor 1.

Online only tables and figures:

Figure 1(Online): Flowchart Summary of Analytical Samples of Early Life Exposures in Mexico to ENvironmental Toxicants (ELEMENT) Cohort:

Table 1 (Online): Baseline Characteristics of the Early Life Exposures in Mexico to ENvironmental Toxicants (ELEMENT) Analytic Sample According to the Sex-specific Median Breastfeeding Duration:

Table 1: Baseline Characteristics of the Early Life Exposures in Mexico to ENvironmental Toxicants (ELEMENT) Analytical Sample:

	Total (N=634)	**Boys** N=307 (48.42%)	**Girls** N=327 (51.58%)
Maternal characteristics (at the time of the child's birth)			
Years of education, %			
< 12 years	342 (53.94)[1]	158 (51.47)[2]	184 (56.27)[2]
12 years	205 (32.33)[1]	104 (33.88)[2]	101 (30.89)[2]
> 12 years	85 (13.41)[1]	44 (14.33)[2]	41 (12.54)[2]
Age at childbirth, (years)	26.15 (5.39)[2]	26.11 (5.32)	26.19 (5.46)[2]
Parity, %			
1	245 (38.64)	111 (36.16)	134 (40.98)
2	224 (35.33)	118 (38.44)	106 (32.42)
≥ 3	165 (26.03)	78 (25.41)	87 (26.61)
Marital Status, %			
Married	443 (69.87)[1]	222 (72.31)	221 (67.58)[1]
Others	189 (29.81)[1]	85 (27.69)	104 (31.80)[1]
Enrollment in RCTs, %			
None or control group	452 (71.29)	216 (70.36)	236 (72.17)
During pregnancy	148 (23.34)	72 (23.45)	76 (23.24)
During lactation	34 (5.36)	19 (6.19)	15 (4.59)
Child characteristics			
Gestational age, (weeks)	39.09 (1.09)	39.14 (1.06)	39.05 (1.13)
Mode of delivery, %			
Vaginal delivery	420 (66.25)[3]	201 (65.47)	219 (66.97)[3]
Cesarean section	211 (33.28)[3]	106 (34.53)	105 (32.11)[3]
Birth weight, (kg)	3.19 (0.45)	3.25 (0.45)	3.13 (0.44)
Age introducing foods or drinks, (months)	2.74 (2.67)[4]	2.50 (2.48)[5]	2.98 (2.83)[6]
Age introducing foods, drinks, or milk formula, (months)	2.18 (2.25)[7]	2.10 (2.20)[8]	2.25 (2.30)[9]

Breastfeeding duration, (months)	8.19 (6.32)	8.33 (6.35)	8.06 (6.30)

Means (standard deviation), or frequency (percentage) are presented for continuous or categorical variables, respectively

Number of missing values 1.n=2; 2. n=1; 3.n=3; 4.n=81; 5.n=35; 6.n=46; 7.n=71; 8.n=29; 9.n=42

Table 2: Youth Characteristics of the Early Life Exposures in Mexico to ENvironmental Toxicants (ELEMENT) Analytic Sample Stratified by Study Visits:

	Study visit 1		**Study visit 2**		**Study visit 3**		**Study visit 4**	
	Boys (N=93)	Girls (N= 84)	Boys (N= 107)	Girls (N= 124)	Boys (N= 242)	Girls (N= 261)	Boys (N= 221)	Girls (N= 251)
				Child Characteristics				
Age, (years)	13.32 (2.56)	13.2 (2.49)	10.36 (1.63)	10.3 (1.73)	14.52 (2.05)	14.52 (2.17)	16.45 (2.04)	16.48 (2.2)
Pubertal onset, %	82 (88.17)[1]	75 (89.29)[2]	94 (87.85)	76 (61.29)	242 (100)	256 (98.08)[3]	221 (100)	249 (99.20)[2]
				Cardiometabolic risk factors				
WC, (cm)	72.89 (12.06)[4]	69.08 (10.83)[3]	70.08 (9.81)	72.04 (11.31)	78.5 (11.29)	80.47 (11.2)	83.02 (11.56)	87.63 (11.37)
SBP, (mmHg)	94.71 (11.51)[4]	90.43 (7.73)[3]	104 (10.36)	101.52 (10.04)	100.59 (10.27)	97.05 (9.04)	103.82 (10.26)	99.59 (8.93)[4]
DBP, (mmHg)	59.27 (9.6)[4]	57.52 (6.92)[3]	65.44 (7.52)	65.63 (7.33)	63.96 (7.11)	62.34 (6.54)	65.17 (7.63)	63.32 (6.68)[4]
TC, (mg/dL)	N/A	N/A	150.49 (27.34)[4]	158.23 (27.67)[4]	150.1 (26.17)[5]	161.78 (26.71)[6]	146.74 (28.26)[7]	157.28 (26.03)[8]
TG, (mg/dL)	104.51 (56.18)[9]	112.09 (60.25)[10]	75.13 (36.9)[4]	98.59 (48.13)[4]	96.83 (51.91)[5]	110.1 (60.68)[6]	102.34 (52.01)[7]	108.91 (48.27)[8]
HDL-C, (mg/dL)	46.81 (13.04)[9]	45.16 (10.96)[10]	60.25 (12.25)[4]	57.21 (11.94)[4]	41.81 (7.83)[5]	44.29 (9.46)[6]	43.61 (8.05)[7]	45.56 (10.11)[8]
LDL-C, (mg/dL)	N/A	N/A	75.22 (23.69)[4]	81.3 (21.91)[4]	88.92 (21.02)[5]	95.46 (21.06)[6]	94.84 (29.81)[7]	101.45 (24.6)[8]
Glucose, (mg/dL)	91.84 (13.54)[9]	89.87 (16.7)[10]	87.56 (7.59)[4]	86.36 (10.69)[4]	78.66 (7.38)[5]	76.86 (7.09)[6]	91.38 (9.7)[7]	88.64 (7.2)[8]
Insulin, (μIU/mL)	7.67 (3.67)[11]	11.74 (12.4)[12]	3.99 (7.55)[13]	7.44 (12.37)[14]	17.65 (10.03)[5]	20.48 (13.49)[6]	17.6 (12.6)[15]	20.85 (12.47)[8]
HOMA-IR	1.79 (0.92)[11]	3.41 (4.78)[12]	0.91 (1.7)[13]	1.93 (4.08)[14]	3.46 (2.06)[5]	3.92 (2.59)[6]	4.02 (3.0)[15]	4.6 (2.8)[8]
				Body weight-related biomarkers				
C-peptide, (ng/mL)	N/A	N/A	1.63 (1.19)[4]	1.91 (1.28)[4]	2.14 (1.19)[5]	2.42 (1.17)[6]	2.43 (1.47)[7]	2.78 (1.41)[8]
Leptin, (ng/mL)	N/A	N/A	8.26 (6.52)[4]	14.32 (10.22)[4]	14.07 (12.69)[5]	33.96 (17.46)[6]	N/A	N/A
IGF-1, (ng/mL)	N/A	N/A	233.24 (102.71)[4]	281.77 (105.86)[4]	319.84 (87.93)[5]	365.7 (92.85)[6]	265.55 (65.7)[7]	274.51 (72.1)[8]

Adiponectin, (ng/mL)	N/A	N/A	N/A	N/A	11377.6 (4085.5)[5]	12147.68 (4005.48)[6]	9626.24 (3919.67)[15]	10449.81 (3818.05)[8]
Body composition								
Fat mass, (%)	N/A	N/A	N/A	N/A	21.13 (8.87)[4]	32.02 (7.95)[4]	20.16 (8.08)	34.35 (7.64)[4]
Trunk fat mass, (%)	N/A	N/A	N/A	N/A	9.77 (5.33)[3]	15.81 (4.86)[2]	9.79 (5.13)	17.44 (4.42)[4]
Lean mass, (%)	N/A	N/A	N/A	N/A	74.36 (8.45)[18]	63.92 (7.45)[19]	77.71 (6.35)[20]	64.71 (3.38)[21]
Muscle mass, (%)	N/A	N/A	N/A	N/A	43.21 (5.15)[4]	36.35 (3.95)[4]	44.5 (4.4)	35.42 (3.91)[4]
Lean trunk mass, (%)	N/A	N/A	N/A	N/A	35.38 (3.98)[3]	31.26 (2.8)[2]	36.51 (3.59)	30.94 (2.79)[4]
Fat-free mass, (%)	N/A	N/A	N/A	N/A	67.97 (16.95)[22]	71.22 (15.59)[21]	79.73 (8.13)[23]	65.51 (7.74)[24]

Means (standard deviation), or frequency (percentage) are presented for continuous or categorical variables, respectively

Number of missing values 1.n=6; 2.n=2; 3.n=3; 4.n=1; 5. n=64; 6.n=77; 7.n=57; 8.n=75; 9.n=50; 10.n=29; 11.n=86; 12.n=76; 13.n=87; 14.n=72; 15.n=59; 16.n=24; 17.n=28; 18.n=4; 19.n=5; 20.n=212; 21.n=241; 22.n=224; 23.n= 9; 24.n=11

Abbreviations: WC= waist circumference; SBP= systolic blood pressure; DBP= diastolic blood pressure; TC= total cholesterol; TG= triglycerides; HDL-C =high density lipoprotein cholesterol; LDL-C =low density lipoprotein cholesterol; HOMA-IR= Homeostatic Model Assessment of Insulin Resistance; IGF-1= Insulin-like Growth Factor 1

Table 3: Associations between Cardiometabolic Health and Quartiles of Breastfeeding Duration among Boys:

Breastfeeding duration (months)[1]		**SBP** (mmHg)	**DBP** (mmHg)	**Log TG** (mg/dl)	**HDL-C** (mg/dl)	**TC** (mg/dl)	**LDL-C** (mg/dl)	**Log glucose** (mg/dl)	**Log insulin** (μIU/mL)	**Log HOMA-IR**	**Log C-peptide** (ng/mL)	**Log leptin** (ng/mL)	**IGF-1** (ng/mL)	**Adiponectin** (ng/mL)	**WC** (cm)	**Total fat** (%)	**Trunk fat** (%)	**Trunk lean** (%)	**Lean** (%)	**Skeletal muscle** (%)	**Fat-free** (%)
		N= 270	N= 270	N= 214	N= 214	N= 189	N=189	N= 214	N=186	N=186	N=189	N=188	N=189	N=178	N=270	N=215	N=215	N=215	N=210	N=215	N=196
Crude model [2]																					
Q 1 =2		**(Ref)**	**(Ref)**	**(Ref)**	**(Ref)**	**(Ref)**	**(Ref)**	**(Ref)**	**(Ref)**	**(Ref)**	**(Ref)**	**(Ref)**	**(Ref)**	**(Ref)**	**(Ref)**	**(Ref)**	**(Ref)**	**(Ref)**	**(Ref)**	**(Ref)**	**(Ref)**
Q 2=5	β	-1.9697	-1.4517	-0.00971	2.4870	-2.6607	-5.1576	-0.02635	-0.1208	-0.1466	-0.1648	-0.2718	-15.7525	60.3175	-2.9500	-3.4154	-1.8840	1.1653	3.4275	1.9182	3.2611
	SE	1.5324	1.0372	0.08267	1.8752	5.1687	4.85	0.01547	0.1242	0.1260	0.09495	0.1542	12.9424	795.74	1.9273	1.5625	0.9740	0.6881	1.6369	0.8702	1.9157
	P	0.1998	0.1629	0.9066	0.1862	0.6073	0.2898	0.0900	0.3319	0.2462	0.0842	0.0796	0.2252	0.9397	0.1270	**0.0299**	0.0544	0.0918	**0.0375**	**0.0286**	0.0902
Q 3=8	β	0.7012	0.3517	-0.04699	2.7891	-3.7583	-6.4742	-0.02579	-0.1463	-0.1763	-0.05959	-0.1940	-12.3228	-241.72	-2.1682	-2.0963	-1.4565	0.5554	1.8680	1.0526	2.4983
	SE	1.6438	1.1087	0.08724	1.9654	5.2840	4.9671	0.01605	0.1289	0.1309	0.09709	0.1567	13.2121	829.66	2.0759	1.6894	1.0531	0.7434	1.7631	0.9405	2.0806
	P	0.6700	0.7513	0.5907	0.1574	0.4778	0.1940	0.1099	0.2580	0.1795	0.5401	0.2171	0.3523	0.7711	0.2972	0.2160	0.1681	0.4558	0.2906	0.2643	0.2312
Q 4= 13	β	0.6441	0.6154	0.1146	1.0200	3.1967	1.1347	-0.01771	-0.02110	-0.05441	-0.03936	-0.2826	-10.9346	-560.61	-1.1288	-3.4844	-1.6586	1.6046	4.2285	2.2905	2.4295
	SE	1.5020	1.0138	0.08026	1.8163	5.0081	4.7066	0.01492	0.1204	0.1222	0.09198	0.1493	12.5213	776.94	1.8965	1.5240	0.9501	0.6707	1.5992	0.8483	1.8361
	P	0.6684	0.5444	0.1547	0.5750	0.5241	0.8098	0.2369	0.8610	0.6565	0.6692	0.0598	0.3837	0.4715	0.5522	**0.0232**	0.0823	**0.0176**	**0.0088**	**0.0075**	0.1873
Linear	β	0.1327	0.1104	0.01087	0.03686	0.3661	0.2321	-0.00097	0.000593	-0.00200	0.001466	-0.01906	-0.5990	-57.5805	-0.03002	-0.2390	-0.1093	0.1196	0.3052	0.1649	0.1483
	SE	0.1302	0.08761	0.006941	0.1572	0.4309	0.4067	0.001294	0.01044	0.01061	0.007963	0.01283	1.0752	66.8943	0.1645	0.1327	0.08264	0.05826	0.1389	0.07391	0.1597
	P	0.3093	0.2089	0.1189	0.8148	0.3966	0.5689	0.4530	0.9548	0.8509	0.8541	0.1391	0.5782	0.3905	0.8553	0.0732	0.1872	**0.0413**	**0.0290**	**0.0268**	0.3543
Adjusted model [3]																					
Q 1 =2		**(Ref)**	**(Ref)**	**(Ref)**	**(Ref)**	**(Ref)**	**(Ref)**	**(Ref)**	**(Ref)**	**(Ref)**	**(Ref)**	**(Ref)**	**(Ref)**	**(Ref)**	**(Ref)**	**(Ref)**	**(Ref)**	**(Ref)**	**(Ref)**	**(Ref)**	**(Ref)**
Q 2=5	β	-1.8643	-1.3152	-0.01745	2.4405	-2.8259	-5.5226	-0.02445	-0.1494	-0.1767	-0.1566	-0.2713	-15.6505	412.30	-2.7415	-3.2190	-1.7816	1.0758	3.0922	1.7860	3.0288
	SE	1.4930	0.9994	0.08134	1.9100	5.3137	4.6807	0.01559	0.1270	0.1308	0.09587	0.1622	12.6582	800.30	1.8729	1.5352	0.9738	0.6478	1.5588	0.8207	1.9032
	P	0.2130	0.1894	0.8304	0.2028	0.5955	0.2395	0.1184	0.2408	0.1786	0.1042	0.0963	0.2180	0.6071	0.1444	**0.0372**	0.0687	0.0982	**0.0486**	**0.0306**	0.1131
Q 3=8	β	1.4703	0.9479	-0.03590	1.7633	-4.7571	-5.9787	-0.02226	-0.1249	-0.1524	-0.02396	-0.1721	-12.3919	-4.7246	-0.6601	-2.1044	-1.3323	0.7178	2.2011	1.2104	2.1901
	SE	1.6054	1.0722	0.08568	2.0103	5.4299	4.7849	0.01621	0.1317	0.1360	0.09799	0.1650	12.9528	831.36	2.0201	1.6558	1.0500	0.6981	1.6706	0.8849	2.0698
	P	0.3606	0.3775	0.6756	0.3815	0.3821	0.2130	0.1715	0.3444	0.2639	0.8071	0.2984	0.3401	0.9955	0.7441	0.2051	0.2059	0.3051	0.1891	0.1728	0.2913
Q 4= 13	β	0.6410	0.6770	0.09013	1.9322	3.3032	-1.1176	-0.01352	-0.06325	-0.1074	-0.04811	-0.2881	-12.9227	372.77	-1.1033	-2.5140	-1.3013	0.9909	2.8699	1.5052	1.3359
	SE	1.4939	0.9985	0.08141	1.9117	5.3149	4.6831	0.01559	0.1278	0.1318	0.09591	0.1621	12.6936	812.08	1.8807	1.5284	0.9686	0.6445	1.5542	0.8172	1.8837
	P	0.6682	0.4984	0.2694	0.3134	0.5351	0.8116	0.3871	0.6212	0.4161	0.6165	0.0773	0.3101	0.6468	0.5580	0.1014	0.1805	0.1256	0.0662	0.0669	0.4790
Linear	β	0.1392	0.1192	0.008888	0.1134	0.3730	0.03805	-0.00059	-0.00209	-0.00559	0.000985	-0.01914	-0.7779	19.9854	-0.01698	-0.1517	-0.07694	0.06502	0.1870	0.09507	0.04891
	SE	0.1296	0.08630	0.006994	0.1643	0.4560	0.4025	0.001349	0.01100	0.01136	0.008269	0.01391	1.0873	69.5831	0.1628	0.1330	0.08418	0.05590	0.1345	0.07116	0.1641
	P	0.2838	0.1685	0.2052	0.4906	0.4144	0.9248	0.6608	0.8499	0.6232	0.9053	0.1706	0.4753	0.7743	0.9170	0.2555	0.3617	0.2460	0.1659	0.1830	0.7660

1: median values of breastfeeding duration in months at each quartile

2: model includes breastfeeding duration quartiles as fixed effects and compound symmetry error matrix structure.

3: additionally adjusted for the following fixed effects: mother's marital status, gestational age, and child's age and pubertal onset.

*$P < 0.05$

Abbreviations: WC= waist circumference; SBP= systolic blood pressure; DBP= diastolic blood pressure; TC= total cholesterol; TG= triglycerides; HDL-C =high density lipoprotein cholesterol; LDL-C =low density lipoprotein cholesterol; HOMA-IR= Homeostatic Model Assessment of Insulin Resistance; IGF-1= Insulin-like Growth Factor 1

Table 4: Associations between Cardiometabolic Health and Quartiles of Breastfeeding Duration among Girls:

Breastfeeding duration (months)[1]		**SBP** (mm Hg)	**DBP** (mm Hg)	**Log-TG** (mg/dl)	**HDL-C** (mg/dl)	**TC** (mg/dl)	**LDL-C** (mg/dl)	**Log glucose** (mg/dl)	**Log insulin** (μIU/mL)	**Log HOMA-IR**	**Log C-peptide** (ng/mL)	**Leptin** (ng/mL)	**IGF-1** (ng/mL)	**Adiponectin** (ng/mL)	**WC** (cm)	**Total fat** (%)	**Trunk fat** (%)	**Trunk lean** (%)	**Lean** (%)	**Skeletal muscle** (%)	**Fat-free** (%)
		N=273	N=273	N=227	N=227	N=196	N=196	N=227	N=189	N=189	N=196	N=196	N=196	N=178	N=273	N=219	N=220	N=219	N=215	N=219	N=206
Crude model [2]																					
Q 1= 2		**(Ref)**	**(Ref)**	**(Ref)**	**(Ref)**	**(Ref)**	**(Ref)**	**(Ref)**	**(Ref)**	**(Ref)**	**(Ref)**	**(Ref)**	**(Ref)**	**(Ref)**	**(Ref)**	**(Ref)**	**(Ref)**	**(Ref)**	**(Ref)**	**(Ref)**	**(Ref)**
Q 2 = 5	β	-0.6733	-0.7239	0.03991	1.2331	1.8696	0.2348	-0.01334	0.1480	0.1372	0.05495	-0.08668	-6.9347	-384.99	-0.1618	-0.2019	0.02533	0.2185	-0.3987	0.3325	0.2000
	SE	1.2814	0.9234	0.06860	1.8437	4.6631	4.0491	0.01442	0.1138	0.1174	0.08205	2.8313	12.5716	756.28	1.8679	1.3742	0.8242	0.4944	1.3644	0.6874	1.6049
	P	0.5997	0.4338	0.5613	0.5043	0.6889	0.9538	0.3563	0.1949	0.2439	0.5038	0.9756	0.5819	0.6113	0.9311	0.8833	0.9755	0.6590	0.7704	0.6290	0.9010
Q 3= 8	β	-0.1085	-0.7143	0.000478	0.6479	3.9472	4.2014	0.01141	-0.05398	-0.04565	0.006440	-1.4401	-4.9379	-689.69	-0.1155	0.4126	0.5636	0.1481	-0.2349	-0.05074	-0.5550
	SE	1.3625	0.9828	0.07268	1.9532	4.9175	4.2714	0.01526	0.1191	0.1231	0.08659	2.9799	13.2753	806.39	1.9823	1.4635	0.8775	0.5263	1.4724	0.7320	1.7031
	P	0.9366	0.4680	0.9948	0.7404	0.4232	0.3266	0.4556	0.6509	0.7111	0.9408	0.6295	0.7104	0.3935	0.9536	0.7783	0.5214	0.7786	0.8734	0.9448	0.7448
Q 4=14	β	0.2936	0.4864	-0.03712	0.5511	2.2101	4.0294	-0.00290	0.09597	0.1047	0.008662	-2.7537	-1.8277	171.42	-1.4853	-2.0569	-0.7920	1.1446	1.9280	1.3650	2.5438
	SE	1.2784	0.9219	0.06759	1.8161	4.6310	4.0225	0.01426	0.1122	0.1158	0.08154	2.8155	12.5021	758.81	1.8596	1.3910	0.8339	0.5004	1.3758	0.6958	1.6580
	P	0.8185	0.5982	0.5834	0.7618	0.6337	0.3178	0.8390	0.3932	0.3669	0.9155	0.3293	0.8839	0.8215	0.4252	0.1406	0.3433	**0.0231**	0.1626	0.0511	0.1264
Linear	β	0.03808	0.04957	-0.00388	0.02078	0.1650	0.3505	0.000201	0.003604	0.004650	-0.00056	-0.2312	-0.00583	17.7976	-0.1152	-0.1541	-0.05797	0.08678	0.1599	0.09967	0.1888
	SE	0.09516	0.06874	0.005031	0.1352	0.3445	0.2994	0.001066	0.008342	0.008598	0.006060	0.2080	0.9241	56.4251	0.1384	0.1038	0.06224	0.03730	0.1027	0.05192	0.1238
	P	0.6893	0.4715	0.4416	0.8780	0.6326	0.2433	0.8506	0.6662	0.5892	0.9262	0.2678	0.9950	0.7528	0.4062	0.1390	0.3527	**0.0209**	0.1209	0.0562	0.1288
Adjusted model [3]																					
Q 1= 2		**(Ref)**	**(Ref)**	**(Ref)**	**(Ref)**	**(Ref)**	**(Ref)**	**(Ref)**	**(Ref)**	**(Ref)**	**(Ref)**	**(Ref)**	**(Ref)**	**(Ref)**	**(Ref)**	**(Ref)**	**(Ref)**	**(Ref)**	**(Ref)**	**(Ref)**	**(Ref)**
Q 2 = 5	β	-0.5166	-0.6648	0.03489	1.4840	1.5769	-1.5779	-0.01253	0.02934	0.01610	0.03231	-0.9019	-1.8255	-18.9146	-0.3782	-0.5612	-0.2558	0.2247	0.005438	0.4397	0.1401
	SE	1.2939	0.9284	0.06921	1.8382	4.5970	4.0323	0.01463	0.1106	0.1154	0.07993	2.9088	12.0302	763.21	1.9748	1.3831	0.8320	0.4984	1.3513	0.6965	1.5829
	P	0.6900	0.4746	0.6147	0.4203	0.7320	0.6960	0.3928	0.7911	0.8892	0.6865	0.7569	0.8796	0.9803	0.8483	0.6853	0.7588	0.6526	0.9968	0.5285	0.9296
Q 3= 8	β	-0.00076	-0.6371	-0.00090	0.03838	2.4229	3.0944	0.01108	-0.01288	-0.01246	0.03990	-0.2394	-0.8638	-635.23	-0.3234	0.1941	0.3948	0.1367	-0.1433	0.006043	-0.8358
	SE	1.3704	0.9844	0.07343	1.9495	4.8580	4.2607	0.01551	0.1167	0.1218	0.08447	3.0721	12.7252	815.14	2.0775	1.4683	0.8830	0.5290	1.4543	0.7394	1.6754
	P	0.9996	0.5181	0.9902	0.9843	0.6185	0.4686	0.4756	0.9122	0.9186	0.6372	0.9380	0.9460	0.4369	0.8764	0.8950	0.7588	0.7963	0.9216	0.9935	0.6184
Q 4=14	β	0.5461	0.6135	-0.05704	1.1438	1.0516	1.6054	-0.00171	0.02054	0.02504	-0.00795	-2.8246	-2.6830	417.56	-1.4604	-2.2761	-0.9786	1.0869	2.1958	1.3928	2.2481
	SE	1.3169	0.9457	0.06935	1.8390	4.6608	4.0877	0.01474	0.1113	0.1161	0.08104	2.9448	12.2133	784.45	1.9981	1.4376	0.8645	0.5180	1.4020	0.7240	1.6855
	P	0.6787	0.5171	0.4117	0.5346	0.8217	0.6950	0.9078	0.8538	0.8295	0.9220	0.3388	0.8264	0.5952	0.4655	0.1148	0.2589	**0.0370**	0.1188	0.0557	0.1837
Linear	β	0.05672	0.06058	-0.00544	0.05646	0.06685	0.1916	0.000284	0.000791	0.001522	-0.00106	-0.2059	-0.1760	28.9240	-0.1102	-0.1643	-0.06715	0.08180	0.1727	0.09940	0.1629
	SE	0.09766	0.07026	0.005150	0.1367	0.3466	0.3048	0.001098	0.008199	0.008554	0.006029	0.2190	0.9027	58.3368	0.1482	0.1071	0.06445	0.03856	0.1045	0.05396	0.1259
	P	0.5619	0.3894	0.2923	0.6800	0.8473	0.5304	0.7963	0.9232	0.8590	0.8606	0.3485	0.8456	0.6207	0.4579	0.1265	0.2986	**0.0350**	0.0997	0.0668	0.1971

1: median values of breastfeeding duration in months at each quartile

2: model includes breastfeeding duration quartiles as fixed effects and compound symmetry error matrix structure.

3: additionally adjusted for the following fixed effects: mother's marital and parity status, mode of childbirth, and child's age and pubertal onset.

*$P < 0.05$

Abbreviations: WC= waist circumference; SBP= systolic blood pressure; DBP= diastolic blood pressure; TC= total cholesterol; TG= triglycerides; HDL-C =high density lipoprotein cholesterol; LDL-C =low density lipoprotein cholesterol; HOMA-IR= Homeostatic Model Assessment of Insulin Resistance; IGF-1= Insulin-like Growth Factor 1

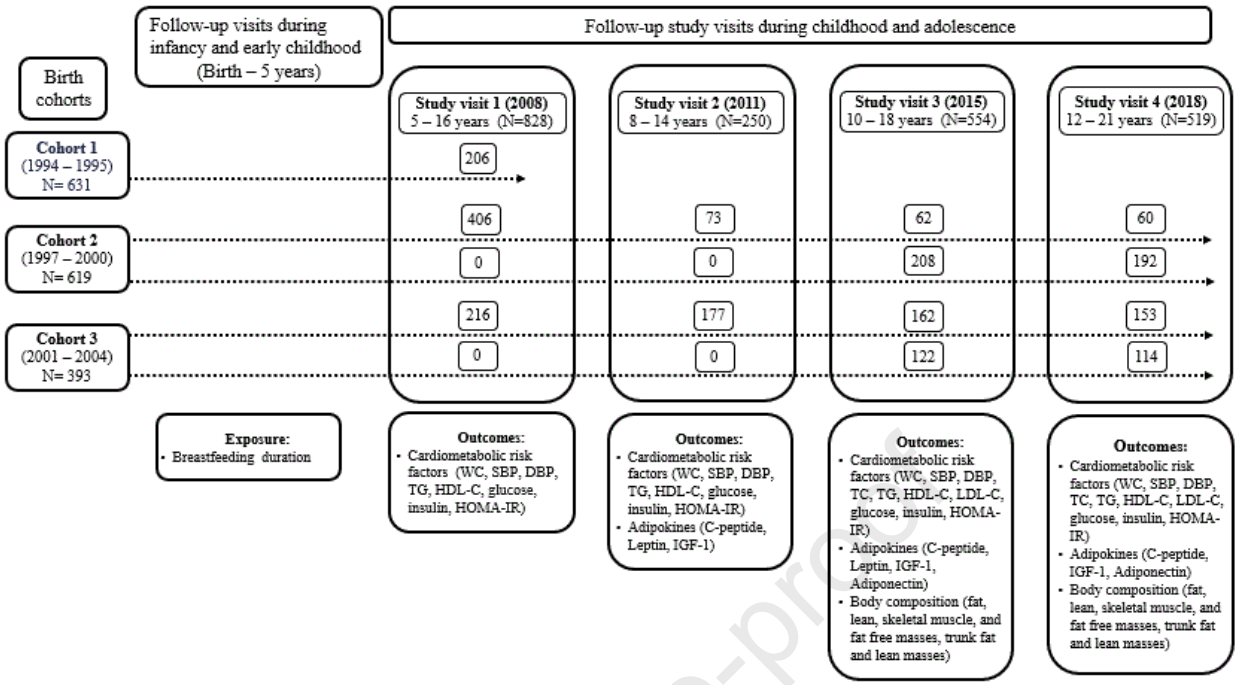

Table 1 (Online): Baseline Characteristics of the Early Life Exposures in Mexico to ENvironmental Toxicants (ELEMENT) Analytic Sample According to the Sex-specific Median Breastfeeding Duration:

Variables	Boys			Girls		
	< 7 months (N= 152)	**≥ 7 months** (N= 155)	**P-value**	**< 7 months** (N= 157)	**≥ 7 months** (N= 170)	**P-value**
Maternal age, (years)*	25.76 (5.22)	26.45 (5.42)	0.2580	26.26 (5.85)	26.12 (5.09)	0.8185
Maternal education, %**						
< 12 years	76 (50.33)[1]	82 (52.90)		88 (56.41)[1]	96 (56.47)	
12 years	51 (33.77)[1]	53 (34.19)	0.7491	51 (32.69)[1]	50 (29.41)	0.6208
> 12 years	24 (15.89)[1]	20 (12.90)		17 (10.90)[1]	24 (14.12)	
Maternal parity, %**						
1	60 (39.47)	51 (32.90)		77 (49.04)	57 (33.53)	
2	54 (35.53)	64 (41.29)	0.4495	45 (28.66)	61 (35.88)	**0.0164**
3 or more	38 (25.00)	40 (25.81)		35 (22.29)	52 (30.95)	
Maternal marital status, %**						
Married	102 (67.11)	120 (77.42)	**0.0435**	97 (62.58)[2]	124 (72.94)	**0.0455**
Others	50 (32.89)	35 (22.58)		58 (37.42)[2]	46 (27.06)	
Mother enrollment in RCTs, %**						
None or control group	104 (68.42)	112 (72.26)		110 (70.06)[1]	126 (74.12)	
During pregnancy	37 (24.34)	35 (22.53)	0.6716	39 (24.84)[1]	37 (21.76)	0.7088
During lactation	11 (7.24)	8 (5.16)		8 (5.10)[1]	7 (4.12)	
Gestational age, (weeks)***	39.03 (1.00)	39.26 (1.00)	**0.0594**	39.05 (1.11)	39.05 (1.15)	0.9570
Mode of delivery, %**						
Vaginal delivery	102 (67.11)	99 (63.87)	0.5512	100 (64.10)	119 (70.83)	**0.1959**
Cesarean section	50 (32.89)	56 (36.13)		56 (35.90)	49 (29.17)	
Birth weight, kg***	3.26 (0.47)	3.23 (0.44)	0.5543	3.16 (0.46)	3.11 (0.42)	0.2724

Means (standard deviation) and frequency (percentage) were presented for continuous, and categorical variables, respectively

Number of missing values 1.n=1; 2.n=2; 3.n=13; 4.n=22; 5. n=14; 6.n=32; 7.n=9; 8.n=20; 9.n=11; 10.n=31
* Independent T-test used for *p*
** Chi-squared test used for *p*
*** Mann Whitney U test used for *p*