doi.org/10.15392/2319-0612.2025.2962
Braz. J. Radiat. Sci., Rio de Janeiro
2025, 13(4) | 01-12 | e2962
Editor: Prof. Dr. Bernardo Maranhão Dantas
Editor: Prof. Dr. Alfredo Lopes Ferreira Filho
Submitted: 202506-047
Accepted: 2025-10-21

Preliminary Studies on the Distribution of Stable Pb and Pb-210 in the Maternal and Fetal Portions of Human Placentas

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Abstract: Fetal growth and survival are solely dependent on the placenta, making the characterization of toxic elements in this tissue crucial for understanding exposure during pregnancy. Stable lead (Pb) and Pb-210 are toxic elements of particular interest in this context. Stable Pb has been linked to developmental changes in children, while Pb-210, a beta-emitting radionuclide with a 22.3-year half-life, can increase cancer risk, particularly bone sarcomas, when present in excess. Placental uptake of stable Pb and Pb-210 can occur through ingestion of food and water, as well as inhalation of air, with smoking and air pollution being significant contributing factors. Recent research suggests that even low levels of environmental chemicals, especially potentially toxic elements, can significantly disrupt placental homeostasis. This preliminary study aimed at determining the concentrations of stable Pb and Pb-210 in the maternal and fetal portions of placentas from eight women who delivered at the Hospital das Clínicas, Faculdade de Medicina, University of São Paulo. Concentrations from 5.7 ± 1.2 ng g^{-1} to 210.3 ± 2.4 ng g^{-1} and from 31.5 ± 2.9 Bq kg^{-1} to 43.3 ± 3.1 Bq kg^{-1} were obtained for stable Pb and Pb-210, respectively. The results showed that both elements can cross the placental barrier and reach the fetal compartment, albeit at lower concentrations than in the maternal portion.

Keywords: stable Pb, Pb-210, placenta, smoking.

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Estudos preliminares sobre a distribuição de Pb estável e Pb-210 nas porções materna e fetal de placentas humanas

Resumo: O crescimento e a sobrevivência do feto dependem exclusivamente da placenta, portanto a caracterização de elementos tóxicos neste tecido pode fornecer informações importantes sobre sua exposição durante a gestação. Chumbo estável e Pb-210 são elementos tóxicos de interesse durante a gestação. O Pb estável pode estar associado a alterações no desenvolvimento da criança, enquanto o Pb-210, por ser um elemento radioativo emissor de radiação beta com meia-vida de 22,3 anos, quando presente em excesso no organismo pode induzir câncer, especialmente sarcomas ósseos. A entrada de chumbo estável e Pb-210 na placenta pode ocorrer pela ingestão de alimentos e água e pela inalação de ar, neste caso hábitos de fumar e/ou poluição do ar são fatores importantes. De acordo com pesquisas recentes, mesmo baixos níveis de produtos químicos ambientais, particularmente elementos potencialmente tóxicos, podem perturbar consideravelmente a homeostase placentária. O objetivo deste estudo é determinar a concentração de Pb e Pb-210 estáveis nas porções materna e fetal da placenta, de oito parturientes que deram à luz no Hospital das Clínicas da Faculdade de Medicina da Universidade de São Paulo. Concentrações variando de 5.7 ± 1.2 ng g^{-1} até 210.3 ± 2.4 ng g^{-1} e de 31.5 ± 2.9 Bq kg^{-1} até 43.3 ± 3.1 Bq kg^{-1} foram obtidas para Pb estável e Pb-210, respectivamente. Os resultados obtidos para a concentração desses elementos nas porções materna e fetal mostram que eles podem atravessar a barreira placentária e atingir o compartimento fetal, embora em concentrações menores.

Palavras-chave: Pb estável, Pb-210, placenta, tabagismo.

1. INTRODUCTION

In mammals, fetal growth and survival are solely dependent on the placenta during development; therefore, characterizing toxic elements in this tissue provides crucial information about maternal and fetal exposure [1].

Stable lead and Pb-210 are toxic elements of interest during pregnancy. Stable Pb may be associated with changes in the child's development, while Pb-210, a radioactive element emitting beta radiation with a half-life of 22.3 years, when present in excess in the body can induce cancer, especially bone sarcomas [2].

Placental uptake of Pb-210 can occur through ingestion of food and water, as well as inhalation of air, with smoking and air pollution being significant contributing factors [3].

Human exposure to stable lead, on the other hand, is mainly due to diet, inhalation of airborne contamination or ingestion of surface contamination. Several studies in literature focus on the determination of stable lead in the placenta. In a 2012 review of 79 studies, Esteban-Vasallo et al. [4] examined Hg, Cd, and Pb levels in placentas, finding that Pb exhibited the greatest variability, ranging from 1.18 ng g^{-1} in China (Shanghai) to 500 ng g^{-1} in a polluted area of Poland. More recent research indicates that even low levels of environmental chemicals, particularly toxic elements, can significantly disrupt placental homeostasis. In a 2022 review, Stojsavljević et al. [5] aimed to determine the levels of As, Cd, Pb, and Hg and their impact on placental health. Based on their reported data, placental Pb levels were notably higher in smokers and occupationally exposed pregnant women. They concluded that even low-level exposure to As, Cd, Pb, and Hg could be detrimental to proper fetal development.

The placenta is also recognized as a biomarker of maternal and fetal exposure to various toxic elements. In 2021, Molina-Mesa et al. [6] determined toxic element concentrations (Pb,

As, Cd, and Hg) in 103 placentas from women who gave birth in the Regional Maternity Hospital of Malaga (Spain), analyzing the influence of lifestyle and dietary habits. Detectable Pb concentrations were found in 84 of the 103 samples, with a mean of 70.08 ng g^{-1} (SD: 65.2). The authors concluded that tap water intake was the only variable associated with Pb presence in the studied placentas, likely due to lead contamination from pipes and plumbing materials. Falcón et al. [7] carried out a study to determine placental lead, as it was believed to be a good biomarker for fetal exposure. In this study, the average Pb concentration found was 113.4 ng/g of dry tissue. These authors were unable to relate higher levels of placental lead to lower birth weight, head and abdominal circumference, or shorter length.

Few studies have assessed Pb-210 presence in placentas. Thomas et al. [8] investigated the transfer of Po-210 and Pb-210 through the lichen-caribou-wolf food chain of northern Canada. Caribou fetuses exhibited lower Po-210 but higher Pb-210 activities compared to maternal muscle and placenta, suggesting more efficient placental transport of Pb-210 than Po-210. Salmon et al. [3] review of publications measuring both inhalation and ingestion of Pb-210 indicated that atmospheric inhalation, diet, and domestic radon contribute an average of 12, 86, and 2% to total Pb-210 uptake, respectively, with alcoholic beverages and cigarettes potentially adding a further 75%.

Despite the established high toxicity and the confirmed presence of stable Pb and Pb-210 in the placenta, leading to fetal exposure, the literature contains few studies on the transplacental transport of this element [9,10]. The aim of this study is to perform a cross-sectional assessment of the concentration of stable Pb and Pb-210 in the maternal and fetal portion of placentas to verify the transport of these elements. Therefore, the intention was not to conduct a population study, but rather an exploratory preliminary analysis of the situation. The placenta of eight women who delivered at the Hospital das Clínicas, Faculdade de Medicina, University of São Paulo were collected and analyzed.

2. MATERIALS AND METHODS

2.1 Collection and pretreatment of placentas

Placentas were collected in 2020 from eight parturient women who delivered vaginally or by cesarean section. Fragments of placental cotyledons were separated into fetal and maternal portions, then immediately frozen and lyophilized to a constant weight.

Inclusion criteria for this study were pregnant women without fetal malformations, mental disorders, or cognitive alterations, who received prenatal care as residents of São Paulo city. All participants provided written informed consent. The Research Ethics Committee of the University of São Paulo approved this study (2020/4.421.835).

2.2 Determination of Pb-210

Pb-210 determination was performed by beta counting using a low background gas flow proportional counter (Berthold, model LB770-1) following radiochemical separation of lead as $PbCrO_4$ [11]. Briefly, 0.5 g of dried placenta was digested in nitric acid and hydrogen peroxide, then diluted to one liter with ultrapure water. Lead was coprecipitated with barium as $Ba(Ra,Pb)SO_4$ by adding 50 mL of H_2SO_4. Radium and lead were then separated by dissolving the sulfate precipitate with nitrilotriacetic acid (NTA) and reprecipitating lead sulfate by adjusting the pH to 4.5-5.0 with acetic acid, discarding the radium-containing precipitate. Pb-210 in the supernatant was subsequently precipitated as PbS. After sulfide elimination with nitric acid, lead was precipitated as $PbCrO_4$ by adding 2.5 mL of Na_2CrO_4. The precipitate was filtered, and after a 10-day ingrowth period, Pb-210 was quantified by total beta counting of its daughter Bi-210. The methodology's validity was confirmed using the International Atomic Energy Agency's fish standard reference material, yielding a relative standard deviation of 3.9% and a relative error of 5.3%, indicating good precision and accuracy. Pb-210 results are expressed as the value corresponding to one determination and the associated uncertainty. The limit of detection for the determination of Pb-210 was 0,8 Bq kg^{-1}.

2.3 Determination of stable Pb

The determination of stable Pb was carried out by Triple Quadrupole Inductively Coupled Plasma Mass Spectrometry - ICP-MS (iCAP TQ ICP-MS, Thermo Fisher ScientificTM, Bremen, Germany). The methodology was adapted from EPA Method 3052 [12].

Placenta dried samples (0.05-0.10 g) were digested in Teflon vials via microwave-assisted digestion with 4 mL of HNO_3 (65% w/v), 4 mL of ultrapure water, and 0.5 mL of H_2O_2 (30% w/v). Complete digestion was confirmed by the absence of visual solid residue, and samples were diluted 250-fold. A 1.0 mL aliquot was transferred to a 15 mL polypropylene conical centrifuge tube, followed by the addition of 1.0 mL of an internal standard solution containing 10 µg L^{-1} each of Rh, Y, and Tb. The final volume was adjusted to 10 mL with 0.01% Triton X-100 and 0.5% HNO_3. Blank solutions were prepared in triplicate. A specific calibration curve for Pb was established using a 1000 mg L^{-1} mono-elemental standard solution (Plasma CAL, SCP Science TM). Method accuracy was verified through spike and recovery experiments, yielding values between 93.8% and 112.5%. Pb results were expressed as the mean of two measurements of the same sample and the corresponding standard deviation. The limit of detection for the determination of Pb was 0.0035 ng g^{-1} and the limit of quantification was 0.011 ng g^{-1}.

3. RESULTS AND DISCUSSIONS

The age of the participating parturient women ranged from 16 to 38 years, with only one reporting smoking during pregnancy. Gestational age at delivery was between 37 and 40 weeks, and newborn birth weights ranged from 2.300 to 4.300 g. Placenta weights varied from 430 to 900 g.

Table 1 presents the results obtained for the concentration of Pb (ng g^{-1} dry weight) and Pb-210 (Bq kg^{-1} dry weight) in the maternal and fetal portions of the placenta and Figure 1 presents the respective Boxplots.

Table 1: Concentration of Pb (ng g^{-1} dry weight) and of Pb-210 (Bq kg^{-1} dry weight)

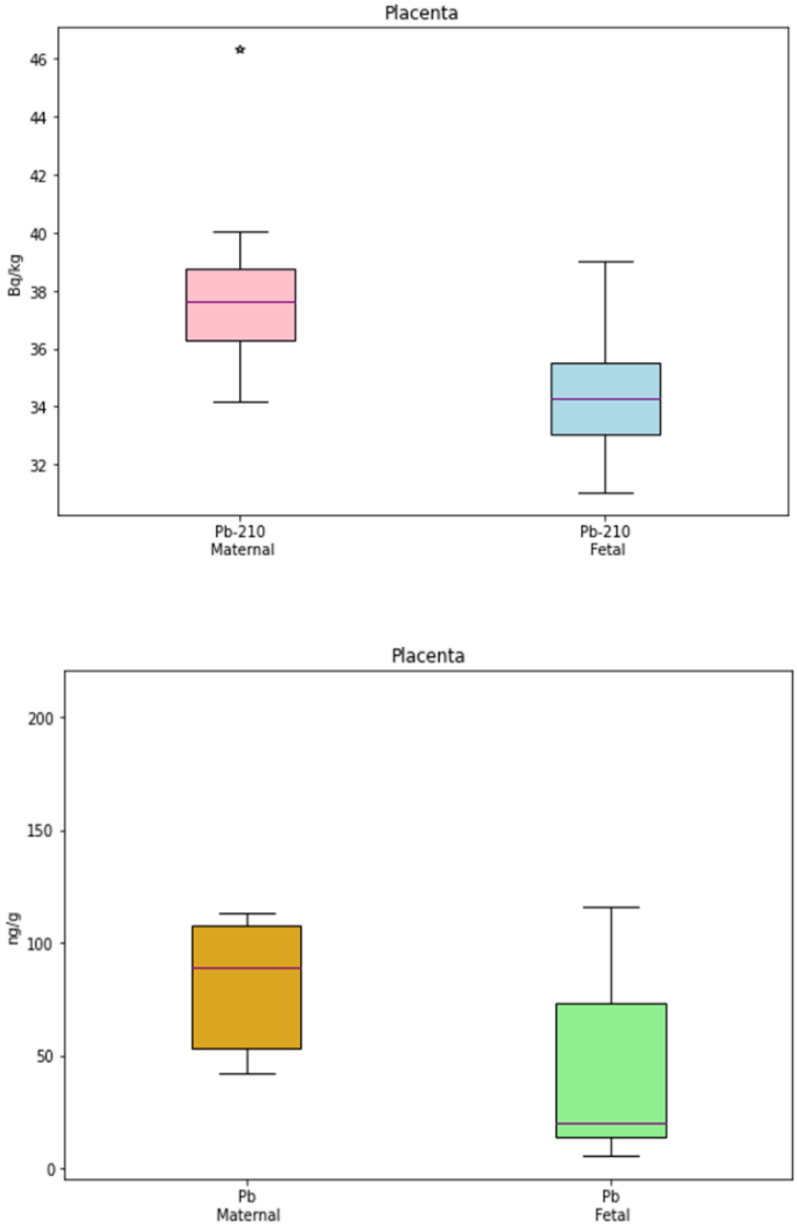
	Minimum value	**Maximum value**	**Mean**	**RSD ***
Pb-210 maternal placenta	34.2 ± 3.1	43.3 ± 3.1	37.9	7.3
Pb-210 fetal placenta	31.5 ± 2.9	39.3 ± 3.3	34.6	7.4
Pb maternal placenta	42.2 ± 10.1	210.3 ± 2.4	94.2	80.5
Pb fetal placenta	5.7 ± 1.2	116.2 ± 7.5	42.6	45.6

*RSD: Relative Standard Deviation (%).

The results of Pb-210 were homogeneous, ranging from 31.5 ± 2.9 Bq kg^{-1} to 43.3 ± 3.1 Bq kg^{-1}, with a relative standard deviation of 7,2%. The mean values found for Pb-210 were higher in the maternal portion of the placenta (37.9 Bq kg^{-1}) than in the fetal portion (34.6 Bq kg^{-1}). On the other hand, stable Pb results, although also presenting higher mean values in the maternal portion (94.2 ng g^{-1}) in relation to the fetal portion (42.6 ng g^{-1}), showed a great dispersion of the results, varying from 5.7 ± 1.2 ng g^{-1} to 210.3 ± 2.4 ng g^{-1}, with a relative standard deviation of 78.2%.

This great variability of the Pb results in the placenta was also observed by Esteban-Vasallo (2012) review of 79 studies, who reported concentrations varying from 1.18 ng g^{-1} in China (Shanghai) to 500 ng g^{-1} in a polluted area of Poland [4]. Molina-Mesa et al. (2022) also found detectable concentrations of Pb in 84 samples of 103 placentas studied in Malaga, with a mean concentration of 70.08 ng g^{-1} (SD: 65.2) [6].

Figure 1: Box plot distribution of stable Pb and Pb-210 in the Maternal and Fetal Portions of Placenta



The Anderson-Darling test was performed to verify the normality of the results. The test indicated that Pb-210 and Pb do not have a normal distribution of data for a 95% confidence interval ($p>0.05$), consequently non-parametric tests were used to carry out the statistical analysis of the results. The Mann-Whitney U test was used to determine whether there is a significant difference between the distributions of these elements in the maternal and fetal placenta. The test evaluates the null hypothesis that the probability of a randomly

selected value from one population being greater than a randomly selected value from another population is equal to the probability of the reverse. In other words, it tests whether the two populations have the same distribution. Both elements Pb-210 and stable Pb presented significant differences between the maternal and fetal portion of the placenta ($p=0.04$ and $p=0.02$, respectively).

While acknowledging the limitation of the present study, namely the analysis of a small and statistically non-representative cohort of parturient women, the findings nevertheless demonstrate the transplacental transfer of stable Pb and Pb-210 to the fetal compartment, albeit at reduced concentrations. Previously, Goyer investigation into the transplacental transport of Pb revealed the absence of a placental-fetal barrier to lead [9].

The Spearman's correlation coefficients obtained for Pb-210 and stable Pb in the maternal and fetal portion of the placenta, were 0.98 and 0.40, respectively. The placenta, as seen in Figure 1, works as a barrier, because the concentrations decrease from the maternal to the fetal parts. Nevertheless, in the case of the stable Pb a much higher dispersion was observed.

Several authors stated that smoking is the main source of Pb-210 in the body [3, 13]. Due to the small number of placentas analyzed, it was not possible to correlate Pb-210 concentration with the smoking habits of the parturient women. However, in the boxplot representation of Pb-210 and stable Pb concentrations (Figure 1), the outlier values found in the maternal placenta and the upper values found in the fetal placenta correspond to the single parturient who reported smoking during pregnancy. The study of the correlation between Pb-210 concentration and smoking habits will be addressed in a future work, once we have a more significant sample size.

4. CONCLUSIONS

In conclusion, the results obtained in this study showed that both stable Pb and Pb-210 are found in the placenta in concentrations ranging from 5.7 ± 1.2 ng g^{-1} to 210.3 ± 2.4 ng g^{-1} and from 31.5 ± 2.9 Bq kg^{-1} to 43.3 ± 3.1 Bq kg^{-1}, respectively. The concentrations observed in the maternal and fetal portion of the placenta gave evidence that there is no placental barrier and that Pb and Pb-210 are reaching the fetal compartment, albeit at reduced concentrations than in the maternal compartment. Although the literature on human exposure to stable lead and radon progeny is extensive, no studies have investigated the simultaneous placental transfer of stable Pb and Pb-210. This represents the most significant contribution of the present study.

ACKNOWLEDGMENT

This work was supported by Conselho Nacional de Desenvolvimento Científico e Tecnológico (CNPq), grant number 300835/95-7. The ICP-MS used for the determination of Pb was financed by "Fundação de Amparo à Pesquisa do Estado de São Paulo," FAPESP, 2017/20752.

Ethical approval: This study was approved by the Research Ethics Committee of the University of São Paulo (2020/4.421.835).

CONFLICT OF INTEREST

The authors declare no competing financial interests.

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