Correlation between maternal and fetal umbilical cord blood lead concentrations in Libya

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Abstract

Background: People are exposed to lead from car exhaust fumes (leaded petrol), lead-based paints, plumbing systems, cigarette smoking, contaminated soil and dust, foods grown in polluted areas, and water sources. Among the vulnerable subpopulations are pregnant women, fetuses and infants.

Aims: To estimate and correlate maternal and neonatal blood lead levels and compare these between neonates and their mothers in Tripoli and Ghadames.

Methods: In this cross-sectional study, blood was collected from 120 and 116 mothers and their neonates from Tripoli and Ghadames, respectively. Lead levels were determined using atomic absorption spectrophotometry. A simple questionnaire was filled by the participants using face-to face interview. Data were analysed using SPSS version 20.0 and Excel.

Results: Mean blood and umbilical cord lead levels were 6.83 (standard deviation 4.96) and 6.05 (4.89) µg/dl in mothers and neonates from Tripoli, respectively, and 5.91 (4.02) and 4.54 (4.09) µg/dl from Ghadames. There was no significant difference in blood lead level between mothers from Tripoli and Ghadames. However, there was a significant correlation between maternal blood and umbilical cord blood in Tripoli and Ghadames. Linear regression revealed that neonatal umbilical cord blood lead levels reflected the levels in maternal blood. Blood lead in this study was higher than that reported in industrialized western countries.

Conclusion: We detected moderate blood lead levels among pregnant women in Tripoli and Ghadames. It is important to detect the source of lead in the Libyan population to treat this problem effectively.

Keywords: blood, lead, maternal, neonatal, neonate, umbilical cord, Tripoli, Ghadames, Libya

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Introduction

Environmental pollution with toxic heavy metals represents a major problem to human health worldwide, and especially in cities. These metals accumulate in the human body and cause serious health disorders (*1*,*2*). Lead is a toxic heavy metal that is widely used in different industries and it has no known function in the human body. Humans are exposed to lead from car exhaust fumes (leaded petrol), tyres, lead-based paints, plumbing systems, cigarette smoking, contaminated soil and dust, foods grown in polluted areas, lead-contaminated opium, and water sources (*3–5*). Previously, the United States Centers for Disease Control and Prevention proposed a population-based paediatric blood lead concentration of 10 µg/dl as an *acceptable* level (*6*). Deficits in cognitive and academic functions have been shown to occur at blood lead levels < 5 µg/dl (*7*). In addition, blood lead concentration was inversely and significantly associated with individuals' IQ level (*8*). These studies have shown that there is no safe lead level for fetal intellectual development.

Pregnant women, fetuses and infants are among the vulnerable subpopulations affected by lead exposure. It has been proposed that lead is transferred across the placenta, probably by simple diffusion in the umbilical cord blood (*9*), and there is a suggestion that placental transfer of lead is facilitated by Ca^{2+} transport mechanisms during late gestation (*10*). Embryonic life is a critical stage in human life, and exposure of the fetus to chemicals including heavy metals affects pregnancy outcome and subsequent life stages (*11*). Heavy metals accumulate in the maternal blood circulation system and reach the fetus through the placenta (*12*), leading to negative effects on pregnancy progression and fetal growth, such as spontaneous abortion, stillbirth, neonatal death, fetal physical dysmorphology, and mental retardation (*13*,*14*). Lead exposure may also cause gestational hypertension (*15*).

Several studies have investigated lead levels in the blood of pregnant mothers and their fetal umbilical cord in different populations, with contradicting results. To the best of our knowledge, no such studies have been conducted among the Libyan population. The present study was designed to estimate and compare blood lead levels in neonatal umbilical cord and mothers in the coastal city of Tripoli and desert city of Ghadames.

Methods

Study location and setting

This cross-sectional study was conducted at the labour wards and neonatal units of the Tripoli Medical Center and Ghadames General Hospital, Libya. Tripoli is the capital of Libya and located in Northwestern Libya along the *Mediterranean coast*. It is the largest commercial and manufacturing centre in Libya, and is therefore a major source of the population's environmental lead exposure. It is an overcrowded city with over 2.3 million inhabitants and a heterogeneous population. In comparison, Ghadames is a small desert city, located about 543 km southwest of Tripoli with about 15 000 inhabitants and a homogeneous population. Tripoli has heavier traffic levels than Ghadames. Tripoli Medical Center is a 1200-bed hospital providing healthcare to inhabitants of Tripoli and neighbouring cities, while Ghadames General Hospital is a 136-bed hospital providing healthcare to inhabitants of the city and neighbouring villages. Blood lead concentration analysis was carried out at the Biotechnology Research Center, Tripoli (BRTC). This study was conducted from January 2014 to May 2015, with some interruptions anytime there was an eruption of armed conflicts.

Sample size estimation

The sample size was derived using the following formula (*16*).

$$n \geq \frac{(Z1-\frac{\alpha}{2}+Z1-\beta)^2\ (\frac{\delta_1^2+\delta_2^2}{r})}{(\mu_1-\mu_2)^2}$$

where $Z_{\alpha/2}$ is the critical value of the normal distribution at $\alpha/2$ (e.g., for a confidence level of 95%, α is 0.05 and the critical value is 1.96); Z_β is the critical value of the normal distribution at β (e.g., for a power of 80%, β is 0.2 and the critical value is 0.84); and σ^2 is the population variance for each city, and r is the ratio between Group 2 and Group 1. This study involved the measurement of lead in blood of mothers and their fetal umbilical cord . Since there are no local published studies on lead in umbilical cord blood and maternal blood, the mean and standard deviation (SD) for Tripoli was estimated at 3.5 and 1.4, respectively, compared with 3 and 1.4 for Ghadames, and the ratio between Group 2 and Group 1 was 1.1. The sample size calculated was 118 per group.

Ethical approval and recruitment of subjects

Before initiation, the study protocol was approved by the Ethics Committee of BTRC. The participant mothers signed informed consent for themselves and their neonates. The mothers were invited to take part in the study on their arrival in the ward for delivery. Detailed information about the study was explained to all mothers, who were consecutively recruited until the appropriate sample size was reached. However, cases with pre-eclampsia, fetal death, antepartum haemorrhage, and those who did not sign the consent were excluded. Thereafter, a simple self-made questionnaire was filled through face-to-face interview. The questionnaire included maternal age, body weight, height, prior pregnancies, infants' weight, primiparity, previous abortion, caesarean delivery, maternal education, and mothers on supplements.

Blood sample collection

One hundred and twenty mothers and their neonates from Tripoli Medical Center and 116 from Ghadames General Hospital were recruited. Five millilitres of maternal venous blood was collected immediately before delivery, while umbilical cord blood samples were collected at delivery prior to cutting of the cord. Both blood samples were collected in trace-metal-free EDTA tubes (Vacutainer; Becton Dickinson, Franklin Lakes, NJ, USA). The samples from Tripoli were stored in the ward refrigerator at 4°C and transported within 24 hours, and samples from Ghadames were stored at −20°C and transported within 1 week to the BTRC laboratories. A cold box was used for sample transportation.

Blood lead analysis

Total blood lead concentration was determined by a well-trained laboratory technician at the BTRC laboratories using graphite furnace atomic absorption spectrometry (Varian SpectrAA 250+, Varian Australia Pty Ltd., Mulgrave, VIC, Australia) that was calibrated with serial standard concentrations of 0, 1, 6.25, 12.50, 25, 50 and 100 µg/dl. The readings were taken at a wavelength of 283.3 nm.

Statistical analysis

Data were analysed using SPSS for Windows version 20. Medians and mean (SD) of different parameters were calculated. The χ^2 test was used to compare proportions. Correlation between maternal and umbilical cord blood lead concentrations was tested. Linear regression was used to test the relation of lead concentrations between mothers and their neonates. For variables with skewed distribution the Mann–Whitney *U* test and Kruskal–Wallis *H* test were used for comparison. The significance threshold was set at 0.05

Results

A total of 120 women and their neonates from Tripoli and 116 women an their neonates from Ghadames participated in this study. Maternal age, body mass index (BMI), infants' weight, number of previous pregnancies and lead concentrations were tested for normality using the Shapiro–Wilk test, and none of them appeared to be normally distributed. Hence, we decided to use nonparametric tests. We used the Mann–Whitney test to compare differences between 2 independent variables and the Kruskal–Wallis *H* test to determine if there were significant differences between more than 2 groups of independent variables.

The Mann–Whitney test indicated that age was significantly higher for mothers from Tripoli (median = 33 years) than from Ghadames (median = 29 years) (Table 1). BMI was significantly greater for mothers from Ghadames (median = 26) than from Tripoli (median = 24.85). There was no significant difference in the number of previous pregnancies between mothers from Tripoli and Ghadames (both median = 3). Infants' weight was significantly higher for infants from Tripoli (median = 3.0 kg) than from Ghadames (median = 2.35 kg).

Table 1 **Characteristics of the participating mothers and their neonates from Tripoli and Ghadames**

Characteristics	Tripoli (N = 120) Median/IQR, mean (SD)	Ghadames (N = 116) Median/ IQR, mean (SD)	*P*
Age (yr)	33/28–38[a], 32.65 (6.31)[b]	29/26–35[a], 30.33 (5.79)[b]	0.007[c]
BMI	24.85/23.54–26.37[a], 25.02 (2.4)[b]	26/24.55–26.81[a], 25.76 (1.90)[b]	0.004[c]
No. of prior pregnancies	3/2–4[a], 2.90 (1.20)[b]	3/2–4[a], 2.70 (1.22)	0.231[c]
Infants weight (kg)	3/2.35–3.02, 2.76 (0.53)	2.35/2.05–3.0, 2.50 (0.60)	< 0.001[c]
	N (%)	N (%)	
Maternal age, yr			
20–30	44 (36.67)	67 (57.76)	
31–40	56 (46.67)	43 (37.07)	< 0.001[d]
41–50	20 (16.67)	6 (5.17)	
Primiparity	17 (14.17)	24 (20.69)	0.19[d]
Previous abortion	69 (57.50)	32 (27.59)	< 0.001[d]
Caesarean delivery	57 (47.50)	26 (22.41)	< 0.001[d]
Maternal education			
Higher education	87 (72.5)	58 (50.00)	
Secondary	5 (4.17)	31 (26.72)	< 0.001[d]
Preparatory	28 (23.33%)	27 (23.28%)	
Mothers on supplements	71 (59.17%)	41 (35.34%)	< 0.001[d]

[a]Median/IQR; [b]median (SD); [c]Mann–Whitney U test; [d]χ^2 test. IQR = interquartile range; SD = standard deviation.

The highest percentage of the pregnant women from Tripoli were aged 31–40 years and the highest percentage of pregnant women from Ghadames were aged 20–30 years, which showed a significant difference (Table 1). There were more women aged 40–50 years from Tripoli than from Ghadames. Of the 120 mothers from Tripoli, 14.17% were primiparous compared with 20.69% of women from Ghadames. For abortion, 57.50% of mothers from Tripoli had a previous abortion compared with only 27.59% of mothers from Ghadames. The percentage of mothers who delivered through caesarean section was significantly higher in Tripoli (47.50%) than in Ghadames (22.41%). Significantly more mothers from Tripoli than from Ghadames received higher education. In Tripoli, 59.17% of mothers were taking supplements compared with 35.34% of mothers from Ghadames.

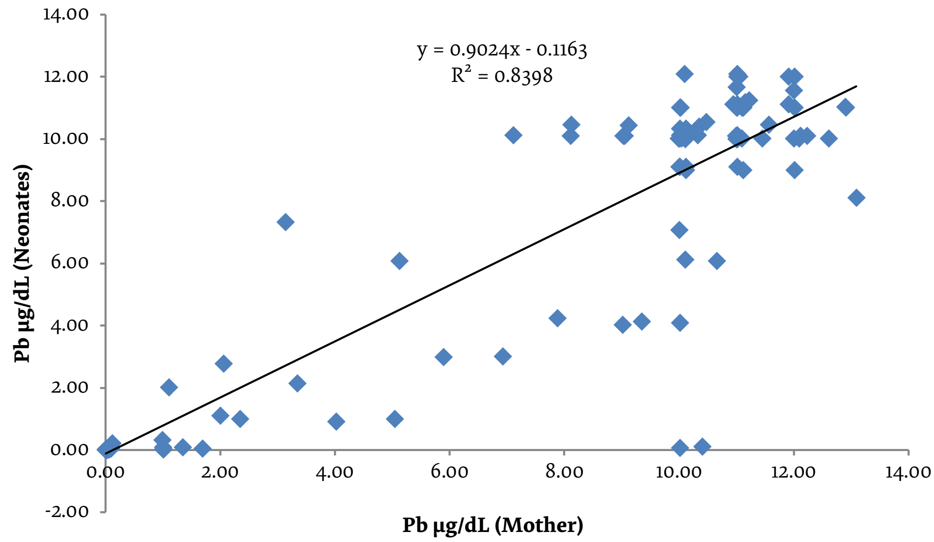
Lead concentration was measured in neonatal umbilical cord blood and maternal blood in Tripoli and Ghadames. The highest concentrations of lead recorded in this study were 13.09 µg/dl in mothers from Tripoli, 12.92 µg/dl in mothers from Ghadames, 12.10 µg/dl in neonates from Tripoli, and 12.0 µg/dl in neonates from Ghadames. The lead concentration ranged from 0 to 13.09 µg/dl and from 0 to 12.10 µg/dl in mothers and their neonates from Tripoli, respectively. For mothers and their neonates from Ghadames, the lead concentration ranged from 0.03 to 12.92 µg/dl and from 0.02 to 12.0 µg/dl, respectively. The lead concentration in neonatal blood from Tripoli was about 88.58% of that in maternal blood, and lead concentration in neonatal blood from Ghadames was about 76.82% of that in maternal blood. Mean blood and umbilical cord lead levels were 6.83 (4.96) and 6.05 (4.89) µg/dl in mothers and neonates from Tripoli, respectively, and 5.91 (4.02) and 4.54 (4.09) µg/dl from Ghadames. There was a significant positive correlation between lead concentrations in maternal and umbilical cord blood in Tripoli (r = 0.916) and Ghadames (r = 0.938). There was a general positive correlation (r = 0.924) between lead concentrations of all mothers and their infants.

We used simple linear regression to investigate the relation between maternal and neonatal lead concentrations. Figure 1A shows that, for Tripoli cases, the linear regression line equation was: $y = 0.9024x - 0.1163$ with $r^2 = 0.84$ and Figure 1B shows that, for Ghadames cases, the linear regression line equation was: $y = 0.9525x - 1.0927$ with $r^2 = 0.88$.

The Kruskal–Wallis *H* test was used to investigate the difference in lead concentrations in the maternal and neonatal blood according to maternal age. There was no significant difference in lead concentration between different age categories in mothers and their neonates from Tripoli [P = 0.796, degrees of freedom (df) = 2] for mothers and *P* = 0.894, df = 2 for neonates]. However, there was a significant difference in lead concentration between different age categories in mothers and neonates from Ghadames: $P < 0.001$, df = 2 for mothers and $P < 0.001$, df = 2 for neonates. Pairwise comparison of the latter showed that the difference was between mothers aged 20–30 years and 31–40 years and their neonates.

The Mann–Whitney *U* test indicated that the lead concentrations in the blood of mothers in Tripoli who had a previous abortion were significantly greater (median = 11.0) than in mothers who had not (median = 0.08, $P < 0.001$). Similar results were obtained for mothers from Ghadames; lead concentrations in those who had

Figure 1 (A) Simple linear regression of neonatal blood lead concentrations as a function of maternal blood lead concentrations in Tripoli; *n* = 120; r2 ≈ 0.84; y = 0.9024x – 0.1163



a previous abortion were significantly greater (median = 11.01) than in mothers who had not (median = 4.19, *P* < 0.001).

Correlation analysis of the relationship between neonatal blood lead concentrations and birth weight showed that the correlation coefficient was −0.05 (*P* = 0.598) and 0.21 (*P* = 0.025) for Tripoli and Ghadames, respectively.

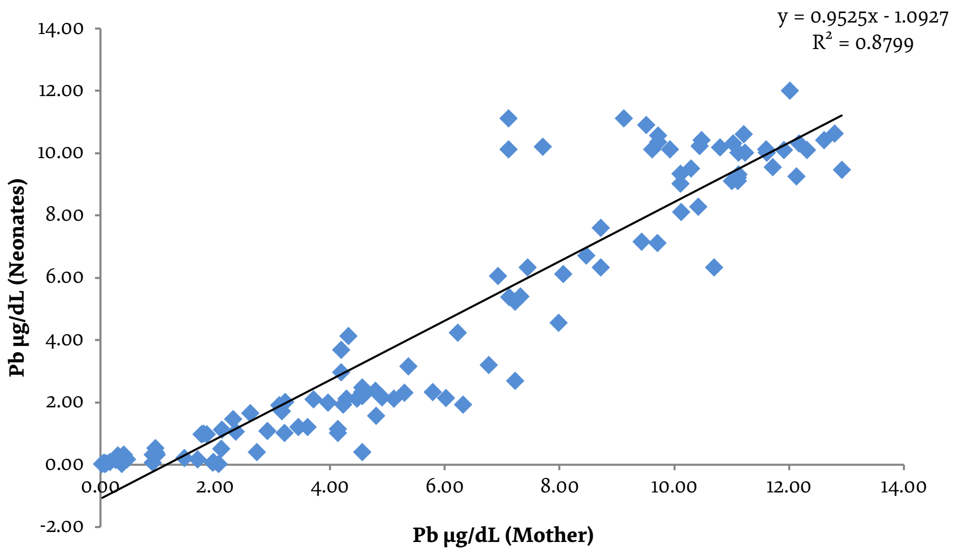
Discussion

To the best of our knowledge, the current cross-sectional study was the first to investigate blood lead concentrations in mothers and their neonates in Tripoli and Ghadames in different environmental settings. Our results clearly show that lead was present in the blood of most mothers and their neonates. This suggests that more studies are needed to detect the sources of lead in the environment to resolve this problem, especially since Libya has been using lead-free petrol (the major source of lead) since 2006.

One of the measures taken in Libya and other countries was to stop the use of leaded petrol. Blood lead concentrations in countries that have stopped using leaded petrol, such as the United States of America (USA) have improved to satisfactory levels (*17*).

The highest lead concentrations in neonatal umbilical cord blood and maternal blood in Tripoli and Ghadames were lower than those obtained in India and Spain (*18*,*19*), but higher than in Sweden, USA and Republic of Korea (*20*,*21*). The lead concentrations in neonatal blood in Tripoli and Ghadames compared to those in maternal

Figure 1 (B) Simple linear regression of neonatal blood lead concentrations as a function of maternal blood lead concentrations in Ghadames; *n* = 116; r2 ≈ 0.88; y = 0.9525x – 1.0927



blood is consistent with previous reports (*20–22*). There was a clear correlation of lead concentrations between mothers and neonates in Tripoli and Ghadames. In other words, the neonatal lead concentration reflects that in mothers. This confirms that lead can readily cross the placenta from mother to fetus (*9,20,23*).

The distribution of lead concentrations in maternal and neonatal blood according to maternal age revealed that, in Tripoli, there were no significant differences between the three age categories. However, in Ghadames, there were significant differences, with the highest concentrations seen in mothers aged 31–40 years. The reason for that is not clear. In all age categories, the mean blood lead concentrations were higher in the mothers than in their neonates.

We investigated the relation between maternal lead concentrations and previous abortion. The Mann–Whitney *U* test showed that there was increase in previous abortion in mothers with higher lead concentrations compared to those with lower lead concentrations in Tripoli and Ghadames. This is in agreement with previous studies (*24–27*). Our results indicate that there was no correlation between neonates from Tripoli and their birth weight but there was a relation in neonates from Ghadames, and the latter is in agreement with previous studies (*28,29*).

The main limitation of this study is that it did not represent the whole of Libya, which makes it important to conduct more studies to investigate the extent of lead contamination throughout the country.

Conclusions

The current study clearly shows that lead is present in the blood of most mothers and neonates studied. Preventive measures should be taken to reduce environmental lead contamination caused by human exposure. The possible sources of lead contamination in our population may be food or water. However, to detect sources of lead contamination are needed.

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Corrélation entre la concentration de plomb dans le sang maternel et du cordon ombilical fœtal en Libye

Résumé

Contexte : Les populations sont exposées au plomb provenant des gaz d'échappement des voitures (essence au plomb), aux peintures à base de plomb, aux systèmes de plomberie, au tabagisme, aux sols et poussières contaminés, aux aliments cultivés dans les zones polluées et aux sources d'eau. Les femmes enceintes, les fœtus et les nourrissons font partie des sous-populations vulnérables.

Objectifs : Estimer les niveaux de concentration de plomb dans le sang maternel et néonatal, établir une corrélation entre ces niveaux et les comparer chez les nouveau-nés et leurs mères à Tripoli et Ghadamès.

Méthodes : Dans la présente étude transversale, le sang a été prélevé sur 120 et 116 mères et leurs nouveau-nés à Tripoli et Ghadamès, respectivement. Les concentrations de plomb ont été déterminées par spectrophotométrie d'absorption atomique. Les participants ont rempli un questionnaire simple lors d'un entretien en face à face. Les données ont été analysées à l'aide du logiciel SPSS version 20.0 et Excel.

Résultats : La concentration moyenne de plomb dans le sang et le cordon ombilical était de 6,83 µg/dl (écart type 4,96) et 6,05 µg/dl (écart type 4,89) chez les mères et les nouveau-nés à Tripoli, respectivement, et de 5,91 µg/dl (écart type 4,02) et 4,54 µg/dl (écart type 4,09) à Ghadamès. La concentration de plomb dans le sang ne variait pas de manière considérable entre les mères de Tripoli et de Ghadamès. Cependant, il y avait une corrélation significative entre le sang maternel et le sang du cordon ombilical à Tripoli et à Ghadamès. La régression linéaire a révélé que la concentration de plomb dans le sang du cordon ombilical néonatal reflétait celle du sang maternel. Les concentrations de plomb dans le sang observées dans cette étude étaient plus élevées que celles rapportées dans les pays occidentaux industrialisés.

Conclusion : Nous avons détecté des concentrations modérées de plomb dans le sang chez les femmes enceintes à Tripoli et à Ghadamès. Il est important d'identifier la source d'exposition au plomb dans la population libyenne pour traiter ce problème efficacement.

الارتباط بين تركيزات الرصاص في دم الحبل السري للأم والجنين في ليبيا

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الخلاصة

الخلفية: يتعرض الناس للرصاص من الأبخرة المنبعثة من عوادم السيارات (إذ يحتوي البنزين على الرصاص)، والدهانات القائمة على الرصاص، ونظم السباكة، وتدخين السجائر، والتربة والغبار الملوثيْن، والأطعمة المزروعة في مناطق ملوثة، ومصادر المياه. ومن بين الفئات السكانية الفرعية الأعلى عرضة للخطر النساء الحوامل، والأجنة، والرضعَ.

الأهداف: هدفت هذه الدراسة الى تقدير مستويات الرصاص في الدم لدى الأمهات والحديثي الولادة والربط بينها ومقارنتها في صفوف الحديثي الولادة وأمهاتهم في طرابلس وغدامس.

طرق البحث: في هذه الدراسة المقطعية جُمعَت عينات الدم من 120 أمًّا و116 من أطفالهن الحديثي الولادة من طرابلس وغدامس. وحُددت مستويات الرصاص بقياس الطيف الضوئي للامتصاص الذري. وملأ المشاركون استبيانًا بسيطًا عبر مقابلة شخصية جرت وجهًا لوجه. وحُلِّلت البيانات باستخدام الإصدار 20.0 من برمجية SPSS وبرنامج إكسل.

النتائج: بلغ متوسط مستويات الرصاص في الدم والحبل السري 6.83 (انحراف معياري 4.96) و6.05 (4.89) ميكروجرام/ ديسيلتر لدى الأمهات والحديثي الولادة في طرابلس، على التوالي، و5.91 (4.02) و4.54 (4.09) ميكروجرام/ ديسيلتر لدى الأمهات والحديثي الولادة في غدامس. ولم يكن هناك اختلاف يُعتد به في مستوى الرصاص في الدم في صفوف الأمهات في المدينتين. ولكن ظهر ارتباط ملحوظ بين دم الأم ودم الحبل السري في كلتيهما، وكشف الانحدار الخطي عن أن مستويات الرصاص في دم الحبل السري لحديث الولادة تعكس مستويات الدم لدى الأم. وكانت نسبة الرصاص في الدم في هذه الدراسة أعلى من تلك المسجلة في الدول الغربية الصناعية.

الاستنتاجات: رصدنا مستويات متوسطة من الرصاص في الدم لدى النساء الحوامل في طرابلس وغدامس. ومن المهم الكشف عن مصدر الرصاص في صفوف السكان الليبيين لمعالجة تلك المشكلة على نحو فعَّال.

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