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Iron deficiency anaemia and blood lead concentrations in Brazilian children

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ABSTRACT

This study investigated the relationship between iron deficiency/iron deficiency anaemia, assessed by several parameters, and blood lead concentration in children.

This cross-sectional study involved 384 Brazilian children, aged 2–11 years, who lived near a lead-manipulating industry. Complete blood counts were obtained by an automated cell counter. Serum iron, total iron binding capacity (TIBC) and ferritin were determined respectively, by colorimetric, turbidimetric methods and chemiluminescence. Blood lead was measured by atomic absorption spectrophotometry. The impact of several parameters for assessment of iron status (haemoglobin, serum iron, TIBC, transferrin saturation, ferritin, red cell indices and red cell distribution width) and variables (gender, age, mother's education, income, body mass index, iron intake, and distance from home to lead-manipulating industry) on blood lead concentration was determined by multiple linear regression.

There were significant negative associations between blood lead and the distance from home to the lead-manipulating industry ($P < 0.001$), Hb ($P = 0.019$), and ferritin ($P = 0.023$) ($R^2 = 0.14$). Based on these results, further epidemiological studies are necessary to investigate the impact of interventions like iron supplementation or fortification, as an attempt to decrease blood lead in children.

1. Introduction

The interaction between nutritional deficiencies and toxic metals, especially lead, has been of great interest in view of the concerns about environmental pollution. Children are considered a high risk group for iron deficiency and lead poisoning. Iron deficiency is the most common nutritional disorder in the world and the main cause of anaemia in childhood, with a high prevalence in developing countries. Children are at particular risk of iron deficiency due to their high demands for iron during a period of rapid growth and because their diet is often too low in available iron.[1]

Lead is a toxic metal with no physiological function in the body. Lead poisoning has resulted from fast industrialization, including mining, food can solders, dyes (mainly paints), and the manufacture and use of glazed household pottery, in developing countries without environmental controls. In a lead contaminated environment children are more exposed to lead because they have more hand-to-mouth activity and absorb lead more efficiently than do adults.[2]

Both iron deficiency and lead toxicity are detrimental to the growth and development of children causing behavioural and cognitive problems, and poor school performance.[1,3,4] Even blood lead concentrations below

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10 μg/dL (0.48 μmol/L) have been associated with negative outcomes in infancy and childhood.[3,5] Deficient iron stores not only seem to augment the risk of lead absorption considering the existence of a common intestinal iron-lead transporter (divalent metal transporter 1),[6] but also increase lead retention in tissues as well as toxicity of this metal.[7]

There are still controversies regarding the association between iron deficiency/iron deficiency anaemia and blood lead concentrations; some studies have shown an association[8–12] whereas others have not.[13,14] Therefore, the objective of this study was to assess the relationship between blood lead concentration and several parameters for assessment of iron status.

2. Materials and methods

This cross-sectional study involved 384 pre-school and school children, aged 2–11 years, who participated in a prospective cohort epidemiological study carried out in Santo Amaro da Purificação city, Northeast Brazil, from 2001 to 2003. The city was chosen for its vicinity to a lead-manipulating metal industry which had been in activity for 33 years until its closure at the end of 1993. According to a previous study carried out in Brazil, lead poisoning seems to constitute a public health problem in this region of the country.[15]

All the children aged 2–11 years attending a pre-school or school in Santo Amaro city were invited to participate in the study. Their parents or guardians received detailed information about the study, and gave formal consent prior to data collection. They were interviewed before blood collection to obtain information on demographic and socioeconomic factors, and area of residence. The anthropometric data were obtained according to Jelliffe and Jelliffe[16] recommendations. The children were weighed, after having fasted for 10–12 hours, by a portable electronic scale (Sohnle®, model 7500, Nassau, Germany), with accuracy of 100 g. Their height was measured using a SECA® stadiometer (Leicester Portable Height measure model, Hamburg, Germany), with accuracy of 0.1 cm. The body mass index (BMI) was classified according to the Centers for Disease Control and Prevention (CDC):[17] low weight (<5th percentile); normal weight (5–85th percentile); risk of overweight (>85–95th percentile); overweight (≥95th percentile).

Fasting venous blood samples were collected from the children by a trained nurse, in the main laboratory of the city, into dry tubes, and tubes with EDTA and trace metal-free heparin. Complete blood counts were performed on the samples within 4–6 hours of collection using a CellDyn 3000 CD® (Abbott Laboratory, Maidenhead, Berkshire, UK) automated cell counter. Serum iron and total iron binding capacity (TIBC) were determined by colorimetric and turbidimetric methods respectively, using the SYNCHRON CX® system (Beckman Coulter, Miami, USA). Serum ferritin was assessed by chemiluminescence in the DPC 1000 IMMULITE® equipment (Diagnostic Products Corporation - DPC, Los Angeles, USA). All the measurements were performed in duplicate, including lead determination (coefficient variation = 3%).

The blood samples for lead determination were stored in a refrigerator at 6 °C, properly transported to the Toxicology section of Adolfo Lutz Laboratory in São Paulo city, and analysed within 15 to 30 days. Blood lead was measured by graphite furnace atomic absorption spectrophotometry method with Zeeman background correction (Model SIMAA 6000AA Spectrometer, Perkin-Elmer, Norwalk, CT, USA). The samples were diluted 1:10 with 1% Triton X-100 in 0.1% nitric acid, and a mixture of ammonium dihydrogen phosphate and magnesium nitrate was used as chemical modifier.[18] The quantification limit obtained for lead was 0.01 μmol/L (0.2 μg/dL) in 1:10 blood dilution, corresponding to 0.10 μmol/L in total blood. For determination of the quantification limit, a blood sample was obtained from a non-exposed person. Lead concentrations were determined in 10 preparations, and the calculation was made according to the International Union of Pure and Applied Chemistry (IUPAC) recommendations.[19] We gave the blood samples that showed lead levels below the quantification limit a value corresponding to 0.048 μmol/L (half of the limit value of the quantification method). To determine the accuracy of the method, we used a lead reference material in bovine blood (NIST 955b, level 2), obtaining a 96% recovery. Children were considered as being lead contaminated if their blood lead concentrations were equal to or greater than 0.48 μmol/L (10 μg/dL).[5]

The cut-off points adopted for the diagnosis of iron deficiency anaemia were haemoglobin (Hb) <11 g/dL for children aged less than 6 years, and <12 g/dL for those children aged 6 years or more, ferritin values <12 μg/L, TIBC ≥410 μg/dL, serum iron <40 μg/dL, and transferrin saturation (TS) <10%.[20] Reference ranges for mean corpuscular volume (MCV) (75–87 fl for children <6 years; 77–95 fl for children ≥6 years), mean corpuscular haemoglobin (MCH) (24–30 pg for children <6 years; 25–33 pg for children ≥6 years) and mean corpuscular haemoglobin concentration (MCHC) (31–37 g/dL for children <12 years) were established according to the age of the children.[20] There is no clear cut-off point for red cell distribution width (RDW) in infancy. Therefore, the <15% cut-off point established by the equipment was adopted.

To estimate the intake of foods rich in iron a 24 h diet recall was used three times, together with a food frequency questionnaire, applied to the parents or guardians of the children. The values obtained were compared with the dietary reference intake (DRI) for iron.[21] The Recommended Dietary Allowances (RDA) cut-off points for children aged 1–3 years, 4–8 years, and 9–13 years were respectively 7, 10 and 8 mg/day of iron. To estimate the foods most ingested by the children, a total of 100 women in the region were interviewed three times (two weekdays and one day in the weekend), by two dieticians from our team, in the rainy and dry seasons, with a month interval, using a 24 h diet recall. In a study carried out by the same authors in Santo Amaro city (unpublished data), we asked how often on average fruits and vegetables (with seasonal variation) were consumed in season. A list of seasonal fruits and vegetables and the length of season for each item were calculated, allowing us to take seasonality into