ORIGINAL ARTICLE

Correlation between blood lead concentration and iron deficiency in Iranian children

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ABSTRACT

Background: Iron deficiency anaemia is the most common nutritional anaemia among children. Lead toxicity is a serious health threat, especially in developing countries due to environmental pollution. It was thus aimed to investigate correlation between blood lead concentration and iron deficiency in children of Mashhad, Iran. **Materials and Methods:** This cross sectional study was performed on children between 1 year and 10 years, in Imam Reza teaching hospital of Mashhad, Iran, in 2010. Indeed during complete blood count (CBC), we measured iron and total iron binding capacity (TIBC) by colorimetric methods, ferritin by radioimmune assay and blood lead concentration by atomic absorption method. Results were analysed by Statistical Package for Social Sciences (SPSS) (version 11.5), using statistical tests including independent sample *t*-test, Mann-Whitney U test, Spearman's test and analysis of variance (ANOVA) and Pearson's or Spearman's correlation coefficient. *P* value ≤ 0.05 was considered as a significant level. **Results:** We studied 223 cases including 98 control children and 125 patients. All children had lead intoxication. Mean (±SD) blood lead concentration in the control group was 57.1 ± 25.3 (ranged 20-212) µg/dl and in the patient group was 57 ± 20.4 (ranged 10.9-159) µg/dl with no significant difference (*P* value = 0.713). We also did not find any correlation between blood lead concentration and haemoglobin, ferritin, iron, TIBC, mean corpuscular volume (MCV), mean corpuscular haemoglobin (MCH), mean corpuscular haemoglobin concentration (MCHC), white blood cells (WBC) and platelets. **Conclusion:** Based on these results, no correlation was found between blood lead concentration and iron deficiency in the children. Because all children had lead intoxication, further studies in highly polluted and a comparison with a low polluted area are necessary to make a general conclusion.

Key words: Anaemia, iron deficiency, lead

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INTRODUCTION

Iron deficiency (ID) is the most common nutritional disorder among children and lead toxicity, especially in developing countries, is the most common environmental health threat, because of rapid urbanisation and uses of leaded fuels, dyes and glazed household pottery and so on.[1,2] Children especially infants are at high risk for ID because of high demand for iron and low diet iron during a period of rapid growth. Both ID and lead poisoning are harmful for early development and growth in children and may cause profound neurologic and developmental effects such as cognitive and behaviour problems.[3-5] During 1976-1980, blood lead concentration was more than 10 µg/dl in 78% of people in the United state, but it was reduced to 20% in 1998.[3] However, in developing countries such as Iran lead pollution is a serious problem[6] and previous studies in children have shown a blood lead concentration > 10 µg/dl in 41-75% of children in large crowded cities.[1,7] The US Environmental Protection Agency has suggested a threshold level of 20-40 µg/dl for anaemia in children.

There are still controversies about the association between ID and blood lead concentration. Although some studies especially in children have showed an association between ID and high blood lead concentration,[3,8-15] some other studies have not confirmed this.[4,10,16] It have been speculated that iron and lead compete for absorption in the small intestine and

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in children with inadequate amounts of iron consumption, lead absorption will be increased.[17,18] Even some other study such as Wolf A *et al*., showed that iron supplement therapy in children with ID could reduce blood lead level.[18]

There has been controversy on the association between ID and blood lead concentration in children and due to high frequency of ID and lead toxicity in this age group especially in underdeveloped and developing countries like Iran, we evaluated this association. In addition, if this association is causative, then preventing ID persons in target high risk group might prevent lead poisoning.[4,18]

MATERIALS AND METHODS

This cross sectional study was approved by local ethic committee and performed on 230 children aged 1-10 years, in Imam Reza teaching hospital of Mashhad (a big city located in northeast Iran) in 2010. After obtaining a informed consent and a short history from children referred to laboratory for evaluation of ID, 2 ml anticoagulated blood with ethylene diamine tetraacetic acid (EDTA)-K2 for measurement of complete blood count (CBC) and blood lead concentration and 4 ml blood without anticoagulant for determination of iron, total iron binding capacity (TIBC) and ferritin was taken. Because ferritin is an acute phase reactant, children with any evidence of acute or chronic infection in medical history and clinical examination were excluded from this study.

Blood lead concentration was measured by an atomic absorption spectrophotometer using heated graphite atomisation technique (Perkin Elemer, Model 3030). Quality control for this analysis was done with two normal and high levels of commercial control material (Seronorm™, Sweden) everyday. According to the U.S. Centres for Disease Control and World Health Organisation (WHO) standards, blood lead concentration ≥ 10 µg/dl was considered as lead intoxication.[4,7,19] CBC, haemoglobin, haematocrit and red blood cells (RBC) indices were measured by a cell counter (Sysmex K-21, Japan). Serum ferritin was determined by radioimmune assay (Kavoshyar reagent-Iran) and serum iron and TIBC by colorimetric methods. Iron deficiency anaemia (IDA) in this age range group was defined as haemoglobin < 11 gr/dl[20] and ferritin < 20 µg/L and/or iron < 50 µg/dl plus TIBC > 350 µg/dl (transferrin saturation < 15%). Children with similar decrease in ferritin or transferrin saturation without anaemia were defined as iron ID.[21] Children with normal ranges of Iron, TIBC, ferritin and haemoglobin were considered as a control group. Sequencing effects in developing IDA is initially as ID and then IDA. This shows that patients with IDA have had more severe and longer time of iron deprivation that can cause more lead absorption. Therefore, we separate these groups from each other in this study for better comparison.

Statistical analysis

Data were analysed by the Statistical Package for Social Sciences (SPSS, version 11.5). Frequency distributions were applied for continuous variables and cross tabulations for categorical variables. We used independent samples Student *t*-test, Mann- Whitney U test and Chi-Square test for comparison of variables between patients (ID and IDA) and the control group. Lead levels in the control group, ID and IDA in patients, were compared by analysis of variance (ANOVA). Correlations between Blood Lead Concentration and ferritin, haemoglobin and RBC indices [mean corpuscular haemoglobin (MCH), mean corpuscular volume (MCV) and mean corpuscular haemoglobin concentration (MCHC)] were assessed by Pearson's or Spearman's correlation coefficient test. The Kolmogorov-Smirnov normality test was done to evaluate normality of the variables. *P* value ≤ 0.05 was considered as a significant level.

RESULTS

Seven children that have evidences of infection or blood sampling problems were excluded from the study. Finally, 223 cases including 98 control children and 125 patients were studied. Mean (±SD) and age range in the control children were 4.8 (±2.2) and 1-10 years, respectively, and in the patients were 4.2 (±2.8) and 1-10 years, respectively. Difference in mean age between two groups was not significant (*P* value < 0.071) as shown in [Table 1]. In the control group, 54 (55.1%) subjects were males and 44 (44.9%) subjects were females, and in the patients group 74 (59.2%) patients were males and 51 (40.8%) patients were females. Difference between males and females in the control group was not significant (*P* value = 0.312) but it was significant in patient group (*P* value = 0.04).

All children (100%) in the both groups had lead intoxication with mean (±SD) blood lead concentration of 57 ± 22.7 µg/dl

Table 1: General characteristics, haematologic values, serum ferritin and blood lead concentrations in patient and control groups

Variables	Patient Group Mean (±SD)	Control Group Mean (±SD)	*P* value *
Age (years)	4.2±2.8	4.8±2.2	<0.071
Lead (µg/dl)	57±20.4	57.1±25.3	0.713
Iron (µg/dl)	72±36	94±38	0.002
TIBC (µg/dl)	390±54	370±58	0.059
Ferritin (µg/l)	21±12	68±68	<0.001
Haemoglobin (gr/dl)	11.1±1.4	12.4±0.8	<0.001
MCV (fl)	75.8±6.8	80.1±5.2	<0.001
MCH (pg)	24.1±3.2	26.7±2.1	<0.001
MCHC (gr/dl)	31.5±2.1	33.1±1.6	<0.001
WBC (×10³µl)	4.67±0.51	4.64±0.40	0.923
Platelets (×10³µl)	330±99	299±81	0.015

**P* value for the *t*-test or Mann-Whitney test

(ranged 10.9-212). Mean (±SD) blood lead concentration in the control group was 57.1 ± 25.3 (ranged 20-212) μg/dl and in the patient group was 57 ± 20.4 (ranged 10.9-159) μg/dl; this difference was not significant (*P* value = 0.713). Of 125 patients, 75 (60%) cases had ID and 50 (40%) cases had IDA. ANOVA also didn't show a significant difference in Blood Lead Concentration among ID, IDA, and control groups (*P* value = 0.315, F = 1.16). Blood lead concentration > 40 μg/dl was observed in 80.6% of children in control group and 82.6% of children in patient group with no significant difference (*P* value = 0.117). Table 1 also shows mean differences between ferritin, iron, TIBC, haemoglobin, MCV, MCH and MCHC in two groups [Table 1].

We also did not find any correlation between blood lead concentration and haemoglobin (r = –0.09, *P* = 0.186), ferritin (r = 0.045, *P* = 0.632), iron (r = 0.105, *P* = 0.252), TIBC (r = –0.064, *P* = 497), MCV (r = 0.051, *P* = 457), MCH (r = –0.007, *P* = 0.913), MCHC (r = –0.096, *P* = 0.156), WBC (r = 0.092, *P* = 0.174) and platelets (r = –0.02, *P* = 0.764).

DISCUSSION

Chronic lead intoxication may affect children because they have more hand-to-mouth activities and they absorb lead in small intestine more efficiently than adults.[10,19,22] All children evaluated in this study had lead intoxication. It shows children breath high concentration of lead in this polluted big city that can be associated with renal, cardiovascular, hematologic, and irreversible neurologic toxicity.[7] This high prevalence of lead poisoning has to decrease with a preventive national program especially with reducing leaded fuels. IDA normally develops during consecutive stages. Initially, iron stores and ferritin are depleted and iron absorption increase but serum iron is sufficient, in the second stage, serum iron is decreased and eventually in third stage, IDA is created.[23] Hence, serum ferritin is a valuable marker of ID showing iron stores. Children with high blood lead levels are more probably to show evidence of ID and children with ID probably have higher blood lead even after controlling for age, sex and socioeconomic status; however, these pathways are different.[18]

According to the results of this study, we didn't observe any relation between blood lead concentration and ID and/or IDA [Table 1]. Many studies especially in paediatric group have revealed that ID and/ or IDA can elevate blood lead concentration with increase blood lead absorption in gastrointestinal tract.[3,4,9,11,22,24,25] There is a hypothesis for this increase in lead absorption. Recent research have shown an iron transport channel in the intestine named the divalent metal transporter (DMT), which is regulated by iron regulatory proteins 1 and 2.[23,26] DMT1 is not specific for iron; it can transport many of divalent metal ions, such as copper, zinc and lead. Therefore, absorption of some other ions such as lead increase in low iron diet or in the high exposure of body to lead in the situation like pica observed specially in infants.[3,10,11,27] However, Bannon *et al*., (2003) in a study on cell lines in a knockdown model confirmed that although DMT is main way of lead absorption, it can also enter the cells by other mechanism,[28]

Willows *et al*., (2002) in a study for evaluating of association between blood lead concentration and IDA on infants characterised that infants with IDA had a significantly higher blood lead concentration than infants without anaemia. They also found a significant negative correlation between blood lead and haemoglobin (r = –0.203, *P* = 0.006) and blood lead and ferritin concentrations (r = –0.245, *P* = 0.003). In another study, Shah *et al*., (2010) evaluated Environmental exposure of lead and IDA in children 1-5 years and observed similar results.[2] Even some researchers have shown that iron fortification of food to children with high lead-exposed may decrease blood lead levels.[10,27] Wright *et al*., (2003) in a longitudinal study on 1,275 children evaluated blood lead concentration, haematologic parameter and iron status in a 3-year period with two consecutive visits. Logistic regression analysis showed ID was associated with subsequent lead intoxication.[4]

Relation between blood lead concentration and IDA in some other studies especially in adults is inconsistent.[1,11,16] They believed, initially, that environmental lead exposure is as aerosols that absorb from the respiratory tract not gastrointestinal tract. Secondly, both diseases are more common in the lower socioeconomic class and, therefore, this relation might be secondary to common environmental risk factors, and ID may merely be a marker of high environmental blood lead.[1,9] Some other studies have shown the relationship of iron status and blood lead concentration varied within ethnic groups. They assumed genetic polymorphism in lead binding proteins can affect blood lead concentration independently of iron status.[11]

As we mentioned, our finding also didn't show any association between blood lead concentration and ID or IDA. We speculate various reason for this result: It may be due to genetic polymorphism in proteins transmitting the iron and lead;[11] this finding also can be cause by chance alone; in addition, the studies have shown that haematopoiesis affects in blood lead concentration more than 25 μg/dl, and anaemia is seen with blood lead concentration more than 50 μg/dl.[1,9] In this study, all children had lead intoxication and mean blood lead concentration was more than 50 μg/dl in each group. Therefore, the high blood lead concentration in the two groups, could affect the haematologic parameter evenly between them and it may be a reason that mean differences in haematologic parameter between two groups were not significant. In addition, it is possible that at this high level of lead in environment/blood, all children, regardless of whether ID or IDA or not, will have similar blood lead concentration. It can be for this reason that lead will still find another ways of getting into the body, indeed absorption in intestine by DMT, when it is very abundant, and in the

event of over abundance, it may not be very dependent on or limited by iron status. We suggest performing a similar study that also includes evaluation of children with low blood lead concentration such as children living in the rural area.

RBCs indices were lower and platelets were higher in patients compared with control group [Table 1]; ID decrease RBC indices and can cause increase in platelets.[23] We didn't determine any significant difference between blood lead and White Blood Cells (WBC). However, Choi *et al*., showed that blood lead elevation can be with increase in leukocyte counts.[13]

CONCLUSION

We didn't find any association between ID and blood lead concentration in children. Further studies in highly polluted and also unpolluted area are necessary to evaluate this association. Indeed, because of high prevalence of lead toxicity in children in this area, performing environmental health programs for reducing air pollution is necessary.

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