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Impacts of Blood Lead Level on Trace Element Status and Hematological Parameters in Anemic Children from Beni-Suef, Egypt

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Abstract

Anemia is a world widespread health problem among infants and children, and it is often associated with an alteration in blood level of some heavy metals and essential trace elements. The aim of our study is to evaluate the association of blood lead levels (BLL) ≥ 10 µg/dl with anemia, and its effect on hematological parameters and some essential trace elements in children. This study was performed on 100 children (mean age 8.2 ± 2); they fulfilled the inclusion criteria, 75 anemic group (HB ≤ 10 g/dl) and 25 non-anemic control group (HB>10 g/dl). Blood samples were taken from subjects for estimating hematological parameters and ferritin levels along with serum level for lead, zinc, copper and iron which were determined using an atomic absorption spectrophotometer. Approximately 79% of the studied children had blood lead levels (BLL) ≥ 10 µg/dl, and the blood lead level range of 1.56-26.7 µg/dl. The Serum zinc, iron and ferritin levels in children of the anemic group were significantly (p<0.001) lower than control. However, The Serum copper concentration of the anemic group were not found to significantly (p=0.92) differ from the control group. There were significant negative correlations of blood lead levels with iron (r=-0.395), zinc (r=-0.401) and serum ferritin (r=-0.609) levels among all studied children with (P<0.01). In addition to a significant negative correlations of blood lead levels with hemoglobin (HB) (r=-0.884), hematocrit (HCT) (r=-0.819) and mean corpuscular volume (MCV) (r=-0.452) levels among anemic group with (P<0.01). In conclusion, blood Lead level ≥ 10 µg/dl was significantly associated with risk of anemia, hematological parameters affection and also altered the status of essential trace elements. Therefore, theses parameters can be used as biomarkers for chronic lead toxicity.

Keywords: Children; Anemia; Lead; Copper; Zinc; Iron; Trace elements; Hematological system

Background

Lead is considered to be one of the major environmental pollutants and lead poisoning is an important problem in humans [1]. Diet, air, drinking water and ingestion of paint chips are considered the primary sources of lead Human exposure; with increased severity and frequency in developing countries through contaminated soil, water and air pollution. Lead poisoning leads to adverse interaction in cellular biochemical reactions, causing many organ and physiological malfunction [1].

Environmental lead exposure can affect the pharmacokinetics of some trace elements in animal and human bodies on the level of absorption, extraction and metabolism. Furthermore, anemia associated with low dietary consumption of essential elements is not uncommon in children of general population [2]. Alterations of trace element by deficiency or excess may cause abnormalities in the absorption, distribution, metabolism and elimination of other trace elements. For example, increased absorption of lead from gastrointestinal tract is enhanced by iron deficiency. Hence, Iron deficiency has been found to be correlated with elevated Blood lead levels in children [3]. Furthermore, Lead is considered a pernicious element for iron metabolism, as it is absorbed by the same iron absorption machinery, and also blocks iron by competitive inhibition. Lead inhibits SH-dependent enzymes activities, involved in heme biosynthesis. At higher concentration of lead in the blood, The Hemoglobin content of blood becomes lower. Although there is insufficient evidence to stat that iron deficiency leads to higher levels of lead in children, it can be concluded that blood lead levels increases with iron deficiency and decreases after iron supplementation [2,4].

Trace elements can cause adverse health effects through their deficiency, imbalance, or toxicity [5]. Trace mineral deficiencies usually associated with inadequate dietary intake or result from abnormal metabolic interactions among metals. For instance, zinc absorption in small intestine is decreased by calcium, phosphate, copper, phytates and fiber in the diet. On the other hand, excess zinc intake is a cause of copper deficiency [6]. Zinc and copper have an important biological role in many physiological function and pathological conditions. Zinc is a component of more than 200 enzymes, plays an essential role in tissue repair and growth, nucleic acid metabolism and cell replication. Copper is an important element of several metalloenzymes as cytochrome oxidases, amino oxidases, superoxide dismutase, ferroxidases, ascorbic acid oxidase and tyrosinase that are essentials for oxidative metabolism [7,8].

Lead exposure due to Environmental contamination and iron deficiency anemia associated with low dietary consumption is a common issue in children of developing countries, including Egypt. Therefore, this work was designed to evaluate the effect of blood lead level >10 µg/dl on alteration of Trace Element Status, and its impact on hematological system in children residing in Beni-Suef governorate, Egypt.

Subjects and Methods

Human subject

Our study was performed on a total of 100 children, from the clinic of pediatric in Beni Suef University hospital. Children were classified into two groups, anemic group (75 children) with Hb levels <10 g/dl and non-anemic control group (25 children) with Hb levels ≥ 10 g/dl), aged 6-15 years. Informed consent was obtained from Parents of children. Beni Suef University ethics committee approves the study. The studied groups did not report any history of chronic hemolytic anemia, chronic illness associated with anemia or occupational/accidental exposure to lead, and also no history of any iron or vitamin containing drugs intake three months before starting of the study. Data regarding age, sex, source of drinking water residence, level of parent's education, occupation and socioeconomic level was collected from the mothers.

Blood collection and laboratory investigations

Blood samples were obtained from all subjects by venipuncture using Vacutainer tubes and divided into three tubes. The first one was EDTA-tube used for hematological parameters assessments using Sysmex KX-21N Automated Hematology Analyzer (Sysmex Asia Pacific, Japan) for cell count, these parameters are: the red blood cell count (RBC), hematocrit (HCT), hemoglobin (Hb), mean corpuscular hemoglobin (MCH), mean corpuscular volume (MCV), mean corpuscular hemoglobin concentration (MCHC), and white blood cells (WBC). The second heparinized tube used for estimation of lead, copper, zinc and iron by Inductively Coupled Plasma-Mass Spectrometry (ICP-MS) (Thermo Scientific™ iCAP™ Q ICP-MS, Germany). The detection limit for lead was 1.0, 1.0, 0.1 and 0.2 µg/dL for Lead, Copper, Iron and Zinc, respectively [9]. The third tube was used to measure Serum ferritin using chemiluminescent immunoassay on AxSYM (Abbott Laboratories, Chicago, IL, USA) [10].

Statistical analysis

Statistical analysis was done by SPSS statistical package Version 19 (IBM corp. Armonk, NY). Chi-square test was performed to compare individual characteristics and the t-test was performed to compare the hematological parameters between the two groups. P-value was considered statistically significant if <0.01. Pearson correlation test was used to determine the significant correlations between variables.

Results

This study was performed on a total of 100 children with ages ranging from 6 to15 years with a mean value of (8.23 ± 2) years. The male/female ratio was 57:43 in the total participants. According to the BLL (Range 1.56–26.7 µg/dl), approximately 79% of children had a blood lead ≥ 10 µg/dl and 21% had a blood lead level <10 µg/dl. The distribution of socioeconomic characteristics of all study children are presented in Table 1. Children with illiterate mothers and fathers have higher BLL; also, blood lead level was higher in those of low social standard. In addition, it was higher in children consuming tap water. However, there is no significance in BLL in regard to age and sex.

Characters of the Studied children	**Blood lead level (BLL)**		**P-Value**
	High ≥ 10 µg/dl (N=79) **No. (%)**	**Low <10 µg/dl (N=21)** **No. (%)**	
Age Mean of age (years)	8.24 ± 1.979	8.20 ± 2.121	0.932
Gender Male Female	45 (57.0%) 34 (43.0%)	13 (61.9%) 8 (38.1 %)	0.726
Mother Education Educated Illiterate	31(39.0%) 48 (61.0%)	18 (86.0%) 3 (14.0%)	<0 .001
Father Education Educated Illiterate	60 (76.0%) 19 (24.0%)	21 (100.0%) 0 (0.0%)	0.007
Source of drinking water Tap water Hand pump water	61 (77.2%) 18 (22.8%)	21 (100.0%) 0 (0.0%)	0.009
Socioeconomic level Middle Low	33 (41.7%) 46 (58.3%)	14 (67.0%) 7 (33.0%)	0.028
Risk of Lead Exposure	57 (72.2%)	1 (4.8%)	0.012

Exposed to machinery exhausts Non-exposed	22 (27.8%)	20 (95.2%)	

Table 1: Distribution of Individual Characteristics of the studied children in relation to blood lead levels.

Mean values of trace element concentrations and iron parameters in the studied children are summarized in Table 2. The results revealed a significant high BLL among anemic group in comparison to non-anemic control group (p<0.01) (Table 3). However, a significant decrease in the level of zinc, iron and serum ferritin among the Anemic Group than the control group (p<0.01). Moreover, there no significant difference in serum copper level (p=0.92). As regard different hematological parameters, most of values were found decreased significantly among anemic group in comparison to non-anemic control group except for WBC, which showed a significant elevation among the anemic group (p<0.01) (Table 2).

Trace Elements	Anemic Group (Hb ≤ 10 g/dl) Mean ± SD	Non-anemic Group (Hb >10 g/dl) Mean ± SD	P-Value
Lead (µg/dl)	19.59 ± 3.85	5.89 ± 2.98	<0.01
Zinc (µg/dl)	65.97 ± 18.24	97.07 ± 3.85	<0.01
Copper (µg/dl)	120.48 ± 22.21	120.97 ± 15.41	0.92
Iron (µg/dl)	52.33 ± 19.58	70.29 ± 17.31	<0.01
S. Ferritin (ng/ml)	37.82 ± 6.36	46.99 ± 8.42	<0.001

Table 2: Concentration of Trace Elements and serum ferritin in Anemic and Non- Anemic Control Groups.

The correlations between BLL with trace element concentrations, iron parameters and different hematological parameters were demonstrated in Table 4, Figure 1 and Figure 2. BLL had significant negative correlations with serum zinc (r=-0.401), iron (r=-0.395) and serum ferritin (r=-0.609). However, there is no significant correlation between BLL and copper (r=+0.21, p=0.839). All hematological parameters had significant negative correlations with BLL expect WBC had a positive correlation with BLL (r=+0.401).

Hematological & Parameters	Anemic Group (Hb ≤ 10 g/dl) Mean ± SD	Non-anemic Group (Hb >10 g/dl) Mean ± SD	P-Value
Hb (g/dl)	9.20 ± 0.599	12.38 ± 0.958	<0.01
RBC (×10^6/mm^3)	3.74 ± 0.45	4.39 ± 0.31	<0.01
HCT (vol %)	28.52 ± 2.01	35.79 ± 2.64	<0.01
MCV (μ^3)	75.59 ± 4.51	82.66 ± 4.22	<0.01
MCH (pg)	24.51 ± 2.12	29.02 ± 1.29	<0.01
MCHC (%)	32.62 ± 1.56	35.18 ± 0.807	<0.01
WBC (×10^6/mm^3)	7.89 ± 1.56	5.63 ± 1.15	<0.01

Table 3: The Comparison of hematological parameters in Anemic and Non- Anemic Control Groups.

Hematological & Trace Elements Parameters	Blood lead level (r –value)	P-Value
Hb (g/dl)	- 0.884	<0.01
RBC (×106 /mm3)	-0.588	<0.01
HCT (vol%)	-0.819	<0.01
MCV (µ3)	-0.452	<0.01
MCH (pg)	-0.647	<0.01
MCHC (%)	-0618	<0.01
WBC (×106 /mm3)	+0.401	<0.01
S. Ferritin (ng/ml)	-0.609	<0.01
Iron (µg/dl)	-0.395	<0.01
Zinc (µg/dl)	-0.401	<0.01
Copper (µg/dl)	+0.21	0.839
Correlation is significant at the <0.01 level		

Table 4: Correlation of blood lead level in relation to different hematological parameters, serum ferritin, iron, zinc and copper.

Discussion

Anemia is a known health- problem result from chronic lead toxicity. Red blood cells are the most affected hematological system parameter and have more affinity for blood lead and typically contain most of lead circulating in the blood stream. Inhibition of heme synthesis and microcytic hypochromic anemia are the most common effects of lead on hematological system [3,11]. Furthermore, it is obvious that high blood lead levels and Iron deficiency are a common linked problem in children all over the world as stated in many studies [2,12-14]. Both conditions are known to produce microcytic hypochromic anemia and their combination induce a severe form of anemia. Therefore, the present study aimed to estimate the effect of blood lead level on abnormalities of Trace Element Status and parameters of hematological system in children.

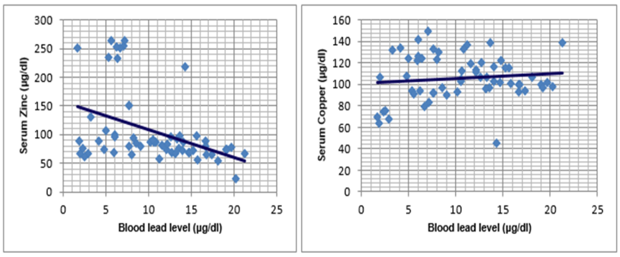

Figure 1: A scattered Plot Chart showing the correlation between Blood lead levels with Serum Zinc, and Serum Copper.

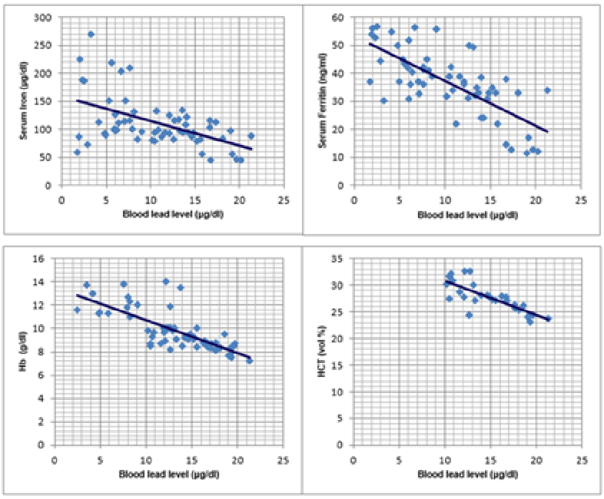

Figure 2: A scattered Plot Chart showing a significant indirect correlation between Blood lead levels with Serum Iron, Serum Ferritin, Hemoglobin (Hb) and Hematocrit (HCT).

In the present work, the blood lead showed significantly higher level in the anemic group than in the non-anemic control and all anemic children (75) had BLL ≥ 10 µg/dl with 10.21-26.7 µg/dl blood lead levels, these results were in accordance with a study done by Hegazy et al. [15], who also approved an association of anemia with 10-20 µg/dl blood lead levels in Egyptian children, also these results agreed with that of Jain et al. [16] and Ahamed et al. [17] about estimation of BLL among children in India . In our study a value of 10 µg/dL was considered as the cut-off for increased blood lead levels as estimated by the Center for Disease Control and Prevention in the past as a limit for an elevated blood lead level mainly is based on neurological toxicity [18]. Recently, the Centers for Disease Control and Prevention accepted recommendations of its Advisory Committee on Childhood Lead Poisoning Prevention to define elevated blood lead as lead level higher than or equal to 5 µg /dL[19]. Recent studies have proven that there is no cutoff value for elevated BLLs; furthermore, children with BLLs < 10 µg /dL are at risk for reduced cognitive development and functioning [20].

Several previous studies have found that the mean BLLs were higher in school-age children, as in this age group children play outdoors, with increased risk of environmental exposure to lead poisoning, such as automobile exhaust, smoking, and a variety of toys [21-23]. In addition to, BLLs in children showed significant correlation with socioeconomic status. Many Studies in developing countries like Egypt concluded that low socioeconomic status and maternal educational levels are one of the risk factors that definitely affect the BLLs during childhood [24-26]. In pediatric age group, exposure by ingestion is the essential route .and as well known the absorption *via* the gastrointestinal tract is much more efficient than that in adults; resulting into elevated BLLs [27]. In our study, BLLs levels in all participated children were significantly affected by socioeconomic status and lead environmental contamination.

Iron, zinc, and copper are essential trace elements for the maintenance of human life and health. Lead can cause many health hazards in human. Therefore, recent studies have focused on the blood level, distribution and interaction of some toxic metals like lead and its interaction with some essential trace elements in children [8,28]. Nutrition, physiological characteristics in different life periods, and underlying pathological diseases also affect essential trace element status. Children during infancy and early childhood age period are particularly susceptible to deficiencies of zinc, copper and iron deficiency which occur mainly in infancy. This susceptibility is due to increased daily requirements for rapid growth which are frequently not met by the diet [29,30]. In addition, there are interactions between essential trace elements and each other, as Deficiency in one trace element may affect the absorption of another e.g., copper deficiency decrease iron absorption and Zinc absorption is impaired by iron [31]. The deficiency of zinc, iron and copper increases lead absorption and toxicity by affecting the physiological and biological functions of the body through interactions with these essential trace metals [32].

In the present study blood iron level and serum zinc level of the anemic group is significantly lower than the non-anemic control group, while serum copper levels elevated insignificantly. Furthermore, in our study, results revealed that blood lead levels showed significant negative correlation with blood iron level and serum zinc level. Therefore, the results of this study revealed the existence of a relationship between elevated blood lead levels and iron deficiency. These results run in parallel with a study done by Hegazy et al. [15] and by Angelova et al. [28], who found a decline in blood iron level and serum zinc level in the anemic group in comparison to the control group. Iron is well known that it plays a crucial role in many metabolic pathways and its deficiency causes several health problems, especially for rapidly growing adolescents and infant. Children known to be at greatest risk of chronic lead exposure are more susceptible to Iron deficiency. Many studies especially in children have showed an association between iron deficiency and high BLLs [17,32-34]. It has been considered that lead and iron compete for absorption in the small intestine and children with inadequate iron intake, lead absorption will be increased. Furthermore, iron supplement therapy in children with iron deficiency could reduce BLLs [35].

Chronic exposure to lead contributes to a decrease of serum zinc levels in children. The contemplated mechanisms explaining decreased serum zinc level in anemic group are the interaction between zinc and lead at the absorptive and enzymatic sites, Most probably due to the competition of zinc and lead for the same binding sites on metallothioneins (metal-binding proteins)-like transport protein in gastrointestinal tract. As well as the evident ability of zinc to inhibit lead absorption, hence decreasing incidence of lead toxicity, zinc interacts with lead systematically [8,36,37]. Furthermore, there is an antagonism between absorption of Zinc and iron from the gastrointestinal tract, as an elevated iron level in the intestinal lumen may antagonize zinc uptake [38].

Our study results showed a significant decrease in Hb, RBC, HCT, MCV, MCH and serum ferritin values in children of anemic group (which have high BLLs) in comparison to non-anemic control group, while WBC values exhibited a significant increase among the anemic group. Lead chronic toxicity causes anemia by impairment of heme biosynthesis by interaction with a number of essential iron dependent metabolic steps and by increasing rate of RBCs destruction, in addition to iron level inhibition will lead to enhancement of lead absorption that in turn affects heme synthesis, thus negatively affecting hematological parameters. For example, the ferrochelatase enzyme that mediates the ferrous insertion into protoporphyrin shows higher sensitivity to lead effects with co-existing Fe deficiency [39,40]. Lead also known as a pernicious element to iron metabolism as it is taken up by the iron absorption machinery instead of iron, and through competitive inhibition. The effect of lead toxicity on this system results in inhibition of heme synthesis and anemia [41]. This study revealed a significant correlation of high BLLs with lower iron and ferritin concentration and significant negative correlation with different hematological parameters. Our detected results are agreed with other studies, who found significant correlation between high BLLs and significant decrease in Hb, RBC, MCV, MCH HCT, and serum ferritin values [2,15].

Conclusion

In conclusion, blood Lead level ≥ 10 μg/dl was significantly associated with increased risk of childhood anemia, decreasing iron and ferritin levels with a significant negative correlation with different hematological parameters and also altered the status of essential trace elements like zinc and copper in children. Evaluation of other environmental pollutants e.g. mercury and cadmium also recommended as it may act synergistically for enhancement lead toxicity. On the basis of the findings of this study, we need to Implementation of standardized lead screening program for children in our country. Establishment of public awareness about source and hazards of lead exposure through conducting health education programs, as well as increase the parent's awareness of the problem and altering the attitudes related to prevention. Finally, our study was a relatively small study due to limited sample size; thus, a larger study is needed to verify our results.

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