

Correlation Between Iron Deficiency and Lead Intoxication in the Workers of a Car Battery Plant

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ABSTRACT

Iron deficiency anemia is the most common nutritional anemia in developed and developing countries. In addition, lead intoxication especially in developing countries is an increasing risk for health, because of rapid urbanization and consumption of leaded fuels. Many studies particularly in children have showed a correlation between iron deficiency and high blood lead concentration. In this study, we have evaluated this association in workers of a car battery manufacturer.

This research was performed on workers who exposed to lead in a factory of car battery of Mashhad, Iran in 2006. Hematological tests including complete blood counts (CBC) and serum ferritin concentration (radioimmunoassay method) were measured. Blood lead concentration (BLC) was estimated by heated graphite atomization technique of an atomic absorption spectrophotometer (Perkin Elmer, Model 3030). Results analyzed by the statistical package for social sciences (SPSS, version 11.5), using statistical tests including independent samples t-test, Mann-Whitney U test, Fisher's exact test and Pearson's correlation coefficient. P value < 0.05 was considered as a significant level.

Based on clinical (lead line) and laboratory observation, all workers had lead intoxication with mean BLC of 32.2 ± 13.7 µg/dl. There were no statistical significant difference on mean BLC in iron deficient (n= 11) and non iron deficient workers (n= 78). There were also no significant correlation between BLC and either serum ferritin or blood hemoglobin (r= 0.18, p value= 0.091 and r= 0.051, p value= 0.682, respectively).

In this study, we did not observe any correlation between BLC with either serum ferritin or hemoglobin or the other blood parameters. However, similar research in a larger population is required to make a general conclusion.

Keywords: Lead, Anemia, Ferritin, Iron deficiency, Hemoglobin, Intoxication

ÖZET

Akü Sanayiinde Çalışan İşçilerde Demir Eksikliği Anemisi ile Kurşun İntoksikasyonu İlişkisi

Demir eksikliği anemisi, gelişmiş ve gelişmekte olan ülkelerde en çok görülen beslenmeye bağlı anemidir. Ayrıca, kurşun intoksikasyonu da gelişmekte olan ülkelerde, hızlı kentleşme ve kurşunlu yakıtların tüketilmesine bağlı olarak, artan bir sağlık problemidir. Bazı çalışmalarda, çocuklarda yüksek kan kurşun değerleri ile demir eksikliği anemisi arasında korelasyon olduğu gösterilmiştir. Bu çalışmada akü sanayiinde çalışan işçilerde bu korelasyonu araştırdık. Bu çalışma, 2006 yılında Meşhed, İran'da akü fabrikasında kurşuna maruz kalan işçiler üzerinde yapıldı. Tam kan sayımı ve serum ferritin (radyoimmünoassay) düzeylerini içeren hematolojik çalışmalar yapıldı. Kan kurşun düzeyi atomik absorpsiyon spektrofotometresinde (Perkin Elmer, Model 3030) termal grafit atomizasyon yöntemi ile ölçülmüştür.

Sonuçlar, SPSS (V 11.5) programında bağımsız değişkenlerde t-testi, Mann-Whitney U testi, Fisher exact testi ve Pearson korelasyonu kullanılarak elde edilmiştir. $P < 0.05$ anlamlı olarak kabul edilmiştir.

Klinik veriler ve laboratuvar bulgularına dayanılarak bütün işçilerde kurşun intoksikasyonu izlenmiştir. Ortalama kan kurşun değeri 33.2 ± 13.7 $\mu\text{g}/\text{dl}$ olarak bulunmuştur. Demir eksikliği olan ($n=11$) ve olmayan ($n=78$) işçiler arasında kan kurşun değerleri açısından istatistiksel olarak anlamlı bir fark bulunmamıştır. Kan kurşun değeri ile serum ferritin düzeyleri ve kan hemoglobin düzeyleri arasında istatistiksel olarak anlamlı bir korelasyon izlenmemiştir (sırasıyla, $r=0.18$, $p=0.091$ ve $r=0.051$, $p=0.682$).

Bu çalışmamızda kan kurşun düzeyleri ile serum ferritin, hemoglobin ve diğer kan parametreleri arasında bir korelasyon izlenmemiştir. Ancak, daha geniş gruplar üzerinde yapılacak çalışmalardan sonra genel sonuçlara varılabileceği kanısındayız.

Anahtar Kelimeler: Kurşun, Anemi, Ferritin, Demir eksikliği, Hemoglobin, İntoksikasyon

INTRODUCTION

Iron deficiency anemia is the most common nutritional anemia in developed and developing countries.^{1,2} In addition, lead intoxication especially in developing countries is an increasing risk for health, because of rapid urbanization and uses of leaded fuels.^{4,5} During 1976-1980, 78% of the united state population had blood lead levels > 10 $\mu\text{g}/\text{dl}$, but it decreased to 20% in 1998.⁶ In some studies in pediatric group of large crowded cities in Iran, blood lead levels had been >10 $\mu\text{g}/\text{dl}$ in 41-75% cases.^{7,8} Other studies also showed increase lead intoxication in some careers such as drivers, painters and workers of oil related industries.⁹⁻¹¹

Both iron deficiency (ID) and lead poisoning are detrimental to early development and may have lasting and profound neurologic and developmental effects.^{6,12} Many studies particularly in children have showed a correlation between iron deficiency and high blood lead concentration (BLC).^{1,5,6,13-15} In adults, fewer studies have been reported and the results have been controversial. Because of these conflict studies, it remains unclear whether ID has a causal association with lead poisoning or whether it merely is a marker of high environmental lead exposure. If the association is causative, then preventing ID in target high risk populations might prevent lead poisoning.¹² It was thus aimed to study BLC in the workers of a car battery plant with high environmental lead exposure and its causal association between ID and lead poisoning.

MATERIAL AND METHODS

This study was approved by the research council and ethics committee of Mashhad University of Medical Sciences, Iran. In this cross sectional study following informed consent, all of 105 workers of a car battery plant have been evaluated. Initially, medical history and clinical examination of the workers was performed. Duration of occupational lead exposure, underlying acute and chronic disease and signs of lead intoxication were investigated and recorded. Then blood was drawn and divided into separate tubes for laboratory tests including complete blood counts (CBC), Hemoglobin, hematocrit, red blood cells indexes, peripheral blood smear, erythrocytes sedimentation rate, BLC, glucose, urea, creatinin and ferritin concentrations. Whole blood collected for determination of BLC and CBC. BLC was determined by an atomic absorption spectrophotometer using heated graphite atomization (HGA) technique (Perkin Elmer, Model 3030). According to the U.S centers for disease control and prevention and world health organization standards, $\text{BLC} \geq 10$ $\mu\text{g}/\text{dl}$ was defined as lead intoxication.^{1,12,16-18} CBC, hemoglobin, hematocrit and red blood cells indexes including mean corpuscular volume (MCV), mean corpuscular hemoglobin (MCH) and mean corpuscular hemoglobin concentration (MCHC) were analyzed by a cell counter (Sysmex K-21, Japan). Hemoglobin <14 g/dl in males and <12.5 g/dl in females, were defined as anemia.¹ Serum ferritin was measured by radio immune assay method (Kavoshyar reagent-Iran). Ferritin <20 $\mu\text{g}/\text{l}$ with normal hemoglobin, was defined ID.²⁰ Any evidence of acute or chronic infection, leukocytosis, $\text{ESR} >20$ mm/h and ferritin >200 $\mu\text{g}/\text{l}$ were excluded from the study.

Statistical analysis

Results were analyzed by the statistical package for social sciences (SPSS, version 11.5). In exploratory data analysis, frequency distributions were used for continuous variables and cross tabulations for categorical variables. Difference between the means of lead in ID and none ID workers was assessed by independent samples t-test. We also used Mann-Whitney U test for comparison of BLC in anemic and non anemic and Fisher's exact test for assessment of lead line in ID and non ID groups. Correlations between BLC and ferritin, hemoglobin and its related parameters (MCH, MCV, MCHC) were assessed by Pearson's correlation coefficient. $P < 0.05$ was considered as a significant level.

RESULTS

Following exclusions, 89 workers were studied. Summary of data in ID and non ID subjects are shown in Table 1. Mean age of the workers was around 30 years with no significant difference between two groups as shown in Table 1. Out of 89 workers, 85 (95.5%) individual were males and 4 (4.5%) were females. Range and mean (\pm SD) weight of subjects was 53-93 kg and 69.1 (\pm 10.4) kg, respectively. The workers have been working about 7 hours per day in a duration period from 1 to 7 years with a mean (\pm SD) of 2.9 \pm 1.6 years in this

factory. Duration of lead exposure between ID and non ID individuals were not significantly different (Table 1).

In clinical examination lead line in the mouth was seen in 9% (n= 8) of workers with no significant difference between ID and non ID workers ($p > 0.05$).

All workers (100%) had lead intoxication with mean (\pm SD) BLC of 32.2 \pm 13.7 μ g/dl, (ranged 10.7-68.2 μ g/dl). BLC was 10-19.9 μ g/dl in 21.3%, 20-39.9 μ g/dl in 48.1% and >40 μ g/dl in 30.6% (Table 2). ID (without anemia) was seen in 12.3% (n= 11) of individuals but we did not observe a significant difference in BLC between ID and non ID subjects (Table 1). We also didn't find any significant correlation between BLC and serum ferritin ($r = 0.180$, $p = 0.091$). Mean hemoglobin concentration in males had not significant difference in ID with non ID workers, but we observe a significant difference in MCV between these groups (Table 1).

Anemia was observed in 6.7 % (n= 6) of workers including 5 males and 1 female, yet BLC in them did not show any significant difference with non anemic individuals. In addition, no significant correlations were found between BLC and hemoglobin ($r = 0.051$, $p = 0.682$), MCV ($r = -0.21$, $p = 0.078$), MCH ($r = -0.2$, $p = 0.106$) and MCHC ($r = -0.15$, $p = 0.207$) (Figure 1).

Table 1. General characteristics, hematologic values, serum ferritin and blood lead concentrations in Iron deficient (ID) and non ID workers

Variable	Non ID	ID	P Value
Age (years)	29.4 \pm 5	30.5 \pm 10.6	0.674
Exposure duration (years)	3.2 \pm 1.7	2.1 \pm 0.9	0.162
Hemoglobin (g/dl)	15.6 \pm 1.1	14 \pm 3.1	0.311
MCV (fl)*	85.4 \pm 6.6	79.1 \pm 9.4	0.041
RDW (%)**	13.6 \pm 0.9	16.4 \pm 4.1	0.207
Ferritin (μ g/l)	64.1 \pm 33.1	11.8 \pm 3.1	<0.001
Lead (μ g/dl)	34 \pm 14.1	25.4 \pm 10	0.055

MCV*: Mean Cell Volume, RDW**: Red cell distribution width

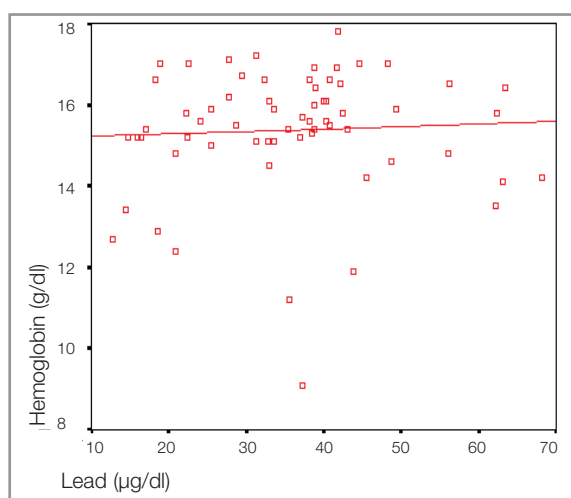


Figure 1. Correlation between blood lead concentrations and hemoglobin levels demonstrated by linear regression line ($r=0.051$, $p=0.682$).

DISCUSSION

Occupational lead poisoning is a health problem in workers of the factories with lead exposure such as car battery plant. Lead line is a sign of lead intoxication which occurs due to lead sulfide precipitation between tooth and gums junctions.²¹ As a result of high lead intoxication in workers, lead line was observed in about 20% of workers.

Many studies particularly in children have revealed that ID and ID anemia can increase blood lead absorption in gastrointestinal tract.^{1,4-6,13-16} Chronic lead poisoning mainly affects young children because they have more hand-to-mouth activity and absorb lead more efficiently than adults.^{4,5,18} There is a theoretical basis for this observation. Iron absorption from the diet is small and limited. Duodenal enterocytes are responsible for iron absorption. Iron is transferred across the apical membrane of the ente-

rocyte into the cell using a protein named divalent metal transporter 1 (DMT1). DMT1 is not specific for iron; it can transport a wide variety of divalent metal ions, including copper, zinc and lead. Therefore, if the iron content of the diet is low, the other divalent metal ions may be absorbed instead including trace quantities of lead.^{5,6,19,22} As ID is associated with pica, there is opportunity for lead to be absorbed if present because of increased exposure rather than increased absorption.^{5,6}

In other studies especially in adults, the results are inconsistent. Although some studies in adults reported higher BLC in low iron status but many other studies have not shown any association.^{5,6,12} Occupational lead exposure is as aerosols that absorb from the respiratory tract.¹ In addition, both diseases do occur more frequently in lower socioeconomic classes; thus, the relationship may be secondary to common environmental risk factors, and ID may therefore merely be a marker of high environmental lead levels.^{5,12}

ID normally develops via successive stages. In the first stage, iron store and ferritin are depleted and iron absorption increase but serum iron is sufficient, then in the second stage, serum iron is depleted and finally in third stage, iron deficiency anemia is appeared. Thus, serum ferritin measurement is a good marker of ID, showing iron stores.^{1,20} Therefore, we measured serum ferritin as a marker of iron stores. Ferritin is an acute phase reactant protein and increase in inflammations^{13,20}, so workers with any evidences of inflammation were excluded from this study. We didn't observe a significant difference on BLC between ID and non ID workers and also could not find any correlation between BLC with either serum ferritin or blood hemoglobin. (Tab & Figure 1). Some studies have shown, a negative re-

Table 2. Distribution of workers among degree of lead intoxication

Severity	Mild	Moderate	Severe
BLC* (µg/dl)	10-19.9	20-39.9	≥40
Percent of workers	21.3%	48.1	30.6

* Blood Lead concentration

lation between high BLC and hemoglobin and hematocrit levels^{1,23,24}, but in spite of lead intoxication in all of the workers, we did not observe such a correlation. The reasons may be due to low numbers of workers with ID or short duration of lead exposure in this study. Longer duration of exposure particularly in high concentration may reveal this correlation. The studies have shown, Hematopoiesis affects in BLC >25 µg/dl, and anemia is appeared in occupational lead exposed subjects with BLC >50 µg/dl.^{1,23} The US Environmental Protection Agency suggests a threshold lead level of 20-40 µg/dl for risk of childhood anemia, but there is little information relating lead levels >40 µg/dl to anemia.¹⁶ Coarse basophilic stippling in peripheral blood smear is seen in lead intoxication²⁵ but we didn't observe it in this study.

Conclusion

In this study, we did not observe any correlation between BLC with either serum ferritin or hemoglobin or the other blood parameters. However, similar research in a larger population is required to make a general conclusion.

Acknowledgments

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REFERENCES

- Kim HS, Lee SS, Hwangbo Y, et al. Cross-sectional study of blood Lead effects on iron Status in Korean lead workers. *Nutrition* 19: 571-576, 2003.
- Andrews NC. Iron deficiency and related disorders. In: Greer JP, Forester J, Lukens JN et al. *Wintrobe's clinical Hematology*. 11th ed, Philadelphia: Lippincott Williams and Wilkin; 2004: 979-1007.
- Javadzadeh SH, Attar M, Taher Yavari M. A study of the prevalence of iron deficiency and its related factors in blood donors of Yazd, Iran, 2003. *Transfus Med* 15: 287-293, 2005.
- Rondo PH, Carvalho Mde F, Souza MC, Moraes F. Lead, hemoglobin, zinc protoporphyrin and ferritin concentrations in children. *Rev Saude Publica* 40 : 71-76, 2006.
- Zimmermann MB, Muthayya S, Moretti D, Kurpad A, Hurrell RF. Iron fortification reduces blood lead levels in children in Bangalore, India. *Pediatrics* 117: 2014-2021, 2006.
- Alabdullah H, Bareford D, Braithwaite R, Chipman K. Blood lead levels in iron-deficient and noniron-deficient adults. *Clin Lab Haematol* 27: 105-109, 2005.
- Tali'e Z, Hosseinzadeh. Lead poisoning in a healthy polluted district of tehranian high school children. *Iran J Ped* 9: 207-212, 1998.
- Farhat A.Sh, Pari Zadeh SMJ, Balali M, Khademi Gh.R. The serum Lead level of children in emergency ward. *Medical journal of Mashhad University of Medical Sciences* 48: 405-408, 2007.
- Yartirah HA. Determination of blood and urine Lead level among workers of Kermanshah refinery in 1994. *Scientific Medical Journal* 31:60-65, 2001.
- Abdollahi M, Shohrati M, Nikfar S, Jalali N. Monitoring of lead poisoning in bus drivers of Tehran. *IJMS* 20: 29-33, 1995.
- Abdollahi M, Sadeghi A, Jalali N. Lead toxicity in paint industry employees. *Medical Journal of Islamic Republic of Iran* 10: 203-206, 1996. (Persian with English abstract).
- Wright RO, Tsaih SW, Schwartz J, et al. Association between iron deficiency and blood lead level in a longitudinal analysis of children followed in an urban primary care clinic. *J Pediatr* 142: 9-14, 2003.
- Bradman A, Eskenazi B, Sutton P, et al. Iron deficiency associated with higher blood lead in children living in contaminated environments. *Environ Health Perspect* 109, 1079-1084, 2001.
- Eden AE. Iron deficiency and blood lead levels. *Pediatrics* 114: 329, 2004.
- Lanphear BP, Hornung R, Ho M, et al. Environmental lead exposure during early childhood. *J Pediatr* 140: 40-47, 2002.
- Jain NB, Laden F, Guller U, et al. Relation between blood lead levels and childhood anemia in India. *Am J Epidemiol* 161: 968-973, 2005.
- Lech T. Exhumation examination to confirm suspicion of fatal lead poisoning. *Forensic Sci Int* 158: 219-223, 2006.
- Albalak R, Noonan G, Buchanan S, et al. Blood lead levels and risk factors for lead poisoning among children in Jakarta, Indonesia. *Sci Total Environ* 301: 75-85, 2003.
- Perkins SL. Normal blood and bone marrow value in human. Greer JB, Forester J, Lukens JN et al, *Wintrobe's clinical hematology*. 11th ed, Lippincott Williams and Wilkins, 2004: 2697-2702.
- Elghetany MT, Banki K. Erythrocyte disorders. In: Mcpherson RA, Pincus MR. *Henry's Clinical diagnosis and management by laboratory methods*. 21st ed, Philadelphia, Saunders Elsevier; 2007: 504-508.
- Pearce JM. Burton's line in lead poisoning. *Eur Neurol* 57: 118-9, 2007.

22. Kwong WT, Friello P, Semba RD. Interactions between iron deficiency and lead poisoning: epidemiology and pathogenesis. *Sci Total environ* 330: 21-37, 2004.
23. Di LL, Soleo L, Cassano F, et al. Anemia in workers exposed to lead: update on differential diagnosis. *G Ital Med Lav* 27: 54-61, 2005.
24. Schwartz J, Landrigan PJ, Baker EL, Jr, Orenstein WA, von Lindern IH. Lead-induced anemia: dose-response relationships and evidence for a threshold. *Am J Public Health* 80: 165-168, 1990.
25. Vajpayee N, Susan S. Graham SS, Bem S. Basic examination of blood and bone marrow. In: Mcpherson RA, Pincus MR. *Henry's Clinical diagnosis and management by laboratory methods*. 21st ed, Philadelphia, Saunders Elsevier; 2007: 468-469.

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