

**BLOOD LEAD LEVELS AND KIDNEY FUNCTION  
AMONG ADOLESCENTS IN DUHOK**

ALI H. AL-DOSKY, BSc,MSc,PhD \*

DHIA J. AL-TIMIMI<sup>1</sup>, BSc(Pharm),Mphil,PhD \*\*

SAMIM A. AL-DABBAGH, MBChB,DTM&amp;H,D.Phil,FFPH \*\*\*

*Submitted 16 May 2014; accepted 6 Nov 2014***ABSTRACT**

**Background and Objectives** The adverse association between low-level lead exposure and kidney function has attracted much attention. The aim of this study was to examine the association between blood lead levels and kidney function in a sample of adolescents in Duhok, Iraq.

**Methods** A cross-sectional study was conducted by estimating blood lead levels, serum creatinine and creatinine-estimated Glomerular Filtration Rate (GFR) among 837 adolescents randomly selected from intermediate and secondary schools.

**Results** Mean blood lead level in the overall adolescents was  $3.55 \pm 0.98$  ug/dl and mean serum creatinine level was  $0.72 \pm 0.07$  mg/dl. Mean creatinine-estimated GFR was  $106.47 \pm 7.39$  ml/min/1.73m<sup>2</sup>. Adolescents with blood lead levels of  $>5$  ug/dl had  $101.66 \pm 4.32$  ml/min/1.73m<sup>2</sup> lower creatinine-estimated GFR compared with those with lead levels  $<3$  ug/dl ( $109.42 \pm 6.78$  ml/min/1.73m<sup>2</sup>),  $P < 0.001$ . Blood lead levels were inversely correlated with creatinine-estimated GFR ( $r = -0.38$ ,  $P = 0.001$ ) and positively with serum creatinine ( $r = 0.25$ ,  $p = 0.01$ ) for all adolescents.

**Conclusion** Our results indicate that the higher blood lead levels in a range below the acceptable limit reported by the Centers for Disease Control and Prevention (10 ug/dl) were associated with a lower creatinine-estimated GFR. Environmental factors has been hypothesized to contribute to this burden

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Lead in the environment is still a major risk factor and its effects are mainly observed in developing countries 1,2. At lower levels of exposure (blood levels  $<10$  ug/dl) adverse associations between blood lead and kidney function have been observed in adults 3. Few studies examined the association between low-level lead exposure and kidney function in children and adolescents 4, 5. In Iraq, most studies on lead exposure have conducted on exposure among risk groups 6, 7, 8, and the adverse association between low-level lead exposure and

kidney function is less well known. The present study designed to examine the association between blood lead level and kidney function of school adolescents in urban area of Duhok city, Kurdistan Region, Iraq.

**METHODS****Setting and sample**

A cross-sectional study carried out during the period 1st, November 2012 until the 31st, August 2013. Adolescent boys and girls from intermediate and secondary schools (n= 837) were included

\* Lecturer, Department of Clinical Biochemistry; 2 School of Medicine, College of Medicine, Faculty of Medical Sciences, University Of Duhok, Duhok, Iraq.

\*\* Professor and chairman of Clinical Biochemistry Dept., School of Medicine, College of Medicine, Faculty of Medical Sciences, University Of Duhok, Duhok, Iraq.

\*\*\* Professor and chairman of Family & Community Medicine Dept. School of Medicine, College of Medicine, Faculty of Medical Sciences, University Of Duhok, Duhok, Iraq.

,Correspondence to Dhia J. Al-Timimi Email : altmimidj@yahoo.com; altmimidj7@gmail.com

in the study sample.

The study conducted in Duhok city, Kurdistan Region, Iraq; which accommodates a population of nearly one million people. The city is located in a valley between 2 mountains and areas were chosen at different altitude in the valley: low (540 - <560 m) and high (>630 m) 9 .The schools in Duhok were grouped according to the resident areas. Of these, two distinct altitude areas located on left side and two on the right side on the highway which divide the city. At each area, the schools were grouped into four groups; intermediate and secondary schools for boys; and intermediate and secondary for girls. Therefore, out of 32, 16 schools randomly selected. Students in these schools represented our target population. The required number of students from each class selected randomly from school records by systematic random sampling procedure. The sample size calculated according to the World Health Organization formula to be 76710. Among the adolescents selected, 418 were urban living in low altitude area of both side of Duhok city and 419 were urban living in high altitude area. They were apparently healthy individuals with an age range from 13 to 19 years. Smokers, age more than 20 years and those having a medical history of diabetes mellitus or kidney disease excluded from the study.

#### **Data collection**

A pre-tested questionnaire was designed to obtain information on age, gender, and residence (high and low altitude). The age of the student was taken from the school records. Each student was interviewed directly and separately in a special room. A verbal consent for participation and approval to give blood samples for testing was obtained from the adolescents, after the nature of the study had been explained to them.

#### **Blood lead measures**

Blood lead (BPb) was measured at the College of Science Analytical Laboratory by flame atomic absorption spectrophotometer using a previously published procedure 11. Briefly, EDTA – blood precipitated with 20% TCA solution. The supernatant solution aspirated directly to the spectrophotometer and the samples run in batches using standard lead solution of 1, 3, 5 and 10 ug/dl. To correct the sensitivity of the instrument, a reagent blank was prepared by mixing an equal volume of 20% TCA with deionized water. The blank gave a reading of 1 ug/dl and this value subtracted from the reading of the samples examined.

#### **Kidney function measures**

Estimated GFR (measured in milliliters per minute per 1.73 m<sup>2</sup>) was calculated using the creatinine based formula of Matzke et al<sup>12</sup>. Serum creatinine (S.Cr) level measured by the modified kinetic Jaffe reaction using a Cobas 6300 analyzer (Roche Diagnostics).

#### **Statistical analysis**

All statistical analyses performed using the Statistical Package for Social Science, version 19. Independent student t-test used to compare differences between the different groups. Linear regression used to assess associations between blood lead levels and estimated GFR. Pearson correlation coefficient<sup>®</sup> was used to assess the correlations between blood lead levels with serum creatinine and estimated GFR.

## **RESULTS**

Blood lead levels and kidney function measures in the adolescents shown in Table 1. The mean blood lead level in the overall adolescents was 3.55 ug/dl (range 1.8-6.7 ug/dl) .The mean serum creatinine level was 0.72 mg/dl (range 0.7-1.2 mg/dl) and the mean creatinine-estimated GFR was 106.47 ml/min/1.73m<sup>2</sup> (range 85-120ml/min/1.73m<sup>2</sup> ). The mean blood lead

levels in adolescents living in low altitude area was higher than in high altitude areas group, ( $p < 0.01$ ). The mean blood lead levels were found to be higher among males and older adolescents than in females and younger age group, but this difference was not significant. The mean serum creatinine and creatinine-estimated GFR values in adolescents living in different altitude areas were significantly different ( $p < 0.01$  and  $< 0.05$  respectively). In linear regression analyses, higher blood lead levels consistently associated with a lower creatinine-estimated GFR. Higher blood

lead levels was also associated with a high serum creatinine values (Table 2). Adolescents with blood lead levels of  $> 5$  ug/dl had  $101.66 \pm 4.32$  ml/min/1.73m<sup>2</sup> lower creatinine-estimated GFR (95% CI for mean  $100.61$ - $102.71$  ml/min/1.73m<sup>2</sup>) compared with those with lead levels  $< 3$  ug/dl ( $109.42 \pm 6.78$ ; 95%CI;  $108.70$ - $110.14$  ml/min/1.73m<sup>2</sup>),  $P < 0.001$ . Adolescents blood lead levels were inversely correlated with creatinine-estimated GFR ( $r = -0.38$ ,  $P < 0.001$ ) (Fig. 1) and positively with serum creatinine ( $r = 0.25$ ,  $p = 0.01$ ); (Fig.2).

**Table 1. Blood lead level, serum creatinine, and creatinine-estimated GFR by participant characteristics**

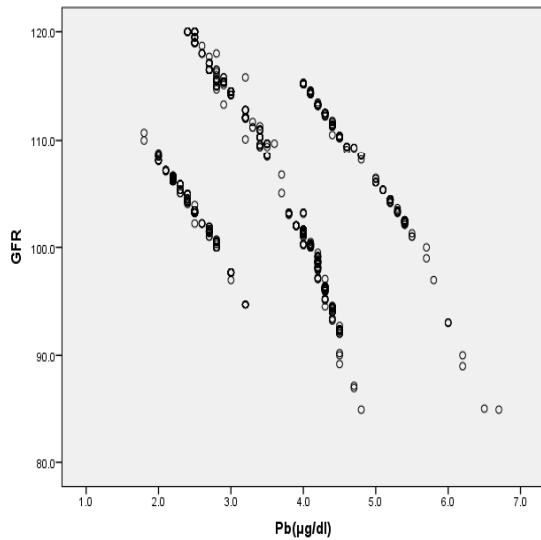
Characteristic	No. (%)	BPb ug/dl	P value	S.Cr mg/dl	P value	Estimated GFR ml/min/1.73m <sup>2</sup>	P value
Total	837(100)	$3.55 \pm 0.98$		$0.72 \pm 0.07$		$106.47 \pm 7.39$	
SEX							
Male	421(50.3)	$3.81 \pm 1.00$	0.82	$0.76 \pm 0.08$	0.57	$104.57 \pm 7.22$	0.61
Female	416(49.7)	$3.30 \pm 0.90$		$0.68 \pm 0.06$		$108.39 \pm 7.56$	
Age(yr)							
13-15	417(49.8)	$3.23 \pm 0.85$	0.71	$0.66 \pm 0.06$	0.09	$108.31 \pm 8.65$	0.07
>15-19	420(50.2)	$3.86 \pm 1.10$		$0.77 \pm 0.08$		$104.61 \pm 6.12$	
Residence							
Low altitude	418(49.9)	$4.43 \pm 0.51$	$< 0.01$	$0.80 \pm 0.09$	$< 0.01$	$103.52 \pm 6.30$	$< 0.05$
High altitude	419(50.1)	$2.68 \pm 0.41$		$0.64 \pm 0.05$		$109.41 \pm 8.47$	

**Table 2. Mean and SD of serum creatinine and creatinine-estimated GFR associated with blood lead levels**

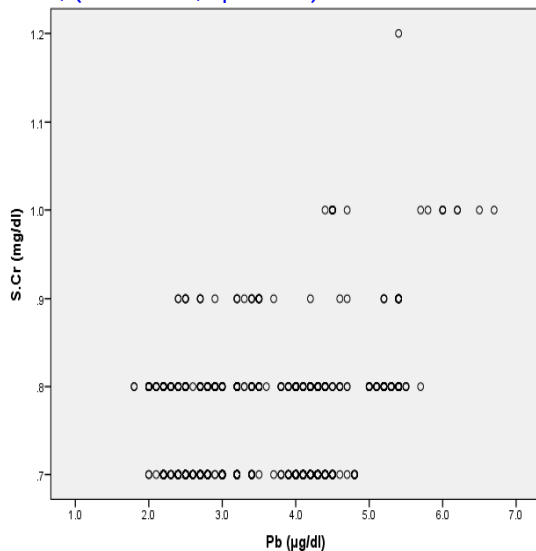
BPb Ug/dl	No. (%)	S. Cr mg/dl	P value*	Estimated GFR ml/min/1.73m <sup>2</sup>	P value*
$< 3$	341(40.70)	$0.73 \pm 0.05$	$< 0.01$	$109.42 \pm 6.78$	$< 0.001$
3-5	426(50.9)	$0.74 \pm 0.06$		$104.90 \pm 7.37$	
$> 5$	70(8.4)	$0.84 \pm 0.08$		$101.66 \pm 4.30$	

\* Onaway ANOVA for serum creatinine and estimated GFR grouped by Pb levels

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**Figure 1.** Creatinine-estimated GFR by blood lead levels, ( $r = -0.381$ ,  $p < 0.001$ )



**Figure 2.** Serum creatinine by blood lead levels, ( $r = 0.25$ ,  $p < 0.01$ )

## DISCUSSION

In this study, we found that, overall, adolescents had blood levels below 10 µg/dl, the acceptable limit reported by others 13,14. Nevertheless, we found a significant association between blood lead levels and kidney function, higher blood lead levels were associated with lower estimated GFR and higher serum creatinine. The association was strong and graded throughout the range of blood lead levels. Previous studies conducted in children and adolescents suggest an inverse relation between low-level

environmental lead exposure and kidney function in cross-sectional and prospective analyses 15, 16. Our study extended those findings to adolescents sample at two levels of lead exposure, i.e. adolescents group living at low altitude area and the other group living at high altitude area, indicating that lead exposure at a level common in low altitude areas is associated with lower kidney function. Our previous study conducted in urban individuals living at different altitude areas, has shown that in low altitude area, crowded area in which exposure to lead is higher owing to the greater number of vehicles, gasoline generators, and industrial emissions, also probably due to less wash by air currents, blood lead levels were higher compared to the other area groups. However, increased risk of impaired kidney function suggests that low-level exposure may affect kidney function through early declines in the glomerular filtration rate.

Our study revealed no significant association between the values of blood lead and the factors known to affect blood lead levels and/or GFR of adolescents, such as sex and age. This is probably due to the low lead exposure among the studied population. However, some recent studies found a tendency towards increased blood lead levels with older age 17, 18.

Our results confirm the previously reported finding that higher blood lead levels in a range below the CDC level of concern (10 µg/dl) associated with lower estimated GFRs in a representative sample of US adolescents 5.

Our data of kidney function based on serum creatinine. This already known highly affected by age and sex, limiting the precision of creatinine-based GFR estimates. However, remarkable percent (8.4%) of adolescents with blood lead levels above 5.0 µg/dl had a lower estimated GFR; moreover, blood lead levels seems to have a negative correlation with values of creatinine-estimated GFR

and a positive correlation with serum creatinine levels. Controversial reports exist about a consistent association of low blood lead levels with kidney function 19, 20. A number of studies have found evidence against reverse causation, as an explanation for observed association between lead level and kidney function even in patients with chronic kidney damage, 21, 22. Prospective studies have shown that baseline lead levels are associated with subsequent decline in kidney function, adding evidence to the cause-effect relationship between lead exposure and subsequent kidney function decline. 23. Such inconsistent findings may be due to differences in the study population and research methodologies.

Some limitations of our data need to be considered in the interpretation of these findings. Firstly, our study was cross-sectional which lacks follow up. Secondly, assessment of kidney function was done by creatinine-based GFR estimates, creatinine-based estimates are known to perform less well at higher levels of GFR, and it has been repeatedly suggested that cystatin-based GFR estimates may be a superior marker of early dysfunction. 24 In conclusion, our results indicate that higher blood lead levels below the acceptable limit reported by the current Centers for Disease Control and Prevention (<10 ug/dl) were associated with a lower creatinine-estimated GFR in a sample of adolescents, particularly among those living in low altitude areas. Environmental factors hypothesized to contribute to this burden. Measures to reduce exposure to the metal should be considered, especially in low altitude areas where children and adolescents are particularly at a higher risk of decline in kidney function. Further studies in this area are needed to seek the association of environmental lead exposure with chronic kidney damage.

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## پوخته

## ئاستین رصاصی دناف خوینی دا دگه ل کارین گولجیسکا لدهف گه نجین دهوکی

**پیشهکی و ئارمانج:** پسته پیدانه کا گرنه هه به ل په یوه ندیا نیگه تیف لنافه ینا کارین گولجیسکا و به رهنکاربوون بو ئاستی نزم یی رصاصی.

**ریکین فه کولینی:** ئەف فه کولینه هاتیه کرن ل سه ر دیارکرن ریزا رصاصی دناف خوینیدا و کریاتینین دا دناف خوینیدا. کریاتینین تیته دهست نیشانکرن ب ریزه یا (الترشیح الکبیبی GFR) ل سه رجه می 837 گه نجا هاتیه ژنگرتن ل قوتابخانین ناوه ندی و ئاماده یی.

**ئه نجام:** تیکرایا ئاستی رصاصی لناف خوینا گه نجا بگشتی  $3.55 \pm 0.98 \mu\text{g/dl}$  و تیکرایا ئاستی کریاتینین  $0.72 \pm 0.07 \text{ mg/dl}$ . دهست نیشانکرن ئاستی کریاتینین  $106.47 \pm 7.39 \text{ ml/min/1.73 m}^2$  GFR. گه نجین ئاستی رصاصی ل دهف وان  $5 \mu\text{g/dl} >$  ئاستی  $101.66 \pm 4.32 \text{ ml/min / 1.73 m}^2$  GFR به راوردی دگه ل گه نجین ئاستی رصاصی 3  $\mu\text{g/dl} <$  ئاستی  $109.42 \pm 6.78 \text{ ml/in/ 1.73m}^2$  GFR چونکه کاریگه ری په یوه ندی نیگه تف بو دگه ل کریاتینین  $r = -0.38$ .  $P = 0.001$  به ل یی پوزه تیف بو دگه ل دهست نیشانکرن کریاتینین  $r = 0.25$ ,  $P = 0.01$  ل دهف هه می گه نجا.

**دهرئه نجام:** ئه نجامین بدهستقه هاتین دیارکر به رزبونا ئاستی رصاصی دناف خوینیدا لدهف گه نجا کیتر بو ئاستی دیارکری ژلای سته نته ری کونترولی یی خو پاراستنا به رهنکاربونا رصاصی یی خوجه کو  $10 \mu\text{g/dl}$  ئه و هاتیه گریدان دگه ل نزمبونا ئاستی (GFR) دگه ل وه رگرتنا هه می کارتیکه رین ژینگه هه ئه وین گریدایفه لسه رفی باری.

## الخلاصة

### مستويات الرصاص في الدم مع وظيفة الكلى لدى المراهقين في دهوك

**خلفية وأهداف البحث:** يوجد اهتمام كبير للعلاقة المعكوسة بين وظيفة الكلى والتعرض الى مستوى منخفض للرصاص. طرق البحث: أجريت دراسة مستعرضة من خلال تقدير مستويات الرصاص في الدم، كرياتينين مصل الدم والكرياتينين المقدر بمعدل الترشيح الكبيبي GFR لدى 837 مراهقاً تم اختيارهم عشوائياً من المدارس المتوسطة والثانوية.

**النتائج:** معدل مستوى الرصاص في دم المراهقين العام  $3.55 \pm 0.98 \mu\text{g/dl}$  في الدم وكان معدل تقدير مستوى الكرياتينين  $0.72 \pm 0.07 \text{ mg/dl}$  بمعدل الترشيح الكبيبي  $106.47 \pm 7.39 \text{ ml/min/1.73 m}^2$  GFR. أكثر من  $5 \mu\text{g/dl}$  كان معدل GFR هو  $101.66 \pm 4.32 \text{ ml/min / 1.73 m}^2$  مقارنة مع المراهقين الذين كان عندهم مستوى الرصاص أقل  $3 \mu\text{g/dl}$  ووجدت  $109.42 \pm 6.78 \text{ ml/in/ 1.73m}^2$  GFR وحيث علاقة عكسية بين مستوى الرصاص في الدم والكرياتينين المقدر بمعدل الترشيح الكبيبي  $r = - 0.38$ .  $P = 0.001$  وعلاقة ايجابية مع تقدير كرياتينين مصل الدم بلغ  $r = 0.25$  ,  $P = 0.01$  عند كل المراهقين.

**الاستنتاج:** تشير النتائج الى وجود علاقة بين المستويات العالية من الرصاص في الدم والتي هي بمستوى أقل من الحد المقبول  $10 \mu\text{g/dl}$  والمثبت من قبل مراكز السيطرة على الأمراض والوقاية مع انخفاض مستوى الكرياتينين المقدر بمستوى الترشيح الكبيبي والاخذ بنظر الاعتبار كافة العوامل البيئية المقترنة بهذا العبء.