

Study of Lead Measurement in Drinking Water and Blood in Children with Chronic Kidney Disease

Wesam E. Afifi ^a, Maha M.Mokhtar ^b, Abd El Hameed A.Abd El Hameed ^a, Hend G. Makled ^a, Mostafa G. Elbalshy ^a

Abstract:

^a Pediatric Department, Faculty of Medicine Benha University, Egypt.

^b Forensics Medicine and Clinical Toxicology Department, Faculty of Medicine Benha University, Egypt.

Corresponding to:

Dr. Hend G. Makled. Pediatric Department, Faculty of Medicine Benha University, Egypt.

Email: drhendmakled@gmail.com

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Background: Environmental lead exposure as a risk factor for chronic kidney disease (CKD) we evaluated the association between lead exposure and CKD. **Aim of the study:** The aim of the study to assess lead in the drinking water and blood lead level in children with chronic kidney disease. **Subjects and Methods:** This case and control study included 30 cases diagnosed with chronic kidney disease on hemodialysis, 10 cases diagnosed with chronic kidney disease and on conservative therapy according to Schwartz formula and 10 healthy children as controls. All subjects were subjected to detailed history taking, general examination, and laboratory investigations. Also, examination for signs of lead poisoning and measurement of lead in blood and water were performed. **Results:** Our study showed that a male predominance. lead was significantly increased in cases compared to controls, and that was evident in both blood and water lead. Urea and Creatinine was significantly increased in cases compared to controls ($p < 0.001$) GFR was significantly lowered in cases compared to controls ($p < 0.001$) The study revealed positive correlation between blood lead, Urea and

Creatinine ($p < 0.001^*$) There was negative correlation between blood lead and GFR ($p < 0.01^*$) Lead level had no significant association with neither of age, sex nor duration of renal disease. **Conclusion:** exposure to lead, even at low level, is associated with increased risk of chronic kidney disease. Reduction of lead exposure may reduce the risk of chronic kidney disease.

Keywords: chronic kidney disease, hemodialysis, lead toxicity.

Introduction

Chronic kidney disease (CKD) is a major health problem worldwide with increasing incidence and prevalence that is threatening to bring on the onset of a real 'epidemic' (1) chronic kidney disease (CKD) refers to a state of irreversible kidney damage and/or reduction of kidney function that can lead to a progressive decrease in kidney function. It is the accepted term in the pediatric nephrology community, CKD is renal dysfunction of varying degrees from severe to mild in nature. CKD more clearly defines renal dysfunction as a continuum, rather than a discrete change in renal function' (2) Lead is the most notable and best studied environmental nephrotoxicant. Acute lead poisoning disrupts both proximal tubular structure and function. Characterized by the development of Fanconi syndrome. Manifestations of acute lead poisoning are usually reversible after cessation of lead exposure. Chronic lead poisoning may also result in lead nephropathy, which is characterized by tubulointerstitial fibrosis, tubular atrophy, glomerular sclerosis, and ultimately diminished glomerular filtration rate (GFR). Chronic lead exposure has also been shown to cause hypertension' (3) Epidemiological studies of the general population have reported associations between blood lead levels (BLLs) < 10 µg/dL increase the risk of chronic kidney disease (CKD), decreased estimated glomerular filtration rate (eGFR) and creatinine clearance. The associations are typically stronger in people with hypertension or diabetes. Individual with BLLs < 10 µg/dL during adulthood may have had higher BLLs earlier in life. It is unknown if blood or bone lead levels are more consistently associated with kidney

effects' (4) The association between lead exposure and GFR was evaluated in. Median blood lead level. In analyses stratified by CKD diagnosis, the association between lead level and GFR was stronger among children with glomerular disease underlying CKD; increase in lead level was associated with decrease in GFR. (5)

Subjects and Methods

This case and control study included 30 cases diagnosed with chronic kidney disease on hemodialysis, 10 cases diagnosed with chronic kidney disease and on conservative therapy according to Schwartz formula and 10 healthy children as control group' (6) Our case study will be conducted on patients attending Pediatric Nephrology unit and Clinic of Benha University Hospitals from (February 2021 - December 2021). An informed written consent was obtained from child parents before the study after complete description of the benefits of these investigations. Also, the study was approved by the Local Ethical Committee of Benha University {MS.16.7.2021}. All cases were subjected to complete history taking, thorough general examination, examination for signs of lead poisoning and measurement of lead in blood and water and Laboratory investigations.

➤ Inclusion criteria:

- All children diagnosed with chronic kidney disease less than 18 years.
- Chronic kidney diseases patients on dialysis and conservative therapy
- Both sexes will be included.

➤ Exclusion criteria: Children above 18 years.

➤ History taking:

- **Personal history:** Age, sex, residence, and socioeconomic status

• **Present history:**

Full history taking including the onset, course and duration of renal disease, manifestation of chronic kidney disease (oliguria, polyuria, hypertension, oedema, hematuria, abdominal pain and growth retardation), manifestation of lead toxicity (abdominal pain, constipation), History suggestive of acute metabolic complications, as (sweating, headache, Blurring of vision, tremors, convulsions, and coma), Drugs used and their doses.

• **Past history:** Other diseases and operations.

• **Family history:** renal problems.

➤ **Examination:**

- **General:** Vital signs (pulse, temperature, respiratory rate and blood pressure), Anthropometric measurements (weight and height), presence or absence of edema and skin rash.
- **Local:** abdominal, cardiac, CNS and chest examination.

➤ **Laboratory investigations:**

- CBC, Blood Urea Nitrogen (BUN, Serum creatinine, Serum electrolytes (sodium, potassium, calcium, phosphorus), Blood lead, Lead in drinking water.

Statistical analysis:

The clinical data were recorded on an "Investigation report form". These data were tabulated, coded then analyzed using the computer program SPSS Statistical package for social science (IBM SPSS statistics for windows version 26 .Armonk, NY:IBM Corp) to obtain. Descriptive statistics were calculated for the data in the form of Mean, Standard deviation (\pm SD) for quantitative data and Number and percent for qualitative data. In the statistical comparison between the different

groups Student's t-test was used to compare between mean of two groups of numerical (parametric) data, for continuous non-parametric data, Mann-Whitney U- test was used for inter-group analysis. ANOVA (analysis of variance) was used to compare between more than two groups of numerical (parametric) data, for continuous non-parametric data, Kruskal-Wallis's test was used for inter-group analysis, post-hoc test was used to detect intergroup comparison. Inter-group comparison of categorical data was performed by using chi square test (X^2 -value), Pearson correlation coefficient (r) test was used correlating different parameters. Some investigated parameters were entered into a regression model to determine which of these factors is considered as a significant predictor. A P value <0.05 was considered statistically significant (S).

Results

This case and control study was carried out (February 2021 - December 2021). It included 30 cases diagnosed with CKD on regular hemodialysis, 10 cases diagnosed with CKD and on conservative therapy according to Schwartz formula and 10 healthy children as controls after obtaining an informed consent from the children care givers. Ages of the children included in this study ranged from 3 to 17 years and there was a significant difference between groups regarding age. The study shows male predominance as (62 %). Regarding anthropometric measurement 3rd percentile of weight and height were the most frequent in group (I)

This study shows that obstructive uropathy were the most common causes of CKD which represent 60% in group I and 40% in group II as showed in (table1,2)

Table (1): causes of CKD in group I

Cause of CKD	No.	%
Congenital renal hypoplasia	4	13
Glomerulonephritis	1	3
nephrotoxic drug	2	6
Obstructive uropathy	18	60
SLE	3	10
Nephrocalcinosis	1	3
Vasculitis	1	3

Table (2): causes of CKD in group II.

Cause of CKD	No.	%
Caroli disease	1	10
Glomerulnep	1	10
HUS	2	20
Nephrotic	2	20
Obstructive	4	40

Although some patients had abnormal electrolyte levels (calcium, sodium, potassium and phosphorus) the mean values of these electrolytes were within normal ranges. Except potassium was statistically significant difference between

Group I, Group II and Group III (p0.001). mean level of creatinine and urea were high in patients compared to controls but the mean level of hemoglobin was low because most of patients were anemic as shown in Table (3).

Table (3): Laboratory investigation among studied groups

Characteristics	Gr. I (n=30)		Gr. II (n=10)		Gr. III (n=10)		Test of sig.	p-value
Na⁺ (mEq/dl) (mean ± SD)	147.97	5.52	151.38	33.28	137.70	1.34	2.3	0.1
K (mEq/dl) (mean ± SD)	5.52	0.77	4.03 ^a	0.54	4.01 ^a	0.20	31.2	<0.001*
Ca⁺ (mg/dl) (mean ± SD)	8.46	1.18	8.18	2.58	9.50	0.19	2.44	0.1
Urea (mg/dl) (mean ± SD)	67.28	8.79	85.6 ^a	31.30	12.4 _{a, b}	2.55	40.9	<0.001*
Creatinine (mg/dl) (mean ± SD)	7.32	5.45	2.22 ^a	0.86	0.69 ^a	0.10	11.5	<0.001*
HB (mean± SD)	11.97	3.38	9.53	2.07	12.91 ^b	0.85	3.9	0.03*

This study shows that mean value of blood lead was significantly higher among Cases (5.27 and 3.73). There is a statistically significant difference between Group I, Group II and Group III regarding water lead as shown in table (4).

There is a positive significant correlation between blood lead and urea, creatinine as shown in (Figure1) There were statistically

significant negative correlations between blood lead &GFR (Figure2).

There were no statistically significant correlations between lead level and (age, sex, duration of renal disease, onset and course of CKD as showed in (table 5)

Table (5) shows that linear regression analysis reveals that none of variables were significant predictors for lead level.

Table (4): Comparison of study groups regarding lead level

Characteristics	Gr. I (n=30)		Gr. II (n=10)		Gr. III (n=10)		Test of sig.	p-value
blood lead ug/dl (mean ± SD)	5.27	6.44	3.72	1.31	0.16	0.21	3.8	0.03*
					a,b			
water lead ug/L (mean ± SD)	0.18	0.17	0.10	0.11	---	---	6.6	0.003*

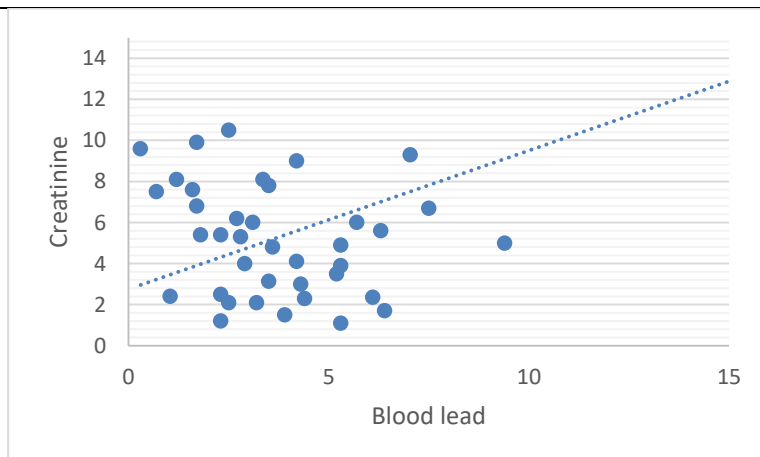


Figure1

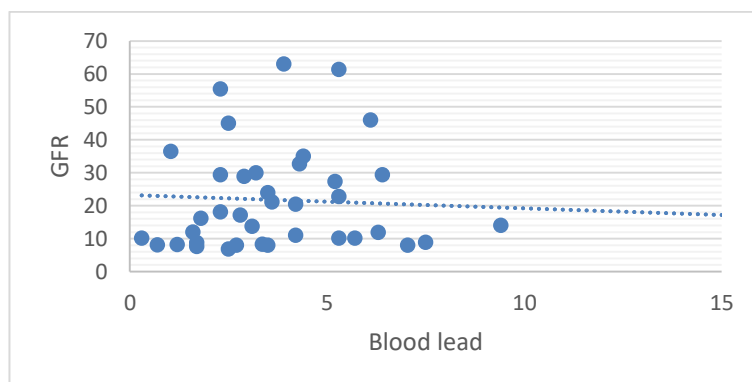


Figure 2

Table (5): Regression analyses of various variables for prediction of lead level.

	Univariate analysis	
	β	p-value
Age	-0.104	0.634
Sex	-0.832	0.610
Disease duration	-0.497	0.210
Onset	-0.927	0.628
Course	-1.548	0.459

Discussion:

The result of the current study revealed that there was statistically significant difference between patient Groups and controls regarding age. This agrees with a study that found positive significant differences between the groups of patients regarding age (7). In the present study males are more affected in CKD in group I (53.3%) and group II (90%) And this agrees with study revealed that the incidence and prevalence of CKD is greater in males than females because of the higher frequency of congenital abnormalities of the kidney and urinary tract (CAKUT) in males (8). In contrast the study conducted by, showed that 18% of women were diagnosed with CKD compared to 13 percent of men. When women battle chronic illness such as CKD (9). In our study the duration of renal disease is 1-10 years, with the duration of hemodialysis is 1-10 years, with 3 sessions of hemodialysis per week and each session lasted for 4 hours. In agreement with current study stated that three sessions per week for 3 to 4 hours per session, achieve the minimum target prescription of hemodialysis required for adequate hemodialysis in children (10,11). The most common cause of chronic kidney disease in those children was obstructive uropathy which represented 60% in group I and 40% in group II. This is positively

matched with study, reported that congenital obstructive uropathy is the most common cause of CRF in children and is among the top three etiologies of pediatric end-stage renal disease (12,13). In current study congenital renal hypoplasia and SLE were the second common cause. In the current study, there were statistically significant differences between patient groups and control regarding weight percentiles. Group I are more affected. in agreement with current study, who found the degree of weight impairment increases as GFR declines, even though a significant decrease in weight was seen at all levels of kidney function (14) Also current results are in agreement with those who found that, under weight is a common and perhaps the most visible complication of CKD in children (15). In the present study height percentiles are affected among the studied cases than controls. On the other hand, data from developed countries generally show a less severe effect on height.(16) the increased effect on height may be due to delay in the diagnosis as well as implementing interventional measures in CKD patients In the current study, there was statistically significant decrease in hemoglobin and hematocrit level among the studied cases than controls in agreement with the present study that found there was significant decrease in

hemoglobin level in patients when compared to the controls.(17) also present study agrees with stated that the anemia of CKD is due to reduced renal erythropoietin production and shortened red cell survival(18) . In contrast to present results reported that among chronic dialysis patients, hemoglobin levels have markedly increased due to widespread use of erythropoiesis-stimulating agents and intravenous iron over past 15 years. (19) The present study showed that there was significant increase in serum creatinine and blood urea in the studied patients when compared to the control group and this matched with, which detected significant high level of blood urea and serum creatinine. (20) In the current study, there was statistically significant increase in potassium among the studied patients when compared to the control group.

In the same line with current result ,who found that there was a highly significant increase in potassium (K+) level inpatients as compared to control(17)hyperkalemia generally develops in the patient who is oliguric or who has an additional problem such as a high potassium diet, increased tissue breakdown or hypoaldosteronism (due in some cases to the administration of an ACE inhibitor or ARB) (21) The result of current study revealed that high blood lead is associated with an elevated serum creatinine and CKD .The current study was positive with , which confirmed that chronic lead poisoning may also result in lead nephropathy, which is characterized by tubule interstitial fibrosis, tubular atrophy, glomerular sclerosis, and ultimately diminished glomerular filtration rate (GFR):(3)

In agreement with current study, who found the blood lead level was higher in the ESRD patients who were on MHD than in the healthy patient (22) Its supported by, which

revealed that associations between blood lead levels (BBLs) < 10 µg/dL increase the risk of chronic kidney disease (CKD)(5). Lead is the most notable and best studied environmental nephrotoxicant. Acute lead poisoning (blood lead levels > 80–100 µg/dL) disrupts both proximal tubular structure and function (4)

In the present result there was positive correlation of blood lead level and serum creatinine and urea in patient groups (high blood lead associated with high serum creatinine and urea), present result agrees with study that revealed the prevalence of elevated serum creatinine and CKD were higher at higher blood lead among patient group, (23) our result revealed that there was negative correlation of blood lead level and glomerular filtration rate. It is supported by, that found higher blood lead level was associated with a lower estimated GFR. (23) Our result agrees with, reported that association between lead exposure and GFR was stronger among children with glomerular disease underlying CKD increase in lead level was associated with decrease in GFR. (5) In contrast, there was no significant association between BLL and directly measured GFR in this relatively large cohort of children with CKD, although associations were observed in some subgroups. Higher lead levels due to reduced lead excretion as a consequence—rather than cause—of decreased kidney function and is raised as an explanatory factor for negative associations between higher blood lead and kidney function in cross-sectional studies. (24)The current study showed that, there was statistically significant difference between patient groups and control group regarding water lead level mean lead level in tap water in group I and group II (0.18 ± 0.17) and (0.10 ± 0.11) It is below the recommended levels of WHO guideline value (10µg/L) and

USEPA (5 µg/L). In agreement with the present results, found that the lead levels in tap water from Cairo and Giza were within recommended WHO level. (25) also concluded that the drinking water mean lead concentration in Greater Cairo was below the international standards. (26)

Conclusion:

The brain and kidney are the main parts affected by lead toxicity in both adults and children. Exposure to lead, even at low level is associated with increased risk of chronic kidney disease.

Reduction of lead exposure may reduce the risk of chronic kidney disease. Children are more prone to lead toxicity due to certain habits such as putting hands that might be contaminated in their mouth. Antioxidants, especially vitamin C, are used for the treatment and improvement of oxidative stress-induced toxicity of lead until now. Chelation treatment is employed for blood lead toxicity if the level is 45 g/dL or greater. Lead toxicity and associated morbidity and mortality can be reduced by regulating ongoing medical diagnosis, creating health awareness, and timely medical treatment.

Recommendation:

1-Need studies on more children with more variation, different age and different sociodemographic standard.

2-further studies need to support our finding, additional studies are needed to investigate the role of lead in pathogenesis of CKD.

3- Every parent should frequently wash their children's hands and prevent children from placing their hands in mouth habitually.

4-Every family should use cold water because hot water contains high amounts of lead.

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