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Original Article

Biochemistry Section

Blood Lead in End-Stage Renal Disease (ESRD) Patients who were on Maintainence Haemodialysis

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ABSTRACT

Background: In India, there is rising burden of chronic diseases like hypertension and diabetes. It has been estimated that 25-40% of these patients are likely to develop CKD, with a significant percentage requiring renal replacement therapy. Haemodialysis is the most common method which is used to treat advanced and permanent kidney failure. The derangements in the metabolism of several toxic and trace elements such as antimony, arsenic, cadmium, molybdenum, nickel, and selenium have been reported for several decades in patients with chronically reduced renal function. Overall, the available literature suggests that the blood levels of some elements such as cadmium, chromium, fluorine, iodine, lead and vanadium are high in ESRD.

Aim and Objectives: Our aim was to study the levels of blood lead in the End-Stage Renal Disease (ESRD) patients who were on Maintenance Haemodialysis (MHD), and to study whether there was any relationship between the blood lead concentration and the duration of MHD.

Methods: The blood lead level was determined in 50 healthy subjects with normal renal function and in 50 patients with ESRD who were on MHD. None of them had a history of smoking or any industrial exposure.

Results: The results of this study revealed that the blood lead level was higher in the ESRD patients who were on MHD than in the healthy adults. The blood lead concentration was found to increase with the duration of the MHD.

Conclusion: The mild increase in the blood lead level with an increase in the duration of MHD in the study population, may be viewed in the wider context that the prolonged exposure to lead, even at low levels may result in CKD by causing interstitial nephritis, hypertension, hyperuricaemia, an increased incidence of hypertension, cerebrovascular disease and cardiovascular disease or the progression of an already existing CKD.

Key Words: Lead, End-stage renal disease, Maintenance haemodialysis

INTRODUCTION

End-Stage Renal Disease (ESRD) is the most debilitating condition for patients with renal diseases and a point of no return on the renal disease spectrum. It increases the patient morbidity and mortality and puts a major economic strain on the health care system. ESRD represents a clinical state or a condition in which there has been an irreversible loss of the endogenous renal function to a degree which is sufficient to render the patient permanently dependent upon Renal Replacement Therapy (RRT) which may be dialysis or kidney transplantation [1]. Haemodialysis is a more accessible treatment option of ESRD; it is the most commonly employed line of treatment as well. Globally, the number of ESRD patients who are on Maintenance Haemodialysis (MHD) has gone up in virtually all the countries in the last two decades. Haemodialysis can lead to the accumulation of certain toxic elements which may be deleterious and the depletion of certain trace elements which will affect the normal functions of the body and may have significant clinical implications, which include an increased risk for cardiovascular disease,immune deficiency, anemia, renal function impairment and bone disease. In ESRD, the most important factor which affects the trace element concentration is the degree of renal failure and the modality of the renal replacement therapy [2,3]. Considering the magnitude of the problem of CKD/ESRD in India and the availability of RRT, it is needed to further our knowledge about the effect of CKD and RRT/MHD on the trace and toxic element homeostasis. Toxic elements are ubiquitous in the environment. When the renal system is not functioning properly, the clearance of many toxic elements are also affected. The accumulation of aluminium and strontium in haemodialysis patients results from the dialysate contamination. Several trace and toxic elements have been implicated in the decline of the renal functions.These include arsenic, cadmium, copper, germanium, lead and mercury [4]. Lead toxicity affects many organs, resulting in encephalopathy, anaemia, peripheral neuropathy, gout and renal failure. Recent investigations have shown that the environmental exposure to lead is related to a progressive renal insufficiency in patients with and without diabetes [5]. This study was done to assess the level of blood lead in ESRD patients who were on MHD and to compare the blood lead levels of healthy adults with normal renal functions with those of end-stage renal disease patients who were on maintenance haemodialysis.

MATERIAL AND METHODS

This study was conducted on 100 subjects. The study design called for two groups: the normal subjects (control) included both males and females with normal renal functions, who were in the age group of 40 to 60 years. The study subjects (cases) included both male and female end-stage renal disease patients who were undergoing chronic haemodialysis for 6 months, 12 months and 24 months, who were in the age group of 40 to 60 years. All measures were taken to maintain a strict confidentiality about the personal details of the participants of the study. This study was done in conformity with the Declaration of Helsinki and it was approved by the Sri Ramachandra University Institutional Ethics Committee.

Group A: Consisted of the control subjects of 50 apparently healthy adult male and female volunteers with normal renal functions. Their mean age was 52.5 years. There were 29 males and 21 females. They were normal healthy adults who are employees of the Sri Ramachandra University, Chennai and individuals who attended the routine health check-ups and were selected randomly.

Group B: Consisted of 50 end-stage renal disease subjects, both males and females with a mean age of 52.5 years, who were on MHD treatment at the Hemodialysis Unit, Department of Nephrology, at the Sri Ramachandra Medical Centre. Of the 50, 31were males and 19 were females.

The conventional technique of low-flux haemodialysis was employed. All the patients had been on the regular bicarbonate haemodialysis on a polysulfone membrane dialyzer for more than 6 months; there were 4 hours per session, which was three times per week. Those with a history of occupational exposure to heavy metals or metal intoxication and those patients who were on haemodialysis for < 6 months and for causes other than ESRD were excluded from the study. The group B subjects were further grouped, based on the duration of their MHD. Group C – ESRD patients who were on MHD for 6 to 12 months; Group D – ESRD patients who were on MHD for 12 to 24 months ; Group E – ESRD patients on MHD for above 24 months .

All the patients were interviewed regarding their full medical and occupational history, the duration on their MHD, the presence of any associated illness, their dietary history and their current medications. For the normal healthy controls, their diet history, occupation history, medication history and tobacco intake history were taken. Blood samples were withdrawn randomly from the healthy individuals (group A) and from the ESRD patients who were on maintenance haemodialysis (group B) for the estimation of serum urea, creatinine, and blood lead. The appropriate blood samples for group B were collected just before the start of the mid-week dialysis session for the elemental estimation. The blood samples were drawn from the peripheral veins into sterile royal blue topped BD vacutainers for the element analysis. The blood samples were stored and the analysis was done in batches within one week of the blood sample collection.

The sample analysis was done by using an inductively coupled plasma-optical emission spectrophotometer (ICP-OES) of the make Perkin Elmer Optima 5300 DV. The sample analysis was done in batches. Calibration curves were plotted before running each batch. The wavelength of the blood lead analysis was 220.353 and the lower detection limit of the instrument was 4.2 µg/dL. Blood urea and serum creatinine were estimated by using the automated ADVIA centaur.

RESULTS

The SPSS, version 15 statistical software tool was used for the data processing. All the values were expressed as mean ± one standard deviation unless was otherwise indicated. The differences in the mean values between the group A and group B were analyzed by using the Student's t-test. The one-way analysis of variance (ANOVA) was used to compare the different groups of haemodialysis, based on the duration of the dialysis treatment (groups C, D, and E). A p-value of < 0.05 was considered as statistically significant. The clinical characteristics of the study group have been shown in [Table/Fig-1]. The blood lead concentrations of the groups A,B,C, D, and E have been shown in [Table/Fig-2].

	Group A (Control)	Group B (Cases)
Age (years) (mean)	52.5	52.5
MHD duration (months)		6 to 24
Diabetes (yes/no)	nil	50/0
Hypertension (yes/no)	nil	45/5
Total n= (male/female)	50 (29/21))	50(31/19)
Tobacco use	nil	Nil
Medication % Erythropoietin Lipid lowering agents		 100 20

[Table/Fig-1]: Clinical characteristics of study groups

Study Group	UREA Mean ± SD (mg/dL)	CREATININE Mean ± SD (mg/dL)	Lead Mean ± SD (µg/dL)	P value
Group A	17.00 ± 2.01	0.70 ± 0.15	07.32 ± 1.67	0.000
Group B	78.62 ± 5.12	8.13 ± 1.69	14.00 ± 1.2	
Group C	69.06 ± 4.01	7.08 ± 1.05	13.13 ± 1.57	0.000
Group D	77.25 ± 5.05	8.06 ± 1.72	14.20 ± 0.48	
Group E	89.55 ± 8.30	9.24 ± 2.30	14.69 ± 1.55	

[Table/Fig-2]: Comparing the concentration of blood urea, serum creatinine and blood lead level between groups A, B, C, D, E

DISCUSSION

The present study observed that the blood lead was high in the haemodialysis patients than in the normal subjects, with a p value of 0.000. A statistically significant increase in the blood lead concentration with an increase in the MHD duration was seen, with a p value of 0.000 [Table/Fig-2]. The present study's results correlated with the results of many other similar studies.

Michael Krachler et al., had demonstrated a higher concentration of lead than the high limits for healthy adults [6]. Martegani et al., described a significant increase in the erythrocyte [7] protoporphyrin IX levels in patients with chronic renal failure and in those who were on haemodialysis. Bernd Winierberg et al measured the bone lead levels in patients without any known lead exposure at various stages of the renal dysfunction, in those who were on haemodialysis and in those who had undergone a renal transplantation and found it to increase correspondingly with the serum creatinine, with the highest level being seen in the haemodialysis patients [8].

Bing Chen et al., who studied the whole blood and the serum samples of Chinese stable chronic renal failure patients, haemodialysis patients, post-transplant patients and subjects with normal renal functions, found a low prevalence of the elevated lead levels (>200 µg/L) in the dialysis patients, which was similar to the findings of Su-Hui Lee et al., [9,10]. Ja-Liang Lin et al., studied the blood lead levels in 315 patients who were on chronic peritoneal dialysis in an 18-month prospective study. The median blood lead level in the study subjects was 7.3 µg/dL (0.1, 29.9 µg/dL) which was higher than the level of 5.8 µg/dL [1.6, 19.1 µg/dL] in patients with chronic kidney disease and than the level of 4.8 µg/dL [1.6, 33.6 µg/dL] in stroke patients with normal serum creatinine levels in Taiwan [5,11,12]. Colleoni N et al and Kessler M et al., demonstrated elevated blood lead levels in patients who were on chronic renal dialysis [13,14]. A study which was done by Muntner P et al., demonstrated that there was an association between the blood lead level and the bone lead concentrations [15].

Ja-Liang Lin et al., in their study, by using the low blood lead level group (<5.62 µg/dL) as the reference (hazard ratio [HR] =1.00),

found that the high blood lead level group (>8.66 µg/dL, HR=3.745, 95% CI=1.218-11.494, p=0.001) and the middle blood lead level group (5.62-8.66 µg/dL, HR=1.867, 95% CI=1.618-2.567, p=0.001) were associated with an increased HR for the 18-month all-cause mortality for the chronic peritoneal dialysis patients [5]. These results were similar to the findings of previous studies in the general population [16-18]. The recent epidemiological investigations have shown that in a nationally representative sample of the US population, the blood lead levels were associated with an increased risk of death from all causes, cardiovascular diseases and cancer [17,18]. A previous study found that the individuals with a baseline blood lead level of 20-29 µg/dL had a 46% increased all-cause mortality than the general population [16]. Consequently, the environmental exposure to lead remains a significant determinant of the mortality in the general population and in the haemodialysis patients.

Ja-Liang Lin et al., in their study, demonstrated that the environmental exposure to lead, even at low levels, may accelerate the progressive renal insufficiency of the nondiabetic patients with CKD [5,16]. The findings of another study which was done by Ja-Liang Lin and Chun-Chen Yu et al., suggested that the low level environmental lead exposure was associated with an accelerated deterioration of the chronic renal insufficiency [19].

From the above discussion, it is clear that the lead exposure, even at low levels, may accelerate the progression of the renal insufficiency. The increased serum/blood lead levels which was seen in the haemodialysis patients may be partially due to the nearly complete loss of the renal functions and due to the difficulty in removing the lead during the haemodialysis. Hence, an environmental exposure to lead, even at low levels, may increase the blood lead levels in the haemodialysis patients. These results support the continued efforts which are being made to reduce the environmental lead exposure in patients with chronic renal diseases. From the above evidence which was provided, it seems that the annual screening for blood lead may provide more information and that it can be considered for better care of the chronic kidney disease patients. A variety of limitations of this study need however to be addressed. The small sample size did not allow a multivariate approach for incorporating additional, potentially meaningful factors for modifying the level of the blood lead. Further studies are needed to elucidate the role of the toxic and the trace elements, their clinical relevance and their effect on the course of chronic kidney disease, which will help in providing a better management for CKD.

Conflict of Interest: The authors declare no conflict of interest.

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