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Studies on the Influence, Reltionship and Alteration in Serum Cadmium Concentrations in Renal Diseased Patients

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Abstract: *Background and Objective: Chronic renal disease (CRD) is a growing worldwide problem. The worldwide prevalence of CRD is high and the number of patients with end–stage renal disease (ESRD) has dramatically increased in the past few decades. The aim of the present study was to assess the influence, relationship and alteration in serum cadmium concentrations in renal diseased patients. Subjects were selected from Sumathi Hospital, Madurai, Tamil Nadu, India for the study. A sample size of 75 from in and out-patients was selected and serum samples were collected from them after proper consent and subjected to cadmium analysis by Atomic absorption spectrophotometry. Among the age group of 51 to 60 years, 53% of the patients were found to have cadmium influenced renal disease. Cadmium toxicity induced renal disease was observed in men and they constituted 69% of the study population. Among those with cadmium influenced renal disease, 56% were smokers. Among the study group, 45% had diabetic nephropathy while 31% had chronic renal failure. Those with glomerulonephritis and interstitial nephritis were 19% and 5% respectively. Thirty three percent of the patients were found to contain serum cadmium levels between 0.001 – 0.01ppm. The results showed that the influence of cadmium was significant on the majority of the renal diseases. A study focussing on a single renal disease and cadmium levels would shed a clearer light on the relationship between cadmium and its deleterious effect on kidney functions.*

Keywords: *Cadmium, Chronic Renal Disease, Heavy Metals, Occupational Hazards*

INTRODUCTION

Cadmium is a well-known and widespread pollutant derived from industrial and agricultural activities (WHO, 2011). Cadmium is one of the most nephrotoxic metals available along with lead and it's toxicity results in the increased release of ß- 2 microglobulin in urine indicative of damage to the proximal tubule (Gonick, 2008). Cadmium has a long biological half life (more than 30 years). Cadmium exposure over a long time leads to increased accumulation in certain tissues like the kidney (Gonick, 1978). Kidney is considered as

the main organ affected by cadmium toxicity and environmental exposure of cadmium is considered as the significant contributory factor for the progress of chronic kidney disease. Upon chronic exposure, it accumulates in the proximal tubules. The chronic kidney disease due to cadmium toxicity is exacerbated in the presence ofother morbidities such as diabetes and hypertension (Johri Et Al., 2010). After absorption by the lungs and the gastrointestinal system, cadmiumis bound to the serum albumin and accumulates in the liver, where metallothionein-1- cadmium complex is formed. cadmium-metallothionein-1 complex is filtered by the kidney. The bound cadmium is taken in by the cells of the proximal tubule which has transporters for free and bound forms of Cadmium. This transport of bound cadmium interferes with the function of the proximal tubule (Ferraro et al., 2010).Cigarette smoke is also considered as one of the greatest sources of cadmium with cadmium levels five times higher in the blood of smokers compared to non-smokers (Rahimzadeh et al., 2017). Though smoking is considered as an independent risk factor for kidney disease, it is strongly discouraged if there is exposure to cadmium either through the environment or through exposure at work places. This makes smoking one of the risk factors which precipitates cadmium nephropathy (Price, 2017). It has been observed that the socio-economic status of individuals play a significant role in the risk of cadmium exposure and toxicity (Figueroa et al., 2017; Wu et al., 2018).The study area, Madurai, Tamil Nadu is beset with heavy metal pollution. Given this condition and the widespread kidney diseases observed, the present study was designed to understand the extent of cadmium nephropathy among the population.

Materials and Methods

The objective of the study was to find out the influence of cadmium in renal disease among the outpatient subjects of Sumathi Hospital. It is situated in the heart of the city of Madurai. The subjects were taken from Madurai and nearby districts belonging to the very poor socio-economic status and illiterate class with poor health and nutritional status. As per these criteria they were selected for the present study.

Selection of clinical cases for the study

A group of 75 patients with chronic renal failure who were attending Madurai Sumathi Hospital outpatient department (OPD) were recruited for the present study after getting consent from the medical superintendent. The study was carried out in 2007 to 2008. The suitable clinical cases (patients suffering from chronic renal failure) were selected by a qualified nephrologist on the basis of clinical history and diagnostic findings. The age, gender, socio-economic status, locality, symptoms of cadmium toxicity and the type of renal diseases were the details collected in the form of questionnaires from the patients. Symptoms of cadmium toxicity such as Hypertension, Hypoglycemia, Anaemia, Allergy, Nausea, Vomiting, Fever, Joint pain, Muscle weakness and Perspiration were obtained as secondary data from hospital records.

Collection of blood samples

Five millilitre of venous blood was collected from the volunteers by venepuncture. Then the blood was transferred to the test tube and kept at room temperature for thirty minutes, in order to allow it to clot. After that, the clotted blood sample was centrifuged at 3000 rpm for ten minutes with the help of a clinical centrifuge. The serum was separated using Pasteur pipette and transferred to a separate tube and stored at 4°C till further use (Tuck et al., 2008).

Sample preparation procedure

The following preparation procedure was employed for the acid digestion of serum samples. Five millilitre of serum sample was taken into a conical flask and to this 10 mL of acid mixture (a mixture of nitric acid and sulphuric acid) was added and covered. The flask was kept over the sand bath for digesting the contents. A clear solution was obtained. The above solution was transferred into a volumetric flask. Double distilled water was added to the solution to get 100 ml as the total quantity. From this, one ml of the solution was taken into an Eppendorf tube and subjected to Atomic Absorption Spectrophotometric (AAS) analysis (Oliveira, 2003).

Results

Patients suffering from various renal diseases were taken as the subjects and their personal details, habits and investigation reports were collected from Sumathi Hospital, Madurai. The serum samples were analysed for cadmium concentration employing AAS.

Age, sex and weight of the study population

Age-wise distribution of patients is tabulated (Table 1). Sex-wise breakdown of the sample population showed that 69% of them were males while 31% of the patients were females.

Table 1: Age-wise distribution of patients with renal diseases

S. no	Age (Yrs)	Frequency (%)
1	41- 50	44
2	51- 60	53
3	61- 70	3

Table 2: Weight of the patients included in the study

S. no	Weight (Kg)	Frequency (%)
1	51-60	37
2	61-70	55
3	71- 80	8

Table 3: Variation in blood pressure observed among the study population

S. no	Blood pressure (mm Hg)	Frequency (%)
1	120/90 to 130/80	12
2	140/100 to 150/90	48
3	160/100 to 170/110	36

Among the patients, 44% were non- smokers while the rest were smokers. Eighty percent of the patients were residents of Madurai while 14 % came from Thirumangalam, a town in the outskirts of Madurai and the rest of them were from other places.

Socio-economic status of the patients studied

Table 4: Employment status of the patients under study

S. no	Details of employment	Frequency (%)
1	Employment in Government or Private concerns	49
2	Unemployed	20
3	Self- employed	17
4	Labourers	14

Table 5: Monthly wages of the patients studied

Based on monthly income the patients could be divided into four groups.

S. no	Details of employment	Frequency (%)
1	No income (housewives)	16

2	Rs 3001- 4000	49
3	Rs 2001- 3000	20
4	Rs 1001- 2000	14

Details of renal diseases observed in the patients under study

The various symptoms of renal disease prevalent among the group of patients under study were: hypertension (47% of the patients), hypoglycaemia (32%), anaemia (28%), allergic effects (20%), joint pain and muscle weakness (16%) and perspiration (13%) (Table 6).

Table 6. Symptoms of cadmium toxicity seen among the study population

S. No	Symptoms	Frequency (%)
1	Hypertension	47
2	Hypoglycemia	32
3	Anaemia	28
4	Allergy	20
5	Nausea, vomiting, fever	20
6	Joint pain, muscle weakness	16
7	Perspiration	13

The prevalence of cadmium influenced renal diseases and their side effects were shown (Table 7); Nineteen percent of the patients had glomerulonephritis with increased urea creatinine, low haemoglobin and high A/G ratio with side effects such as joint pain, hypertension, and anaemia. Diabetic nephropathy was seen in 45% of the patients showing increased urea creatinine, glycosuria and low haemoglobin. The range of side effects seen in these patients include hypoglycaemia, hypertension and 31% had increased urea creatinine and albuminuria with side effects such as hypertension, allergy and muscle weakness. Only 5% of the subjects had interstitial nephritis with high urea creatinine levels and glycosuria. Hypertension, perspiration, vomiting and fever were the side effects seen in these patients. All these patients were recommended a low protein diet.

Table 7: Various renal diseases observed in the study population

S. no	Type of renal disease	Frequency (%)
1	Diabetic nephropathy	45
2	Chronic renal failure	31
3	Glomerulonephritis	19
4	Interstitial nephritis	5

The clinical blood report of the patients showed that the patients had various conditions such as proteinuria/albuminuria (47%), glycosuria (42%), low haemoglobin (41%) and high A/G ratio (25%). Figure 1 shows the level of cadmium in the sera of the patients under study.

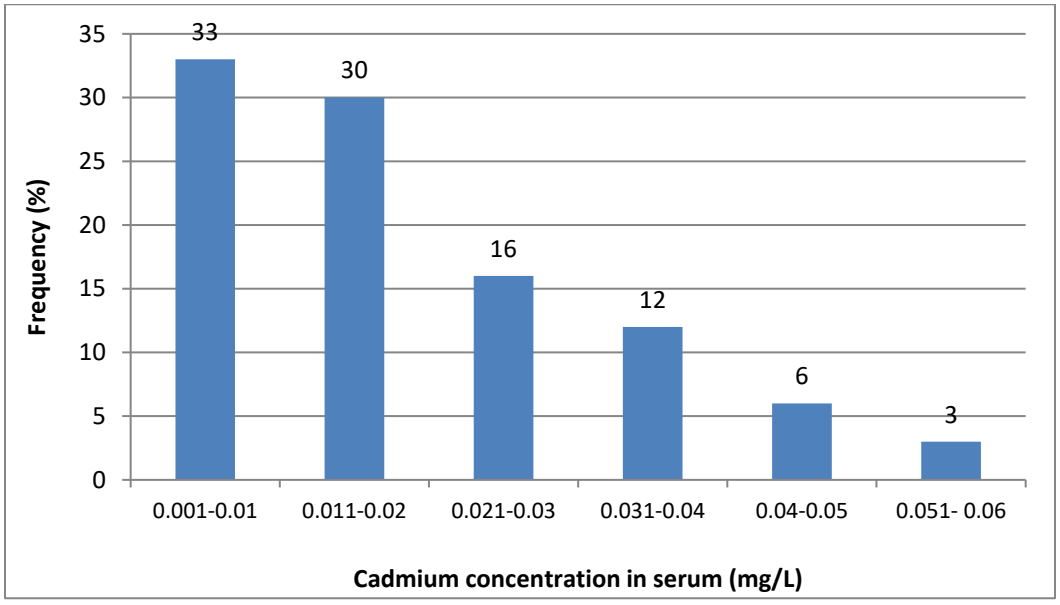

Figure 1. Serum cadmium concentration among the patients under study

Discussion

The present study aims to assess the influence, relationship and alteration in serum cadmium concentrations in renal diseased patients in Sumathi Hospital, Madurai. The study group consisted of 75 subjects with various types of renal diseases. Serum cadmium concentrations of the entire group of subjects were related to the age, gender, socio-economic status and types of renal diseases. The serum cadmium concentration fluctuated with the different types of renal diseases. Proteinuria, the hallmark of Cadmium nephropathy was observed in majority of the patients. Serum cadmium levels were low ranging from 0.001 to 0.06 mg/L.

In the present work, age and gender were significant indicators of cadmium influenced renal disease. Cadmium concentration in serum increased with age. People may develop the adverse health effects at an old age. Cadmium reaches the maximum accumulation in people around and over 50 years of age (Olsson et al., 2002). The present study also shows that gender differences are also associated with the cadmium influenced renal disease. Regarding gender, males are more prone to cadmium accumulation than females. Men were more susceptible to trace element toxicity than women. In contrast to the present observation, a study among Sri Lankans has shown that chronic kidney disease was more in females than males. But severe stages of chronic kidney diseases were seen in males (Jayatilake et al., 2013). The risk of cadmium influenced renal disease was also related to socio-economic status. The members of families with working professionals had a higher risk and this was mainly confined to men. The effect of socio-economic status on chronic renal failure was reported in a population based case- control study in Sweden (Vahter et al., 2007). They inferred that that low socio-economic status is associated with an increased risk of chronic renal failure. This observation is supported by different studies (Fored et al., 2003; Said and Hernandez, 2015). In Sri Lanka, being a farmer increased the risk of chronic kidney disease (Jayatilake et al., 2013).

In the present study, it was observed that the highest percentage of patients falling in the group of blood pressure (140/100 to 150/90) as 48 and 56% subjects were smokers. The major source of cadmium apart from occupational exposure and diet is smoking. Cigarettes contain nicotine as well as cadmium which also has nephrotoxic effects (Price, 2017). Blood pressure and heart rate are increased by smoking (Kim et al., 2015). Smoking indirectly causes chronic kidney disease by causing hypertension. Among Korean population, hypertensive patients with high serum cadmium levels were prone to have chronic kidney disease (Robles-

Osorio and Sabath, 2016). This indicates the complex interaction between blood pressure, smoking, cadmium exposure and chronic kidney disease.

In the present work, proteinuria was observed in 45% of the study population. The first sign of cadmium-related damaged kidneys is usually an increase of low molecular weight proteins in the urine (proteinuria). Marker proteins includeß- 2 microglobulin and retinol binding protein. These proteins are normal constituents of plasma, and are normally filtered through the glomerular membrane and then reabsorbed from the proximal tubules of the kidney. Proteinuria is a sign of damage to the tubules (Wallin et al., 2014). The significant association between low level cadmium exposure and proteinuria (damaged tubules) was observed in a study among Swedish adults (Orth, 2004).

In the present work, serum analysis showed the alteration in the cadmium concentration of the subject altering with various types of renal diseases. Considering alteration of the subjects, between 0.001 to 0.01ppm the patients were 33%, while 30% were found to be between 0.011 to 0.020ppm and 16% between 0.02-0.03ppm. The next variation between 0.031 to 0.04ppm had 9% and 6% between 0.041 and 0.05ppm and 3% from 0.051 to 0.06ppm. Such low serum cadmium levels were observed in many studies (Ferraro et al., 2010; Wallin et al., 2014). The public health implications of environmental clearance was also inversely proportional to the concentrations of lead and zinc protoporphyrin in the blood. Thus environmental exposure to cadmium and lead was associated with alterations in renal function (Lauweryset al., 1990; Harounet al., 2003; Nordbergetal., 2007).

Although the alterations in the serum concentration of cadmium do not reflect the real bodystatus of this trace element, it can be easily determined in routine practice and may give a quick insight and warning about possible disorders of cadmium metabolism. Serum cadmium levels are not enough to monitor cadmium exposure as they are less reliable. In the future, along with serum cadmium, urine cadmium should also be measured since the accumulation of cadmium in the cortex of the kidney can be understood accurately by analysing the urine cadmium rather than blood cadmium levels (Friberg, 1984; Barbieret al., 2005; Bernard, 2008)

Conclusion

The observations showed that the influence of cadmium was significant on the majority of the renal diseases. To implicate the definitive role of cadmium in renal diseases among the population of Madurai, the study group must be increased and should be restricted to people living in industrial areas of the city which would reveal a clearer picture of cadmium nephropathy.

Significance statement

This study discovered the extent of cadmium toxicity among patients with chronic kidney diseases in Madurai that can be beneficial for understanding and mitigating cadmium pollution in the city. This study will help the researchers to uncover the extent of cadmium toxicity and the adverse effects it has on the kidneys of the people of Madurai. It will help in accelerating the efforts to reduce cadmium pollution and also will highlight the role of smoking on cadmium nephropathy.

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