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Review Article

Ochratoxin A and its Relationship with Biochemical Markers in Human with Chronic Kidney Disease

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Abstract: ***Background*:** Ochratoxin A (OTA) is a nephrotoxic mycotoxin, which potentially leads to development of chronic kidney disease (CKD). Its exposure in the human body may alter several biochemical indicators that include serum creatinine, urea, and alkaline phosphatase (ALP). ***Objective*:** The study was conducted with the aim of examining the connection between OTA levels in the serum and the biomarkers (creatinine, urea and ALP) in patients of kidney renal diseases. ***Procedures*:** This was done by taking fifty samples of the kidney failure patients and fifty samples of the healthy persons. Each patient had their blood collected during September 2024 to April 2025. ***Results*:** The results depicted that the levels of Alkaline phosphatase in both the 'with OTA CKD patients' and the without OTA CKD patients were increased (188-212.26) mg/dl as compared to the controls. In the current research, it was revealed that the levels of Creatinine and Urea are also increased in the patients with OTA or without OTA, it was between (6.7-12) mg/dl, (166-120) kg/dl respectively, compared with healthy individuals with significant differences. ***Conclusion*:** The results of the current study indicated that serum blood compositions in patients of chronic kidney disease (CKD) were still high regarding Ochratoxin a (OTA). Further, the findings showed that women patients seemed to be more sensitive of the toxic effects of OTA compared to men. Notably, the OTA in the blood samples obtained in CKD patients are above the safety levels recommended across the globe. In general, the authors proved the existence of the strong relationship between OTA exposure and the occurrence of CKD, which proves the possibility of the involvement of this mycotoxin into the development of the kidney dysfunction.

Keywords: CKD, OTA, Urea, Creatinine, ALP.

1. INTRODUCTION

Chronic Kidney Disease (CKD) is a life-threatening clinical syndrome of lasting impairment in kidney structure and/or functioning and highlighted with progressive, slow progression and its ending nature [1]. Chronic Kidney Disease (CKD) is a serious problem in the global community as it is predicted that its prevalence in the United States is 14 percent [2]. The Chronic Kidney Disease (CKD) is a global problem as more that 800 million people live with this problem and is associated with decreased health-related quality of life [3]. The secondary metabolites of molds, called mycotoxins, are a serious threat to human lives. The following qualitative characteristic that defines these naturally occurring compounds is their low molecular weight, which is usually less than 1000 Da [4]. Scientists have so far discovered more than 500 mycotoxins though many of them are still undergoing state checks or without a uniform testing procedure. In addition to that, emerging findings still identify new mycotoxins. Moreover, plant metabolisms are capable of generating what are known as masked mycotoxin, for instance modified forms that cannot be readily collected by conventional analytical techniques which are used to detect the parental compound [5]. Ochratoxins: It is a type of mycotoxin, considered to be secondary metabolites, mainly derived by a variety of fungal species in the Aspergillus and penicillium genera. And the notable producers are Aspergillus westerdijkiae, A. ochraceus, A. niger, A. carbonarius, and A. steynii and Penicillium verruscum and P. viridicatum [6]. Urea is an organic compound [7]. The excessive conversion of proteins results in the formation of urea which is mainly disposed of through the kidneys as a urinary product. The urine and blood urea measures

are valued more than 150 years of clinical measuring of renal functions [8]. Creatinine is the resultant product during the manipulation taking place in the metabolism of creatine and creatine phosphate. Creatine, an organic acid containing nitrogen, is produced mainly in the liver and kidneys, and also additionally in the pancreas, by metabolic processes that employ the amino acid glycine, arginine and methionine. It is estimated that 10 percent of glycine, 22 percent of arginine and 42 percent of methionine is consumed during the biosynthesis of creatine daily [9]. Generally, alkaline phosphatase (ALP) has been divided into four isozymes depending on their tissue-specific expression as tissue-nonspecific ALP known also as liver/bone/kidney (L/B/K) ALP, intestinal ALP, placental ALP, and germ cell ALP [10]. ALP isoforms in serum depend on a number of factors such as age of patient, use of medications, endocrine disorders, gestational age, and existence of neoplastic conditions [11].

2. MATERIALS AND METHODS

2.1 Study Design

The case-control study was carried out between 9/2024 and 4/2025.Sample of patients with end stage chronic kidney disease was taken in Al-Hussian Hospital in Karbala.

2.2 Study Sample

One hundred subjects were studied (50) that were patient with kidney failure and (50) not having any disease. These figures are separated as (Table1).

Table 1: Study groups

No	Groups	Description
1	M, CKD, TX	Male, chronic Kidney disease with OTA
2	M,CKD,NTX	Male, chronic Kidney disease without OTA
3	F,CKD,TX	Female, chronic Kidney disease with OTA
4	F,CKD, NTX	Female Chronic Kidney disease without OTA
5	M, C, NTx	Male, control, with OTA
6	M,C, NTX	Male, Control, without OTA
7	F, C,TX	Female, Control with OTA
8	F,C,NTX	Female, Control, without OTA

2.3 Biochemical Measure

Each of the expected subjects (both physician-confirmed patients of CKD, and healthy subjects) underwent a collection of their 10 mL of venous blood using sterile syringes. Out of this volume 8 mL were pipetted to tubes containing gel and were left to clot at room temperature for 15 minutes. The samples were subsequently centrifuged at 4000 rpm in 15min in order to separate the serum. Micropipetter was used to aliquot each serum sample into 2 mL sterile eppendorf tubes and then kept in -20 C until further analysis. These serum samples which were stored were used to conduct the evaluation of levels of urea, creatinine, and alkaline phosphatase and also ochratoxin A (OTA) in the blood serum using thin- layer chromatography (TLC).

2.4 Statistics Analysis

The statistics used in the analysis of the data have been performed with the help of the IBM SPSS statistical software version 23. Analysis findings have been summarized through the execution of descriptive statistics. Besides, the experimental data was annexed with a p-value criterion (0.05) in establishing the statistical significance. Standard deviation and mean were tabulated too. There was also a multi-comparison within groups which was performed by Duncan post-hoc tests.

3. RESULTS AND DISCUSSION

3.1 To Carry Out Qualitative Measurement of Ochratoxin A, Thin Layer Chromatography (TLC) Was Used

The results showed that a proportion of 92% (46) of the serum samples of patients with the chronic kidney disease had the toxin and 8% [4], does not have the toxin. In a different view, the blood serum samples taken were of the fruit of healthy individuals which had 10 percent [5], of toxin and 90 percent (45) without toxin. The difference was highly significant on a group compare basis (Table 2).

Table 2: Distribution of OTA in healthy individuals and patients according to the TLC

Group	With OTA	Without OTA	P. value
Patient	(46)92%	(4)8%	0.00003***
Healthy	(5)10%	(45)90	

Table 3: Distribution of OTA in Patients According to sex

Sex	Number and percentage of patients with OTA	Number and percentage of patients without OTA	P. value
Female	24(96%)	1(4%)	0.00001***
Male	23(92%)	2(8%)	

3.2 Measurement of Biochemical Parameters

Alkaline Phosphatase

The finding presents a comparison between chronic kidney disease that has been exposed to the toxin and the chronic disease that has not been exposed along with a comparison between the health individuals that have been exposed to the toxin and those that have not been exposed. The (M,CKD,TX),(M,CKD,NTX),(F,CKD,TX),(F,CKD,NTX) were raised to (212.265, 219.500,188.429,239.000)mg/Dl respectively as compared to the count of this enzyme in the blood serum of controls groups (49.238 to 64.667) (Table 4).

Table (4). The Comparisons between control and patients according to Alp.

Groups	Mean (mg/dL)	Duncan Post hoc test	Std. Deviation	P. value
M, CKD, TX	212.265	b	81.642	
M, CKD, NTX	219.500	b	14.849	
F, CKD, TX	188.429	b	94.494	
F, CKD, NTX	239.000	b	12.728	
M, C, TX	64.667	a	9.292	0.00001***
M, C, NTX	59.158	a	22.933	
F, C, TX	46.000	a	5.657	
F, C, NTX	49.238	a	14.649	

The difference between the litters mean that there is a significant difference between the groups.

Creatinine

The findings were portrayed that the creatinine concentrated in the blood serum of all the group of CKD patients with or without OTA is high with more creatinine in (M,CKD,NTX) and (M,CKD,TX) of 12.000 and 9.140 respectively as compared to the control groups (Table 5).

Table 5: The Comparisons between patients and controls according to Creatinine

Groups	Mean (mg/dL)	Duncn Post hoc test	Std. Deviation	P. value
M,CKD,TX	9.140	c	2.204	
M,CKD,NTX	12.000	d	0.707	
F, CKD, TX	7.514	bc	1.681	
F,CKD,NTX	6.700	b	0.283	0.00003***
M, C, TX	0.680	a	0.026	
M,C, NTX	0.671	a	0.109	
F, C, TX	0.510	a	0.014	
F, C, NTX	0.511	a	0.089	

The difference between the litters mean that there is a significant difference between the groups.

Urea

The outcome indicates that the comparison is between patients with chronic kidney disease (CKD) who have been exposed to the toxin or not and those without chronic kidney syndrome and healthy controls. The concentration of urea in (M,CKD,TX) cases was (136.765,166.000,136.105,129.000) in (M,CKD,NTX), (F,CKD,TX), (F, CKD, NTX) respectively (Table 6).

Table 6: The Comparisons between patients and controls according to Urea

Groups	Mean (mg/dL)	Duncan Post hoc test	Std. Deviation	P. value
M, CKD,TX	136.765	bc	26.708	0.00005***
M,CKD,NTX	166.000	c	53.740	
F, CKD, TX	136.105	bc	32.626	
F, CKD,NTX	129.000	b	12.728	
M, C, TX	27.333	a	9.074	
M,C, NTX	23.895	a	6.054	
F, C, TX	21.000	a	2.828	
F, C, NTX	18.524	a	4.622	

The difference between the litters mean that there is a significant difference between the groups.

Thin Layer Chromatography (TLC) Was Used to Entail Qualitative Determination of Ochratoxin A

The present findings are similar to Hassan and Ali , who showed that the frequency of patients with chronic kidney disease of unknown etiology were shown to test positive to OTA to be 90 percent, and there was a significant variation as compared to 30 percent of OTA-positive samples in healthy individuals [12], and also Zaied, when they compared the OTA concentration in human serum of healthy individuals and in the nephropathy groups, the results showed a significant difference (P value<0.001) [13] . The outcome also complies with Kosicki who discovered that concentration of ochratoxin A was higher in kidney disease samples as compared to healthy individuals [14], and even with Meucci who also discovered that CKD dog group has a significantly (P<0.01) higher incidence of OTA-positivity compared to healthy subjects and significantly (P<0.001) higher median value of plasma concentrations [15].

Biochemical Parameter Measurement

Alkaline Phosphatase

This finding concurred with that of Zhu, who observed that the serum values of ALP level rose in the rats [16]. The outcome also corresponded with Malekinejad, who reported that an increase in Animals exposed to OTA alone exhibited slight yet significant rise in the level of the ALP activity compared to the untreated controls [17]. The finding concurs with that of Pleadin who discovered that elevated level of ALP in pigs increases [18]. Alkaline phosphatases (APs) are enzymes which catalyze the release of phosphate group in a variety of substrates and this crucial process occurs in multiple metabolic pathways. These are very important enzymes in mineralization of bones. Nevertheless, ironically, their exercise can as well lead to the pathological disorders like vascular calcification. This duality not only emphasizes the mutually intricate relation between skeletal and vascular systems, more widely known as bone vascular cross-talk. The division between the useful and harmful impact of APs is also becoming even more difficult to accomplish in patients with chronic kidney disease (CKD) [19].

Creatinine and Urea

Table (5) and Table (6) findings are in agreement with Falayh who established that the level of creatinine and urea is elevated in chronic kidney disease in the presence of OTA [20]. They also agreed with Stoev, who noticed an increase in the concentration of urea and creatinine in pigs [22]. The results found in Table (5) and Table (6) also matched that of Abidin who has noted an increase in the level of creatinine and urea in birds [22]. The findings were also in agreement with the findings of Damiano who discovered that there was a rise of urea and creatinine in the rat [23]. The kidneys are the most dominant in removing urea which is derived as a result of digestion of dietary protein and tissue protein sources. This elimination entails filtering by the glomeruli and remodeling. The main rationale in the accumulation of urea in the blood in case of chronic kidney disease is the impaired capacity of the kidneys to excrete it [24]. Creatinine is a byproduct of the metabolism of creatine which goes into the plasma at a relatively stable speed. The glomeruli filter it freely and are not reabsorbed or metabolized by renal tissues. Despite being a standard test that measures the residual renal function, its levels in the serum can vary with the nutritional intake and muscle mass, age and sex of the patient [25].

CONCLUSIONS

The current research paper has revealed that there was a high degree of concentration of Ochratoxin a (OTA) in the serum samples of chronic kidney disease (CKD) patients. Moreover, the evidence indicated that women patients are more vulnerable to the toxicity of OTA as opposed to male patients. It is worth mentioning that OTA concentrations in the blood of CKD patients surpassed internationally accepted safe levels. These results confirm that there might be a correlation between OTA and the development or progression of global CKD disease, and the mycotoxin may have a potential linkage with renal impairment.

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