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TOXICITY OF AFLATOXIN B1 TOWARDS THE INDUCING ALTERATIONS IN THE LIVER FUNCTIONS

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ABSTRACT

Since 2003, the world's developing countries are home to more than 5 billion people thought to be at danger of prolonged consumption of contaminated foods that are aflatoxic according to a number of study efforts conducted in South Africa, Egypt, and other countries in west and east Africa. Additionally, the presence occurrence of aflatoxins and their byproducts in animal tissues used to make food (such as beef and sheep meat) may contaminate human diets. As a result of their increasing prevalence, aflatoxins have recently been identified as a significant public health concern. Aflatoxins are dangerous second-generation byproducts of Aspergillus species. Due to their chemical makeup, the majority of aflatoxins are highly liposoluble substances that can be absorption from the exposed site, such as the gastro-intestinal and respiratory tracts, into the bloodstream, where they can then spread throughout the body and reach various organs, including the liver and kidneys. The primary goals of the study were to monitor and screen for levels of aflatoxin B1 in the Karbala Province using a case-control study. The connection between Aflatoxin B1 concentrations and the common biochemical indicators of liver function as well investigated. How alter liver function by Aflatoxin B1. The study also emphasised the necessity to determine the pathophysiology of AFB1's involvement in the rising number of patients with liver dysfunction. AFB1 levels were quantitated using utilising thin layer chromatography, together with High Pressure liquid chromatography being employed for the quantitative identification (HPLC). In the province of Karbala, an analysis of case-control studies was done to look at the Aflatoxin B1 affects (AFB1) exposure on kidney disease patients. AFB1 levels were quantitated using utilising thin layer chromatography with high-performance liquid chromatography to provide quality results. The evaluations of the samples that tested positive for AFB1 as well as the lipid profile and indicators of liver function tests. The findings indicated that the population under investigation had afflatoxins exposure. AFB1 was found in 100% of individuals with unknown kidney disease (KD) and in 24%, 20%, and 100% of patients with known CKD, respectively. AFB1 concentrations in serum samples ranged from 0.68 to 8.33 ng/mL for patients with questionable KD, 1.21 to For patients, 5.60 ng/mL with known KD, likewise, healthy controls ranged from 0.11 to 1.30 ng/mL. The presence of AFB1 was positively and strongly linked with liver enzymes, specifically ALT and ALP. AFB1 levels among serum samples from KD sufferers and wholesome controls showed a prolonged contact with the poison, suggesting an unknown cause. The evaluation of the biochemical marker of liver functioning supported the effect of AFB1 exposure. This work may help build effective nationwide programmes for tracking AFs exposure. The study also emphasised the necessity to determine the pathophysiology of AFB1's involvement in the rising number of patients with liver dysfunction. Future research is urged to concentrate on more comprehensive topics that cover the entire nation (Iraq).

INTRODUCTION

Aflatoxins, which include Aspergillus flavus and Aspergillus parasiticus, are harmful byproducts of fungi, primarily Aspergillus. It is accessible in a variety of crops that provide food, including sorghum, millet, rice, corn, and groundnuts (1).

The four main aflatoxins that are naturally generated by the Aspergillus species are mould identified as Where "B" and "G," we have AFB1, AFB2, AFG1 and AFG2 represent for the fluorescence hues produced thin layer chromatography plates exposed to UV light in the colours green and blue while the subtitle number 1 and 2 stand for major and minor compounds, respectively. When aflatoxins B1 and B2 are subjected to UV light, they glow in a blue colour, while similar compounds fluoresce in a yellow-green colour, earning them the designations G or B (2).

Production of mycotoxins in cereal crops occurs in inadequate temperature and humidity both in the field in storehouses (3). Considering the issue of food security as well as due to the financial losses that this causes, AF infestation in agricultural products is a severe issue (4). The USA's maize harvest is predicted to lose 52 million dollars annually (5). In addition to their presence in food as well as agricultural items, Following dietary ingestion, aflatoxin can be found in biological samples. In fact, assessing aflatoxin exposure in humans and animals by looking for indicators for aflatoxin in biological fluids such as serum and urine is important for figuring out the level and frequency of exposure to aflatoxin (6).

According to reports, aflatoxins are quickly absorbed in the gastrointestinal tract after ingestion (due to their low molecular weight) through an unidentified passive device. They then emerge swiftly as metabolites in the blood after only fifteen min and within 12 hours of feeding, in milk (7). Aflatoxins produce aflatoxicosis in outbreaks of episodic poisoning and are hepatocarcinogenic, especially when combined with Hepatitis B virus infection that is ongoing. Additionally, involvement with aflatoxin in Gambian children has been linked to a lower amount of salivary IgA (8). Aflatoxins are mostly processed, Aflatoxin M1, a less harmful form of reactive epoxide intermediate, is produced by the liver (9). The primary method of contact to AFB1 is through the consumption of contaminated food) (10). However, individuals exposed to the environment have reported using the dermal and inhalation channels (11). The two AFs' and their metabolites' hazardous mechanisms are still unknown (12). AFB1 was classified as a Group 1 human carcinogen by the International Agency for Research on Cancer in 1993. There is currently a tone of information showing liver toxicity (the main organ for which AFB1) and how it affects liver cancer (hepatocellular) in cells, animals, and people at various doses (13). AFB1 is a powerful mutagen, teratogen, carcinogen, and immunosuppressant, and all of these properties may disrupt normal protein synthesis processes and block a number of metabolic systems, resulting in harm to numerous organs among them are the kidney, liver and heart (14).

According to Lu et al. (15), the main metabolic consequences of acute AFB1 exposure are dyslipidemia and gluconeogenesis. These effects were discovered while looking for possible biomarkers employing AFB1-induced acute hepatotoxicity Earlier diagnosis using transcriptomics and metabolomics. According to reports, AFB1 can change the amounts of lipids in the liver and plasma (16). The Knowledge Gap may be caused by persons who consume small levels of mycotoxins in their diets without manifesting any symptoms of sickness. Since Mycotoxins can cause major health issues when consumed in high doses or repeatedly spanning a considerable amount of time. The strongest known toxins are mycotoxins, which are secondary metabolites. Mycotoxins are extremely potent because they have low molecular weights and are not antigenic, which means they cannot provoke the immune systems of humans or other animals to create antibodies to them. Additionally, it demonstrated tolerance to high temperatures, meaning that the temperature at which food is cooked did not cause it to fail. Mycotoxins are not completely eliminated from meals when the diseased portion is removed, despite the fact that this is something that many people do. This is because mycotoxins migrate swiftly from fungus colonies to food. The majority of foods sold in nearby marketplaces may contain aflatoxins. Regarding the association between AflatoxinB1 and the liver illnesses in Iraq, no prior research has been done.

Only a few worldwide researches have demonstrated a link between toxic effect to AFs and malignancies of the bile duct, salivary glands, multiple myeloma, and the liver (17). Although there have been signs that inhaling Aflatoxin is associated with liver malignancies, no studies have yet connected malignancies caused by AFs consumption of the respiratory system. In addition, despite reports of the toxicological pathophysiology of aflatoxin-induced Hepatocellular carcinoma, the relationship among It is yet uncertain whether liver cancer cells are exposed to AFB1 and have lipid-based dysmetabolism (18).

AIM

Find out to how alter liver function by Aflatoxin B1

OBJECTIVE

The study also emphasised the necessity to determine the pathophysiology of AFB1's involvement in the rising number of patients with liver dysfunction. TLC, or thin layer chromatography, was utilized for the qualitative data of serum AflatoxinB1 in accordance with the AL-Mosoui technique (2015, together with High Pressure liquid chromatography being employed for the quantitative identification (HPLC).

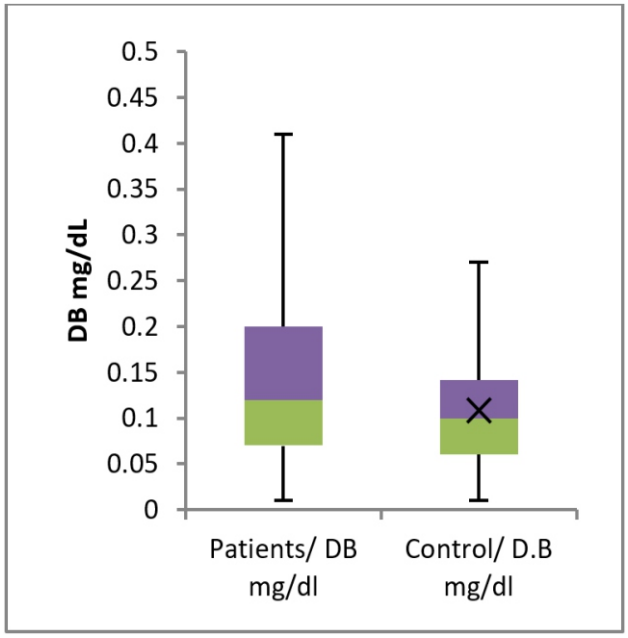
MATERIALS AND METHODS

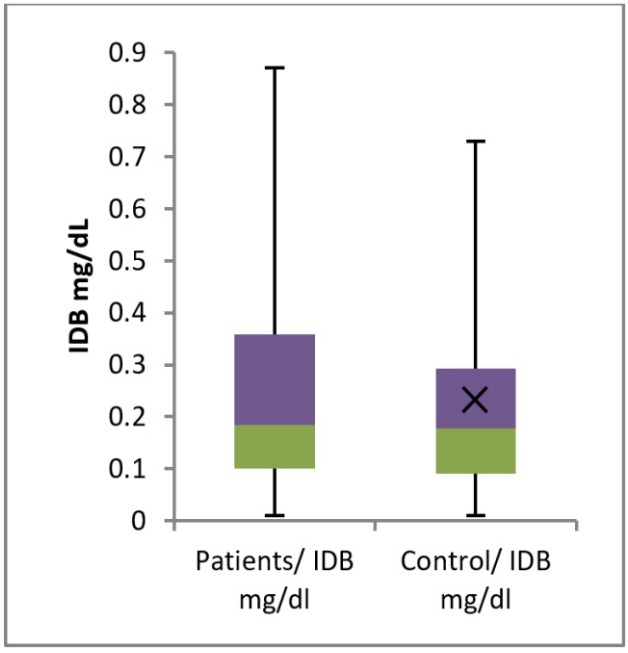
Case-control research was part of the current investigation, and patients' samples were taken at the AL-Zahraa Medical Center and Advising Center in Kerbala's AL-Hussain Teaching Hospital. Patients were split into groups based on whether their renal disease had a known or unknown origin for relationship-building reasons. Groups of patients were contrasted with a control subject group that appears to be healthy and free of disease.

This study also looked at how serum levels of direct, indirect, and total bilirubin varied between the KD patient group and the healthy group.

In contrast to the healthy group in figure 2, the KD patient group displays a modest hyperbilirubinemia. In patients who already have KD, serum bilirubin levels have a connection to the development of liver disease (36).

The mean blood the levels of total, direct, and indirect bilirubin in the KD patient group were 0.5, 0.55, and 1.24 mg/dL, respectively, while these values were 0.34, 0.1, and 0.23 mg/dL in the healthy control group. Long used as a sign of liver disease, elevated blood bilirubin concentrations.





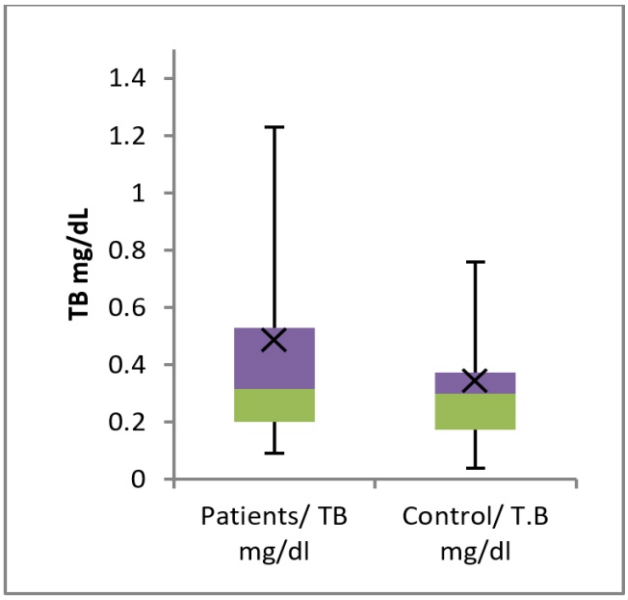


Fig. 2: Distribution of Serum Direct. Indirect and Total Bilirubin Levels as a Liver Dysfunction in KD Patients Group Compared to the Healthy Group

Comparing the availability of blood lipid profile levels between the group of KD patients and the healthy group also revealed aberrant distribution, as illustrated in figure 3. The studied lipid profile typically showed decreased values in KD patients. The mean levels of TC, HDL, LDL, TG, and VLDL in the patient group were, respectively, 144.04, 34.4, 80.3, 166.23, and 33.9 mg/dL. Mean values of TC, HDL, LDL, TG, and VLDL were, respectively, 172, 41.4, 105.32, 174.49, and 34.89 mg/dL in controls.

A substantial difference between the cholesterol levels of KD patients and the healthy control group was shown through analysis (P values are presented in Table). (1).

In addition, KD patients' HDL levels compared to those in the group of healthy controls were substantially lower (P values are presented in Table 1) Patients with KD may have low HDL levels as a result of a variety of causes, which are typically signs of poor reverse cholesterol transport. Thus, apolipoprotein AI and AII levels are typically lower in uremic individuals (the main protein constituent of HDL). LCAT, the enzyme that converts free cholesterol in HDL particles to cholesterol esters, has decreased activity, and cholesterol TG-rich lipoproteins can transfer proteins and lipids from HDL more easily thanks to an ester transfer protein, has increased activity. These changes result in lower serum concentrations of HDL cholesterol. One of the independent risk variables for the advancement of renal disease in KD patients was low HDL levels (42). Numerous changes in lipoprotein metabolism are also linked to renal impairment (40). A deficiency in lecithin-cholesterol acyl-transferase (LCAT) results in poor HDL

A total of 136 people were examined, 86 (46 men and 40 women) of whom had renal issues, and 17 (11 men and 6 women) of whom had kidney illness with no known cause. An apparently healthy control group of 50 subjects (28 men and 22 women) was selected volunteered by renowned individuals.

Important sociodemographic traits, general health condition, dietary habits, and family history of chronic diseases were all assessed using a questionnaire.

5ml of blood was drawn from each participant's vein using a sterile syringe and sent to the main lab in a gel tube container. Serum was separated from samples by centrifuging them for 15 minutes at 3000 rpm after they had been settled for 15 minutes. Following the methods of (19-22) respectively, serum concentrations the activities of aspartate aminotransferase and alanine aminotransferase were measured using a kinetic UV enzymatic method, and serum concentrations of alkaline phosphatase, Using a colorimetric approach, the levels of direct and total bilirubin were assesse.

Following the procedures of (23-26) respectively, an enzyme colorimetric test was performed to determine the levels of blood total cholesterol, triglycerides, high-density lipoprotein, and low-density lipoprotein.

TLC, or thin layer chromatography, was utilized for the qualitative data of serum AflatoxinB1 in accordance with the AL-Mosoui technique (2015) (27-32) together with High Pressure liquid chromatography being employed for the quantitative identification (HPLC).

RESULTS

Figure from this study depicts the variation of serum liver enzyme levels in the group of renal disease patients in comparison to the healthy group (1). Comparing the control group to the study group, the degree of liver enzymes in KD patients was clearly elevated. Alkaline phosphatase (ALP), aspartate aminotransferase, and alanine aminotransferase (ALT) (AST) mean blood levels in KD patients were higher (29.1, 132.9, and 21.68 mg/dl, respectively) than in controls (21.6, 82.04, and 20.93 mg/dl). Only ALP, nevertheless, distinguished KD patients from controls in a statistically significant way (P values are provided in Table 1).

A drop in pyridoxal-5-phosphate, an aminotransferase coenzyme, the occurrence of elevated amounts of uremic toxins, affects on the production of releases Hepatocyte-derived AST and ALT or serum-based rapid clearance are some of the processes that have been hypothesised for generating a variation in transaminase levels in KD (33). The results of our study, which showed greater ALP levels in KD patients, are in line with those of many previous investigations. (34-35).

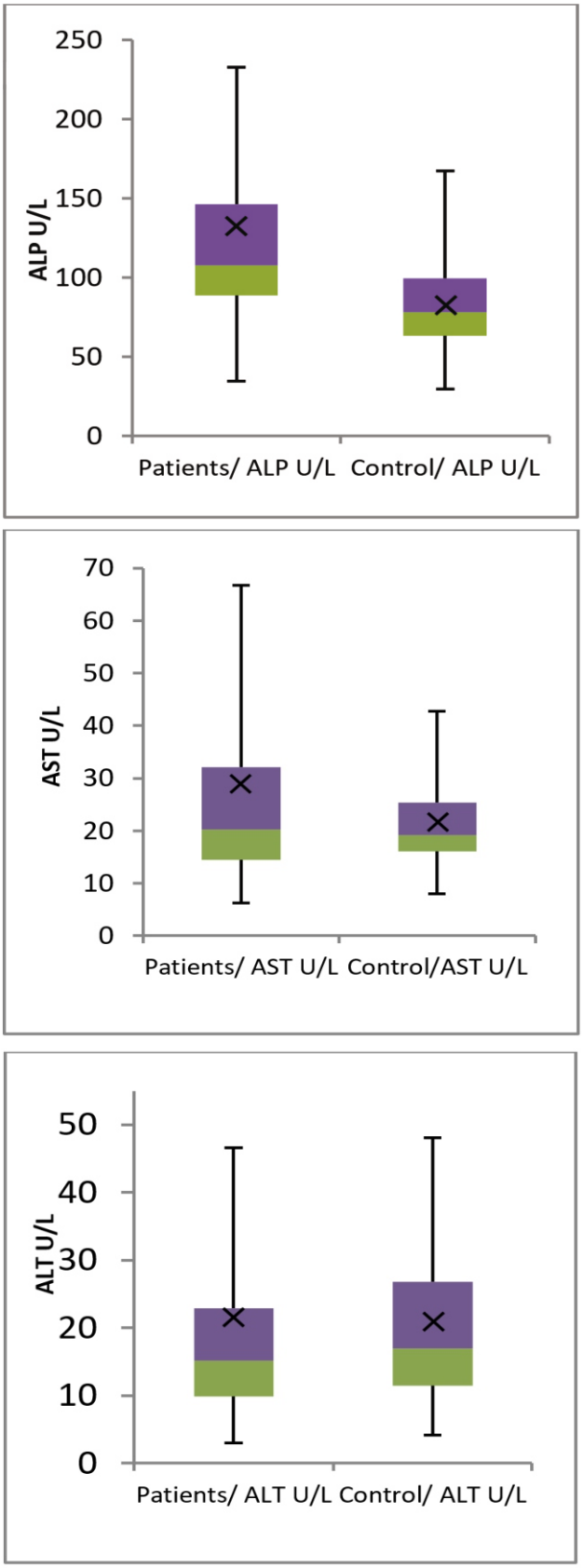
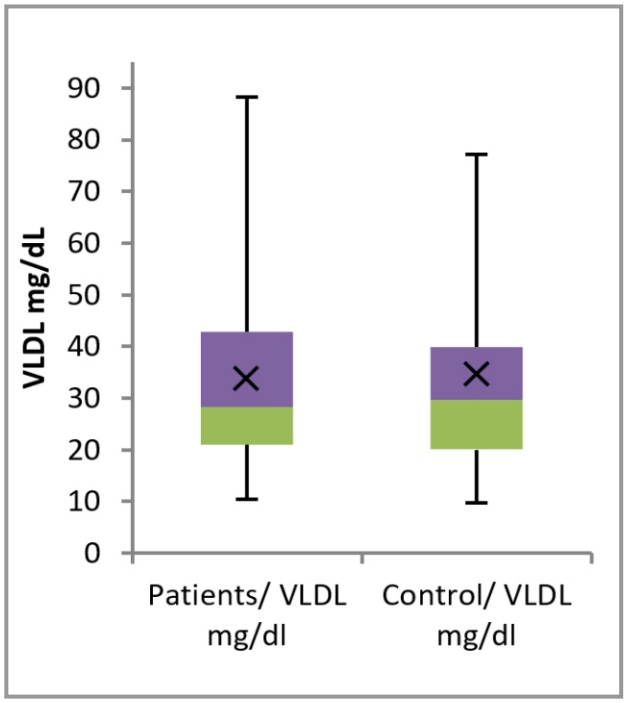


Fig. 1: Distribution of Serum Liver Enzymes Levels in KD Patients Group Compared to the Healthy Group



Cont. Fig. 3: Distribution of Serum Lipid Profile Levels as a Liver Dysfunction in KD Patients Group Compared to the Healthy Group

It was determined how exposure to toxins and CKD interacted. AflatoxinB1 estimation was done on 136 individuals. In order to look for potential correlations between AFB1 levels and liver functions depending on the known and uncertain causes of CKD, the patient group was divided into two categories. The variation in quantitative data employing the, comparisons between the groups were nonparametric Spearman rank test (Coefficient rs).

According to Table, 20% of the control group had Aflatoxin B1 detected, compared to 24% and 100%, respectively, in certain and doubtful patients (2).

Samples of:	Mean of AFB1 Conc. ng/ml (Range)	Samples with AFB1 (%)	Samples without AFB1 (%)
KD/ Certain	3.07 (1.21-5.6)	24%	76%
KD/ Un-certain	3.53 (0.68-8.33)	100%	0%
Control	0.41 (0.11-1.4)	20%	80%

Table 2: The mean of AFB1 Concentration (ng/ml) in the Blood Samples of the Patients Infected with CKD and Healthy Control

Characteristic	Patients		Control Group Confidence Level(95.0%) Median(Lower Cl-Upper Cl)	P value (ANOVA)
	Certain Etiology Patients Confidence Level(95.0%) Median(Lower Cl-Upper Cl)	Un Certain Etiology Patients Confidence Level(95.0%) Median(Lower Cl-Upper Cl)		
ALT (U/L)	14.68 (5.51-23.84)	17.95 (12.11-23.78)	16.96 (12.07-21.84)	0.94
ALP (U/L)	110.18 (76.23-144.12)	96.35 (77.54-115.15)	78 (69.9-86.09)	0.01
AST (U/L)	20.1 (12.62-27.57)	22.45 (9.20-35.69)	19.135 (16.91-21.35)	0.20
DB (mg/dL)	0.12 (0.1-0.52)	0.13 (0.11-1.81)	0.1 (0.07-0.12)	0.07
IDB (mg/ dL)	0.161 (0.1-2.48)	0.22 (0.10-0.57)	0.17 (0.11-0.23)	0.64
TB (mg/ dL)	0.28 (0.24-3.003)	0.4 (0.32-2.41)	0.3 (0.22-0.37)	0.62
TC (mg/ dL)	148.09 (136.29-159.88)	126 (104.99-147.01)	170.54 (159.43.181.85)	0.0002
HDL (mg/ dL)	30.82 (26.82-34.74)	31.1 (20.31-41.88)	40 (36.70-43.29)	0.04
LDL (mg/ dL)	80.2 (68.57-91.82)	49.88 (29.91-69.91)	100.7 (89.64-111.75)	0.0007
TG (mg/ dL)	139.8 (115.03-164.56)	123.34 (78.46-168.21)	148.25 (118.08-178.41)	0.84
VLDL (mg/ dL)	28.76 (23.72-33.79)	24.66 (15.69-33.64)	29.65 (32.61-35.68)	0.84

Table 1: The Confidence Level of all Laboratory Parameters in CKD Patients Group Compared to Healthy Control Group

metabolism in KD, which prevents HDL-3 from maturing into HDL-2 (43). These alterations are all connected to oxidative stress, Endothelial dysfunction is a crucial risk factor for the expansion of KD and its consequences and is brought on by chronic and oxidative stress inflammation (44). Due to dysfunctional HDL cholesterol and a deficiency in Small dense LDL (sdLDL), a subtype of the protein linked to the LDL receptor, is produced by KD patients (LRP) (40).

Despite the fact that normative ranges for serum LDL cholesterol can exist, when kidney function declines, the amount of sdLDL, a highly atherogenic subtype of LDL that is quickly oxidised, increases in the serum (45). As a result, even if your levels of LDL cholesterol are within the normal range, IDL as well as sdLDL cholesterol cause the development of coronary artery plaques (46).

One of the most important lipid types that kidney disease affects is serum triglycerides, which are commonly increased in the early stages of KD due to aberrant triglyceride synthesis and decreased triglyceride breakdown. Due to lipoprotein lipase's deactivation (LPL), the breakdown of triglycerides is altered (45). LPL inactivation is accelerated by a higher apolipoprotein C-III/C-II ratio because apolipoprotein C-III inhibits LPL whilst apolipoprotein C-II activates it (47).

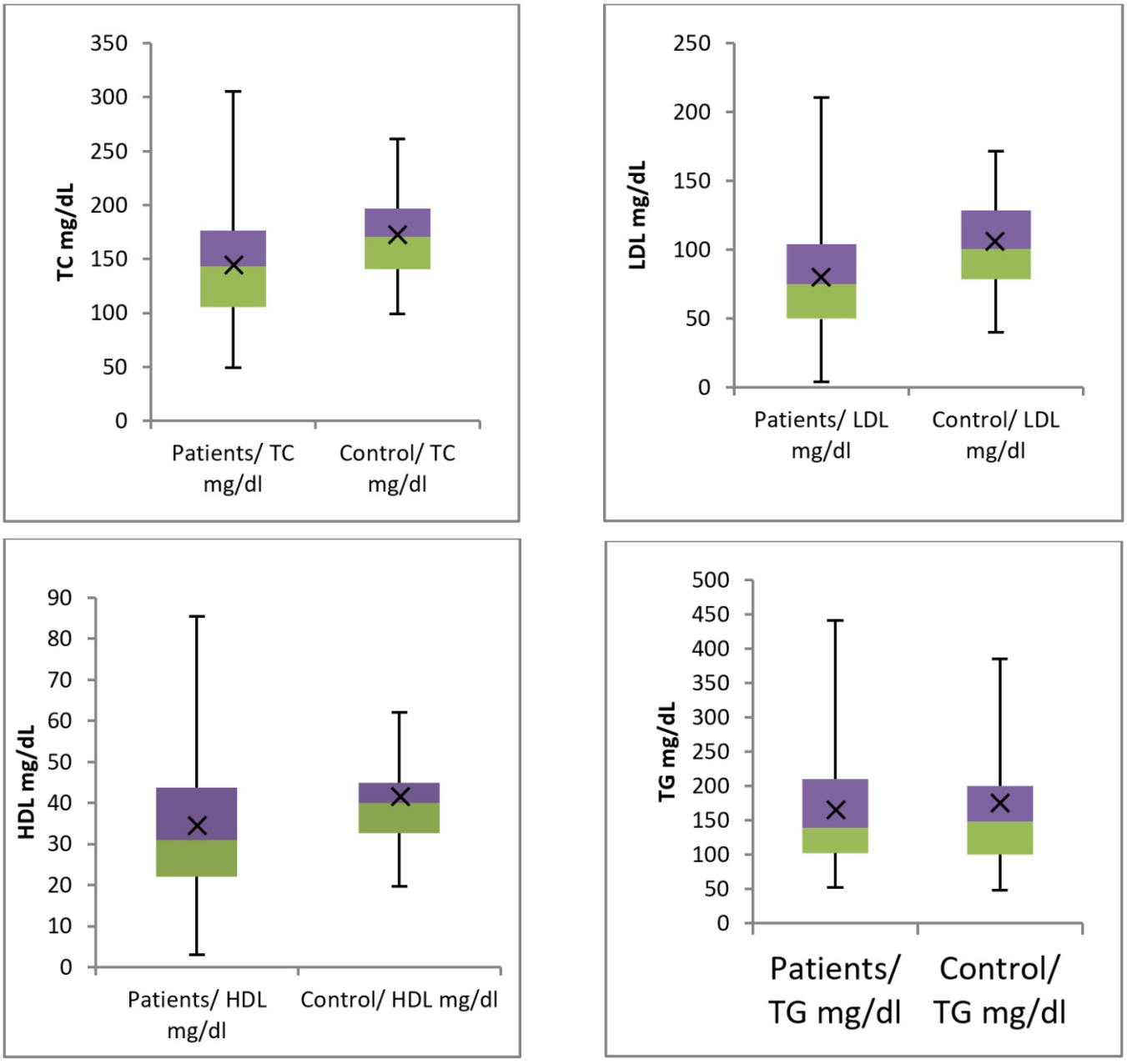


Fig. 3: Distribution of Serum Lipid Profile Levels as a Liver Dysfunction in KD Patients Group Compared to the Healthy Group

While the age range for AFB1-negative individuals was between (22- 30) years, that of AFB1-positive individuals ranged from (67- 75) years in both the patient and control groups. AflatoxinB1 level and patient age evidence of a statistically significant connection (rs = 0.76, p=0.01), and the Sturgess formula was used to categorise patients by age (48).

Assessment of the Unknown aetiology CKD Patients who tested positive for AFB1 using the measured biochemical indicators of liver function:

Human liver is the primary organ affected by the poisoning and carcinogenicity of AF. One of the metabolic adverse consequences of AF is the inhibition of DNA, RNA, and protein synthesis as well as the activity of several enzymes, the inhibition of the synthesis of lipids, particularly phospholipids, NEFA, TAG, cholesterol, and its esters, as well as the slowing down of the metabolism of glucose, and the inhibition of the synthesis of clotting factors (49).

Only an increase in ALT and ALP levels with P0.05 statistically substantially raised AFB1 levels in patients with Uncertain Etiology, according to analysis of the correlation. Liver enzymes in the form of ALT, AST, and ALP were evaluated in Uncertain Etiology KD patients. Table provided the correlation coefficient and p value for both enzymes (3).

liver enzymes ALT, ALP, and AST were elevated depending on how high the level of AFB1 increased; these results were in perfect agreement with our findings. The NADPH-dependent aldo-keto reductases (AKR7A), an enzyme crucial for bioactivation and biodetoxification, showed down-regulated expressions in the aldehyde metabolite of AFB1, which consequently affected the intracellular stress in the liver (54).

DISCUSSION

The liver, which is typically in charge of detoxifying chemicals and poisons, was where aflatoxin had its most severe effects on people. AFB1-epoxide may attach to different cellular macromolecules during acute aflatoxicosis, which causes hepatocellular damage and mortality. Aflatoxin exposure in humans and animals resulted in substantial bile duct growth and considerable necrosis of parenchymal cells in liver tissue samples (28).

AFB1 is classified by the World Health Organization as a class 1 carcinogen (WHO) (29).

AFB1 may also contribute to the clinical occurrence of gastroenteric cancers among Asians and Africans, according to a number of epidemiological studies. (30).

The most prevalent and serious chronic condition brought on by lifetime exposure to modest levels of

Variables groups	Characteristic	AFB1 levels in Un-Certain Etiology Patients	P value
		Coefficient rs	
	Age (Year)	0.76	0.01
	BMI (Kg/m^2)	0.43	0.22
Liver Function	ALT (U/L)	0.73	0.01
	ALP (U/L)	0.65	0.04
	AST (U/L)	0.29	0.4
	DB (mg/dL)	0.39	0.2
	IDB (mg/ dL)	0.15	0.9
	TB (mg/ dL)	0.29	0.8
	TC (mg/ dL)	0.21	0.5
	HDL (mg/ dL)	0.23	0.52
Lipid profile	LDL (mg/ dL)	0.09	0.8
	TG (mg/ dL)	0.35	0.3
	VLDL (mg/ dL)	0.35	0.31

Table 3: Correlation Between AFB1 Positive Samples of Un-Certain Etiology Patients Group and the Biomarkers

According to a toxicologic pathogenesis investigation, liver cancer cells with lipid-based dysmetabolism and AFB1 exposure are related. The study evaluated lipid-based compounds and liver functional enzymes. The aflatoxins is cancer. Despite the fact that consumption of aflatoxins has historically been associated with hepatocellular carcinoma, such as HCC and bile duct hyperplasia (31).

Alkaline phosphatase levels are thought to be raised because of accelerated bone turnover in KD. Vascular cells in KD differentiate into osteoblasts and express a number of proteins linked with bone, including alkaline phosphatase. When osteodystrophy, a KD consequence, occurs, the ALP bone isoenzyme will be released in excessive amounts. A feature of chronic renal illness is a mineral bone problem called osteodystrophy (KD-MBD). Numerous investigations have shown that advanced KD patients had higher levels of bone-specific ALP. In KD, vascular cells differentiate into osteoblasts and express a number of proteins linked with bone, including alkaline phosphatase. (35).

Serum bilirubin is not just a byproduct the deterioration of heme; Additionally, it is a strong anti-inflammatory that prevents the activity of NADPH oxidase and protein kinase C, two significant enzymes that both non-phagocytic and phagocytic cells use to create oxidants (37).

The fact that bilirubin is both an antioxidant and possesses anticomplementary characteristics that guard against inflammation may be a factor in the rise in bilirubin levels in CKD patients (38). Additionally, it has been hypothesised that bilirubin possesses cytoprotective qualities due to its effect on protein kinase C. (39). However, patient age distribution, anthropometry, risk factors, and medication use could all have an impact on the variations in bilirubin levels.

Numerous changes in lipoprotein metabolism are also linked to renal impairment. (40). a deficiency in lecithin-cholesterol acyl-transferase (LCAT) results in poor HDL metabolism in KD, which prevents HDL-3 from maturing into HDL-2 (43). These alterations are all connected to oxidative stress; Endothelial dysfunction is a crucial risk factor for the expansion of KD and its consequences and is brought on by chronic and oxidative stress inflammation. (44). Due to dysfunctional HDL cholesterol and a deficiency in Small dense LDL (sdLDL), a subtype of the protein linked to the LDL receptor, is produced by KD patients (LRP) (40).

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According to recent reports, all of AFB1's biotransformation products may persist in the liver as residues, as seen in various species (50). Covalent connections between proteins, cellular DNA, ribonucleic acid (RNA), and other macromolecules are swiftly reacted with by this AFB1 metabolic active form (51). The tumour suppressor gene p53's codon 249 produces adducts containing guanine at the site of N7 as a result of the connection with DNA (52). Additionally, a cytoplasmic enzyme found in the liver homogenates' soluble fraction that is NADPH-dependent can reduce AFB1 to generate aflatoxicol (AFL). (53).

According to a toxicologic pathogenesis investigation, liver cancer cells with lipid-based dysmetabolism and AFB1 exposure are related. The study evaluated lipid-based compounds and liver functional enzymes. The liver enzymes ALT, ALP, and AST were elevated depending on how high the level of AFB1 increased; these results were in perfect agreement with our findings. The NADPH-dependent aldo-keto reductases (AKR7A), an enzyme crucial for bioactivation and biodetoxification, showed down-regulated expressions in the aldehyde metabolite of AFB1, which consequently affected the intracellular stress in the liver. (54).

CONCLUSION

Not only are aflatoxins a significant issue for cultivation of crops; they have also emerged as a global health concern due to the negative effects that exposure to this toxin has on both humans and animals. In order to limit aflatoxin exposure, governments at all levels-local, regional, national, and global must devote appropriate resources and work together with the fields of agriculture and public health.

REFERENCES

1. Komsky-Elbaz A., Saktsier M., Roth Z. Aflatoxin B1 impairs sperm quality and fertilization competence. Toxicology. 2018; 393: 42-50.
2. Thrasher J. D. Aflatoxicosis in animals. Aflatoxins and Health. 2012; 32: 24-44.
3. Singh R., Mandal A. B. Efficacy of fumaric and citric acids in preventing biosynthesis ofaflatoxins in poultry feed with variable moisture content. ndian Jounal of Animal Science. 2014; 84: 453-456.
4. Kumar P., Mahato D. K., Kamle M. Aflatoxins: a global concern for food safety, human health and their management. Frontiers in microbiology. 2017; 7: 2170.
5. Mitchell NJ, Bowers E, Hurburgh C. Potential economic losses to the US corn industry from aflatoxin contamination. Food Addit Contam A. 2016; 33: 540-550.
6. Siti Husna Sulaiman, Rosita Jamaluddin. Association between Urinary Aflatoxin (AFM1) and Dietary Intake among Adults in Hulu Langat District, Selangor, Malaysia. Nutrients. 2018; 10: 460.
7. Moschini R, Sisterna M, Carmona M. Modelling of wheat black point incidence based on meteorological variables in the southern Argentinean Pampas region. Australian Journal of Agricultural Research. 2006; 57: 1151-1156.

8. Turner PC, Moore SE, Hall AJ, et al. Modification of immune function through exposure to dietary aflatoxin in Gambian children. Environ Health Perspect. 2003; 111: 217-220.
9. Wu F., Khlangwiset, P. Health economic impacts and cost-effectiveness of aflatoxin reduction strategies in Africa: Case studies in biocontrol and postharvest interventions. Food Additives & Contaminants. 2010; 27: 496-509.
10. Iqbal SZ, Asi MR, Hanif U, et al. The presence of aflatoxins and ochratoxin A in rice and rice products; and evaluation of dietary intake. Food Chem. 2016; 2010: 135-140.
11. Malik A, Ali S, Shahid M, et al. Occupational exposure to Aspergillus and aflatoxins among food-grain workers in India. Occup Env Health. 2014; 20: 189-193.
12. N. Polychronaki, C. P. Wild, H. Mykk¨anen, et al. Urinarybiomarkers of aflatoxin exposure in young children from Egypt and Guinea. Food and Chemical Toxicology. 2008; 46: 519-526.
13. S. Mohd Redzwan, Jamaluddin Rosita, A.M. Mohd Sokhini, et al. Detection of serum AFB 1-lysine adduct in Malaysia and its association with liver and kidney functions. Int. J. Hyg. Environ. Health. 2014; 217(4-5): 443-451.
14. Mohammed A. M., Metwally N. S. Antiaflatoxigenic activities of some aqeous plant extracts against AFB1 induced Renal and Cardiac damage. J. Pharmacol. Toxicol. 2009; 4: 1-16.
15. Xiaoyan Lu, Bin Hu, Li Shao, et al. Integrated analysis of transcriptomics and metabonomics profiles in aflatoxin b1-induced hepatotoxicity in rat. Food Chem. Toxicol. 2013; 55: 444-455.
16. A.A. El-Nekeety, S.H. Abdel-Azeim, A.M. Hassan, et al. Quercetin inhibits the cytotoxicity and oxidative stress in liver of rats fed aflatoxin-contaminated diet. Toxicol. Rep. 2014; 1: 319-329.
17. Santella RM, Wu HC. Environmental exposures and hepatocellular carcinoma. J Clin Transl Hepatol. 2013; 1: 138-143.
18. Zhou R., Liu M., Liang X., et al. Clinical features of aflatoxin B1-exposed patients with liver cancer and the molecular mechanism of aflatoxin B1 on liver cancer cells. Environ. Toxicol. Pharmacol. 2019; 71:103225.
19. ALT/GPT BR opt., Linear Chemicals, S.L.U., Barcelona Spain.
20. AST/GOT BR opt., Linear Chemicals, S.L.U., Barcelona Spain.
21. Alkaline Phosphatase, Linear Chemicals S.l.,Barcelona, Spain.
22. Bilirubin (total And Direct), Linear Chemicals, S.L.U., Barcelona Spain.
23. Cholesterol Mr, Linear Chemicals, S.L.U., Barcelona, Spain.
24. Triglycerides Mr, Linear Chemicals, S.L.U., Barcelona, Spain.
25. HDL-cholesterol, Linear Chemicals, S.L.U., Barcelona, Spain.
26. LDL-cholesterol, Linear Chemicals, S.L.U., Barcelona, Spain.
27. Study the relationship between some fungi and its toxins with kidney failure of unknown case. AL-Qadisiya university. AL-Musoui, H.R.H. 2015.
28. Jolly P. E., Shuaib F. M., Jiang Y., et al. Association of high viral load and abnormal liver function with high aflatoxin B1–albumin adduct levels in HIV-positive Ghanaians: preliminary observations. Food Additives & Contaminants: Part A. 2011; 28: 1224-1234.
29. Thrasher J.D., Crawley S.L. The Biontaminants and Complexity of Damp Indoor Spacs: More than Meets the Eyes. Toxicology and Industrial Health. 2009; 25: 583-616.
30. M. A. Abdel-Wahhab, A. Ibrahim, A. A. El-Nekeety, et al. Meyer extractcounteracts the oxidative stress in rats fed multi-mycotoxin contaminated. Comunicata Scientiae. 2012; 3:143-153.
31. Katherine A. McGlynn, W. Thomas London. Epidemiology and natural history of hepatocellular carcinoma. Best Pract Res Clin Gastroenterol. 2005; 19(1): 3-23.
32. A, Hamfelt. The effect of pyridoxal phosphate on the aminotransferase assay in blood. Scand J Clin Lab Invest Suppl. 1966; 18(92): 181-188.
33. Ono K, Ono T, Matsumata T. The pathogenesis of decreased aspartate aminotransferase and alanine aminotransferase activity in the plasma of hemodialysis patients: The role of vitamin B6 deficiency. Clinical nephrology. 1995; 43: 405-408.
34. Ray L, Nanda SK, Chatterjee A, et al. A comparative study of serum aminotransferases in chronic kidney disease with and without end-stage renal disease: Need for new reference ranges. Int J Appl Basic Med Res. 2015; 5(1):31-35.
35. Freethi R., Raj A. V., Ponniraivan K. Study of serum levels of calcium, phosphorus and alkaline phosphatase in chronic kidney disease. International Journal of Medical Research & Health Sciences. 2016; 5: 49-56.
36. Sakoh T., Nakayama M., Tanaka S., et al. Association of serum total bilirubin with renal

outcome in Japanese patients with stages 3–5 chronic kidney disease. Metabolism. 2015; 64: 1096-1102.

37. Lanone S., Bloc S., Foresti R., et al. Bilirubin decreases nos2 expression via inhibition of NAD (P) H oxidase: implications for protection against endotoxic shock in rats. The FASEB Journal. 2005; 19: 1890-1892.
38. T. Nakagami, K. Toyomura, T. Kinoshita, et al. A beneficial role of bile pigments as an endogenous tissue protector: anti-complement effects of biliverdin and conjugated bilirubin Biochim Biophys Acta. 1993; 1158(2): 189-193.
39. M Mietus-Snyder, A Friera, C K Glass, et al. Regulation of scavenger receptor expression in smooth muscle cells by protein kinase C: a role for oxidative stress. Arterioscler Thromb Vasc Biol. 1997;17(5): 969-978.
40. Nosratola D Vaziri. Role of dyslipidemia in impairment of energy metabolism, oxidative stress, inflammation and cardiovascular disease in chronic kidney disease. Clin Exp Nephrol. 2014; 18: 265-268.
41. Joel D Kopple. The phenomenon of altered risk factor patterns or reverse epidemiology in persons with advanced chronic kidney failure. Am J Clin Nutr. 2005; 81(6): 1257-1266.
42. Pandya V., Rao A., Chaudhary K. Lipid abnormalities in kidney disease and management strategies. World J Nephro. 2015; 4(1): 83-91.
43. Moradi H., Pahl M.V., Elahimehr R., et al. Impaired antioxidant activity of high-density lipoprotein in chronic kidney disease. Transl Res. 2009; 153(2): 77-85.
44. Ribeiro S, Faria Mdo S, Silva G, et al. Oxidized low-density lipoprotein and lipoprotein(a) levels in chronic kidney disease patients under hemodialysis: influence of adiponectin and of a polymorphism in the apolipoprotein(a) gene. Hemodial. Int. 2012; 16(4): 481-90.
45. Kwan BC, Kronenberg F, Beddhu S, et al. Lipoprotein metabolism and lipid management in chronic kidney disease. 2007; J Am Soc Nephrol. 18: 1246-1261.
46. Quaschning T, Krane V, Metzger T, et al. Abnormalities in uremic lipoprotein metabolism and its impact on cardiovascular disease. Am J Kidney Dis. 2001; 38: S14-S19.
47. K, Nitta. Clinical assessment and management of dyslipidemia in patients with chronic kidney disease. Clinical and experimental nephrology. 2012; 16; 522-529.
48. Sturges HA. The choice of a class. interval. Journal of the American Statistical Association. 1926: 21(156): 65-66.
49. Ronald C. Shank. Mycotoxins and N-nitroso compounds: environmental risks. 1981; 1: 3-29.
50. Park D.L., Pohland A.E. Rationale for the control of aflatoxin in animal feeds. Elsevier Applied Science. 1986; 473-482.
51. Hsieh, D. P., Atkinson, D. N. Bisfuranoid mycotoxins: their genotoxicity and carcinogenicity. Boston: Springer; 1991.
52. Groopman J. D., Jiaqi Z., Donahue P. R., et al. Molecular dosimetry of urinary aflatoxin-DNA adducts in people living in Guangxi Autonomous Region. People's Republic of China. Cancer research. 1992; 52: 45-52.
53. M.L. Biehl, W.B. Buck. Chemical contaminants: their metabolism and their residues. J Food Prot. 1987; 50(12): 1058-1073.
54. Ramalho L.N.Z, Porta L.D., Rosim R.E., et al. Aflatoxin B1 residues in human livers and their relationship with markers of hepatic carcinogenesis in São Paulo, Brazil. Toxicology reports. 2018; 5: 777-784.

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