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Zinc and Abdominal Aortic Calcification in Patients under Regular Hemodialysis

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ABSTRACT

Background: Vascular calcification is known to be significantly influenced by zinc deficiency. Low serum zinc inhibited the osteochondrogenic phenotypic flip of phosphate-induced vasculature smooth muscle cells (VSMCs), which led to the formation of vascular calcification. Abnormal mineral metabolism, like hyperphosphatemia, which leads to the phenotypic conversion of VSMCs into osteoblasts that secrete collagen, is a contributing factor for the development of arterial calcification in CKD.

Aim of the work: To evaluate the link between zinc and abdominal aortic calcification in individuals receiving regular hemodialysis.

Patients and Methods: This Cross-Sectional research included 40 Hemodialysis Patients The study Will Be Conducted In Nephrology Unit Al Hussien Hospital. All patients receive 3 Hemodialysis sessions weekly.

Result: AAC score and age have a strong positive link (r = 0.56) that is statistically substantial (p-value< 0.001). AAC score and BMI have a statistically substantial (p-value = 0.014) negative connection (r = -0.39). AAC score and albumin have a strong negative connection (r = -0.55) that is statistically substantial (p-value < 0.001). AAC score and PTH have a statistically substantial (p-value = 0.036) positive connection (r = 0.33). AAC score and serum zinc have a statistically substantial (p-value = 0.005) negative connection (r = - 0.43).

Conclusion: Low serum zinc is connected with high odds of having AAC.

Keywords: *Zinc; Abdominal Aortic Calcification; Hemodialysis; chronic kidney diseases.*

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INTRODUCTION

The micronutrient zinc, which makes up around 57 percent of skeletal muscle and 29 percent of bone, is a crucial trace element and the second-most abundant divalent cation in the body (2-4 g).[1]

A shortage in zinc may be caused by insufficient consumption, poor absorption, and/or excessive loss of the mineral. More than two billion individuals worldwide suffer from zinc insufficiency.[2]

Several earlier investigations have shown reduced blood zinc levels in patients with chronic kidney disease (CKD), with the incidence of zinc insufficiency in those receiving hemodialysis ranging from 40 to 78 percent.[3]

In a latest in vitro experiment, zinc reduced the osteochondrogenic phenotypic transition of vasculature smooth muscle cells (VSMCs) triggered by phosphate, which resulted in the formation of vascular calcification.[4]

Furthermore, an in vivo experiment showed that zinc can prevent phosphate-induced arterial calcification by promoting the synthesis of the zinc-finger protein tumor necrosis factor (TNF)-a-induced protein 3 (TNFAIP3) and inhibiting the stimulation of nuclear factor kappa-light-chain-enhancer of activated B (NF-k B).[5]

The greatest cause of illness and death worldwide is cardiovascular disease (CVD).[6]

Vascular calcification, another prominent characteristic of chronic inflammatory illnesses like CKD, has also been linked to a greater risk of CVD events.[6]

In the United States, non-institutionalized people who consumed more dietary zinc had a decreased

chance of developing severe abdominal aortic calcification (AAC).[7]

Indeed, a number of cohort investigations have shown a link between inadequate zinc consumption and cardiovascular mortality.[8]

Recent research by Chen et al. shown that increased nutritional zinc intake was substantially linked with a reduced incidence of severe AAC (n = 2535). [7]

In patients receiving regular hemodialysis, the research sought to determine the link between zinc and abdominal aortic calcification.

PATIENTS AND METHODS

This cross-sectional research includes 40 Hemodialysis Patients. The study Will Be Conducted In Nephrology Unit Al Hussien Hospital. All patients receive 3 Hemodialysis sessions weekly.

Inclusion Criteria: Patient`s age between 18 and 60 years, duration of haemodialysis more than 6 months and uses of Native arteriovenous fistula in all patients**.**

Exclusion Criteria: patients less than 18 years Or more 60 years, duration of haemodialysis Less than 6 months, Un controlled hypertension or diabetes mellitus, recent inflammation and known to be collagen disease.

Methods: Measurement of serum zinc in patients under regular hemodialysis.

Standing while utilizing common radiographic tools, lateral radiography was completed. The anterior lumbar spines required to be visible for at least 4 cm: The distance between the camera and the subject was 100 cm, other adjustments were: 33-200 mAs, 94 KPV, and a radiation dosage of around 15 mGy were used. Using a previously established technique, the degree of calcific deposits at each lumbar spinal segment (L1-L4) was assessed, along with their position and size. Two techniques were used to sum up the scores: (a) The composite score for anterior-posterior intensity, often known as the AAC, was created by adding the scores of each individual aorta segment for both the anterior and posterior walls (maximum score 24), and (b) the overall number of aorta segments displaying any degree of calcification is displayed, together with the afflicted segments score (maximum score 4).

Ethics and patient consent: For every operation that will be carried out, the patients' written informed permission has been acquired. All procedures were flow Al_Azhar University Ethical Commitee Regulation.

Statistical analysis: Version 24 of the Statistical Program for Social Science (SPSS) was utilized to analyze the data. Both qualitative and quantitative data were reported utilizing frequency and % for quantitative data. The mean (average) is the middle value in a collection of discrete numbers; it is the sum of values divided by the total number of values. The measure of a collection of values' dispersion is the standard deviation (SD). As opposed to a higher SD, which suggests that the results are dispersed across a greater range, a lower SD implies that the values tend to be near to the established mean. Data correlation was done using the Pearson's correlation coefficient (r) test.

RESULTS

		Studied patients (N = 40)	
Sex	**Male**	29	72.5%
	Female	11	27.5%
Age (years)	**Mean ±SD**	44.6 ± 9.2	
	Min – Max	24 – 57	
Weight (kg)	**Mean ±SD**	66.5 ± 7.02	
	Min – Max	48 – 77	
Height (cm)	**Mean ±SD**	165.7 ± 6.7	
	Min – Max	152 – 177	
BMI (kg/m²)	**Mean ±SD**	25.5 ± 1.5	
	Min – Max	21.3 – 28.9	

Table (1): description of demographic data in all researched patients

Regarding gender, there were 11 girls (27.5%) and 29 men (72.5%) among the patients under study. With a minimum age of 24 and a maximum age of 57, the median age of all patients in the research was 44.6 ±9.2 years.

(n = 40)	Minimum	Maximum	Mean	±SD
WBC	2.9	10.8	6.4	1.8
HB	7	14.6	10.7	1.7
PLT	94	325	207.2	56.3
Cholesterol	140	255	189.0	26.9
TG	123	254	155.8	26.3
LDL	110	177	139.7	18.4
HDL	30	56	43.2	6.6
Albumin	3.1	4.9	3.9	0.4
Corrected Ca	7.4	11.8	9.4	1.1
PO4	2.6	8.39	4.9	1.4
Ca X PO4 product	24.9	80.1	45.5	13.2
PTH	22	645	325.8	152.7

Iron	35	196	68.4	30.3
Ferritin	56	1975	421.0	390.3
TIBC	148	321	225.0	32.7
Transferrin Saturation	9	95	29.0	13.9
ZINC	28	124	53.3	19.3

Table (2): description of laboratory data in all studied patients

Regarding WBCs, the median WBCs for all patients in the research were 6.4 ±1.8, with a minimum WBC of 2.9 and a high WBC of 10.8. Regarding Hb, the mean Hb of all patients that were investigated was 10.7 ±1.7, with a low Hb of 7 and a high Hb of 14.6. The mean TIBC of all patients that were investigated was 225 ± 32.7, with a low TIBC of 148 and a high TIBC of 321. In terms of transferrin saturation, the average for all patients under study was 29 ±13.9, with a minimum and highest value of 9 and 95, respectively. Regarding zinc, the average zinc level across all participants in the study was 53.3 ±19.3, with a range of 28 to 124.

		Studied patients (N = 40)
AAC score	**Mean ±SD**	6.5 ± 5.8
	Min - Max	0 – 18

Table (3): description of AAC score in all researched patients

This table shows the description of AAC in all researched patients. With a lowest AAC score of 0 and a maximum AAC score of 18, the average AAC for all patients in the study was 6.5 ±5.8.

Variables	**r**	**p-value**	**variables**	**r**	**p-value**
AAC vs age	**0.56**	**< 0.001 HS**	**AAC vs Albumin**	**-0.55**	**< 0.001 HS**
AAC vs weight	-0.22	0.168 NS	**AAC vs Corr. Ca**	0.03	0.843 NS
AAC vs Height	-0.09	0.572 NS	**AAC vs PO4**	0.26	0.097 NS
AAC vs BMI	**-0.39**	**0.014 S**	**AAC vs Ca.PO4.pro**	0.17	0.291 NS
AAC vs WBC	-0.05	0.783 NS	**AAC vs PTH**	**0.33**	**0.036 S**
AAC vs HB	0.19	0.24 NS	**AAC vs iron**	0.20	0.228 NS
AAC vs PLT	-0.20	0.216 NS	**AAC vs Ferritin**	0.13	0.427 NS
AAC vs CHOL	0.20	0.209 NS	**AAC vs TIBC**	0.17	0.293 NS
AAC vs TG	- 0.23	0.142 NS	**AAC vs T.SAT**	-0.13	0.428 NS
AAC vs LDL	0.06	0.735 NS	**AAC vs S.ZINC**	**-0.43**	**0.005 S**
AAC vs HDL	-0.02	0.896 NS			

(r): Pearson correlation coefficient. S: p-value < 0.05 is substantial.

HS: p-value < 0.001 is very substantial.

NS: p-value > 0.05 is non- substantial.

Table (4): Correlation study between AAC score and other studied data in all studied groups

In studied patients this table shows that there were: AAC score and age have a strong positive link (r = 0.56) that is statistically substantial (p-value< 0.001). AAC score and BMI have a statistically substantial (p-value = 0.014) negative connection (r = -0.39). AAC score and albumin have a strong negative connection (r = -0.55) that is statistically substantial (p-value< 0.001). AAC score and PTH have a statistically substantial (p-value = 0.036) positive connection (r = 0.33). AAC score and serum zinc have a statistically substantial (p-value = 0.005) negative connection (r = - 0.43).

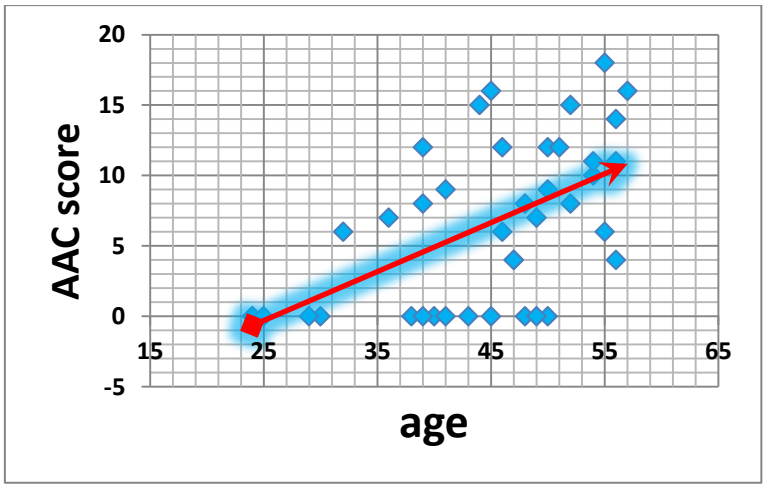

Fig. 1: positive correlation between AAC score and age.

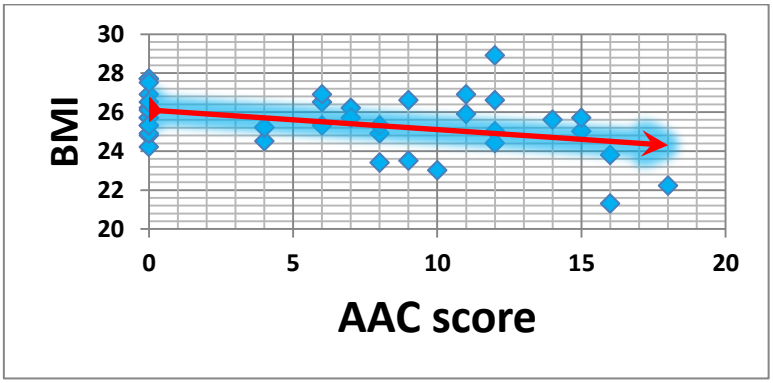

Fig. 2: negative correlation between AAC score and BMI.

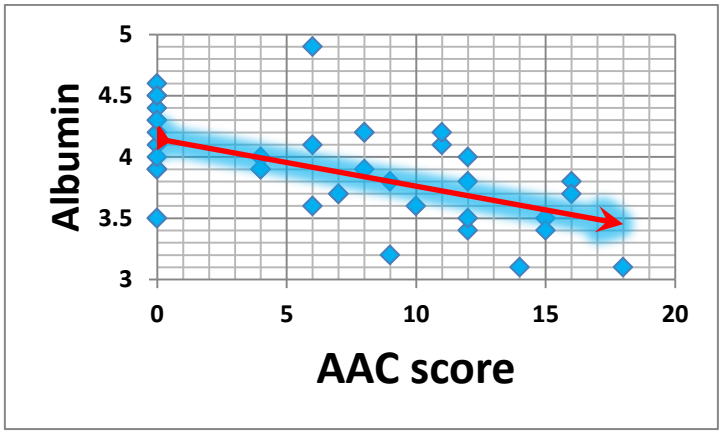

Fig. 3: negative correlation between AAC score and serum albumin.

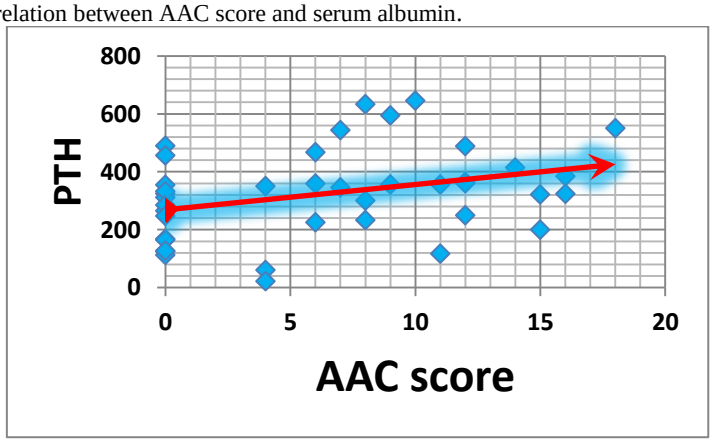

Fig. 4: positive correlation between AAC score and serum PTH.

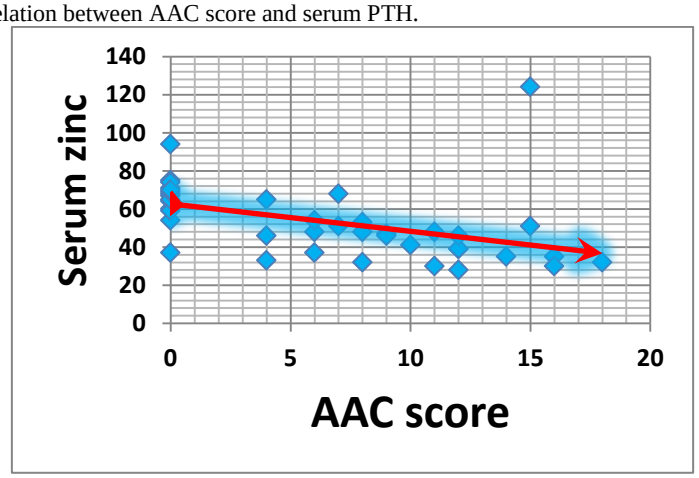

Fig. 5: negative correlation between AAC score and serum zinc.

DISCUSSION

This research was done at Al-Hussein university hospital hemodialysis unit over a period of six month; from November 2021 to July 2022, and conducted on 40 Hemodialysis Patients. Demographic data and Clinical information were recorded. Laboratory data including CBC, calcium, phosphate, albumin, parathyroid hormone (PTH), total cholesterol, triglyceride, high-density lipoprotein (HDL), low density lipoprotein (LDL) Iron profiles (serum iron, TIBC, ferritin, T.SAT) and serum Zinc were evaluated and plain x ray abdomen lateral view was done in the standing position utilizing the standard radiographic equipment's.

In terms of demographic information, the average age of all patients under study was 44.6 ± 9.2 years, with a minimum age of 24 and a maximum age of 57. There were 11 females and 29 men (72.5%). (27.5 percent). Some patients also had other comorbid conditions; 5 of them (12.5%) had diabetes, and 24 had hypertension (60 percent). According to the study's findings, the average AAC score of all patients was 6.5 ±5.8, with the lowest AAC score being 0 and the highest being 18, and the average zinc score was 53.3 ±19.3, with the lowest zinc value being 28 and the highest value being 124.

In the current study, AAC score and age showed a very statistically substantial (p-value< 0.001) positive connection (r = 0.56).

In support of these results Hashim Al-Saedi et al., [9] found in his several investigations that Depending on the patient's age, aortic vascular calcification affects between 18.5 and 95 percent of individuals.

Craver L et al., [10] observed that Common risk factors such as hypertensive, diabetes mellitus, dyslipidemia, age, smoking, and CVD, as well as particular genetic diseases in CKD patients, all contribute to the acceleration of arterial calcification.

Also In support of these results Honkanen et al., [11] observed that In the hemodialysis group, age, the existence of diabetes mellitus, and serum phosphorus were shown to be predictive factors of AAC. In the CORD trial, it was also shown that age, the length of dialysis, and a history of cardiovascular disease were unique predictors for AAC.

Furthermore, Kestenbaum B et al., [12] observed that the main factor influencing vascular calcification is age. Age and AAC have repeatedly been shown to be directly correlated in CKD patients, dialysis patients, and the general population.

In addition, Rapa et al., [13] observed that Age-related increases in abdominal aorta calcifications are linked to conventional cardiovascular risk factors. Age, initial AAC, and hypertension are all independently linked to AAC advancement.

In agreement Honkanen H et al., [11] in his study, found significant association between AACS and age, where calcification score increased rapidly with age.This comes in accordance with Honkanen H et al [11].

Balla J et al., [14] observed that There is an inverse relationship between AAC and demographic factors such age, the frequency of dialysis, and hypertension.

Atkinson J et al.,[15] observed that Vascular calcification worsens with age, and the thoracic aorta at 90 years old has 30 times more calcium buildup than it did at 20 years old in the elastin-rich layer of the media. High blood pressure is linked to age-related medial elastocalcinosis in arteries. In the general public, age-related vascular calcification only affects arteries and doesn't impact additional soft tissues.

Also In support of these results Moe SM et al., [16] observed that His research found a substantial age-related rise in AAC, which has also been seen in HD patients.

Allison MA et al., [17] observed that Age-related increases in abdominal aortic calcifications are linked to conventional CVD risk.

AAC has been shown to increase with time as a consequence of age or dialysis vintage in several investigations.[18]

In this research, the amounts of calcium and phosphorus in the corrected serum did not correspond to the severity of ACC. A number of factors contribute to the pathogenic process of vascular calcification in CKD patients, including abnormalities in the calcium and phosphate metabolic pathways, extracellular matrix metabolism variations, oxidative stress, and inflammation-related disruption of the equilibrium between calcification promoters and inhibitors.[19]

However, our research found no evidence of a connection between serum calcium and AAC rating. Our findings are in accordance with Volkovet al., [20]

In the current study, AAC score and PTH have a statistically substantial (p-value = 0.036) and favorable (r = 0.33) association.

In support of these results Yamada et al., [21] showed a positive connection between vascular calcification parathormone levels of hemodialysis patients.

Nitta K et al., [22] shown that High iPTH levels are VC risk factors. IPTH may boost intracellular Ca levels and cartilage matrix expression, which will aid in the development of VC.

In the current study, AAC score and blood albumin had a very statistically substantial (p-value 0.001) negative connection (r = -0.55).

In support of these results Herselman et al., [23] It was observed in 2010 that lower serum albumin predicted increased all-cause vascular calcification in hemodialysis patients, and that the dynamics of serum albumin level is an effective predictor of all-cause death and cardiac death.

In the current study, there was a statistically substantial (p-value = 0.005) negative connection (r = - 0.43) between AAC score and serum zinc.

In support of the current study Nagy A et al.,[4] observed that Zinc reduced the osteochondrogenic phenotypic transition of vasculature smooth muscle cells (VSMCs) generated by phosphate, which led to the synthesis of vascular calcification.

Also, in accordance with Vervloet M et al., [24] who observed in his numerous investigations that In patients on dialysis, serum Zinc (Zn) concentrations are negatively correlated with VC.

Also, in accordance with Shimizu S et al., [25] who observed that Patients on hemodialysis often have low serum Zn levels because they are frequently malnourished as a result of ongoing inflammation, uremia, and dietary restrictions.

Pasch A et al., [26] observed that decreased zinc concentrations in CKD patients, particularly in dialysis patients.
Also, in support of these results Pasch A et al., [26] observed that An increased arterial calcification was substantially correlated with decreased serum zinc levels.
Also, in support of these results Moe SM et al., [16] observed that Recruiting leukocytes to induce pathological alterations in the vascular endothelium and promoting cardiovascular calcification, low plasma zinc levels in HD patients (mainly as a result of impaired renal function, decreased intestinal zinc absorption, and exogenous elements including food and medicines) stimulate the secretion of many inflammatory mediators and promote cardiovascular disease.
Also, in support of these results de Seigneux S et al., [27] observed that in individuals with CKD, hypozincemia may be linked to an elevated risk of calcification.
Also, in support of these results Chen Z et al., [28] observed that Zinc is crucial for preventing vascular smooth muscle from calcifying.
Also, in support of these results de Carvalho et al., [29] observed that Low dietary zinc intake has been associated with calcification in the general population, and zinc has emerged as a prospective protective factor in cardiovascular calcification. Lack of zinc is linked to the advancement of CVD in those with chronic renal disease.
Also, in support of these results Voelkl et al., [30] observed that zinc sulfate administration 1) reduced the expression of mRNA, which is a bone formation signal and contains the expression of zinc-finger protein TNF-induced protein, and 2) repressed phosphate-induced calcification 3 and 3) prevented NF-kB activation and bone/cartilage reprogramming, which in turn suppressed VSMC phosphate-induced calcification.[30]
The zinc deficit in hemodialysis (HD) patients has been observed to be substantial, ranging from 40% to 78%.[31]
According to reports, consuming more zinc via diet may prevent aorta calcification by 8%.[28]

In the current investigation, serum albumin levels had no effect on the association between serum zinc deficiency and abdominal aortic calcification. The information was comparable to the study indicating zinc deficiency was linked to HD patients' 2-year mortality.[32]

CONCLUSION

AAC risk is increased by low serum zinc levels. Our research points to the advantages of dietary zinc on vascular calcification. Additional research is required to validate this connection.

Conflict of interest : none

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