Research Article

Prevalence of cardiovascular calcification in hemodialysis patients and its correlation with serum calcium and phosphorus level

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Abstract

Introduction: Compared to the general population, hemodialysis patients are at marked increased risk for cardiovascular disease. Vascular calcification, occurring during late-stage vascular and valvular disease, is highly associated with chronic kidney disease-mineral and bone disorders (CKD-MBD), representing a major risk factor for cardiovascular morbidity and mortality. In CKD, Calcitriol levels are reduced and calcium complexes with phosphate, reducing calcium serum levels, causing secondary hyperparathyroidism. This leads to phosphate resorption from the bone, paradoxically causing a phosphate shift from bone demineralization toward vascular mineralization. **Aim of the work:** The aim of the work is to study Prevalence of cardiovascular calcification in patients in hemodialysis unit of Minia university hospital. To evaluate the relationship between cardiovascular calcification and serum calcium and phosphorus level. **Patients and Methods: Subjects:** The current study, The study group comprised 80 of hemodialysis patients, 35 males (43.8%) and 45 females (56.2%) were selected from hemodialysis unit of Minia university hospital (From august 2018 till February 2019). **Results:** Our study sample is 80 patients, 35 males (43.8%) and 45 females (56.2%) were selected from hemodialysis unit of Minia university hospital (From august 2018 till February 2019). Our study Revealed high prevalence of cardio vascular calcification in hemodialysis patients and recommend regular follow up and control of serum calcium and phosphorus level in hemodialysis patients

Key Words: cardiovascular calcification, hemodialysis, calcium, phosphorus

Introduction

Vascular calcification is a common patho-physiological phenomenon in the development of atherosclerosis, hyper- tension, diabetic vascular disease, vascular injury, and chronic kidney disease. It is one of the most important factors for high morbidity and mortality of cardiovascular and cerebrovascular diseases, and even an independent predictor of all-cause mortality. (Chaikriangkrai et al., 2017)

There is no doubt that end-stage renal disease (ESRD) patients have a high prevalence of VC because of multiple risk factors that induce the phenotypic transformation of VSMCs into these osteoblast-like cells capable of inducing tissue mineralization. Vascular calcification causes a decrease in vascular elasticity, an increase in pulse wave velocity, an induction of cardio-myopathy, a decrease in coronary artery flow, and an ischemic change. (Nitta, 2015)

Nowadays, vascular calcification has been an evitable matter to solve in intervention-resistant conditions. Recent technical advances have enabled detection and quantification of coro-nary artery calcifi-cation by multidetector coronary computed tomography. Moreover, calcification patterns on intravenous ultrasound have been reported to be associated with acute coronary syndrome (ACS). In particular, a calcium burden pattern (i.e., spotty or granular microcalcification) was prone to rupture, whereas a homogenous pattern or sheetlike macrocalcification seemed to be resistant to plaque rupture. (Avogaro & Fadini, 2015) Therefore, the diagnosis and treatment of Coronary artery disease (CAD) should not leave out vascular calcification.

Studies revealed two molecular mecha-nisms involved in vascular calcification, which are Ectopic Osteogenesis and Elastin Degradation. (Mori & Inaba, 2018)
There are two patterns of VC. One occurs in the intimal layer and the other in the medial layer of the vessel wall, as in Monckeberg's sclerosis, which is very common in ESRD patients. Both patterns are associated with increased mortality in ESRD patients. (Nitta, Ogawa, Hanafusa, & Tsuchiya, 2019)

An imbalance of calcification promoters and inhibitors in CKD paves the way for the development of extraosseous calcifications. Of note, these factors may act differently on different parts of the arterial tree (Schlieper, 2014)

Promoters of vascular calcification include Ca+2 and P-2 Status (Altered mineral homeo-stasis), Uremic Toxins, Altered vascular extra-cellular matrix, Altered vascular enzyme activity, and Osteocalcin,. (Tesfamariam, 2019) while Inhibitors of vascular calcification include Matrix Gla protein, Vitamin K, fetuin-A, Osteo-protegerin, Klotho, Fibroblast growth factor-23 (FGF23) and Osteopontin. (Lok & Lyle, 2019)

In CKD, a reduced phosphate filtration is compensated by a decline in tubular reab-sorption, attributed to elevations of the phos-phaturic hormones PTH and Fibroblast growth factor 23 (FGF23). With continuing nephron loss, phosphate clearance is reduced and phosphate levels rise. Calcitriol levels are reduced and calcium complexes with phosphate, reducing calcium serum levels, causing secondary hyperpara-thyroidism. This leads to phosphate resor-ption from the bone, paradoxically causing a phosphate shift from bone deminera-lization toward vascular minerali-zation.(Vervloet et al., 2017)

Under physiological conditions, extraoss-eous calcium-phosphate precipitation is prevented by anticalcific mechanisms, including proteins such as fetuin-A, which may encoat calcium-phosphate particles as primary calcium-phos-phate protein particles (calciprotein particles, CPPs). When these anticalcific defenses fail or mineralization pressure of hyperphosphatemia exceeds their capabilities, increased mineral stress with formation of secondary CPPs with a crystalline core occurs. (Pasch, Jahnen-Dechent & Smith, 2018). These strongly stimulate vascular calcification in vitro.
In advanced carotid atherosclerotic plaques, matrix vesicle-like structures derived from vascular smooth muscle cells (VSMCs) were found to contain high levels of BAX (a pro-apoptotic member of the BCL2 family), suggesting that they may be remnants of apoptotic cells. Apoptotic VSMC-derived matrix vesicle-like structures can also concen-trate and crystallize calcium, triggering calci-fication. All these findings have paved the way to the theory that the formation of apoptotic bodies could initiate the ectopic calcification of some cells under certain conditions.(Priante et al., 2019)

Aim of the study

The aim of the work is to study Prevalence of cardiovascular calcification in patients in hemodialysis unit of Minia university hospital

To evaluate the relationship between cardio-vascular calcification and serum calcium and phosphorus level.

Patients and Methods

This study was carried out in department of internal Medicine, hemodialysis unit of Minia university hospital
80 of hemodialysis patients, 35 males (43.8%) and 45 females (56.2%) in hemo-dialysis unit of Minia university hospital were involved in this study after informed written consent. (From august 2018 till February 2019).
All Patients are ESRD, minimum 18 years of age and start hemodialysis from 1 year at least.

Exclusion criteria:

- Poor mobility (inability to walk 100 yards unaided) .
- Malabsorption (extensive bowel surgery, short bowel).
- Generalized carcinomatosis.
- Glucocorticoid therapy.
- Inflammatory disorders (e.g. Active rheumatoid arthritis, inflammatory bowel disease requiring oral glucocor-ticoids).
- Endocrine diseases (e.g. Primary hyper parathyroidism, hyperthyroidism).
- Chronic liver disease.
- Current treatment with teriparatide, strontium ranelate.

- Participation in a trial with an investigational product within the previous 3 months.
- Patients on anti-coagulants such as warfarin.

Clinical Study

All patients were subjected to:

- Thorough history taking (Name, age, sex, residence) and clinical examination. Patients were inter-viewed according to a standard questionnaire about clinical characteristics and included:
  - ✓ **History of hypertension**, duration if present.
  - ✓ **Presence of cardiovascular disease (CVD)**, (Duration, History of Cardiac Catheterization, and History of CABG) & smoking.
  - ✓ **History of diabetes Mellitus**, (Diabetes Type, Duration, treatment "oral hypoglycemic drugs or insulin", and History of peripheral vascular disease).
  - ✓ **Hemodialysis history** (Cause of Dialysis, duration of HD, No. of dialysis sessions per week, Time of each dialysis session, dry weight, UF volume).
- **Calculation of adequacy of Hemodialysis**: by Urea Reduction Ratio (URR)

Radiological investigations including:

- Echocardiography
- Carotid duplex
- Abdominal ultrasonography

Laboratory investigations:

Consent for the collection of 10 ml of blood (predialysis) and 2ml of blood (postdialysis) by sterile venipuncture for laboratory tests was obtained from all study subjects and were subjected to:

- **Renal function test:** (serum creatinine, Blood Urea :"pre and postdialysis") and
- **liver function tests**: Liver enzymes (serum alanine aminotransferase (ALT) and aspartate transaminase (AST), serum albumin, and bilirubin.
- Complete blood picture
- Total calcium, phosphorus and PTH

Results

Our study sample is 80 patients, 35 males (43.8%) and 45 females (56.2%) were selected from hemodialysis unit of Minia university hospital (From august 2018 till February 2019) . **Table (1):** The table shows that mean age of study group is (47.85± 15.78), ranged from (18-77)years. (43.8%) of the study patients were males Vs. (56.2%) of them were females. Percentage of patients from rural areas were (55%), (15%) of them were smokers, (60%) were hypertensive, while (16.3%) were diabetic. About (31%) of patients had history of cardiovascular disease.

Table (1) Sociodemographic and baseline data of the studied patients

Variable	Subtype	Value Frequency Total N=80	Percentage (%) (100%)
Age	**Mean ±SD Range**	47.85± 15.78 (18-77)	-
Sex	**Male**	35	43.8
	Female	45	56.2
Residence	**Urban**	36	45
	Rural	44	55
Smoking	**Smoker**	12	15
	Non-smoker	56	70
	Ex-smoker	12	15
Hypertension	**Yes**	48	60
	No	19	23.7
	Past history	13	16.3
Diabetes	**Yes**	13	16.3
	No	65	81.3
	Past history	2	2.4
CVD	**Yes**	25	31.3
	No	55	68.7

Figure (1): This Figure shows that (60%) of cases had RT IMT more than 7 in duplex , (61%) of cases had LT IMT more than 7 in duplex.

Figure (1) Percentage of IMT more than 7 in duplex

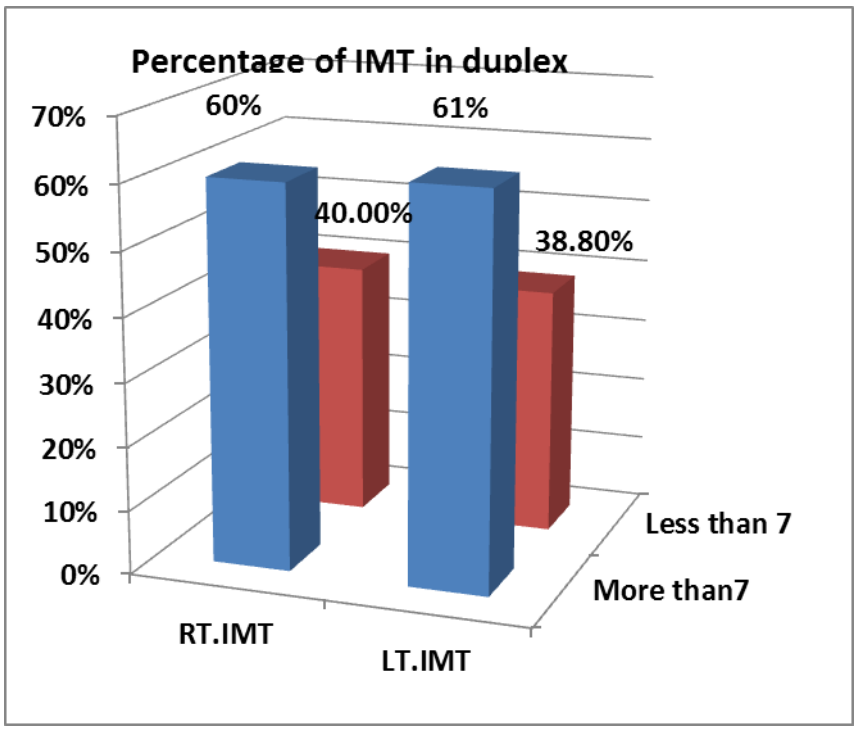

Figure (2): This Figure shows that all hemodialysis diabetic patients (100%) had RT and LT IMT more than 7

Figure (2) Percentage of IMT more than 7 in duplex in diabetic patients

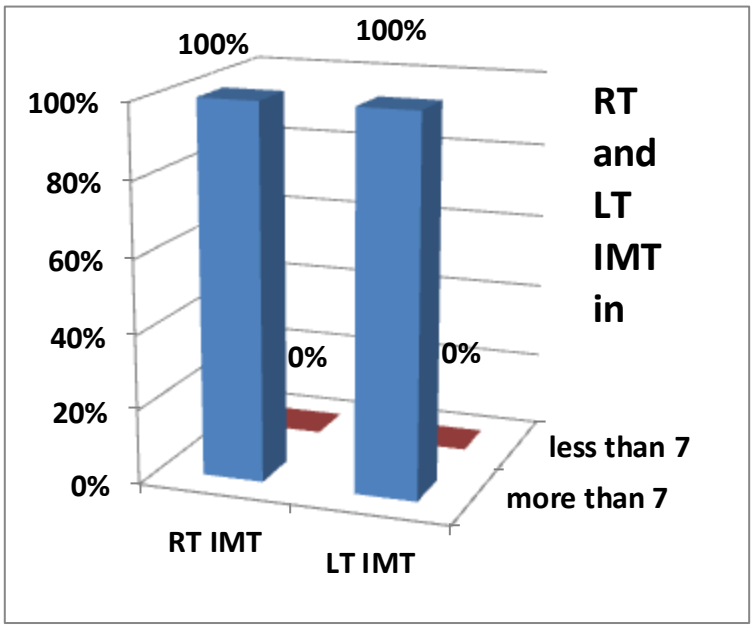

Table (2): The table shows that Calcium**,** Phosphorus**,** and PTH level was higher in patients with atherosclerosis in ascending aortic root.

Table (2) Measuring different variables in patients with atherosclerotic ascending aortic root in Echo

Variable	atherosclerotic ascending aortic root	
	present	Absent
PTH	272.04±120.9	262.58±127.9
Calcium	7.35± 0.61	7.30± 0.5
Phosphorus	9.44± 15.5	6.1± 1.5

Table (3): The table shows that calcium and phosphorus level were higher in patients with LT IMT less than 7.

Table (3) Measuring different variables in patients in relation to LT IMT in duplex

Variable	LT IMT	
	Less than 7	More than 7
PTH	262.58±127.9	272± 120.9
Calcium	7.5± 0.5	7.35 ± 0.6
Phosphorus	9.44± 5.5	6.1± 1.5

Discussion

Vascular Calcification is common in ESRD and is independently predictive of future cardio-vascular events and mortality. Calcification occurs in both the intimal and medial layers of vascular tissue, but medial calcification is the major form in ESRD patients. Medial calcification increases arterial stiffness and pulse pressure, induces left ventricular hyper-trophy, reduces perfusion of the coronary arteries, and ultimately promotes increased cardiovascular mortality. (Nitta et al., 2019)

In genetic and acquired diseases involving hyperphosphatemia, including CKD-MBD, the inability of the kidney to clear excess phosphate causes severe endocrine disturbances as well as leads to calcification of the vasculature. (Hum et al., 2017)

Serum Phosphorus and parathyroid hormone (PTH) were found to be increased in hemodialysis patients. Also, a significant increase in serum Calcium level was found in hemodialysis patients. Also there is a relationship between high levels of Calcium and Phosphorus and presence of cardiovascular calcification.

Vascular calcification is highly prevalent in ESRD as shown in our study (60%) of cases had increase in RT IMT in carotid duplex, (61%) of cases had increase in LT IMT. Also high percentage of patients have evidence of cardiovascular calcification in Echocardiography in the form of Atherosclerotic ascending aortic root, Valvular thickening, or Valvular calcification

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