A Study on carotid IMT as early markers of cardiovascular disease in chronic kidney disease

SangamithraSwaminathan, *SanthaKarunanithi, InmozhiSivakamasundari, Ashok kumar, Krishnan Baskaran,KanagasabaiGanesan.

Department of Biochemistry, Rajah Muthiah Medical College, Annamalai University, Annamalai Nagar, Tamil Nadu, India - 608002 *Corresponding Address:

Dr. K. Santha, Professor and HOD, RMMC, Annamalai University, Annamalai Nagar.

Abstract

BACKGROUND

Chronic Kidney Disease (CKD) was becoming a public health problem in accordance to the increasing non communicable diseases like diabetes and hypertension. The CKD subjects are more prone to complications in terms of increased cardiovascular disease mortality. The non-invasive investigations like Carotid Ultrasonography can measure carotid artery intima media thickness (IMT) and thus can identify CVD complicated with CKD for early intervention preventing subsequent complications. The aim of the study is to assess the role of IMT in subjects with CKD as early markers of cardiovascular disease

MATERIALS AND METHODS:

The study was conducted among 37 subjects in the age group 40-60, identified as CKD patients, undergoing dialysis in Nephrology Department, RajahMuthiah Medical College Hospital and with 17 age matched controls. Blood samples were collected from subjects and were assessed for liver function test, renal function test, haemogram. Carotid IMT was assessed by Doppler Ultrasound using B mode. The data were and analysed using SPSS software. Statistical analysis was performed using student t test. P value less than 0.001, 0.05 was considered as significant.

RESULTS

The mean CIMT of right and left carotid artery was significantly increased in CKD population in comparison with controls. Carotid intima-media thickness positively correlated with blood urea and creatinine. **CONCLUSION**

The study showed that carotid IMT can be used as an early marker to assess the CVD morbidity among CKD subjects. Since carotid artery doppler is a non-invasive procedure it can be widely used as an early marker of CVD complications in CKD patients thereby reducing mortality due to CVD disease in CKD patients.

Key Word: Chronic Kidney disease, Carotid Intima Media Thickness, Cardiovascular disease, Early marker.

Date of Submission: 11-12-2020	Date of Acceptance: 26-12-2020

I. Introduction

Chronic kidney disease (CKD) is featured as a structural or functional kidney defect long-lasting for > 3 months (1). The worldwide occurrence of CKD is observed to be > 10%, and CKD has become a major public health problem (2-4). To prevent mortality due to CVD in CKD patients early screening and treatment is more important. The most frequent modifiable risk factors of CKD are hypertension, diabetes, anaemia like blood disorders, low birth weight, smoking and obese body mass index and non modifiable risk factors are age, genetic component and ethnicity (5). The incidence of CKD is directly linked with diabetes, hypertension, and pre diabetes and is expected to reach 629 million subjects by 2045 (6-8). The risk of cardiovascular mortality is 10–100 times greater in CKD. Structural and functional changes of the cardiovascular system, like endothelial dysfunction, arterial stiffening, left ventricular hypertrophy (LVH), and vascular calcification, contribute to the increasing mortality due to cardiovascular Diseases (CVD) in CKD patient(9-11).

Arterial wall thickness of Carotid Artery can be measured by high resolution B-mode Carotid Doppler. (12-14)The intima-media thickness (IMT) was characterised as the distance between the leading edge of the luminal echo to the leading edge of the adventitia of the media. Carotid intima-media thickness is a validated marker in the assessment of CVD. (15–17) An intima media thickness greater than 0.9 mm and presence of plaque in carotid arteries are known to be strong predictor of CVD events in CKD patients. Carotid IMT is also an independent predictor of CVD mortality in haemodialysis patients (18). Hence the aim of the study is to assess Carotid IMT by Doppler in patients with CKD as an early marker of cardiovascular disease

II. Methodology

A descriptive cross-sectional study was conducted among CKD patients. A total of 37 subjects with CKD who were undergoing dialysis in the Nephrology Department Rajah Muthiah Medical college, Chidambaram over a 6 month period in the age group of 40-60 years were selected for the study. The subjects who need renal replacement were excluded from the study. Institutional ethical committee clearance was obtained and Venous blood samples were collected from the subjects after getting detailed informed written consent. The serum was separated and analysed for baseline biochemical investigations like glucose, lipid profile, liver function test, renal function test, serum electrolytes and haemogram. Carotid IMT was measured using high resolution B mode Carotid Doppler Ultrasonography among the cases and controls. Statistical analysis was performed using student 't' test and results were compared with controls. P value less than 0.001, 0.05 was considered as significant.

III. Results

The study was done among 37 CKD patients and 17 controls. The mean age of the cases was 47 ± 4.95 years among cases and 50.41 ± 6.26 years among controls.

	cases	controls	P value
Blood sugar(mg/dl)	120.46±38.39	89.76±13.51	0.002
Blood urea(mg/dl)	105.54±17.44	20.71±5.05	< 0.001
Creatinine(mg/dl)	9.41±2.23	0.71±0.47	< 0.001
Totalbilirubin(mg/dl)	0.81±0.03	0.79±0.05	0.21
Directbilirubin(mg/dl)	0.20±0.04	0.23±0.47	0.03
SGOT(U/L)	31.46±6.72	33.59±6.79	0.29
SGPT(U/L)	31.95±5.45	31.29±6.57	0.70
ALP(U/L)	168.03±37.55	82.59±31.13	< 0.001
Total protein(g/dl)	6.66±0.77	6.49±0.56	0.43
Albumin(g/dl)	3.59±0.50	3.49±0.37	0.44
Globulin(g/dl)	3.06±0.39	3.01±0.26	0.57

Table no1 Biochemical Parameters among the population

Independent t test, the values are represented by mean \pm SD

*- p value<0.05 is significant

Blood urea [105.54 ± 17.44 vs. 20.71 ± 5.05], creatinine [9.4 ± 2.23 vs. 0.7 ± 0.47], was elevated among cases in comparison to controls (p value<0.05). Liver Function Tests were within normal limits.

Tableno 2Haemogram	. Lipid Profile.	Electrolytes	.carotid IMT	among the cas	es and controls
- asiento	, 21010 1101110,	210001 01 / 000	,	annong me eac	

	cases	controls	P value
Cholesterol(mg/dl)	139.7±23.84	131.71±37.03	0.39
TGL(mg/dl)	88±73,	70±44,94	0.04
LDL(mg/dl)	68.02±13.89	75.58(20.01	0.11
HDL(mg/dl)	37.38±3.3	36.82±3.63	0.58
Sodium(mmol/L)	136.24±6.89	135.35±6.26	0.65
Potassium(mmol/L)	97.10±3.72	97.65±4.01	0.63
Choride(mmol/L)	4.42±0.75	4.38±0.63	0.82
Right IMT(cm)	0.09±0.05	0.05±0.01	0.004
Left IMT(cm)	0.080±0.06	0.050±0.05	< 0.001
Hemoglobin(g/dl)	8.27±1.37	10.94±1.20	< 0.001
TWBC	7337.84±1788.91	4894.12±1592.75	< 0.001
Lymphocyte	21.82±7.67	14.59±2.79	< 0.001
Mixed	5±2.04	15.9±5.91	< 0.001
Neutrophil	48.81±7.09	57.35±8.38	< 0.001
Platelets	228000 ±167000	26000±199000	0.44

Values are represented by mean \pm SD p value <0.05, 0.001 is significant There was significant increase in the carotid IMT (left) (0.080 \pm 0.06) P < 0.001 among cases in comparison to controls.

Tableno 3 Pearson's Correlation	of Carotid	IMT in comparison	with the variables

Variable	Pearson's Correlation coefficient (r)	P value
Right Carotid IMT	0.35	0.01
Blood urea	0.27	0.04
Creatinine		

A Study on carotid IMT as early markers of cardiovascular disease in chronic kidney disease

Left Carotid IMT		
Blood urea	0.54	0.001
Creatinine	0.40	0.003

The above table shows that IMT was positively correlated with urea and creatinine.

IV. Discussion

The aim of the study is to assess the role of IMT by Carotid Doppler in patients with CKD as early markers of cardiovascular disease. The mean age of CKD patients was 47.49 ± 5.52 years. In some studies conducted the mean age of CKD subjects was 51.06 ± 11.90 (17) and 50.03 ± 10.90 .(13) This shows that the major cause of CKD is a chronic inflammatory diseases like diabetes, hypertension and lifestyle changes.

The present study showed that IMT of left common Carotid Artery was in the higher range compared to right Common Carotid among cases in comparison with controls. In CKD, the most common feature is hypovitaminosis D leading to secondary hyperparathyroidism.(22) As a result there is secondary increase in calcium and a decrease in phosphate levels(23)These may alter the vascular smooth muscle cell proliferation and finally leading to increase arterial wall thickness. Paul et al showed that CKD subjects had mean IMT of 0.10 in comparison to 0.07. Kumar et al showed that the mean CAIMT value in CRF patients was 0.10 as compared with 0.070 in healthy control group in their study. Hinderliter et al studied 198 CKD subjects and reported higher CIMT which was associated with other markers of subclinical CVD. Szeto et al followed 203 chinese patients with stage 3 or 4 CKD for an average of 52 months and reported similar findings. This implies that the occurrence of carotid atherosclerosis can be assessed earlier by doing noninvasive study such as carotid Doppler.

V. Conclusions

Since CVD is the most common cause of mortality in CKD patients, early detection of the risk factor is important in the prevention. Also Carotid intima-media thickness was well correlated with many cardiovascular risk factors, CIMT can be used for evaluating CVD risk in CKD patients. Carotid artery IMT by Doppler is also cost effective and non invasive procedure. So Carotid IMT can be used as an early marker in CKD patients, thereby preventing mortality and slowing the progression of kidney disease.

References

- Foundation NK. Clinical practice guidelines for chronic kidney disease: evaluation, classification, and stratification. Am J Kidney Dis. 2002 Feb;39(2 Suppl 1):S1-266.
- [2]. Eckardt K-U, Coresh J, Devuyst O, Johnson RJ, Köttgen A, Levey AS, et al. Evolving importance of kidney disease: from subspecialty to global health burden. Lancet (London, England). 2013 Jul;382(9887):158–69.
- [3]. James MT, Hemmelgarn BR, Tonelli M. Early recognition and prevention of chronic kidney disease. Lancet (London, England). 2010 Apr;375(9722):1296–309.
- [4]. Ji E, Kim YS. Prevalence of chronic kidney disease defined by using CKD-EPI equation and albumin-to-creatinine ratio in the Korean adult population. Korean J Intern Med. 2016 Nov;31(6):1120–30.
- [5]. K. Ogurtsova, J.D. da Rocha Fernandes a, Y. Huang a, U. Linnenkamp a, L. Guariguata a, N.H. Cho a,b, D. Cavan a, J.E. Shaw c, L.E. Makaroff. IDF Diabetes Atlas: Global estimates for the prevalence of diabetes for 2015 and 2040 diabetes research and clinical practice 128 (2017) 40 5 0
- [6]. Alicic RZ, Rooney MT, Tuttle KR. Diabetic Kidney Disease: Challenges, Progress, and Possibilities. Clin J Am Soc Nephrol. 2017 Dec;12(12):2032–45.
- [7]. Thomas MC, Cooper ME, Zimmet P. Changing epidemiology of type 2 diabetes mellitus and associated chronic kidney disease. Nat Rev Nephrol. 2016 Feb;12(2):73–81.
- [8]. Kazancioğlu R. Risk factors for chronic kidney disease: an update. Kidney Int Suppl. 2013 Dec;3(4):368–71.
- [9]. Tuttle KR, Alicic RZ, Duru OK, Jones CR, Daratha KB, Nicholas SB, et al. Clinical Characteristics of and Risk Factors for Chronic Kidney Disease Among Adults and Children: An Analysis of the CURE-CKD Registry. JAMA Netw Open. 2019 Dec 20;2(12):e1918169–e1918169.
- [10]. Hemodial Int. 2007 Jul;11(3):340–8YL, Branley P, Shiel LM, et al. Carotid artery intima-medial thickness is increased in chronic renal failure. ClinExpPharmacol Physiol. 2000 Aug;27(8):639–41.
- [11]. Menon V, Gul A, Sarnak MJ. Cardiovascular risk factors in chronic kidney disease. Kidney Int. 2005 Oct;68(4):1413-8.
- [12]. Manjunath G, Tighiouart H, Coresh J, Macleod B, Salem DN, Griffith JL, et al. Level of kidney function as a risk factor for cardiovascular outcomes in the elderly. Kidney Int. 2003 Mar;63(3):1121–9.
- [13]. Paul J, Dasgupta S, Ghosh MK, Shaw K, Roy KS, Niyogi SM. A study of atherosclerosis in patients with chronic renal failure with special reference to carotid artery intima media thickness. Heart Views. 2012 Jul;13(3):91–6.
- [14]. Gepner AD, Keevil JG, Wyman RA, Korcarz CE, Aeschlimann SE, Busse KL, et al. Use of carotid intima-media thickness and vascular age to modify cardiovascular risk prediction. J Am SocEchocardiogr OffPubl Am SocEchocardiogr. 2006 Sep;19(9):1170–4.
- [15]. Grobbee DE, Bots ML. Carotid artery intima-media thickness as an indicator of generalized atherosclerosis. In: Journal of Internal Medicine. Blackwell Publishing Ltd; 1994. p. 567–73.
- [16]. Bots ML, Hoes AW, Koudstaal PJ, Hofman A, Grobbee DE. Common carotid intima-media thickness and risk of stroke and myocardial infarction: The Rotterdam Study. Circulation. 1997 Sep 2;96(5):1432–7.
- [17]. Lawal OM, Balogun MO, Akintomide AO, Ayoola OO, Mene-Afejuku TO, Ogunlade O, et al. Carotid Intima-Media Thickness: A Surrogate Marker for Cardiovascular Disease in Chronic Kidney Disease Patients.ClinMedInsightsCardiol.2019;13:1179546819852941

- [18]. Sunil Kumar K, Lakshmi AY, Srinivasa Rao PVLN, Das GC, Siva Kumar V. Carotid intima-media thickness in patients with endstage renal disease. Indian J Nephrol. 2009 Jan;19(1):13–4.
- [19]. Cornel BA. The extracranial cerebral vessels. Diagnostic Ultrasound Saint Louis, USA Mosby Inc. 2005;946-7.
- [20]. Stein JH, Korcarz CE, Hurst RT, Lonn E, Kendall CB, Mohler ER, et al. Use of carotid ultrasound to identify subclinical vascular disease and evaluate cardiovascular disease risk: a consensus statement from the American Society of Echocardiography Carotid Intima-Media Thickness Task Force. Endorsed by the Society for Vascular Medicine. J Am SocEchocardiogr OffPubl Am SocEchocardiogr. 2008 Feb;21(2):90–3.
- [21]. Zoungas S, Cameron JD, Kerr PG, Wolfe R, Muske C, McNeil JJ, et al. Association of carotid intima-medial thickness and indices of arterial stiffness with cardiovascular disease outcomes in CKD. Am J kidney Dis Off J Natl Kidney Found. 2007 Oct;50(4):622–30.
- [22]. Zoungas S, Ristevski S, Lightfoot P, Liang Kimata N, Albert JM, Akiba T, Yamazaki S, Kawaguchi T, Fukuhara S, et al. Association of mineral metabolism factors with all-cause and cardiovascular mortality in hemodialysis patients: the Japan dialysis outcomes and practice patterns study. Hemodialysis International 2007; 11:340–348.
- [23]. Kamal LochanBehera, VK. Praveen VarmaD.S. S. Raju, SureshBabuSayana et al. Status of VitaminD, Lipid Profile and Carotid Artery Intima Media thickness in patients With Chronic Kidney Disease. Int J Res Med Sci. 2019 Jun;7(6):2292-2296

SangamithraSwaminathan, et. al. "A Study on carotid IMT as early markers of cardiovascular disease in chronic kidney disease." *IOSR Journal of Dental and Medical Sciences (IOSR-JDMS)*, 19(12), 2020, pp. 41-44.