Original Research Paper

Volume - 12 | Issue - 05 | May - 2022 | PRINT ISSN No. 2249 - 555X | DOI : 10.36106/ijar

General Medicine

CORRELATION BETWEEN CAROTID INTIMA-MEDIA THICKNESS WITH URINE ALBUMIN CREATININE RATIO IN PATIENTS WITH TYPE 2 DABETES MELLITUS

Ourangajeb RMO/SR, Department of Medicine Murshidabad Medical College

Md Hamid Ali* Associate Professor,Department of Medicin, Murshidabad Medical College.
*Corresponding Author

ABSTRACT **Introduction:** Atherosclerotic cardiovascular disease (ASCVD) is the leading cause of morbidity and mortality for individuals with diabetes. Common conditions coexisting with type 2 diabetes (e.g., hypertension and dyslipidemia) are clear risk factors for ASCVD, and diabetes itself confers independent risk. Large benefits are seen when multiple cardiovascular risk factors are addressed simultaneously. Increased urinary albumin excretion (albuminuria) and reduced Glomerular Filtration Rate (GFR) are risk factors for progressive kidney failure and cardiovascular disease. It has been reported that microalbuminuria had a close association with cardiovascular diseases (CVD) as well. It was also reported that microalbuminuria or macroalbuminuria increased the mortality rate by 60 – 80% (1) . Albuminuria can be most easily performed by urinary albumin-to Creatinine ratio (ACR) in a random spot urine collection (2).

Atherosclerosis is the main cause of cardiovascular diseases; measurement of IMT (Intima Media Thickness) enables the detection of atherosclerosis lesions of the arterial wall. CIMT (Carotid Intima Media Thickness) can be measured by high frequency B mode ultrasonography, which provides a high degree of accuracy in estimating the arterial wall thickness. B-mode gray scale sonography allows for imaging of atherosclerotic plaques and intima-media thickness of carotid arteries.

Of these, continuous- wave Doppler and single-gate pulsed-wave Doppler sonography incorporated in duplex systems are reported to be highly accurate relative to angiography for the detection and classification of the degree of obstruction producing a narrowing of lumen more than 50%. In addition, the use of high-resolution B-mode real-time sonography makes it possible to identify small, non stenotic (<50%) plaques and to describe the echo morphology of carotid arteries (3). The carotid IMT is significantly higher in diabetic patients than that in non-diabetic patients (4), and the increased IMT can predict future events of silent brain infarction and coronary heart disease in the patients with T2DM (5).

Carotid IMT is considered to reflect an early stage of macroangiopathy in patients with diabetes. An increasing CIMT above normal level (> 0.8 mm) is associated with increasingly severe coronary artery disease, an increased risk of myocardial infarction and also stroke. Urine ACR is an important marker for the progression of renal dysfunction and is currently recognized as predictive factors for CVD. However, association of IMT with both urinary ACR (Albumin Creatinine Ratio) in type 2 diabetic patients has been investigated in a few reports. Keeping them in mind, a hospital based cross sectional study was performed on the patients presenting with type 2 diabetes mellitus. The study was aimed to establish the role of urine ACR as a leading investigation in patients presenting with type 2 diabetes mellitus for cardiovascular risk assessment. It was intended to evaluate the Carotid IMT in these patients and also detection of atherosclerotic plaque which are clearly related to pathogenesis and aid in planning of management. Our objective is to find out the correlation between urine ACR and carotid intima media thickness (CIMT) in type 2 diabetes patients and whether urine ACR can be used as a screening tool for risk stratification for future cardiovascular disease in Indian population.

KEYWORDS : CIMT-Carotid Intima Thickness, ACR-Albumin Creatinine Ratio, DM

Review Of Literature

Diabetes mellitus is associated with a high risk of cardiovascular disease. It causes aggressive vascular abnormalities in human subjects, and atherosclerosis is regarded as the leading cause of morbidity and mortality in diabetic patients. The Framingham study[13] and Multiple Risk Factor Intervention Trial (MRFIT)(6) showed a 2–3 fold elevation in the risk of clinically evident atherosclerotic disease in patients with T2DM.Similarly, Insulin Resistance Atherosclerotic Study (IRAS) has shown progression of atherosclerosis in persons with T2DM.

The Copenhagen City Heart Study showed that with a history of coronary heart diseases or stroke, subjects with ACR above 5 microgram/min conferred about 100% higher risk of death in comparison with those with ACR below 5 micro g/min (7). In a community-based sample of middle-aged non hypertensive and non-diabetic individuals, an increasing level of ACR that was well below the threshold of microalbuminuria predicted the development of CVD (8). Crouse et al (9) found a strong association between coronary artery status, verified by coronary angiography, and mean aggregate IMT in carotid arteries. Likewise, in our study mean aggregate IMT increased with advancing CAD.

Bots et al (10) used B mode ultrasonography to study the carotid arteries of 7983 patients aged 55 years and over. Throughout 4.6 years of observation (on average), they registered 194 new myocardial infarctions in the study group. Patients who had a myocardial infarction had significantly higher IMTs than did others. The statistical analysis confirmed a strong positive correlation between carotid IMT and the incidence of myocardial infarction, which prompted Bots et al[10] to conclude that IMT may effectively identify patients at high risk of myocardial infarction and cerebrovascular events. A strong association between IMT and risk of stroke and myocardial infarction was established in the Rotterdam study.

O'Leary et al, (11) having examined over 5800 patients (⩾ 65 years of age) with high resolution ultrasonography, found that increased IMT of the carotid arteries is directly associated with an increased risk of myocardial infarction and stroke in older adults without a history of cardiovascular disease. Stehouwer et al. (12) found that microalbuminuria (urine ACR) was linearly associated with impaired endothelium-dependent, flow-mediated vasodilatation in elderly individuals without and with diabetes. It is possible that endothelial leakiness, as reflected by urine albumin excretion, is in part a primary and possibly genetically determined vascular risk factor, or that it mirrors the endothelial dysfunction featuring the atherosclerotic process.

Jadhav et al. (13)in their study on the association of microalbuminuria with CIMT and CAD, observed that microalbuminuria had a strong association with high CIMT in diabetic subjects. Mykkannen et al (14) Investigated the relationship between microalbuminuria (increased urine ACR) and CIMT in 991 non-diabetic and 450 T2DM subjects aged 40 to 69 years. They also reported that subjects with microalbuminuria had greater CIMT than those without microalbuminuria.

The Atherosclerosis Risk In Community (ARIC) (15) study on 15,792 individuals aged 45-64 years reported statistically significant associations of change in CIMT with baseline diabetes, current smoking, HDL cholesterol, pulse pressure during follow up from 1987 to 1998. The ARIC study reported that when compared with internal carotid artery, IMT of common carotid artery (CCA) was found to be a stronger marker of future stroke. Sjoblom et al. investigated the association between reduced eGFR and microalbuminuria against subclinical organ damage, and showed that levels of urinary albumin excretion, but not reduced eGFR, were associated with increased atherosclerosis in patients with T2DM(16).

An analysis of 3,498 patients with diabetes and 5,545 patients without diabetes in the Heart Outcomes Prevention Evaluation (HOPE) study found that microalbuminuria increased the adjusted relative risk (RR)

of major cardiovascular events (RR 1.83, 95% CI1.64–2.05) (17). Participants with diabetes had a RR of 1.97 (95% CI 1.68–2.31) and those without diabetes had an RR of 1.61 (95% CI 1.36–1.90). Data from the RENAAL study also demonstrated that the presence of albuminuria was associated with increased cardiovascular events (18). It was found that patients with a high baseline ACR> (3 g/g) had a 1.92-fold higher risk (95% CI 1.54–2.38) for the cardiovascular end point and a 2.70-fold higher risk (95% CI 1.94–3.75) for heart failure compared with patients with low baseline levels of ACR <(1.5g/g)

MATERIALS AND METHODS

Study Design: Cross sectional, single centre, hospital based prospective and observational study.

Place Of Study: Nilratan Sircar Medical College, Kolkata.
Period Of Study: January 2018 to June 2019.

Study Population: Patients attending OPD and IPD of General Medicine Department, Nilratan Sircar Medical College, Kolkata and fulfill inclusion & exclusion criteria of the study.
Sample Size: 50.
Sample Selection: Randomized

Inclusion Criteria:

Diagnose case of type 2 diabetes mellitus	Age above 18 years	Both sexes

Exclusion Criteria:

Type 1 diabetes mellitus	Secondary diabetes	Gestational diabetes	Connective tissue disorders or vacuities	Overt renal failure
Valvular heart disease or Arial fibrillation	Ischemic heart disease with medications	Patients with ischemic stroke. infection	Urinary tract infection	Congestive cardiac failure

Method Of Data Collection:

Interview & History taking	Physical examination	Laboratory examination,	Record analysis.

Parameters To Be Studies:

Clinical:
Polyuria, polydipsia, or complications of type 2 diabetes mellitus as nephropathy, neuropathy or retinopathy and duration of diabetes.

Laboratory Investigations:
1. The following laboratory parameters were carried out:

Complete haemogram	Fasting Blood Glucose	PPBS	HBA1C	Spot urine ACR	Serum electrolytes-Sodium, potassium, chloride etc.
Blood urea & Creatinine	Urine RE/ME	Lipid profile:.	ECG in all leads	Echocardiography in selected cases	Brain imaging in suspected cases of CVA.

2. Specific Investigation:

A) ACR
Urinary Creatinine was measured by colorimetry. Urinary albumin was measured by immunoturbidimetry. Urinary albumin Creatinine ratio (ACR) was calculated by dividing the urinary albumin concentration in micrograms by the urinary Creatinine concentration in milligrams. Normal UACR is generally defined <30 mg/g Cr, and increased urinary albumin excretion is defined as >30 mg/g Cr. However, UACR is a continuous measurement, and differences within the normal and abnormal ranges are associated with renal and cardiovascular outcomes. Furthermore, because of biological variability in urinary albumin excretion, two of three specimens of UACR collected within a 3- to 6-month period should be abnormal before considering a patient to have albuminuria. Exercise within 24 h, infection, fever, congestive heart failure, marked hyperglycemia, menstruation, and marked hypertension may elevate UACR independently of kidney damage

B) Carotid Artery Doppler Study:
Carotid Artery Doppler study with 7.5 Mhz linear superficial probe was done for all patients to determine CIMT, ICA-IMT and presence of plaques.

Study Procedures:
The proforma were duly filled up and the relevant clinical findings & routine investigations were noted. Consent forms were duly signed by the parents.

Data treatment:
IMT values averaged; Mean IMT values are preferred (more reproducible than maximal values; maximal IMT may reflect more advanced stages with focal thickening or plaque or represent a sampling error); Increased reproducibility of IMT measurement when values from right and left CCA are combined **(19)**; most of the data points for higher values on the left side

RESULTS AND ANALYSIS

Age Distribution:
10 cases out of 50 cases in the study are below the age of forty years Comprising 20.0 % of total cases, 25 cases are between 40-60 years comprising 50.0 % of total cases, 15 cases are 60yrs or more comprising 30.0 % of total cases. (Table-1)

Sex Distribution:
22 cases out of fifty cases in the study are Female Comprising 44.0 % of total cases, 28 cases are male comprising 56.0 % of total cases. (Table-2)

Fasting blood sugar:
Out of 50 cases, 26 cases are in the range OF 100-126 of FBS, comprising of 52 % of cases, 24 cases are >126, comprising 48 % of FBS

PPBS distribution:
Out of 50 cases, 27 cases are in the range of 140-200 of PPBS, comprising of 54 % of cases, 15 cases are >200, comprising 30 % of PPBS

Hba1c Distribution: 43 cases out of fifty cases in the study are HbA1c (>6.5) Comprising 86.0 % of total cases, 7 cases are HbA1c (≤ 6.5) comprising 14.0 % of total cases.

Urine ACR distribution:
Out of 50 cases, 24 cases are abnormal of Urine ACR, comprising of 48 % of cases, 26 cases are normal, comprising 52 % of Urine ACR (Table-4)

Presence of carotid plaque:
30 cases out of fifty cases in the study are no Presence of plaque Comprising 60.0 % of total cases, 20 cases are Presence of plaque (yes) comprising 30.0 % of total cases. CIMT distribution: Out of 50 cases, 11 cases are increased of CIMT, comprising of 22 % of cases, 39 cases are normal, comprising 78 % of CIMT. (Table-5).

Ica-imt Bistribution: Out of 50 cases, 10 cases are increased of ICA-IMT, comprising of 20 % of cases, 40 cases are normal, comprising 80 % of ICA-IMT.

Relation / Association:
Table 6. CIMT* PRESENCE OF PLAQUE: Out of 11cases in increased CIMT, 7 cases are in no group in PRESENCE OF PLAQUE and 4 cases are in YES group.

Table 7. CIMT* SERUM CREATININE: Increased CIMT for 2 cases comprising of 4 % for having abnormal SERUM CREATININE and 9 cases for normal SERUM CREATININE.

Table 8. URINE ACR * PRESENCE OF PLAQUE: there was not statistical significant (as p >0.05) relation

Table 9. CIMT* Urine ACR: Out of fifty patients, urine ACR was increased for 24 patients of them increased CIMT seen in 10 patients and only one patient has increased CIMT out of 26 normal urine ACR patients. As the p value 0.001 so the correlation is statistically significant e.g. the type 2 diabetic patients who have increased urine ACR have increased CIMT.

DISCUSSION:

This study was a hospital-based, observational (cross-sectional) study to evaluate correlation between carotid intima media thickness & urinary Albumin Creatinine Ratio (ACR) in patients of type 2 diabetes who had no history of CVA or heart disease like CCF or AF.

10 cases out of 50 cases in the study are below the age of forty years comprising 20.0 % of total cases, 25 cases were between 40-60 years comprising 50.0 % of total cases, 15 cases were 60yrs or more comprising 30.0 % of total cases. Mean age of the patient was 51.66 with SD 13.3. Out of 50 cases 10 cases bellow the age of 40 years, among them none has increased CIMT, 19 cases between 40-60 years among them 6 cases and 10 cases above 60 years, of them 5 have increased CIMT respectably and there was no statistically significant relation between age and CIMT (P=0.135)

Barry I. Freedman, et al. JASN July 2005(24) The mean ± SD (median) age in the study group was 61.2 ± 9.2 yr (61.0 yr). Hamid Dehdashti Shahrokh et al(21) showed mean age 52.33 with SD 10.96.

22 cases out of fifty cases in the study were Female Comprising 44.0 % of total cases, 28 cases were male comprising 56.0 % of total cases. Out of 28 of male patients only 5 had increased CIMT but out of 22 female patients 6 have increased CIMT there was no statistically significant relation between sex and CIMT (P=0.425) Barry I. Freedman, et al. JASN July 2005 in their study male was 57% and female was 43%. Hamid Dehdashti Shahrokh et al(22) in their study male was 41.5% and female was 58.5%, just opposite to our study.

Jadhav et al. (13)in their study on the association of microalbuminuria with CIMT and CAD, observed that microalbuminuria had a strong association with high CIMT in diabetic subjects. The three glycemic parameters (FPG, PPPG, and HbA1C) and the lipid parameters like total cholesterol, LDL cholesterol, and triglyceride were all significantly higher in patients with increased CIMT.

Out of 28 of male patients 14 have increased urine ACR but out of 22 female patients 10 have increased urine ACR, there was statistically no significant association between URINE ACR with SEX as the p-value is >0.05 (0.749 (at 5 % level of significance) but 10 cases for female and 14 cases female having abnormal URINE ACR. An analysis of 3,498 patients with diabetes and 5,545 patients without diabetes in the Heart Outcomes Prevention Evaluation (HOPE) study found that microalbuminuria increased the adjusted relative risk (RR) of major cardiovascular events (RR 1.83, 95% CI1.64–2.05) (17). Participants with diabetes had a RR of 1.97 (95% CI 1.68–2.31) and those without diabetes had an RR of 1.61 (95% CI 1.36–1.90).

19 cases are of 5 to 10 years DM, 15 cases less than 5 years and 16 cases more than 10 years of DM. Mean duration of diabetes was 7.430 with SD = 4.401..there was maximum increased CIMT for 8 cases out of 16 cases comprising of 16 % for > 10 years of duration of DM and only 3 cases out of 19 cases between age 5-10 years were increased CIMT and no one had increased CIMT bellow the age of 5 years. Hamid Dehdashti Shahrokh et al (22) in their study they showed significant relation with CIMT and duration of diabetes and mean duration of diabetes was 8.66 years with SD 6.07. 30 cases out of fifty cases in the study are no Presence of plaque Comprising 60.0 % of total cases, 20 cases are Presence of plaque (yes) comprising 30.0 % of total cases Out of 11cases in increased CIMT, 7 cases are in no group in PRESENCE OF PLAQUE and 4 cases are in YES group it was not statistically significant p value >0.05 (p=0.167)

Out of 24 cases with increased urine ACR 5 cases had carotid plaque and 4 cases out of 26 normal urine ACR had carotid plaque and it was not statistically significant (p=0.556). **Seong-Woo Choi et al** (23), studied Association between Albuminuria, Carotid Atherosclerosis, Arterial Stiffness, and Peripheral Arterial Disease in Korean Type 2 Diabetic Patients. In this study, after adjusting for other covariates, ACR levels were not significantly associated with carotid plaque (OR 1.36; 95% CI 0.72–2.55 for normo-albuminuria and macroalbuminuria).

11 cases are increased of CIMT, comprising of 22 % of cases, 39 cases are normal, comprising 78 % of CIMT (Table-7), 10 cases are increased of ICA- IMT, comprising of 20 % of cases, 40 cases are normal, comprising 80 % of ICA-IMT and average level of Rt. CCA is 0.857 mm with SD 0.848, for Rt. ICA it is 0.734 mm with SD 0.310, for Lt CCA it is 1.698 mm with SD 5.978, for Lt ICA it is 0.797 with SD 0.414. The Atherosclerosis Risk In Community ARIC (15) study on 15,792 individuals aged 45-64 years reported statistically significant associations of change in CIMT with baseline diabetes, current smoking, HDL cholesterol, pulse pressure during follow up from 1987 to 1998. The ARIC study reported that when compared with internal carotid artery, IMT of common carotid artery (CCA) was found to be a stronger marker of future stroke.

Urine ACR was increased for 24 patients of them increased CIMT seen in 10 patients and only one patient has increased CIMT out of 26 normal urine ACR patients and p value was 0.001 so the correlation is statistically significant e.g. the type 2 diabetic patients who have increased urine ACR have increased CIMT Mykanen et al. investigated the relationship between microalbuminuria and CIMT in 991 non-diabetics and 450 T2DM subjects aged 40 to 69 years. They also reported that subjects with microalbuminuria had greater CIMT than those without microalbuminuria (14).

Diercks et al. similarly showed that urine albumin excretion was strongly related to subclinical atherosclerosis in the presence of increased CIMT in patients with T2DM (24). Also Yokoyama et al. reported that a slight elevation of albuminuria was a significant determinant of IMT independent of conventional cardiovascular risk factors in T2DM patients with no clinical nephropathy or any vascular diseases (25).

CONCLUSION:

There were significant relations between CIMT and lipid profile. TC, TG and LDL-C (P=0.001). HDL had negative effect on CIMT. There was statistically significant correlation between CIMT with hypertension (p= 0.009) and urine ACR with hypertension (p=0.39). CIMT was significantly related to duration of diabetes. CIMT was significantly related with urine ACR. Statistically significant (p=0.001) increased CIMT found among the patients with increased urine ACR, e.g. the type 2 diabetic patients who have increased urine ACR have increased CIMT. Urine ACR can be used as a screening tool for risk stratification for future cardiovascular disease in Indian population.

Limitations Of The Study:

Study Design:

This was a cross-sectional study where CIMT & urinary ACR level were assessed single time. A longitudinal study with baseline and follow up of CIMT & urinary ACR in type 2 diabetic patients would have been more suited to determine the relationship between the occurrence of albuminuria and CIMT.

Selection Bias: The study being a hospital-based study, there is always a chance of selection bias and the subjects might not be the ideal representative of the population.

Sample Size: A larger number of study populations would have made this study more accurate and leaded further weight age to the results. 50 patients were too small to come into a conclusion.

Referral Bias: Referral bias could not be excluded because the study was conducted in a tertiary care hospital like our institution where most of the cases are referred from other primary health care facility. This may have influenced the study result in this study.

There is no conflict of interest. I acknowledge my co-author for his sincere effort.

Tables and Figures

Table 1. Age Distribution

Age (In Years)	Frequency	Percent
<40	10	20.0
40-60	25	50.0
>60	15	30.0

Table2. Sex Distribution

Sex	Frequency	Percent
FEMALE	22	44.0
MALE	28	56.0

Table 3. Urine Acr Distribution

Urine ACR	Frequency	Percentage
Abnormal (> 30 mcg/mg Creatinine)	24	48.0
Normal (<30 mcg/mg Creatinine)	26	52.0

Table 4. Plaque Distribution

Presence of Plaque	Frequency	Percent
NO	30	60.0
YES	20	40.0

Table 5. Cimt Distribution

CIMT	Frequency	Percentage
Increased (> 0.8 mm)	11	22.0

Normal (<= 0.8 mm)	39	78.0

Table 6. CIMT* Presence of Plaque

	CIMT		p-value
Presence Of Plaque	Increased	Normal	0.167
No	7	34	
Yes	4	5	

Table 7. Cimt* Serum Creatinine

		Serum Creatinine		TOTAL	P-VALUE
		Abnormal	Normal		
CIMT	Increased	3	16	19	.112
	Normal	1	30	31	
Total	4	46	50		
P-Value <0.05→ Significance					

Table 8. Urine Acr * Presence Of Plaque

		Presence of Plaque		Total	P-Value
		No	Yes		
URINE ACR	Normal	22	4	26	0.556
	Micro Albuminuria	8	1	9	
	Macro Albuminuria	11	4	15	
Total	41	9	50		
P-Value <0.05→ Significance					

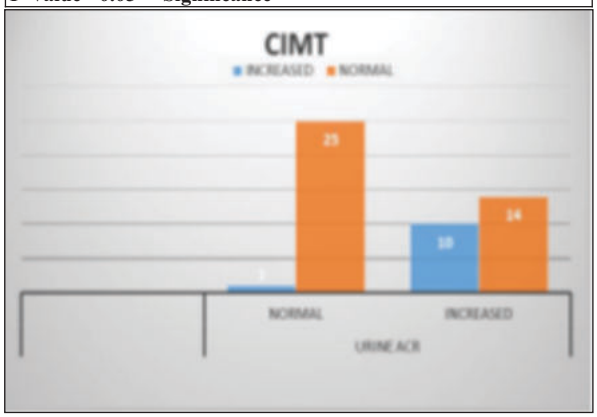

Table 9. CIMT* Urine ACR

CIMT	Urine ACR		P-VALUE
	Normal	Abnormal	
Increased	1	10	0.001*
Normal	25	14	

REFERENCES:

1. Jackson CE, Solomon SD, Gerstein HC, Zetterstrand S, Olofsson B, Michelson EL, Granger CB, Swedberg K, Pfeffer MA, Yusuf S, McMurray JJ; CHARM Investigators and Committees 2009 Albuminuria in chronic heart failure: prevalence and prognostic importance. Lancet 374:543–5501.
2. Tuttle KR, Bakris GL, Bilous RW, et al. Diabetic kidney disease: a report from an ADA Consensus Conference. Diabetes Care 2014;37: 2864–2883.
3. Dietrich ED. Clinical applications of non-invasive cerebrovascular screening, in Zwiebel WJ (ed): Introduction to Vascular Ultrasonography. London, Grune & Tratton Inc 1986: 81-91.
4. Ito H, Komatsu Y, Mifune M, Antoku S, Ishida H, Takeuchi Y, et al. The estimated GFR, but not the stage of diabetic nephropathy graded by the urinary albumin excretion, is associated with the carotid intima-media thickness in patients with type 2 diabetes mellitus: a cross-sectional study. Cardiovasc Diabetol. 2010; 9: 18[DOI][PubMed].
5. Temelkova-Kurktschiev TS, Koehler C, Leonhardt W, Schaper F, Henkel E, Siegert G, et al. Increased intimal-medial thickness in newly detected type 2 diabetes: risk factors. Diabetes Care. 1999; 22(2): 333-8[PubMed].
6. Stamler J, Vaccaro 0, Neaton JD, Wentworth D. Diabetes, other risk factors and 12-yr cardiovascular mortality for men screened in the Multiple Risk Factor Intervention Trial. Diabetes Care. 1993;16:434 44.[PubMed].
7. Klausen KP, Scharling H, Jensen JS 2006 Very low level of microalbuminuria is associated with increased risk of death in subjects with cardiovascular or cerebrovascular diseases. J Intern Med 260: 231–237.
8. Arnlo¨ v J, Evans JC, Meigs JB, Wang TJ, Fox CS, Levy D, Benjamin EJ, D'Agostino RB, Vasan RS 2005 Low-grade albuminuria and incidence of cardiovascular disease events in nonhypertensive and nondiabetic individuals: the Framingham Heart Study. Circulation 112:969–975.
9. Crouse JR, Craven TE, Hagaman AP, et al. Association of coronary disease with segment-specific intimal-media thickening of the extracranial carotid artery. Circulation1995;92:1141–7.
10. Bots ML, Hoes AW, Koudstaal PJ, et al. Common carotid intima-media thickness and risk of stroke and myocardial infarction. The Rotterdam study. Circulation1997;96:1432–7.
11. O'Leary DH, Polak JF, Kronmal RA, et al. Carotid-artery intima and media thickness as a risk factor for myocardial infarction and stroke in older adults. N Engl J Med1999;340:14–22.
12. Stehouwer CDA, Henry RMA, Dekker JM, Nijpels G, Heine RJ, Bouter LM. Microalbuminuria is associated with impaired brachial artery, flow-mediated vasodilation in elderly individuals without and with diabetes: further evidence for a link between microalbuminuria and endothelial dysfunction—the Hoorn Study. Kidney International. 2004;66(supplement 92):S42– 544.
13. Jadhav UM, Kadam NN. Association of microalbuininuria with carotid intima- medial thickness and coronary artery disease - across sectional study in Western India. J Assoc Physicians India. 2002;50:1 124–9.
14. Mykkanen L, Zaccaro DJ, O'Leary DH, Howard G, Robbins DC, Haffner SM. Microalbuminuria and carotid artery intima-media thickness in nondiabetic and NIDDM subjects. The Insulin Resistance Atherosclerosis Study (IRAS). Stroke. 1997;28(9):1710-6. 11.Pub Med].
15. Chambless LE, Folsom AR, Davis V, Sharrett R, Heiss G, Sorlie P, et al. Risk factors for progression of common carotid atherosclerosis: The Atherosclerosis Risk In Community Study, 1987-1998. Am J Epidemiol. 2002;155:38-47.
16. Sjoblom P, Nystrom FH, Lanne T, Engvall J, Ostgren CJ. Microalbuminuria, but not reduced eGFR, is associated with cardiovascular subclinical organ damage in type 2 diabetes. Diabetes Metab. 2014;40(1):49–55. 16.
17. Gerstein HC, Mann JF, Yi Q, Zinman B,Dinneen SF, Hoogwerf B, Halle JP, Young J, Rashkow A, Joyce C, Nawaz S, Yusuf S: Albuminuria and risk of cardiovascular events, death, and heart failure in diabetic and nondiabetic individuals. JAMA 286: 421–426, 2001.
18. de Zeeuw D, Remuzzi G, Parving HH, Keane WF, Zhang Z, Shahinfar S, SnapinnS, Cooper ME, Mitch WE, Brenner BM: Albuminuria, a therapeutic target for cardiovascular protection in type 2 diabetic patients with nephropathy. Circulation 110:921–927, 2004.
19. Reproducibility of carotid intima-media thickness measurements in young adults. http://www.ncbi.nlm.nih.gov/pubmed/18349312 Gonzalez J, Wood JC, Dorey FJ, Wren TA, Gilsanz V. Radiology. 2008; 247(2):465-71.
20. Freedman BI, Langefeld CD, Lohman KK, Bowden DW, Carr JJ, Rich SS, Wagenknecht LE. Relationship between albuminuria and cardiovascular disease in Type 2 diabetes. J Am Soc Nephrol. 2005 Jul;16(7):2156-61. doi: 10.1681/ASN.2004100884. Epub 2005 May 4. PMID: 15872076.
21. Dehdashti Sharokh H, Zakerkish M, Sina AH, Saki A, Forouzan F, Jenabi A. Diagnostic Value of Carotid Artery Intima-media Thickness in Patients with Type 2 Diabetes and Its Correlation with HbA1c Levels. Jundishapur J Chronic Dis Care. 2021;10(2):e111308.
22. Dehdashti Sharokh H, Zakerkish M, Sina AH, Saki A, Forouzan F, Jenabi A. Diagnostic Value of Carotid Artery Intima-media Thickness in Patients with Type 2 Diabetes and Its Correlation with HbA1c Levels. Jundishapur Journal of Chronic Disease Care. 2021;10(2):e111308.
23. Choi SW, Yun WJ, Kim HY, Lee YH, Kweon SS, Rhee JA, et al. Association between albuminuria, carotid atherosclerosis, arterial stiffness, and peripheral arterial disease in Korean type 2 diabetic patients. Kidney Blood Press Res. 2010; 33(2): 111-8[DOI][.
24. Diercks GF, Stroes ES, Van Boven AJ, Van Roon AM, Hillege HL, De Jong PE, et al. Difference in the relation between urinary albumin excretion and carotid intima-media thickness in nondiabetic and type 2 diabetic subjects. Diabetes Care. 2002; 25(5): 936-7.
25. Yokoyama H, Aoki T, Imahori M, Kuramitsu M. Subclinical atherosclerosis is increased in type 2 diabetic patients with microalbuminuria evaluated by intima- media thickness and pulse wave velocity. Kidney Int. 2004; 66(1): 448- 54[DOI][PubMed].