

Carotid artery intima-media thickness in non-diabetic hypertensive patients and their correlation with microalbuminuria: A cross-sectional study

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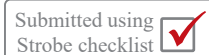
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Cite this article as: Bhusal KR, Khanal U, Pathak S, Khanal P, Bhattarai M, Gyanwali P, Simkhada R, Oli KK. Carotid Artery Intima-Media Thickness in Non-Diabetic Hypertensive Patients and Their Correlation with Microalbuminuria: A Cross-Sectional Study. Nepalese Heart Journal. 2025;22(2):65–69.

Submission Date: 24, Aug, 2025

Acceptance date: 10 Oct, 2025



Abstract

Background: Carotid artery intima-media thickness (IMT) is an early indicator of atherosclerosis and a predictor of cardiovascular disease. Hypertension, prevalent globally, is linked to metabolic risk factors and damages carotid artery characteristics. Microalbuminuria signals endothelial dysfunction, increasing the risk of stroke and cardiovascular events.

Objective: The objective of the study was to determine the prevalence of carotid artery changes in non-diabetic hypertensive patients and its correlation with microalbuminuria.

Methods: A quantitative cross-sectional study was done in 107 participants diagnosed as non-diabetic hypertensive patients visiting Manmohan Memorial medical college and Teaching hospital and Manmohan Cardio-thoracic Vascular and transplant Centre from January 2020 to August 2020. Carotid IMT was measured using B-mode ultrasound, and microalbuminuria was assessed by spot urine albumin-to-creatinine ratio. Data were analyzed using chi-square test and Pearson correlation.

Results: The prevalence of abnormal carotid artery IMT is 16.8% and microalbuminuria is 26.2%. No significant association was found between IMT status and micro-albuminuria status ($p=0.315$). Additionally, there was no significant correlation between IMT and urine albumin level ($r=-0.167$, $p=0.086$).

Conclusions: The level of microalbuminuria was similar in non-diabetic hypertensive patients, whether or not they had carotid artery changes. However, there was no significant difference between the two groups.

Keywords: CCIMT (common carotid artery intima-media thickness); hypertension; microalbuminuria

DOI: <https://doi.org/10.3126/nhj.v22i2.85796>

Introduction

Carotid artery intima-media thickness (IMT) is recognized as an early indicator of atherosclerosis and is strongly linked to the initial onset of cardiovascular disease (CVD) and ischemic stroke across various age groups^{1,2}. Additionally, carotid artery IMT is a powerful predictor of CVD and coronary artery disease^{2,3}. It is measured as

the combined thickness of the innermost two layers of the common carotid artery.

Hypertension, a chronic disease prevalent globally and in Asia, is strongly associated with metabolic risk factors such as obesity, insulin resistance, and abnormal lipid profiles in adults⁴. According



to STEPS survey 2019, prevalence of hypertension of Nepal was 24.5% with higher rates among male (29.8%) as compared to female (19.7%)⁵. Previous studies investigating the relationship between blood pressure and the carotid artery have reported that hypertension is linked to changes in carotid artery characteristics such as intima-media thickness (IMT), lumen diameter (LD), and increased arterial stiffness⁶⁻⁸.

Microalbuminuria (MA) is defined as urinary albumin excretion in the range of 30-300 mg per 24 hours and is considered as an abnormal albumin excretion rate⁹⁻¹¹. Microalbuminuria is linked with several common cardiovascular risk factors. The presence of albuminuria reflects generalized endothelial dysfunction, which is an early sign of atherosclerosis¹². Patients with MA usually have epithelial dysfunction and have a high risk for target organ damage resulting in stroke, retinopathy and adverse cardiovascular events^{10,11}. Its prevalence increases if hypertension is untreated or patients stop using antihypertensive medication¹⁰. There is limited data in our setting correlating carotid IMT changes with microalbuminuria among hypertensive individuals. Understanding this relationship is crucial for early risk stratification and implementing preventive strategies. The objective of the study was to determine the prevalence of abnormal carotid intima-media thickness in non-diabetic hypertensive patients and to assess its association with microalbuminuria among patients with essential hypertension attending a tertiary care center.

Methods

A quantitative cross-sectional study was conducted at Manmohan Memorial medical college and Teaching hospital (MMTH) and Manmohan Cardio-thoracic Vascular and transplant Centre (MCVTC) between June 2020 and June 2021. Ethical approval was obtained from the ethical review board of Nepal Health Research Council.

A total of 107 participants who met the eligibility criteria within the study period were recruited in the study. The sample size was determined based on the availability of eligible patients and the resources available during the study period. Although a formal power calculation was not performed, the sample size is considered adequate for detecting large to moderate effect sizes based on prior studies in similar populations. We included adult patients (≥ 18 years) with a diagnosis of essential hypertension attending the outpatient department. Inclusion criteria was non-diabetic hypertensive patients of age 18 and above years, both sexes having any grade of hypertension as per 2017 American College of Cardiology (ACC)/American Heart Association (AHA) i.e., those with systolic BP = 130 mmHg or more and/or diastolic BP = 80 mmHg or more. Exclusion criteria were patients with diabetes mellitus or impaired glucose tolerance test; renal disease; serum creatinine >1.5 mg/dl; major cerebrovascular events; patients who were not willing to participate and did not give informed consent.

Data were collected and recorded in the proforma through clinical examinations, laboratory investigations, and imaging studies. Sociodemographic information, including age and gender, was recorded. Clinical variables assessed included duration of hypertension (classified as recently diagnosed if ≤ 6 months or chronic if >6 months) and hypertension control status, where controlled hypertension was defined as blood pressure less than 140/90 mmHg and uncontrolled hypertension as blood pressure equal to or greater than 140/90 mmHg. Medication adherence was also evaluated, with patients categorized as regular if they adhered to

daily prescribed medications, or irregular if medications were taken inconsistently or only during symptomatic periods. Blood pressure was taken by manual sphygmomanometer.

Carotid artery IMT was measured with ultrasonography examination by experienced radiologists. B mode imaging of both carotid arteries was performed with 8-12 MHz linear probe and patients in supine position with extended neck facing to opposite side. IMT measurements were taken at the proximal, mid, and distal common carotid arteries on each side. The average value of these three measurements for each side was then calculated, followed by averaging the values from both sides to derive a single value for each patient. IMT was defined as the distance between the lumen-intima interface and the media-adventia interface. All measurements were taken at plaque free site, identified by visual inspection of the B-mode ultrasound images. IMT was classified as normal (≤ 0.79 mm), increased (0.80–1.50 mm), or indicative of plaque formation if greater than 1.50 mm¹³. To ensure the reliability of the measurements, inter-observer variability was assessed by comparing measurements taken by two independent radiologists. Blinding was maintained throughout the process to minimize bias.

Laboratory investigations included measurement of serum creatinine and electrolytes, along with a spot urine albumin-to-creatinine ratio (ACR). Microalbuminuria was defined as an ACR greater than 0.03 mg/mg. In cases where clinical or laboratory data were missing (less than 5% of cases), the affected records were excluded from the final analysis to maintain data integrity. No statistical imputations were performed.

The data was analyzed using IBM SPSS version 27 for analysis. Continuous variables were expressed as mean $\pm$ standard deviation (SD), while categorical variables were presented as frequencies and percentages. Inferential analysis was calculated using chi-square test for categorical independent and categorical dependent variables, independent t-test for categorical independent variable and continuous dependent variable. Similarly, Karl Pearson correlation was done to observe the relationship between two continuous variables.

Results

The study involved 107 hypertensive patients. The mean age of the study participant was 52.08 ± 16.75 years with age ranging from 19 to 92 years. Of the participants, 65 (60.8%) were male. Baseline characteristics such as age, sex, duration of hypertension, hypertension control status, and medication adherence did not show any significant association with the presence of microalbuminuria (Table 1).

Table 1: Association of gender, duration and status of HTN and medical adherence with microalbuminuria group.

Variable	Microalbuminuria		P value
	Yes	No	
Age (in years)	54.20±12.78	51.34±17.92	0.842
Sex (n=107)			
Male	17 (26.2%)	48 (73.8%)	0.789
Female	11(26.2%)	31(73.8%)	
Duration of hypertension (n=107)			

Recently diagnosed (≤6 months)	7(20%)	28(80%)	0.312
Diagnosed for >6 months	21(29.2%)	51(70.8%)	
Hypertension status (n=107)			
Under control	5 (23.8%)	16 (76.2%)	0.342
Not controlled	24(28.2%)	61(71.8%)	
Medication adherence (n=107)			
Regularly taking pre-scribed medicines	18(27.3%)	48(72.7%)	0.578
Taking medicines only when feel difficulty	1 (11.1%)	8 (88.9%)	
Not taking medicines or newly diagnosed hypertensive	6 (18.7%)	26(81.3%)	

Microalbuminuria was present in 28 (26.2%) participants. Regarding carotid artery changes, normal intima-media thickness was found in 89 (83.1%) of participants. Abnormal carotid artery change (increased intima-media thickness) was found in 18 (16.8%) of participants. Of those, 16.7% had microalbuminuria.

Table 2: Association between microalbuminuria and IMT status

Variables	microalbuminuria (n=107)		P value	Karl pearson Correlation test	
	Yes (n=28) N (%)	No (n=79) N (%)		Cor- relation (r)	P value
IMT					
Normal	25 (28.1%)	64 (71.9%)	0.315	-0.167	0.086
Abnormal (>0.79mm)	3 (16.7%)	15 (83.3%)			

Relationship between IMT and microalbuminuria status

No significant difference was observed between IMT status and microalbuminuria status ($p=0.315$) (Table 2). Pearson's correlation analysis showed no significant correlation between IMT and urine albumin level ($r=-0.167$, $p=0.086$) (Table 2).

Discussion

In this cross-sectional study among non-diabetic hypertensive patient, we observed a 26.2% prevalence of microalbuminuria. This is higher than the earlier findings from the study conducted in Nepal among hypertensive patients¹⁴ and diabetic patients¹⁵ where the prevalence of microalbuminuria was 19.16% and 20.3% respectively. The prevalence of abnormal IMT in our study was 16.8% among non-diabetic hypertensive patients with microalbuminuria. In a study by Kaul et al.¹⁶ in asymptomatic Indian individual over 40 years of age, prevalence of abnormal IMT was 41% with higher prevalence

among hypertensive and diabetic patient. Since our population was non-diabetic, that could be the reason that prevalence is high and should not be neglected in clinical settings. The 16.8% prevalence of abnormal IMT among non-diabetic hypertensive patients in this study underscores the importance of incorporating IMT measurements into CVD risk stratification, particularly in those with microalbuminuria. The high frequency of abnormal IMT in this group suggests that hypertensive patients with microalbuminuria may be at high risk for myocardial infarction and stroke in the future. More stringent monitoring and possibly earlier interventions, including more aggressive blood pressure control, lipid management, and lifestyle changes, are necessary for these patients in light of this finding.

Our study found no significant association between IMT and microalbuminuria ($p=0.315$), which aligns with findings from Pedrinelli et al.¹⁷ in Italy among essential hypertensive patient. It suggested microalbuminuria might not be a surrogate measure of subclinical atherosclerosis. Another study from Korea by Shin et al.¹⁸ among newly diagnosed hypertensive or diabetic patients also observed microalbuminuria was not associated with IMT, but with arterial stiffness and vascular inflammation. Conversely, Ravera et al.¹⁹ demonstrated a significantly higher carotid IMT among hypertensive patients with micro-albuminuria as compared to no micro-albuminuria, highlighting the complexity and potential variability of this relationship. Mykkanen et al.²⁰ in their study found an interrelation between carotid IMT and microalbuminuria in nondiabetic and noninsulin-dependent diabetes mellitus subjects, with hypertension partially mediating this relationship.

The lack of association found in our study might be due to the specific non-diabetic population we examined. In diabetic population, study has shown association between microalbuminuria and increased IMT and coronary artery disease²¹. However, in a study by Choi et al.²², albuminuria was associated with peripheral artery disease but not to carotid plaque or carotid IMT in individuals with type 2 diabetes mellitus (T2DM). Similarly, Ishimura et al.²³ and Ito et al.²⁴ found no association between albuminuria and carotid IMT in patient with T2DM.

In Nepal, CVD risk assessment for hypertensive patients is primarily based on traditional risk factors such as blood pressure, cholesterol levels, and family history. However, the use of more advanced tools, such as carotid IMT screening, has not been widely adopted. Ultrasonography equipment is only available in cities, and radiology expertise may not be available on a consistent basis in rural areas. Despite these challenges, the findings of this study indicate that incorporating IMT as a routine screening tool could provide valuable additional risk stratification in hypertensive patients, particularly given the high prevalence of abnormal IMT (16.8%) in this cohort. This is consistent with international guidelines, which recommend IMT as a non-invasive, cost-effective method to identify individuals at higher risk of cardiovascular events.

This study has some limitations. First of all, the sample size was relatively small which restricted in drawing inferences to a full extent. Similarly, the study was limited to two institutions, and thus the results may not be generalized to the population. Another limitation of this study is the lack of a formal power calculation. As a result, the study may have lacked sufficient power to detect weak associations, and the negative findings should be interpreted with caution. Furthermore, microalbuminuria was assessed using a spot morning urine sample instead of a 24-hour urine collection which may not fully reflect albumin excretion over time. Cardiovascular

risk markers such as serum lipids, glucose, HbA1c, and C-reactive protein were not investigated. Likewise, there was also missing information for some responses. Despite limitations, this study provides useful evidence for understanding the prevalence of increased carotid IMT among hypertensive patients and assessing their vascular health in terms of ongoing atherosclerosis. We recommend large-scale longitudinal studies including broader risk factor profiling in the future to understand the burden and impact of abnormal carotid IMT for knowing ongoing atherosclerosis in nondiabetic hypertensive patients.

Conclusion

This study demonstrated a 26.2% prevalence of microalbuminuria with normal IMT and a 16.8% prevalence of abnormal carotid IMT among non-diabetic hypertensive patients. While no significant association was found between IMT and microalbuminuria, it should be interpreted cautiously. This lack of association may be attributed to factors such as sample size, measurement methods, or other unmeasured confounders. Future studies should involve larger, more diverse populations and consider additional biochemical markers to provide a more comprehensive understanding of the relationship between microalbuminuria and subclinical atherosclerosis. We recommend regular monitoring of vascular health in hypertensive patients, including assessments for microalbuminuria and carotid IMT, to independently manage and reduce the risk of cardiovascular and renal diseases in this population.

Conflicts of interest

None

Sources of funding

No funding was received for the study.

Ethical approval

Ethical approval was obtained from the research ethics committee of the Nepal Health Research Council (M) [Ref 2654].

Consent

Written informed consent was obtained from the study participant for publication of this study.

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Literature search KRB, UK, SP

Clinical studies KRB

Experimental studies

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Data analysis UK, SP

Statistical analysis PK, MB

Manuscript preparation KRB, UK, SP

Manuscript edit PK, MB

Manuscript review PG, RS, KKO

Acknowledgement

None

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