

Comparative Burdens of Atherosclerosis in Rural and Urban Communities in South India: Insights from the Kovai Medical Center and Hospital-noncommunicable Disease Studies

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Abstract

Aim: The aim of this study was to describe the distribution and comparison of carotid intima thickness in two completely different demographics in South India. **Materials and Methods:** Data were obtained from 865 participants in rural Nallampatti and 1081 participants from urban Kalapatti in the state of Tamil Nadu. Local ethics committee approval and written and informed consent were obtained from all participants. Carotid intima thickness was measured on all participants using high-resolution B-mode ultrasound. Atherosclerosis was defined as a carotid intima-media thickness of ≥ 1 mm. **Results:** The prevalence of atherosclerosis was 10.3% in rural Nallampatti compared to 7.8% in urban Kalapatti. On binary logistic regression analysis, diabetes and hypertension were associated with atherosclerosis in rural areas, but this significance disappeared after adjustment for confounding factors. In urban areas, diabetes appeared to be significantly associated with atherosclerosis even after adjustment for confounding factors. **Conclusion:** Our data suggest a surprisingly increased prevalence of atherosclerosis in a rural farming population even though traditional risk factors for atherosclerosis such as diabetes and hypertension did not show a significant association after adjustment for confounding factors. If confirmed, this provides a rationale to do large-scale studies to explore the role of nontraditional risk factors in rural India that could have an impact on atherosclerosis and cardiovascular disease.

Keywords: Atherosclerosis, carotid intima-media thickness, Nallampatti-Non communicable disease (NNCD), noncommunicable disease

INTRODUCTION

Mortality, morbidity, and years of lost life from cardiovascular disease (CVD) are escalating immensely in India. Within the last decade alone, there has been a 6% absolute increase in both total deaths and adult deaths related to coronary heart disease in India.^[1] There is always a general perception that cardiovascular events and mortality are higher in an urban population compared to rural counterparts due to westernization, fast food culture, and sedentary lifestyle in urban areas. However, a sea change in dynamics seems to be happening in rural India, which seems to portend a surprisingly rapid increase in cardiovascular risk factors in rural households.^[2] In contrast to some of the regional studies reported from India,^[3,4] the PURE study showed that the rates of major cardiovascular events and deaths from any cause were much higher in rural communities than their urban counterparts

in countries like India.^[5] We recently published data that suggest that we may be seriously underestimating the burden of cardiovascular risk factors and noncommunicable diseases in rural India.^[6] We, therefore, set out to measure carotid intima thickness on two totally different demographics from South India; a completely rural farming population (Nallampatti) and an urban population within Coimbatore city limits (Kalapatti).

Carotid intima thickness is used widely worldwide as a surrogate marker for atherosclerosis and provides a

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How to cite this article: Veerasekar G, Swaminathan K, Sundaresan M, Ramanathan C, Velmurugan G, Alexander T, *et al.* Comparative burdens of atherosclerosis in rural and urban communities in South India: Insights from the Kovai Medical Center and Hospital-noncommunicable disease studies. *Apollo Med* 2018;15:94-8.

Access this article online

Quick Response Code:



Website:
www.apollomedicine.org

DOI:
10.4103/am.am_13_18

noninvasive method for risk assessment of CVD.^[7,8] Carotid intima-media thickness (CIMT) has the additional advantage of being easily available, less expensive, and free from ionizing radiation. There is a huge paucity of large-scale studies in the Indian population evaluating the associations of CIMT. Numerous small-scale studies have looked at the association between CIMT and coronary artery disease, microalbuminuria, and retinopathy.^[9-11] One of the first larger multicenter studies in India assessing 1229 participants provided age- and gender-specific distribution of CIMT in Indian participants free of CVD.^[12] This study showed a progressive increase in CIMT with increasing age, male sex, diabetes, and hypertension. However, the participants were recruited from clinics and hospitals rather than from the community. Therefore, the aim of this study was to evaluate the prevalence of carotid atherosclerosis using CIMT among rural and urban populations in India and to explore associations in respective populations.

MATERIALS AND METHODS

Two demographic areas were chosen after careful deliberations based on contacts with administrative heads, ease of logistics, and ability to perform long-term follow-ups. Local Ethics Committee approval was obtained before the study. Nallampatti is a typical farming village located around 60 km from Coimbatore city and was chosen as representative area for rural setup. Kalapatti located within Coimbatore city was chosen as representative urban area. The Kovai Medical Center and Hospital-Noncommunicable Disease (KMCH-NCD) study is a cross-sectional study that includes rural and urban population of 1946 individuals who were recruited from Nallampatti (Rural – 865) and Kalapatti (Urban – 1081), between April 2015 and June 2016. The study population was informed of our visit through the distribution of leaflets (door to door) and by “word of mouth” through the local heads and volunteers. The exclusion criteria were age <20 years or >85 years, pregnant women, and those not native to the place. The nativity was confirmed through proof of government identity document (Ration card, driving license, or Aadhar card). The convenient sampling method was used to screen participants.

The methodology of the KMCH-NCD study has been published previously.^[6] Briefly, a detailed questionnaire was administered exploring the educational status, employment, alcohol intake, smoking status, pesticide exposure, family disease history, and past medical history. Anthropometric measurements including body weight, height, and waist circumference were obtained using standardized techniques from all participants. All participants had blood pressure measurement in the right arm, with an automatic blood pressure monitor (Model HEM-7130, Omron healthcare, Singapore). Two readings were taken 10 min apart, and the mean of the two was taken as the blood pressure. Carotid intima thickness done using high-resolution B-mode ultrasound machines (GE Healthcare, Venue 40, USA) transported to the venue,

by two radiologists from the department of radiology. Body mass index (BMI) was calculated using the following formula: weight (in kilograms)/height (in meters squared).

Blood investigations included a random glucose (hexokinase/GOD-POD/endpoint method), glycated hemoglobin (automated high-performance liquid chromatography method), and nonfasting lipid profile. Fasting and postmeal glucose were not considered due to logistical issues. Blood investigations were analyzed at Microbiological Laboratory, a accredited laboratory National Accreditation Board for Testing and Calibration Laboratories.

Generalized obesity was defined as a BMI ≥ 25 . Diabetes was defined as either having a history of diabetes on medications or HbA1c level of $\geq 6.5\%$ in those without a history of diabetes. Prediabetes was defined as glycated hemoglobin between 6.0% and 6.4% (International Expert Committee) or 5.7%–6.4% (American Diabetes Association) in those without a history of diabetes. Data were analyzed with both criteria to assess the differences in prevalence between these two groups. Hypertension was defined as either having a history of hypertension on medications or a systolic blood pressure of ≥ 140 mmHg and/or diastolic blood pressure ≥ 90 mmHg on two occasions taken 15 min apart. Generalized hypercholesterolemia was defined as a total cholesterol ≥ 200 mg/dl. Dyslipidemia was defined as a total cholesterol ≥ 200 mg/dl, low-density lipoprotein (LDL)-cholesterol ≥ 130 mg/dl, and high-density lipoprotein-cholesterol (HDL-C) < 40 mg/dl in males and < 50 mg/dl in females. Triglycerides were nonfasting samples due to logistical issues related to fasting samples. People with abnormal CIMT ≥ 1 mm were classified as atherosclerotic.

Statistical analysis

Results were tabulated on Microsoft Excel and transposed to SPSS Statistics Version 20.0. Armonk, New York. Differences between mean and standard deviation were expressed using independent samples T-test. Binary logistic regression was performed to demonstrate the strength of relationship between diabetes and hypertension and abnormal CIMT observations. $P < 0.05$ was considered statistically significant in all analyses (* $P < 0.05$, ** $P < 0.01$, *** $P < 0.001$).

RESULTS

The baseline characteristics of rural and urban populations are outlined in Table 1. Of the 865 participants in rural population, the prevalence of diabetes was 16.2%, 37.8% for hypertension, and 10.3% for atherosclerosis. Compared to rural areas, urban population had a higher prevalence of diabetes 23.1% and hypertension 39.6%, whereas the prevalence of atherosclerosis was 7.8%. There was no significant difference between two groups in the baseline cholesterol levels [Table 1].

Urban participants had significantly higher BMI, HbA1C, LDL, and waist circumference compared to rural population. The rural group had much higher CIMT levels, systolic,

diastolic pressure, and HDL-C. There were no significant differences in age, total cholesterol, and creatinine between the two population areas [Table 2].

Mean and standard deviation of cardiovascular risk markers among the atherosclerotic and nonatherosclerotic groups in rural and urban are tabulated in Table 3. Increasing age, systolic

and diastolic blood pressures, glycosylated hemoglobin, creatinine, uric acid, and waist circumference were associated with atherosclerosis in rural populations whereas increasing age, systolic blood pressure, creatinine, and glycosylated hemoglobin were associated with atherosclerosis in urban population [Table 3].

In the binary logistic regression analysis [Table 4], diabetes, prediabetes, and hypertension in rural areas were significantly associated with atherosclerosis in the unadjusted model. On adjustment for age, sex, and BMI, the significance disappeared in rural population. Similar findings were observed in the unadjusted urban model, but diabetes in urban population appeared to be significantly associated with atherosclerosis even after adjustment for age, sex, and BMI.

DISCUSSION

We report the distribution of CIMT in two totally different demographics in South India. Our findings of diabetes being an independent predictor of carotid intima thickness in urban participants and an unexpected higher prevalence of atherosclerosis in a rural farming South Indian population merit further investigation.

Participants with atherosclerosis in the urban population were significantly older and had higher systolic blood pressures and glycosylated hemoglobin levels. Diabetes was significantly associated with atherosclerosis in urban participants even after adjustment for age, sex, and BMI. This is consistent with previous studies done in urban population around Chennai which show that diabetes is an independent predictor of atherosclerosis in urban participants. In a study of nearly 3000 participants from a representative population of Chennai, a progressive increase in carotid intima thickness was associated with increasing severity of glucose intolerance.^[13] In another study done in a South Indian urban population, at any given age, diabetics had a higher carotid intima thickness than nondiabetics. Multivariate regression analysis showed that diabetes was the most important factor associated with intima-media thickness in this South Indian urban cohort.^[14] Overall, the results of our study along with the above two studies done in Chennai are consistent with diabetes being an independent risk factor for atherosclerosis in an urban South Indian population. This is extremely worrying due to two reasons; first, there is evidence to implicate CIMT as a prognostic indicator of coronary artery disease in diabetic patients,^[15] and second, nearly a quarter of our urban participants had diabetes, which portends a huge coronary artery disease burden for this community in the years to come. This calls for urgent strategies regionally and nationally to reduce diabetes burden in urban communities.

The burden of atherosclerosis among our rural farming population is significant for a variety of reasons. While it is inappropriate to compare two different cohorts with differing baseline characteristics, the prevalence of atherosclerosis based on CIMT was much higher in rural than the urban

Table 1: Baseline characteristics of discrete variables (Nallampatti [rural] and Kalapatti [urban])

Variable	Groups	Rural (%)	Urban (%)
Age	20-40	32.9	31.5
	41-60	46.6	47.8
	>60	20.5	20.7
Sex	Male	48	40.5
	Female	52	59.5
BMI	Underweight	13.2	6.6
	Normal	20.6	14.3
	Overweight	61.3	65.6
	Obese	4.86	13.5
Cholesterol	Abnormal	33.4	37.4
	Normal	66.6	62.6
Hypertension	Hypertensive	37.8	39.6
	Normal	62.2	60.4
Atherosclerosis	Atherosclerotic	10.3	7.8
	Normal	89.7	92.2
HbA1c (ADA)	<5.7	39.7	43.8
	5.7-6.4	42	33.1
	≥6.5	16.2	23.1
HDL	Abnormal	39.4	32.3
	Normal	60.6	67.7
LDL	Abnormal	24.6	38.7
	Normal	75.4	61.3

BMI: Body mass index, HbA1c: Glycated hemoglobin, ADA: American Diabetes Association, HDL: High-density lipoprotein, LDL: Low-density lipoprotein

Table 2: Baseline characteristics of continuous variables (Nallampatti [rural] and Kalapatti [urban])

Variable	Mean (SD)		P
	Rural	Urban	
Age	48.29 (13.71)	48.49 (13.93)	NS
BMI	23.25 (4.10)	25.14 (7.04)	***
Cholesterol	185.64 (38.9)	189.04 (38.62)	NS
CIMT (left)	0.067 (0.019)	0.064 (0.038)	*
CIMT (right)	0.066 (0.018)	0.062 (0.038)	**
Creatinine	0.756 (0.189)	0.772 (0.35)	NS
Diastolic BP	82.13 (11.62)	77.37 (11.62)	***
Systolic BP	130.89 (20.64)	128.74 (21.95)	*
HbA1c	5.98 (1.11)	6.20 (1.47)	***
HDL	44.2 (9.67)	42.2 (11.1)	***
LDL	109.7 (31.45)	121.4 (32.76)	***
WC	89.74 (9.51)	91.97 (10.67)	***

* $P < 0.05$, ** $P < 0.01$, *** $P < 0.001$, BMI: Body mass index, CIMT: Carotid intima-media thickness, BP: Blood pressure, HbA1c: Glycated hemoglobin, HDL: High-density lipoprotein, LDL: Low-density lipoprotein, WC: Waist circumference, NS: Not significant, SD: Standard deviation

Table 3: Mean and standard deviation values of atherosclerosis groups (normal [carotid intima-media thickness <0.1] and atherosclerotic [carotid intima-media thickness ≥0.1]) on cardiovascular risk markers from rural and urban population

Variables	Rural			Urban		
	Normal	Atherosclerosis	Significant	Normal	Atherosclerosis	Significant
Age	46.9 (13.5)	60.6 (8.77)	***	47.2 (13.3)	64.9 (9.90)	***
BMI	23.23 (4.04)	23.43 (4.61)	NS	25.2 (7.21)	24.9 (4.32)	NS
Cholesterol	185.1 (38.1)	190.5 (45.4)	NS	189.1 (38.1)	189.8 (45.2)	NS
Creatinine	0.747 (0.173)	0.83 (0.282)	**	0.76 (0.36)	0.84 (0.21)	**
Diastolic BP	81.8 (11.5)	84.6 (12.1)	*	77.2 (11.5)	79.1 (11.3)	NS
Systolic BP	129.9 (20.3)	139.2 (22.1)	***	127.7 (21.3)	140.6 (24.3)	***
HbA1c	5.9 (1.05)	6.4 (1.52)	**	6.15 (6.84)	6.84 (1.72)	**
HDL	44.4 (9.66)	42.5 (9.64)	NS	42.2 (11.1)	42.0 (10.3)	NS
LDL	109.2 (30.6)	114.7 (37.7)	NS	121.4 (32.4)	122.5 (37.2)	NS
Uric acid	4.71 (1.37)	5.13 (1.36)	**	4.88 (1.40)	5.17 (1.35)	NS
WC	89.4 (9.35)	92.0 (10.5)	*	91.8 (10.7)	93.9 (9.63)	NS

* $P < 0.05$, ** $P < 0.01$, *** $P < 0.001$, BMI: Body mass index, BP: Blood pressure, HbA1c: Glycated hemoglobin, HDL: High-density lipoprotein, LDL: Low-density lipoprotein, WC: Waist circumference, NS: Not significant

Table 4: Binary logistic regression analysis between two groups of atherosclerosis (normal and atherosclerotic)

Population	Parameters	Unadjusted				Adjusted (age, sex, and bmi)			
		Odds ratio	95% CI		Significant	Odds ratio	95% CI		Significant
			Lower	Upper			Lower	Upper	
Rural	Diabetes versus normal	4.97	2.63	9.34	***	1.97	0.98	3.93	NS
	Diabetes versus prediabetes	2.02	1.20	3.40	**	1.24	2.16	2.45	NS
	Hypertensive versus nonhypertensive	3.10	1.96	4.90	***	1.60	0.97	2.64	NS
Urban	Diabetes versus normal	4.78	2.55	9.00	***	2.08	1.03	4.23	*
	Diabetes versus prediabetes	1.61	0.96	2.68	Ns	0.99	0.56	1.71	NS
	Hypertensive versus nonhypertensive	3.50	2.16	5.69	***	1.32	0.76	2.31	NS

* $P < 0.05$, ** $P < 0.01$, *** $P < 0.001$, BMI: Body mass index, CI: Confidence interval, NS: Not significant

cohort. Unlike the urban group, diabetes did not seem to be associated with atherosclerosis after adjustment for confounding factors, and it is pure speculation at this point to link novel nontraditional risk factors with atherosclerosis in rural populations, especially heavy metals used in fertilizers and pesticides. Synthetic phosphate fertilizers are important sources of heavy metals, particularly As, which can accumulate in soil with repeated application.^[16] Recently, we studied urinary heavy metal analysis and serum pesticide levels in all 865 participants from our rural cohort.^[17] The data on urinary heavy metals in our rural cohort suggest significant trends for carotid atherosclerosis associated with the highest quartile of metal compared with lowest quartile of metal for arsenic (As).^[17] There is accumulating evidence for As-induced carotid atherosclerosis,^[18,19] and this may be one “cog in the wheel” for the burden of atherosclerosis in the rural population. Therefore, the role of nontraditional risk factors in the pathogenesis of atherosclerosis in rural population merits further investigations.

There are several limitations to this study. It is possible that there may be a selection bias which could have exaggerated the prevalence data of the study as the sampling of both populations was convenient. Due to logistics and workforce

issues, we were unable to have an independent review of carotid intima thickness nor could we do quality assurance on measurement readings.

CONCLUSION

The overall burden of CVD risk factors in both our urban and rural study population was higher than expected. Diabetes was a significant predictor for atherosclerosis in the urban population. The prevalence of atherosclerosis in the rural cohort was much higher than expected raising valid research questions on the role of nontraditional risk factors in a rural population. Further large-scale studies are warranted to explore these issues, to devise strategies, and to reduce the burden of cardiovascular disease in both the communities.

Acknowledgments

We wish to acknowledge our KMCH Nursing Team, staff from Microbiological Laboratory, Coimbatore, and the village heads of Nallampatti for their help with this study.

Financial support and sponsorship

The study was financially supported by KMCH Ltd., Coimbatore, Tamil Nadu, India.

Conflicts of interest

There are no conflicts of interest.

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