ORIGINAL ARTICLE

PREVALENCE OF CAROTID ARTERY STENOSIS IN PATIENTS WITH ACUTE MYOCARDIAL INFARCTION ADMITTED TO A CORONARY CARE UNIT AND ITS RELATIONSHIP WITH CORONARY ANGIOGRAPHIC FINDINGS

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Objectives: The prevalence and clinical significance of carotid artery stenosis (CAS) in acute myocardial infarction (AMI) patients remain uncertain. This study aims to evaluate CAS prevalence and its association with coronary artery disease (CAD) severity in AMI patients admitted to a coronary care unit (CCU).

Methodology: In this cross-sectional study, 100 consecutively selected AMI patients underwent ultrasound Doppler carotid artery assessments, including measurements of carotid intima-media thickness (cIMT), identification of plaque (stenosis >0%), and calculation of internal carotid artery/common carotid artery (ICA/CCA) peak systolic velocity ratio. Angiographic findings, including the number of diseased vessels and Syntax score (SS), were also recorded.

Results: Among the study cohort (mean age 55.1±11.2 years, 78 males), 32 patients exhibited CAS, with 8 having cIMT>1.2mm, 3 showing ICA/CCA PSV ratio>2, and 25 presenting plaque. CAS prevalence did not significantly correlate with CAD severity, regardless of the number of diseased vessels or SS. Similarly, CAS rates did not significantly differ based on SS categories (low, intermediate, high). While CAS prevalence trended higher in patients with conventional atherosclerotic risk factors (diabetes, hypertension, smoking, obesity), these associations were not statistically significant.

Conclusion: CAS was prevalent in approximately one-third of AMI patients, yet it did not demonstrate a significant association with CAD severity or SS. However, CAS rates tended to increase with the presence of conventional atherosclerotic risk factors. Further research is warranted to elucidate the clinical implications of CAS in AMI patients and its relationship with CAD severity.

Keywords: acute myocardial infarction; carotid artery stenosis; coronary care unit

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INTRODUCTION

Atherosclerotic cardiovascular diseases, including ischemic heart diseases and stroke, represent leading causes of death and disability worldwide.[1] Initiated by sustained low-level inflammation of blood vessel walls, atherosclerosis involves modified monocytes and gradual vascular alterations that predispose individuals to ischemic events and thromboembolism.[2] This process predominantly affects multiple arterial sites, including the coronary, carotid, cerebral, and ilio-femoral arteries, as well as the aorta, resulting in widespread manifestations such as acute coronary syndromes, stroke, and limb ischemia. Consequently, the presence of atherosclerosis in one location is indicative of and contributes to an increased risk of atherosclerosis elsewhere.[2]

A one-year follow-up of patients after an index myocardial infarction event reveals a 25% mortality rate and a 34.4% incidence of major adverse cardiovascular events, including a 4% incidence of stroke.[3] Similarly, the presence of carotid artery stenosis (CAS) is associated with a 77% increased risk of significant coronary artery disease (CAD),[4] and 32% of patients with acute ischemic stroke exhibit atherosclerotic narrowing in at least one coronary artery.[5] Moreover, around 12.8% of patients undergoing coronary angiography harbor unrecognized peripheral arterial disease.[6] These associations likely arise from common risk factors such as male gender, advanced age, diabetes, hypertension, smoking, dyslipidemias, obesity, and chronic kidney disease (CKD).[7] Consequently, modifying and treating risk factors for one arterial bed disease can aid in managing disease in other arterial beds, potentially preventing deaths, disabilities, amputations, and loss of Disability-Adjusted Life Years (DALYs), as well as reducing the cost of care.

In Pakistan, non-communicable diseases, including cardiovascular diseases, have emerged as major causes of morbidity and mortality. Tobacco use and hypertension stand as the leading attributable risk factors for cardiovascular disease-related deaths. However, few studies from our region have explored the relationship between atherosclerotic diseases affecting different regions.[8]

Screening for CAS involves Carotid Artery Ultrasound, with Carotid Intima-Media Thickness (CIMT) defined as the distance from the lumen-intima interface to the media-adventitia interface. CIMT has been shown to predict the presence of CAD and coronary events, correlating well with the burden of Coronary Artery Disease.[9] Prior to Coronary Artery Bypass Grafting (CABG), guidelines from the American College of Cardiology/American Heart Association (ACC/AHA) recommend screening for carotid artery disease in patients over 65 years old, those with left main disease, a history of smoking, a history of transient ischemic attack (TIA)/stroke, carotid bruits, or peripheral artery disease. However, the 2017 ESC Guidelines on the Diagnosis and Treatment of Peripheral Arterial Diseases suggest that carotid screening in patients with CAD cannot be universally recommended, except prior to CABG, due to a lack of evidence regarding its effect on outcomes.[10,11]

As the largest cardiac care center in Pakistan, performing around 8000+ primary PCIs annually, we aim to identify the frequency of carotid artery stenosis in patients presenting with myocardial infarction and its association with coronary angiographic findings.[12] This study will highlight the importance of carotid examination in these patients and contribute to understanding atherosclerosis as a systemic disease rather than a localized one. Tailoring management accordingly will also aid in preventing strokes in these patients. For patients scheduled to undergo CABG after myocardial infarction, screening for carotid artery stenosis will help prevent perioperative neurocognitive complications, including stroke. Furthermore, patients will be followed up at 3, 6, and 12 months as part of a longitudinal study to monitor ongoing issues and manage them accordingly.

Therefore, the aim of our study is to observe the frequency of CAS in patients presenting with myocardial infarction and to correlate the burden of CAS with the severity and complexity of CAD.

METHODOLOGY

Study Design: This cross-sectional study was conducted to investigate the relationship between carotid artery parameters and coronary artery disease severity in patients with acute myocardial infarction (AMI). The study took place over a six-month period, from March 2023 to August 2023, at the National Institute of Cardiovascular Diseases (NICVD) in Karachi, Pakistan. The study design was approved by the institutional review board (IRB) under reference number IRB-12/2023.

Setting: The NICVD, being the largest cardiac center in Pakistan, provided a suitable environment for this study. The critical care units (CCU) within the NICVD were chosen for recruiting participants, given their capacity to handle severe cardiac conditions and facilitate comprehensive ultrasound and coronary assessments.

Participants: The study included adult patients (≥18 years) admitted to the CCU with a diagnosis of AMI. A consecutive sampling method was used to recruit participants who underwent ultrasound Doppler carotid artery assessments. Exclusion criteria were applied to patients who either refused to provide verbal consent or had a history of recent neck trauma, carotid artery compression (e.g., hematoma), or carotid artery thrombosis.

Variables: The primary variables in this study included:

Coronary artery disease severity: Assessed using coronary angiography and quantified by the syntax score.[13]

Carotid artery parameters: Including carotid intima-media thickness (cIMT), plaque thickness, percentage carotid stenosis (CS%), peak systolic velocity (PSV), end-diastolic velocity (EDV), and the ICA/CCA PSV ratio.

Data Sources/Measurement

Data collection involved several steps:

Coronary Angiography: Performed on all participants, with expert cardiologists assessing the coronary artery disease and calculating the syntax score. The score quantifies the complexity of coronary artery disease by assigning weights to different coronary segments and stenosis categories.

Carotid Ultrasound: Conducted by three intensivists trained by a senior radiologist, using B-mode and Color Doppler ultrasound with either the Aplio i-600 series ultrasound machine or Butterfly iQ handheld probe. Patients were examined lying flat or at a 30-degree inclination with the neck rotated 45 degrees to the opposite side.

The following carotid parameters were measured:

Carotid Intima-Media Thickness (cIMTmax): Measured at the common carotid artery (1 cm proximal to the bifurcation) and internal carotid artery (1 cm distal to the bifurcation) for both the right and left sides.[14]

Plaque Thickness: Defined as a cIMT > 1.2 cm, recorded as the maximum thickness of plaques in the CCA and ICA.[15]

Percentage Carotid Stenosis (CS%): Calculated using the formula CS% = (1 - [Residual Diameter/Original Diameter]) × 100% at the most stenotic segment, following the NASCET criteria.[16]

Pulse-Wave Flow Velocities: PSV and EDV measured in the longitudinal view at the stenotic segment. An ICA/CCA PSV ratio >2 indicated >50% stenosis.[17]

Bias: To minimize selection bias, a consecutive sampling method was used. Measurement bias was reduced by standardizing ultrasound procedures and training intensivists. Additionally, the syntax score was determined by a team of expert cardiologists to ensure accuracy and consistency.

Study Size: Based on a prior study by Ozturk et al.[18], which reported significant carotid artery stenosis in 15.9% of patients with multi-vessel coronary artery disease, a sample size of 206 patients was calculated to achieve a 95% confidence level and a 5% margin of error. This report presents interim analysis results from the first 100 patients enrolled.

Quantitative Variables: The main quantitative variables included the cIMTmax, plaque thickness, CS%, PSV, EDV, and the ICA/CCA PSV ratio. Coronary artery disease severity was quantified using the syntax score and the percentage stenosis of each coronary artery segment.

Statistical Methods: Data analysis was performed using IBM SPSS version 21. Continuous data were tested for normality. Normally distributed variables were compared using Student's t-test and reported as means ± SD. Skewed data were compared using the Mann-Whitney U test and reported as medians (IQR). Categorical variables were analyzed using the Chi-square test or Fisher's Exact Test for small sample sizes (n<5). One-way ANOVA was used to explore associations between variables of interest. Binary logistic regression analysis determined factors associated with carotid artery stenosis, with results reported as odds ratios (OR) and 95% confidence intervals (CI).

RESULTS

Participants: A total of 100 patients diagnosed with acute myocardial infarction (AMI) were included in this study. Of these, 78 (78.0%) were male, and 22 (22.0%) were female. The mean age of the participants was 55.1 ± 11.2 years. At baseline, 84 patients (84.0%) were diagnosed with ST-segment elevation myocardial infarction (STEMI), while 16 (16.0%) had non-ST-segment elevation myocardial infarction (NSTEMI). Furthermore, 64 patients (64.0%) exhibited multi-vessel coronary artery disease.

Descriptive Data: Table 1 provides a detailed distribution of clinical, angiographic, and carotid ultrasound findings stratified by the number of vessels involved on coronary angiogram. Patients with multi-vessel disease were significantly older (mean age 58.4 ± 10.4 years) compared to those with single-vessel disease (mean age 49.3 ± 10.0 years), with a significant p-value of <0.001. The majority of multi-vessel disease patients were aged ≥60 years (56.2%), while single-vessel disease patients were predominantly within the 40-59 years age group (69.4%).

Gender distribution showed a higher prevalence of males in both single-vessel (86.1%) and multi-vessel disease groups (73.4%), though this was not statistically significant (p=0.14). Notably, the prevalence of STEMI was significantly higher in single-vessel disease patients (97.2%) compared to multi-vessel disease patients (76.6%) (p=0.007).

Table 1: Distribution of clinical, angiographic, and carotid ultrasound findings by number of vessels involved on coronary angiogram

	Total	Number of Vessels Involved		P-value
		Single Vessel	Multi Vessel	
Total (N)	**100**	**36**	**64**	-
Age (in years)	55.1 ± 11.2	49.3 ± 10.0	58.4 ± 10.4	<0.001
<40 Years	8 (8.0%)	5 (13.9%)	3 (4.7%)	
40 to 59 Years	50 (50.0%)	25 (69.4%)	25 (39.1%)	<0.001
≥60 Years	42 (42.0%)	6 (16.7%)	36 (56.2%)	
Gender				
Male	78 (78.0%)	31 (86.1%)	47 (73.4%)	0.14
Female	22 (22.0%)	5 (13.9%)	17 (26.6%)	
Categorization				
NSTEMI	16 (16.0%)	1 (2.8%)	15 (23.4%)	0.007
STEMI	84 (84.0%)	35 (97.2%)	49 (76.6%)	
Mechanical ventilation				
No	51 (51.0%)	18 (50.0%)	33 (51.6%)	0.88
Yes	49 (49.0%)	18 (50.0%)	31 (48.4%)	
Co-morbid conditions				
Diabetes	34 (34.0%)	12 (33.3%)	22 (34.4%)	0.92
Hypertension	60 (60.0%)	16 (44.4%)	44 (68.8%)	0.017
Smoking	33 (33.0%)	15 (41.7%)	18 (28.1%)	0.17
Dyslipidemia	2 (2.0%)	1 (2.8%)	1 (1.6%)	0.68
Obesity	4 (4.0%)	1 (2.8%)	3 (4.7%)	0.64
Chronic kidney disease	4 (4.0%)	1 (2.8%)	3 (4.7%)	0.64
Chronic obstructive pulmonary diseases	4 (4.0%)	1 (2.8%)	3 (4.7%)	0.64
Congestive heart failure	1 (1.0%)	0 (0.0%)	1 (1.6%)	0.45
Family history of premature CAD	5 (5.0%)	1 (2.8%)	4 (6.2%)	0.44
Family history of ASCVD	6 (6.0%)	2 (5.6%)	4 (6.2%)	0.89
Prior ischemic heart disease	13 (13.0%)	0 (0.0%)	13 (20.3%)	0.004
Atrial fibrillation	1 (1.0%)	0 (0.0%)	1 (1.6%)	0.45
History of previous CVA	2 (2.0%)	0 (0.0%)	2 (3.1%)	0.28
Drug addictions	19 (19.0%)	9 (25.0%)	10 (15.6%)	0.25
Carotid Intima-Media Thickness (cIMT)				
Right CCA (≥ 1.2 mm)	3 (3.0%)	0 (0.0%)	3 (4.7%)	0.19
Left CCA (≥ 1.2 mm)	2 (2.0%)	1 (2.8%)	1 (1.6%)	0.68
Right ICA (≥ 1.2 mm)	3 (3.0%)	0 (0.0%)	3 (4.7%)	0.19
Left ICA(≥ 1.2 mm)	4 (4.0%)	1 (2.8%)	3 (4.7%)	0.64
Percentage Carotid Stenosis (CS %)				
Right ICA (> 0%)	3 (3.0%)	2 (5.6%)	1 (1.6%)	0.26
Left ICA (> 0%)	7 (7.0%)	3 (8.3%)	4 (6.2%)	0.70
Right CCA (> 0%)	9 (9.0%)	2 (5.6%)	7 (10.9%)	0.37
Left CCA (> 0%)	12 (12.0%)	3 (8.3%)	9 (14.1%)	0.40
Internal Carotid Artery/Common Carotid Artery (ICA/CCA) PSV ratio				
Right (≥ 2)	1 (1.0%)	0 (0.0%)	1 (1.6%)	0.45
Left (≥ 2)	2 (2.0%)	0 (0.0%)	2 (3.1%)	0.28
Carotid Artery Stenosis	32 (32.0%)	10 (27.8%)	22 (34.4%)	0.50
CIMT ≥2.0 mm	8 (8.0%)	2 (5.6%)	6 (9.4%)	0.50
Presence of Plaque (stenosis >0%)	25 (25.0%)	8 (22.2%)	17 (26.6%)	0.63
De-ranged Velocity	3 (3.0%)	0 (0.0%)	3 (4.7%)	0.19

ASCVD: atherosclerotic cardiovascular diseases, STEMI: ST-segment elevation myocardial infarction, NSTEMI: non-STEMI, CAD: coronary artery disease, CVA: cerebrovascular accident, CCA: common carotid artery, ICA: internal carotid artery

Table 2: Comparison of angiographic findings between patients with and without significant carotid artery stenosis

	Carotid Artery Stenosis		P-value
	Yes	No	
Total (N)	**32**	**68**	-
Percentage stenosis - Left Main	0.9 ± 5.3	6.0 ± 17.2	0.11
Normal	31 (96.9%)	59 (86.8%)	
0-49 - Insignificant	1 (3.1%)	4 (5.9%)	0.23
≥50 - Significant	0 (0.0%)	5 (7.4%)	

Percentage stenosis - RCA	54.7 ± 42.8	52.0 ± 42.8	0.78
Normal	11 (34.4%)	25 (36.8%)	
1-69 - Insignificant	4 (12.5%)	5 (7.4%)	0.70
≥70 - Significant	17 (53.1%)	38 (55.9%)	
Percentage stenosis - LAD	83.0 ± 24.1	82.3 ± 29.4	0.91
Normal	1 (3.1%)	5 (7.4%)	
1-69 - Insignificant	4 (12.5%)	8 (11.8%)	0.71
≥70 - Significant	27 (84.4%)	55 (80.9%)	
Percentage stenosis - LCx	47.0 ± 44.5	45.3 ± 39.9	0.85
Normal	14 (43.8%)	26 (38.2%)	
1-69 - Insignificant	2 (6.2%)	12 (17.6%)	0.31
≥70 - Significant	16 (50.0%)	30 (44.1%)	
Number of Vessels Involved			
1	10 (31.2%)	26 (38.2%)	
2	9 (28.1%)	13 (19.1%)	0.57
3	13 (40.6%)	29 (42.6%)	
Syntax score I	15.3 ± 5.4	16.5 ± 6.7	0.38
low (≤16)	18 (56.2%)	32 (47.1%)	
Intermediate (16-22)	12 (37.5%)	23 (33.8%)	0.24
High (>22)	2 (6.2%)	13 (19.1%)	
Any intervention done			
Percutaneous coronary intervention	29 (90.6%)	58 (85.3%)	0.46
Left heart catheterization	3 (9.4%)	10 (14.7%)	
Thrombolysis in myocardial infarction (TIMI) flow achieved			
0	0 (0%)	2 (3%)	
I	0 (0%)	1 (2%)	0.35
II	4 (14%)	3 (5%)	
III	25 (86%)	52 (90%)	
Echocardiography			
Left ventricular ejection fraction	32.7 ± 7.1	34.3 ± 7.5	0.29
TAPSE	16.7 ± 2.1	17.2 ± 1.4	0.11
Presence of left ventricular clot	0 (0.0%)	1 (1.5%)	0.49

RCA: right coronary artery, LAD: left anterior descending artery, LCx: left circumflex

Table 3: Binary logistic regression analysis for significant carotid artery stenosis

	Odds Ratio [95% CI]	P-value
Gender		
Female	Reference	Reference
Male	1.8 (0.60 - 5.41)	0.295
Categorization		
Non ST-segment elevation myocardial infarction	Reference	Reference
ST-segment elevation myocardial infarction	1.5 (0.44 - 5.08)	0.514
Co-morbid condition		
Diabetes	1.25 (0.52 - 3.02)	0.613
Hypertension	1.17 (0.49 - 2.77)	0.726
Smoking	2.01 (0.84 - 4.82)	0.120
Obesity	2.20 (0.30 - 16.37)	0.441
Chronic kidney disease	2.20 (0.30 - 16.37)	0.441
Chronic obstructive pulmonary diseases	2.20 (0.30 - 16.37)	0.441
Family history of premature CAD	1.44 (0.23 - 9.10)	0.695
Family history of atherosclerotic vascular disease	1.07 (0.19 - 6.15)	0.942
Prior ischemic heart disease	0.94 (0.27 - 3.30)	0.919
Drug addictions	0.50 (0.15 - 1.67)	0.262
Number of Vessels Involved		
Single Vessel	Reference	-
Multi Vessel	1.36 (0.56 - 3.33)	0.498
Syntax score I		
Low (≤16)	Reference	-
Intermediate (16-22)	0.93 (0.38 - 2.30)	0.871
High (>22)	0.27 (0.06 - 1.35)	0.112
Left ventricular ejection fraction	0.97 (0.91 - 1.03)	0.287
TAPSE	0.81 (0.63 - 1.05)	0.112

CI: confidence interval, CAD: coronary artery disease

Outcome Data: Carotid artery stenosis (CAS) was observed in 32 patients (32.0%). Of these, 8 patients had a carotid intima-media thickness (cIMT) greater than 1.2 mm, 3 patients had an ICA/CCA PSV ratio greater than 2, and 25 patients had detectable plaques (stenosis >0%). The prevalence of CAS showed no significant association with the number of coronary arteries involved (34.4% in multi-vessel vs. 27.8% in single-vessel disease, p=0.50).

Main Results: Comparison of angiographic findings between patients with and without significant CAS is detailed in Table 2. There was no significant difference in the percentage stenosis of the left main, right coronary artery (RCA), left anterior descending artery (LAD), and left circumflex artery (LCx) between those with and without CAS. Notably, the prevalence of CAS did not significantly correlate with the severity of coronary artery disease, as indicated by Syntax scores. CAS was present in 36% of patients with low Syntax scores (≤16), 34% with intermediate scores (17-22), and 13% with high scores (>22) (p=0.24).

Binary logistic regression analysis (Table 3) identified no significant associations between CAS and conventional cardiovascular risk factors, including diabetes (OR: 1.25 [95% CI: 0.52 - 3.02]), hypertension (OR: 1.17 [95% CI: 0.49 - 2.77]), and smoking (OR: 2.01 [95% CI: 0.84 - 4.82]). Similarly, CAS did not show a significant association with gender (OR: 1.8 [95% CI: 0.60 - 5.41]), STEMI (OR: 1.5 [95% CI: 0.44 - 5.08]), or multi-vessel coronary artery disease (OR: 1.36 [95% CI: 0.56 - 3.33]).

Overall, while certain trends were observed, such as higher but non-significant rates of CAS in patients with conventional risk factors and STEMI, no statistically significant predictors of CAS were identified in this cohort. The complexity of coronary artery disease, as measured by the Syntax score, did not show a significant relationship with the prevalence of CAS.

DISCUSSION

Cardiovascular diseases, particularly atherosclerotic conditions like ischemic heart diseases and stroke, present formidable global health challenges, accounting for significant mortality and disability worldwide.[19] Atherosclerosis, characterized by chronic inflammation of blood vessel walls, predisposes individuals to ischemic events and thromboembolism, affecting multiple arterial sites including the coronary, carotid, cerebral, and ilio-femoral arteries.[20] The extensive nature of atherosclerosis necessitates understanding its impact across different arterial beds, as manifestations in one location often signify increased risk elsewhere.

Studies have underscored the substantial mortality and morbidity associated with acute myocardial infarction (AMI), with a significant proportion experiencing major adverse cardiovascular events, including stroke, within a year post-event.[21] Additionally, the prevalence of atherosclerotic-related cardiovascular and cerebrovascular events in South Asian countries underscores the urgency of understanding and managing these conditions in this population due to genetic predisposition and the presence of metabolic syndrome.[22]

Our study aimed to elucidate the relationship between carotid artery stenosis (CAS) and the severity of coronary artery disease (CAD) in patients presenting with AMI. While previous research has suggested an association between CAS and significant CAD, our findings did not reveal a significant correlation between the presence of CAS and the severity or complexity of CAD in our cohort of 100 consecutive AMI patients.[23]

Contrary to our expectations, CAS was prevalent in 32% of cases, with varying degrees of plaque formation, carotid intima-media thickness (cIMT), and peak systolic velocity (PSV) ratios.[24] However, this prevalence did not significantly correlate with the severity or complexity of CAD, as measured by Syntax scores. These findings suggest that while CAS may be common among post-AMI patients, it may not necessarily reflect the extent or complexity of CAD.[25]

Comparisons with previous studies reveal differences in CAS prevalence, potentially due to variations in reference values and patient populations.[26] Moreover, conventional risk factors such as obesity, hypertension, and diabetes did not show significant associations with CAS in our study, challenging their equal impact on both vascular systems.

While previous studies have suggested associations between Syntax scores and cIMT, our study did not find a significant correlation between CAS and Syntax scores.[27] This discrepancy may stem from differences in methodology, including the specific syntax scores used and the cutoff ranges for cIMT thickness.[28, 29]

The clinical implications of our findings are noteworthy. The high prevalence of non-significant CAS among AMI patients underscores the importance of comprehensive vascular assessment in this population.[30] However, the lack of a significant correlation between CAS and CAD severity challenges the routine use of carotid screening in CAD patients, particularly those undergoing percutaneous coronary intervention (PCI) secondary to AMI. Further research is needed to elucidate the clinical utility and cost-effectiveness of routine carotid screening in CAD patients.

LIMITATION

Limitations of our study include its cross-sectional design, relatively small sample size, and observational nature, which precludes causal inference. Future longitudinal studies with larger cohorts are warranted to validate our findings and explore the long-term implications of CAS in AMI patients.

CONCLUSION

In conclusion, our study underscores the systemic nature of atherosclerosis and highlights the need for personalized risk assessment and management strategies. While we found a high prevalence of carotid artery stenosis (CAS) among acute myocardial infarction (AMI) patients, we did not establish a significant association between CAS and coronary artery disease (CAD) severity. This suggests that the relationship between these conditions is complex and requires further investigation. Individualized approaches to risk assessment and management are essential for improving outcomes in this high-risk population.

AUTHORS' CONTRIBUTION

SGA, MYB, MIA, LT, MSA, MH, AURM, MU, and JA: Concept and design, data acquisition, interpretation, drafting, final approval, and agree to be accountable for all aspects of the work. SGA, MYB, MIA, LT, MSA, MH, AURM, MU, and JA: Data acquisition, interpretation, drafting, final approval and agree to be accountable for all aspects of the work.

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