



## Original Article

# Presence of coronary artery disease in diabetic and non diabetic South Asian immigrants

Sunita Dodani<sup>a,\*</sup>, Gyanendra K. Sharma<sup>b</sup><sup>a</sup> Department of Medicine, College of Medicine, Mayo Clinic, Jacksonville, FL, United States<sup>b</sup> Division of Cardiology, Department of Medicine, Medical College of Georgia, Augusta University, Augusta, Georgia

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## ABSTRACT

**Introduction:** South Asian Immigrants (SAIs) are the second fastest growing Asian immigrant population in the US, and at a higher risk of type 2 diabetes (diabetes) and coronary artery disease (CAD) than the general US population. Objectives: We sought to determine in SAIs the; 1) the prevalence of CAD risk factors in diabetics and non-diabetics; and b) the high possibility of CAD in diabetic SAIs. We also assessed the prevalence of sub-clinical CAD in both diabetics and non-diabetics SAIs using common carotid artery Intima-media thickness (CIMT) as a surrogate marker for atherosclerosis.

**Methods:** In a cross-sectional study design, 213 first generation SAIs were recruited and based on the history, and fasting glucose levels were divided into two subgroups; 35 diabetics and 178 non-diabetics. 12-hour fasting blood samples were collected for glucose and total cholesterol levels. Exercise Tolerance Test (ETT) was performed to determine the possibility of CAD.

**Results:** Both diabetics and non-diabetics SAIs in general, share a significant burden of CAD risk factors. The prevalence of hypertension ( $p = 0.003$ ), total cholesterol  $\geq 200$  mg/dl ( $p < 0.0001$ ) and family history of diabetes ( $p < 0.0001$ ) was significantly higher in diabetics compared to non-diabetics. Of the 22/29 diabetic participants without known history of CAD, 45% had positive ETT ( $p < 0.001$ ). Similarly, 63.1% of diabetics and 51.8 % of non-diabetics were positive for sub-clinical CAD using CIMT as a marker.

**Conclusion:** The susceptibility to diabetes amongst SAIs promotes an adverse CAD risk, as evident by this small study. Further research, including larger longitudinal prospective studies, is required to validate the current small study findings with investigation of the temporal association.

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## 1. Introduction

Though death rates attributable to cardiovascular diseases (CVDs) including coronary artery disease (CAD) have declined in the past decade, yet CAD is still number one killer globally and accounts for 30.8% of all deaths in the US.<sup>1</sup> The increasing frequency of global migration to US has highlighted the need for more information on CAD risk factors and diseases in migrant populations from different ethnic backgrounds. The prevalence of Type 2 Diabetes (henceforth, diabetes) worldwide was about 2.8% in 2000 and is projected to be 4.4% in 2030.<sup>2,3</sup> India leads the world with the largest number of diabetics (prevalence of approximately 10%), earning the dubious distinction of being termed the “diabetes capital of the world”. South Asian Immigrants (SAIs), the people from Indian subcontinent (India, Pakistan, Bangladesh, Nepal, and

Sri Lanka) represent a quarter of the world's population, and at 3.4 million, SAIs in the US has exploded over the past decade (over 106% growth rate), and is the second fastest growing immigrant group.<sup>4</sup> Many studies have reported high rates of diabetes and CAD among SAIs worldwide.<sup>5,6</sup> Furthermore, studies have found that SAIs' risk of CAD death is as high as 40% above whites', and they have a 2- to 4-fold higher incidence of diabetes.<sup>2,7</sup> A recent study on SAIs in the US found a diabetes prevalence of 30%.<sup>8</sup> Recently, the South Asian Association for Regional Cooperation (SAARC) reported that mortality and morbidity due to diabetes and CVDs are higher in SAIs than in any other expatriate ethnic group worldwide.<sup>9,10</sup> Metabolic syndrome (MS) is more prevalent in both men and women living in India or abroad.<sup>11,12</sup> Diabetes is a major problem among South Asians still living in Asia, as well as among SAIs who have migrated to other countries.

The principal cause of mortality globally, particularly in diabetics is CAD, as their CAD mortality risk is equal to that of non-diabetics who had a previous episode of myocardial infarction.<sup>9</sup> MS predisposes patients, especially women to CAD, stroke,

\* Corresponding author.

E-mail address: [soni.dodani@gmail.com](mailto:soni.dodani@gmail.com) (S. Dodani).

and diabetes.<sup>10</sup> Insulin resistance is postulated as a central feature of the MS, culminating in atherosclerosis, diabetes and CVD; a pathway potentially accelerated by migration/urbanization.

In the US, SAI population has doubled in the past decade, however, data on CAD with and without among diabetic SAIs is limited and mostly comes from Canada or UK. The awareness about high burden CAD in SAIs in general and in SAI diabetics in particular is low. Since prevalence of diabetes is high in SAIs and to our knowledge, no previous study has reported the incidence of CAD in diabetic SAI population; we sought to determine; a) the prevalence of CAD risk factors in diabetics and non-diabetics; and b) the possibility of CAD in diabetic SAIs living in the State of Georgia, US, which is home to a very large SAI population. We also assessed the prevalence of sub-clinical CAD in both diabetics and non-diabetics SAIs using common carotid artery Intima-media thickness (CIMT) as a surrogate marker for atherosclerosis. Through this small but an eye-opener study, the goal is to create awareness among SAI community of the diabetes and CAD burden and highlight that SAI with diabetes and a positive stress test need more aggressive risk management.

## 2. Methods and study design

The study was approved by Institutional Review Board (IRB) of the Medical College of Georgia, Augusta, Georgia. Using a cross-sectional study design, a total of 213 first generation SAIs (Hindus) were randomly recruited from Hindu Temples, major businesses and other organizations in Augusta and Atlanta, the two largest cities of Georgia. Study information was made available by distributing flyers in the temples and announcements through local newspapers outlining the purpose, rationale, and design of the study. The study included adult SAIs of age 25 years or more. Written informed consent was obtained. Information on socio-demographic status, ethnicity (based on spoken language), personal lifestyle characteristics, as well as CAD risk factors was obtained. Twelve-hour fasting blood samples were collected for measurements of total cholesterol and fasting glucose levels. We also assessed sub-clinical CAD in those without the history of CAD using CIMT as a surrogate marker for atherosclerosis.

### 2.1. Exercise stress test

Due to limited funding, exercise tolerance test-ETT (also called stress test) was offered to only on diabetic participants without known history of CAD (n=29) in order to determine the high possibility of CAD in this group. Standard Bruce protocol was followed for the ETT.<sup>13,14</sup> The exercise goal was to achieve at least a target heart rate of 85% of maximum predicted for age.<sup>14</sup> The test could also be terminated early at the discretion of supervising physician if a participant had any significant symptoms like chest pain, shortness of breath, sustained arrhythmias, or hemodynamic instability (based on BP control) or ST-segment changes.<sup>14</sup> ETT test was considered positive for ischemia (high possibility of CAD) in the presence of exercise induced 1 mm horizontal or down sloping ST-segment depression 80 ms from the J point. A blinded cardiologist interpreted ETT.

### 2.2. Carotid ultrasound doppler

Details on Carotid ultrasound Doppler procedure are provided elsewhere.<sup>15</sup> Briefly, IMT is defined by Pingoli and colleagues as the distance from the leading edge of the lumen-intima interface of the far wall to the leading edge of the media-adventitia interface of the far wall.<sup>16</sup> B-mode ultrasound scanning of bilateral common carotid arteries was performed by a trained non-invasive vascular ultrasound technician at study clinic at the Medical College of

Georgia, using SonoCalc™ IMT machine (SonoSite, Inc Bothell, WA) with a 7.5 MHz linear array transducer. Both arteries were scanned in supine position. A total of eight images were obtained (four on each side), 1 cm proximal to the carotid bulb using an anterior approach. ECG leads were placed to obtain end-diastolic measurements. Images were recorded and stored on a disk. The CIMT approach for IMT measurements was preferred because the CIMT is reproducible and predictive of future cardiovascular events, and the data collection is more complete than other non-invasive markers.<sup>17–19</sup> Measurements of the internal carotid and bifurcation segments tend to have many more missing values.<sup>18</sup> The Mannheim Intima-Media Thickness Consensus suggested that measurement of the common carotid artery is ideal.<sup>20</sup>

Any focal thickening of the intima-media complex or carotid plaque though documented, but was not included in the analysis. A cardiologist, who was blinded to participants' identities and clinical information, analyzed stored images by using automated edge detection technology (SonoCalc™ IMT). Measurement of the far wall of the carotid artery was preferred, since studies comparing ultrasound measurements with histology suggest that far-wall CIMT measurements are more indicative of the true thickness of the arterial wall.<sup>21</sup> Near-wall CIMT measurements, in comparison, are limited by their dependence on the axial resolution, gain settings of the equipment used and show greater variation between repeated measurements.<sup>22–24</sup> Participants with values greater than 0.80 mm were considered to be IMT positive. Previous epidemiological studies suggest that a value of IMT at or above 0.80 mm is associated with a significantly increased absolute risk of CAD.<sup>24</sup> In this study CIMT values of 0.80 mm or more were considered abnormal. CIMT values were adjusted for age as age can influence IMT.<sup>24</sup> We did not include carotid plaque in this study.

### 2.3. Power calculation and statistical analysis

This was a pilot cross-sectional study on SAIs to determine the prevalence of CAD, diabetes and CAD risk factors in diabetic vs. non diabetic participants. Therefore a convenience sample of 213 SAIs was recruited without a specific sample size target. Results obtained from this study will help develop a powered prospective observational trial. The data management and statistical analysis was performed using Windows based SPSS software, version 9.1 of the SPSS system. A detailed statistical analysis was conducted to explore the socio demographic and clinical characteristics of the study participants. Baseline socio-demographic characteristics and laboratory measures were summarized by frequency distributions and percentages for qualitative measures and means and standard deviations for quantitative measures. Maximum likelihood estimates and asymptotic 95% confidence intervals were calculated for the prevalence of clinical parameters. Bivariate tests of association were performed using simple logistic regression. Multiple logistic regression models were used to assess the relative importance of variables found to be significantly associated with the outcome from the bivariate assessments. All statistical tests were two-sided and performed at the 0.05 level of significance.

## 3. Results

The total sample consisted of 213 participants who were categorized into two subgroups on the basis of the presence of diabetes: 35 diabetics and 178 non-diabetics. CIMT was performed on 46 participants who provided consent and had no known history of CAD; 19 diabetic and 27 non-diabetic participants. ETT was offered to 29 participants with diabetes and known CAD, however only 22 consented and completed ETT testing.

The mean age of participants was  $51 \pm 10.63$  years with an almost equal number of males and females (Table 1). As per

**Table 1**  
Clinical Characteristics of study Participants (n=213).

Participants' Characteristics	# of Participants	Percentages (%)
Age		
Sex	213	<sup>a</sup> 50.99 ± 10.63 <sup>b</sup>
Male	105	49.53
Female	108	50.47
Prevalence of CAD <sup>c</sup> and its determinants		
Known CAD (on history)	24	11.21
<sup>f</sup> CIMT	46	21.5
Type 2 diabetes	35	16.82
<sup>d</sup> Hypertension	64	29.91
Cholesterol (≥ 200 mg/dL)	78	36.45
Smoking	5	2.34
Physically active	140	65.42
Family History of CAD	88	41.12
Family history of T2D	105	49.07
<sup>e</sup> Age adjusted CAD risk factors	N = 152	
Two Risk factors	68	44.74
Three risk factors	16	10.52
Four risk factors	10	6.57

<sup>a</sup> Mean.<sup>b</sup> Standard Deviation.<sup>c</sup> Coronary Artery Disease.<sup>d</sup> Defined by Joint National Committee 6 (JNC-6) criteria.<sup>e</sup> Male ≥ 40, female ≥ 50.<sup>f</sup> Common Carotid Artery Intima Media Thickness.

information from the medical history questionnaire, the prevalence of CAD (based on known history of CAD) was 11.2%. The history of diabetes, hypertension and smoking was 16.8%, 21.5%, and 2.3% respectively. Approximately 65% participants reported having physically active lifestyles. Family history of CAD and diabetes was 41.12% and 49% respectively, and 45% had two or more CAD risk factors. Serum cholesterol (≥200 mg/dl) was present in 36.4%. More than 10% of subjects after age adjustment had at least three risk factors (Table 1). Of the total 35 diabetic participants, 6 already had CAD diagnosed previously and among non-diabetics 18/178 had known CAD on history. Among diabetics, 22/29 provided consent for ETT and 19/29 for CIMT. We also performed CIMT measurements on 27 non-diabetics without known history of CAD.

### 3.1. Prevalence of CAD risk factors in diabetics and non-diabetics

On comparison of CAD risk factors among diabetics and non-diabetics (Table 2), the prevalence of hypertension was 31.7% and 15.7% in diabetics vs non-diabetics ( $p=0.003$ ) respectively. Similarly, the prevalence of high total cholesterol (≥200 mg/dL) and family history of diabetes was 54.3% ( $p<0.0001$ ) and 77.1% ( $p<0.0001$ ) respectively in diabetics as compared to lower values in non-diabetics (Fig. 1 and Table 2).

We also compared other CAD risk factors between these two groups, however, these comparisons did not reach significance which could be attributable to a small sample size (Table 2).

**Table 2**  
Prevalence of CAD<sup>a</sup> risk factors among Diabetics and non Diabetics.

Risk factors	% Diabetics (n = 35)	% non-Diabetics (n = 178)	p-value
Hypertension	37.1	15.7	<b>0.003</b>
Total Cholesterol ≥ 200 mg/dL	54.3	24.7	<b>&lt;0.0001</b>
Smoking	5.7	1.7	0.190
Physical inactivity	40.0	33.7	0.475
Family history of diabetes	77.1	43.8	<b>&lt;0.0001</b>
Family history of CAD	48.6	39.9	0.340

Bold values denote highly significance.

<sup>a</sup> Coronary Artery Disease.

### 3.2. Positive ETT amongst diabetics

Of the 22/29 diabetic participants without known history of CAD who consented for ETT (Table 3), 45% had positive ETT and thus pointed towards the high risk of the presence of CAD ( $p<0.001$ , Fig. 2, Table 3). Similarly, 63.1% of diabetics and 51.8% of non-diabetics were positive for sub-clinical CAD using CIMT that further supports the fact that CAD incidence and prevalence is high in SAls irrespective of diabetes status. To see if there was any correlation of CIMT and CAD, we compared to assess if those who were positive for ETT also had high CIMT. We found that out of 10 subjects that were positive for ETT, 7 were also positive for CIMT ≥ 0.8 mm ( $p=0.18$ ) but was not statistically significant (Table 3). Similarly, we could not find statistical association between CAD and diabetes control ( $p=0.56$ ), duration of diabetes ( $p=0.14$ ) and with type of diabetes treatment i.e. with diet ( $p=0.71$ ) and drugs ( $p=0.83$ , Table 4).

## 4. Discussion

SAls have a high burden of traditional risk factors predisposes them at the increased risk of CVD events. Our findings demonstrate that the four traditional modifiable cardiac risk factors (dyslipidemia, hypertension, overweight/obesity and diabetes) originally identified from a white cohort in the Framingham Heart Study (FHS) and subsequently confirmed in major multiethnic epidemiological studies (e.g. Seven Countries Study, INTERHEART, INTERSTROKE) are important contributors to variations in CVD rates in migrant populations from very diverse ethnic backgrounds.<sup>6,25–27</sup> In this small pilot of 213 SAls residing in Georgia, we found higher prevalence of CAD risk factors in all participants, irrespective of the presence of diabetes. Moreover, diabetics had clustering of risk factors as shown by higher prevalence of hypertension, hypercholesterolemia and family history of diabetes, thus increase risk of MS. Subclinical atherosclerosis determined by CIMT was seen in >50% of the entire sample. A positive ETT suggestive of the presence of asymptomatic CAD (45%) was seen in those with diabetes requiring further research on large sample in a prospective study design.

With increasing prevalence of obesity, clustering of cardiac risk factors has increased, particularly in the western countries, also seen in SAls. The high CAD risk factor prevalence rates have consistently been described in countries across the globe: Singapore, Canada, the United Kingdom, South Africa, Trinidad, and the US.<sup>28–31</sup> Studies around the world have shown that from 11% to 20% of all SAls and other South Asian groups have diabetes.<sup>28–31</sup> A population-based study on SAls found the prevalence rate of diabetes to be 20% in the US.<sup>31</sup> Moreover, in the US, SAI men have more than double the incidence (7% vs. 3%) of myocardial infarction than the general US population.<sup>25</sup> The susceptibility of diabetes amongst SAls promotes an adverse CAD risk, even in patients treated for high blood pressure and CV risk as evident in this study. This is higher than the national rates reported

### Prevalence of CAD risk factors among Diabetics and Non diabetics

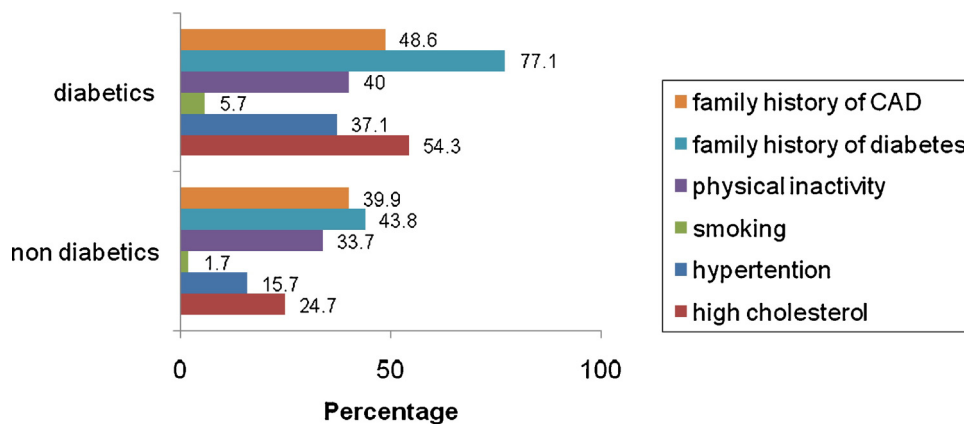


Fig. 1. Prevalence of CAD Risk Factors among Diabetics and Non diabetics.

**Table 3**  
Incidence of Positive ETT and CIMT in the study sample.

Tests	Diabetics (n=22)		Non- Diabetics (n=158)		P value
	n	%	n	%	
<sup>a</sup> CIMT positive ( $\geq 0.8$ )	12/19	63.1	14/27	51.8	0.18
<sup>b</sup> ETT positive	10/22	45%	-	-	<b>&lt;0.0001</b>

Bold values denote highly significance.

<sup>a</sup> Fisher exact Test.

<sup>a</sup> Common Carotid Artery Intima Media Thickness.

<sup>b</sup> Exercise Tolerance Test/Stress Test.

### ETT outcome in diabetics

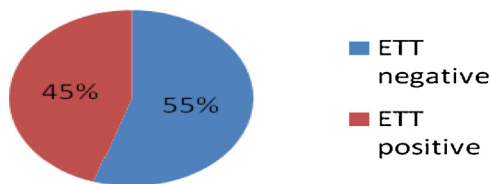


Fig. 2. Exercise Tolerance Test in Diabetics (n=22).

**Table 4**  
Association of Positive ETT with Clinical Parameters among diabetics (n=10) (Outcome-ETT as categorical variable).

Variable	Beta value	Wald Chi-Square	p-value <sup>*</sup>
IMT( $\geq 0.8$ vs. $< 0.8$ )	-0.9945	1.8079	0.18
Blood Glucose( $\geq 125$ vs. $< 125$ )	0.4359	0.2262	0.63
Diabetic treatment			
Diet	-0.3622	0.1402	0.71
Drug	-0.1884	0.0485	0.83

<sup>\*</sup> Multivariate Logistic regression.

by the Centers for Disease Control's (CDC's) National Diabetes Surveillance System.<sup>32</sup> In one of the studies, CAD mortality rate among diabetic SAIs was 3 times higher than that of people with diabetes who were born in England and Wales.<sup>33</sup> The mortality rate difference was greatest in the younger age group, from 30- to 64-year olds. From our analysis, we found that both the diabetic and non-diabetic groups showed high CAD risk factor prevalence with a slight higher figures in diabetics than non-diabetics (Table 2,

Fig. 1). Even non-diabetic participants had a high prevalence of positive CIMT suggesting that true incidence of CAD in this population may be much higher than thought. Of note, 65% of the participants reported to have physically active life style and may represent a health conscious proactive group to volunteer to participate in the study. The true prevalence of CAD in a larger representative population may be even higher.

In this current study, we confirmed the presence of diabetes in 16.82% of the study sample that is higher than any other immigrant as well as general US population<sup>8,34</sup> (Table 1), however this may still be an under estimation. Considering the fact that those who are negligent of their health are also less likely to participate in such research for health assessments; the actual number of people with risk factors could be much higher. Further studies are needed to determine the relative contribution of established and emerging CVD risk factors in SAIs and evaluate clinical outcomes following treatment of these risk factors. Moreover, more research is needed to address the patho-physiological mechanism by which diabetes confers an adverse CV risk in SAIs, and whether there is ethnic variation therein. Studies comparing CAD risk factors amongst South Asians living in India to SAIs in Britain highlighted that CAD risk factors are markedly higher amongst Indian Punjabi<sup>27</sup> and Gujarati<sup>28–30</sup> migrants than their counterparts in India. Greater atherogenic effects of diabetes in SAIs might also explain the higher mean levels of CIMT observed in this study, and these findings strongly argue for specific and intensive strategies for the management of diabetes levels and lipids in SAIs especially with high prevalence of family history of CAD and diabetes.

Differences in association of diabetes with MS have also been observed between Chinese, Europeans and South Asians,<sup>35</sup> suggesting that SAIs may be uniquely susceptible to the effects of metabolic determinants of CVDs. In a study, levels of CIMT were slightly lower in SAIs as compared to locals of European descent;<sup>31</sup> however, CIMT levels were not adjusted for risk factors that may lead to under-estimation of true prevalence.

With a goal to estimate presence of a positive stress test or positive CIMT in SAI diabetics, this small study has provides some evidence of early screening of CAD in diabetics as all diabetics are not same and pts with a positive stress test need more aggressive risk management. In a large cohort of white man, positive ETT was a strong predictor of cardiovascular death.<sup>36</sup> However, the US Preventive Services Task Force does not endorse ETT to detect CAD in asymptomatic individuals because of low diagnostic yield (2.7%) for severe coronary artery obstruction that would benefit from

revascularization.<sup>37</sup> Exercise thallium scintigraphy was found to be useful in the risk assessment of asymptomatic male siblings of patients with premature CAD.<sup>38</sup> However, since the prevalence of sub-clinical disease measured by CIMT is so high in diabetic SAIs in this study, there is little to be gained by testing for CAD but more to be gained by intensively treating known risk factors in this high risk as supported by several.<sup>39,40</sup> Additionally, there is enough evidence available suggesting that though the prevalence of conventional CAD risk factors and MS is high, But, these factors cannot account for all the excess CAD risk among SAIs, and search for non-traditional markers are needed to facilitate more accurate identification of high-risk SAIs and earlier CAD prevention or treatment.<sup>41,42</sup> One such non-conventional risk factor is the presence of dysfunctional HDL in SAIs and some of the recent studies have shown its association with CIMT and MS in SAIs.<sup>43</sup> Further research is warranted to better understand the CAD risk in SAIs and the utility of CAD screening tests in high-risk groups.

Despite interesting and supportive findings, this small pilot study has several limitations and faced many challenges that are worth mentioning. First, while interesting, this data must be considered as “hypothesis generating” due to its limitations in both sample size and selection bias. Nonetheless, the study design was cross-sectional, so caution should be exercised in any causal interpretation of diabetes and the CAD parameters. Moreover the results of this small pilot are just an eye-opener and may not be generalizable to the diverse SAIs. Larger prospective studies are required to support these findings. Second, recruiting eligible participants and having them complete the study was a challenge. Research team made every effort to arrange visits for blood, imaging and ETT testing, including several appointment reminders through phone, emails, personal contacts, however the issue of no-show was significant, and recruiting SAIs in research studies is of a great concern, despite SAIs being the fastest growing immigrant population in the US, a group with high burden of CVD and its risk factors, compared to other racial/ethnic groups. Moreover, SAIs are not significantly well represented in clinical studies. To improve SAI recruitment and retention in research studies, collaborative efforts and partnerships with SAIs communities and organizations including faith-based settings, and academic institution will be fruitful in engaging substantial portion of at-risk population in institutional research projects so that the basic information on the causes of CAD risk is made available for evidence-based disease management. Furthermore, education of SAI community through regular community sessions and health screening events, and endorsing healthy behaviors will be useful. Clearly, for these activities to take place on regular basis, resources, such as time, energy, support, committed staff and funding are critical elements, especially in the face of competing priorities.

Third is the presence of CAD in non-diabetics that may not reflect correct numbers as we did not perform ETT in non-diabetics and figures are based on history of CAD and available medical health records. On the same note, due to its lower sensitivity, ETT may not represent true incidence of CAD in diabetics and further tests are required to confirm CAD diagnosis. Forth is the small sample size due to limited funding, and therefore some of the findings did not reach statistical significance, and additional sub-analyses (adjustments and bonferroni corrections for example) were not performed. Fifth, the convenience sample of the study may cause selection bias. We recruited participants from local Hindu temples, and therefore participants may not be generalizable and representative of the South Asian Indian community. There are no census data on SAIs within the US that provide a true estimate of the SAI population, and the convenience sampling method is mostly used to design studies in SAIs. However, people attending these temples are from mixed ethnic backgrounds, and data were collected from participants who attended weekend

worship services, which in general are attended by SAI Hindus from different and diverse ethnic groups. Seventh, we did not assess diet pattern in this study, and plan to include a detailed nutrition component in our larger future study. And eighth, due to the limited budget and in order to have a homogeneous group, only Hindu SAIs were included, and SAIs of different religions were not included.

## 5. Conclusion

Unexpectedly high rates of CVDs in general and CADs in particular in SAIs have remained largely unexplained since they were first noted. The susceptibility to diabetes amongst SAIs promotes an adverse CAD risk, as evident by this small study. The key to combating the increasing incidence of CAD among SAIs is early CAD screening and an aggressive treatment of known risk factors, and diabetes through both an individual-based as well as a population-based approach aimed at comprehensive risk factor reduction. Further research, including larger longitudinal prospective studies, is required to validate the current small study findings with investigation of the temporal association.

## Conflict of interest

None.

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