

Are US Asian Indians Dying with Atherosclerosis More Likely to have Concurrent Diabetes Mellitus: Analysis of National Multiple Cause of Mortality Data (2012 - 2019)

Deepak Rajendran Nair

Armed Forces Medical College

Abhyuday Chauhan

Armed Forces Medical College

Dhananjay Vaidya (✉ dvaidya1@jhmi.edu)

Johns Hopkins University School of Medicine

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Abstract

Background:

Asian Indians (AI) are at high risk for both atherosclerotic diseases (ATH) and Type 2 Diabetes Mellitus (DM). We analyze the clustering of these two comorbidities as contributing causes of death in AI versus the rest of the US population (Non-AI).

Methods:

Using Mortality Multiple Cause Files (2012–2019) from the National Center for Health Statistics, we included deaths at age ≥ 45 years among US residents where AI versus Non-AI status could be ascertained ($n = 55,461$ AI; $n = 20,090,038$ Non-AI) and identified ATH (ICD10: I20-I25, I63, I70) and DM (ICD10: E10-E14) as contributing causes of death. We calculated the tetrachoric correlation (Rho) between these contributing causes and the difference in the fraction of deaths involving DM in those with versus without ATH.

Results:

Among AI decedents, 29.9% of deaths included ATH as a contributing cause, 16.4% included DM as a contributing cause with 8.3% deaths being included in the overlap (Rho = 0.36, SE = 0.007) whereas, among Non-AI, 22.4% of deaths included ATH as a contributing cause, 10.0% included DM as a contributing cause with 4.1% deaths being included in the overlap (Rho = 0.31, SE = 0.0005). Thus, DM and ATH as co-occurring causes correlated more strongly in AI versus Non-AI ($p < 0.001$). Further, this difference in clustering of DM with ATH was highest for younger AI women (age < 60 years) compared to comparable Non-AI women.

Conclusions:

The more frequent co-occurrence of DM and ATH as causes of death among AI compared to Non-AI suggest that the increased burden of these diseases among AI during life has vicious synergistic consequences in terms of mortality. Public health strategies targeted to AI should focus on prevention and clinical treatment of both conditions jointly, in all adults, and especially in women < 60 years.

1. Introduction

Individuals of Asian Indian national origin (AI) are the largest representative sample of South Asian ethnicity (India, Pakistan, Bangladesh, Nepal, Bhutan, and Sri Lanka) in the US [1]. AI have a higher burden of type 2 diabetes mellitus (DM) [2] in both native settings [3] and diaspora populations [4] and are more likely to succumb to DM complications in comparison to individuals of other national origins [5].

The unique cardiometabolic risk profile of this burgeoning ethnic population in the US has sparked much interest in the medical community lately [4–6].

Atherosclerotic – disease(s) related events (ATH), predominantly coronary heart disease and cerebrovascular disease, are the leading cause of mortality in AI [7]. Although ATH-related mortality has dipped in the US over the past few years, AI have not enjoyed a proportional decrease [2, 8]. AI are also more likely to succumb to ATH prematurely in comparison to other racial/ ethnic groups [9]. While it is not fully established which of the conventional risk factors lend such disparity for excess ATH burden in AI [10–12], South Asian ethnicity itself has recently been recognized as a “risk modifier” for ATH [13] and is second only to DM in ATH risk prediction [14].

DM confers an approximately two-fold increased risk of atherosclerotic disease (ATH) related morbidity and mortality relative to non-DM, more so among the younger ages [15]. Previous studies have shown that AI carry a much higher burden of DM and ATH than individuals of other national origins in the US (Non-AI) [2, 8, 16]. However, it is not known how strongly DM and ATH cluster as contributing causes of death in AI versus Non-AI. We use comprehensive US Vital Statistics Mortality Data to compare the co-occurrence of DM and ATH as causes of mortality in AI versus Non-AI.

2. Methods

2.1 Data

We used annual death records in the Mortality Multiple Cause Files compiled by the National Center for Health Statistics (NCHS) which are available for public use. These datasets are based on information reported on death certificates, which are completed by funeral directors, attending physicians, medical examiners, and coroners. Causes of death were processed by the International Classification of Diseases, Tenth Revision (ICD10). We pooled data from 2012 to 2019 to create our final dataset. The reason for limiting our analysis to these eight years is as follows: 2020 data were excluded due to the disproportionate number of deaths due to COVID-19. Although disaggregated data for the Asian-American population has been reported in US Death Certificates since 2003, consistency in reporting decedents of AI descent by the participating US states improved only by 2012 [17]. For sensitivity analyses, we also added data from 2003–2012 and repeated our analyses, but these are not reported in detail. As this dataset is publicly-available and de-identified, it was exempt from Institutional Review Board approval.

We used the following variables from the NCHS Mortality Multiple Cause Files for analysis: Resident Status, Sex, Age Recode 12, Race, Hispanic Origin Recode, Number of Record-Axis Conditions, and Record-Axis Conditions (numbers 1 to 20). Tape locations for these fields were identified with the help of the accompanying user guide.

2.2 Study population

We restricted our analysis to age 45 years and older as ATH and DM as contributing causes of death are less likely at younger ages. Death records of foreign residents or those with missing data on age were removed. Further, we recoded available data on Race and Hispanic – Origin to exclude death records with any missing data on race, ethnicity, or nationality. Next, we grouped AI decedents as we were primarily interested in understanding differences compared to decedents of Non-AI. The latter group comprised Non-Hispanic White, Non-Hispanic Black, American Indians, Hispanics, Japanese, Chinese, Filipino, Korean, Vietnamese, and Other Asian and Pacific Islanders. Thus, the final number of death records in our 2012 – 2019 dataset was 20,145,499, of which 55,461 (0.28%) were AI decedents.

2.3 Definition of ATH and DM as contributing causes of death

We used ICD10 codes to identify ATH-related deaths (either of the following: ischemic heart disease, ischemic stroke, atherosclerosis; ICD10 range: I20-I25, I63, I70, respectively) and DM-related deaths (ICD10 range: E10-E14) in the AI and Non-AI groups. Any mention anywhere in the multiple causes of death records (Record Axis Conditions) of ATH and DM were included.

2.4 Statistical Analysis

All statistical analyses were implemented using R software, version 4.1 (R Project for Statistical Computing), with the polycor package for calculation of tetrachoric correlation (Rho) and its standard error. We tabulated proportions of patterns of co-occurrence of DM and ATH by AI and Non-AI groups. To determine the association of DM and ATH beyond chance co-occurrence due to their prevalence, we calculated the Rho between DM and ATH separately in the AI and Non-AI groups. Rho describes the relation between two dichotomous variables and represents the correlation of underlying normally distributed latent variables which manifest as the dichotomous DM and ATH causes of death. We further examined whether this association differed by age decade and sex and calculated the difference in the fraction of deaths with DM in those with ATH versus those without ATH as a co-occurring cause of death. The difference of Rho between AI and Non-AI was calculated and the null hypotheses of no difference was tested as a difference between two normal distributions (*Additional File 1*).

3. Results

3.1. Baseline Characteristics

In this dataset of Mortality Multiple Cause Files from 2012–2019, there were 4,518,524 (22.43%) ATH-related deaths and 2,017,221 (10.01%) DM-related deaths (Table 1).

Table 1

title: Proportions of patterns of co-occurrence of DM and ATH by AI and Non-AI groups

Asian Indian national origin status	The cluster of contributing causes of death	n (%) of death records associated with each cluster
AI	ATH & DM	4,603 (8.29%)
	ATH & Non-DM	11,960 (21.56%)
	Non-ATH & DM	4,505 (8.12%)
	Non-ATH & Non-DM	34,393 (62.01%)
Total number of deaths in AI		55,461
Non - AI	ATH & DM	826,262 (4.11%)
	ATH & Non-DM	3,675,699 (18.29%)
	Non-ATH & DM	1,181,851 (5.88%)
	Non-ATH & Non-DM	14,406,226 (71.71%)
Total number of deaths in Non-AI		20,090,038

Table 1 legend: AI indicates Asian Indian; Non-AI, Non-Asian Indian; ATH, Atherosclerotic disease defined as either of the following: - ischemic heart disease (ICD10 I20 – I25), ischemic stroke (ICD10 I63), or atherosclerosis (ICD10 I70); DM, Diabetes Mellitus (ICD10 E10 – E14); Non-ATH: Non-Atherosclerotic disease; Non-DM: Non-Diabetes Mellitus.

3.2. Correlation between ATH and DM as contributing causes of death

The number of ATH deaths when DM also contributed was 830,865 (18.4%). Among AI decedents, 29.9% of deaths included ATH as a contributing cause, 16.4% included DM as a contributing cause with 8.3% deaths being included in the overlap ($Rho = 0.36$, $SE = 0.007$) whereas, among Non-AI decedents, 22.4% of deaths included ATH as a contributing cause, 10.0% included DM as a contributing cause with 4.1% deaths being included in the overlap ($Rho = 0.31$, $SE = 0.0005$) (difference between AI versus Non-AI $p < 0.001$) (Table 1, Fig. 1).

Figure 2 shows the excess fraction of deaths due to DM when ATH also contributed versus when ATH did not contribute in AI compared to Non-AI by age decade and sex.

In sensitivity analyses, adding data from the years 2003–2012 to our analyses did not alter our qualitative results.

4. Discussion

In this study, we have shown that DM and ATH cluster as contributing causes of death more strongly in AI as compared to Non-AI. We also found that the difference in the fraction of deaths with DM when ATH was also a contributing cause relative to when ATH did not contribute, was higher for both AI men and women across all age groups but more so among younger AI women (age \leq 60 years). DM is rarely the primary cause of mortality; it is more likely to serve as an antecedent to vascular dysfunction which can directly cause deaths [18]. In this context, our second finding, though only in mortality data, suggests the interpretation that during life: DM as a risk factor for subsequent ATH and dual DM/ATH contribution to mortality is more salient in AI as compared to a Non-AI for all age groups studied in both men and women. However, the excess contribution of DM in ATH-related deaths in AI was mostly higher among women than men of the same age group and this difference was most apparent at age \leq 60 years.

Our findings are in line with current literature that suggests the existence of excess dual burden of ATH and DM in AI vs Non-AI [2, 8, 16]. Further evidence regarding the subclinical disease during life comes from a recent study performed in the ongoing Mediators of Atherosclerosis in South Asians Living in America (MASALA) cohort which reported that the highest predicted probability for incident coronary artery calcium deposition, a marker of subclinical atherosclerosis, in any US race/ ethnic group with pre-existing diabetes but free from cardiovascular disease at the time initial evaluation, is observed in South Asians [19]. Our first finding takes this understanding a step further by quantitating the excess joint burden of ATH and DM as contributing causes of deaths in AI vs Non-AI. While studies that have relied on electronic health records and health-system based reports for data have reported a higher prevalence of DM and ATH in AI, these contrast with a recent observation by Satish *et al*/ who pooled data using self-reported questionnaires [20]. As several AI were potentially under-diagnosed owing to poorer access to healthcare and were, hence, unaware of their condition, Satish *et al*/ found a significantly lower prevalence of DM and ATH in AI [20]. This observation is notable in the context of our findings as it highlights the need to step up the detection of DM and ATH in AI. Further, it has been noted that the largest disparities due to poorer healthcare access to immigrants in the US are in the metabolic control of DM and ATH [21]. These compound the risk of progression of undetected DM and ATH in an already genetically predisposed group with lower levels of physical activity coupled with culturally derived dietary practices that fuel the risk of development of these two cardiometabolic co-morbidities [8].

Our second finding that the excess contribution of DM as a co-occurring cause of death in ATH-related versus ATH-unrelated deaths was most apparent in younger AI women (age \leq 60 years) is consistent with prior reports that the association of DM and mortality is generally higher in females and at younger ages [15, 22], and that it is most pronounced in women of AI national origin [2].

Our study has a major clinical implication which is in line with a recent observation made by Coles *et al* [23]. Until it is known whether the increased ATH mortality in AI is incited by DM itself or if it is the combined effect of the 'Asian Indian phenotype' ('South Asian phenotype') and DM, our results indicate that public health strategies should focus on joint prevention and treatment of both ATH and DM in AI, especially in young adulthood and middle age. As suggested by the Emerging Risk Factors Collaboration, in those patients first diagnosed with DM, it is essential to prevent subsequent ATH, and conversely, to

prevent DM in those who first develop ATH, because these diseases have multiplicative associations with mortality [22]. Further, our findings quantify the public health implication by quantitating at least a 4% excess co-occurrence of DM and ATH as contributing causes of death in AI versus Non-AI.

Our study has some limitations. Firstly, the data for our study is based on national death certificates, which may contain errors at the time of documentation. Secondly, we were unable to calculate the mortality rate using this dataset compiled by the NCHS as the national origin groups on US Death Certificates are not currently linked to census denominators. Therefore, we can only make indirect inferences about cause-specific rates observed in each subgroup using the cause-specific proportion of overall mortality in that subgroup as a proxy. As a next step to studying the mortality rate owing to concurrent ATH and DM as contributing causes in AI versus Non-AI, mortality data from US Death Certificates could be linked with US Census data. Nevertheless, our results add evidence to the growing field of study of cardiometabolic risk in the South Asian community.

Despite these limitations, our study has notable strengths. While previous studies have characterized mortality related to DM and ATH in Asian American populations using US death certificates [2, 8], to our knowledge, this is the first study to specifically examine DM and ATH clustering as contributing causes of death in AI versus Non-AI using the same mortality data. Our study findings also provide a more informed approach for physicians toward cardiometabolic disease prevention and health promotion in AI.

5. Conclusion

In conclusion, we showed that AI carry an excess burden of ATH and DM clustering as contributing causes of death compared to the rest of the US population. We also showed that the clustering of DM with ATH was higher for both AI men and women across all age groups but more prominent among younger AI women (age ≤ 60 years). Results from future studies are needed to calculate mortality rate rather than mortality fraction in AI to verify and expand on our conclusion. Public health strategies should, therefore, focus on joint prevention and treatment of both ATH and DM in AI, especially in young adulthood and middle age. In addition, renewed efforts are required to improve access to healthcare for immigrant communities in the US.

6. Non-standard Abbreviations And Acronyms

AI	Asian Indian
Non-AI	Non-Asian Indian
ATH	Atherosclerotic disease(s)
DM	Type 2 Diabetes Mellitus

Declarations

7.1. Ethics approval and consent to participate: Not applicable. Deidentified Public Use Data files were used.

7.2. Consent for publication: Not applicable.

7.3. Availability of data and materials: The datasets analyzed during the current study are available in the Mortality Data repository, National Vital Statistics System, NCHS, CDC [https://www.cdc.gov/nchs/nvss/mortality_public_use_data.htm] (Accessed 25th August 2021). The R Language code used for analysis is available in the Additional File 1: Data Download Instructions and R Markdown Analysis Code.

7.4. Competing interests: The authors declare that they have no competing interests.

7.5. Funding: None.

7.6. Authors' contributions: DV conceptualized and designed the study. DRN made the first manuscript draft. DV, DRN and AC were involved in exploratory analysis of data, interpretation of results and manuscript revision. All authors read and approved the final manuscript.

7.7. Acknowledgements: Not applicable.

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Figures

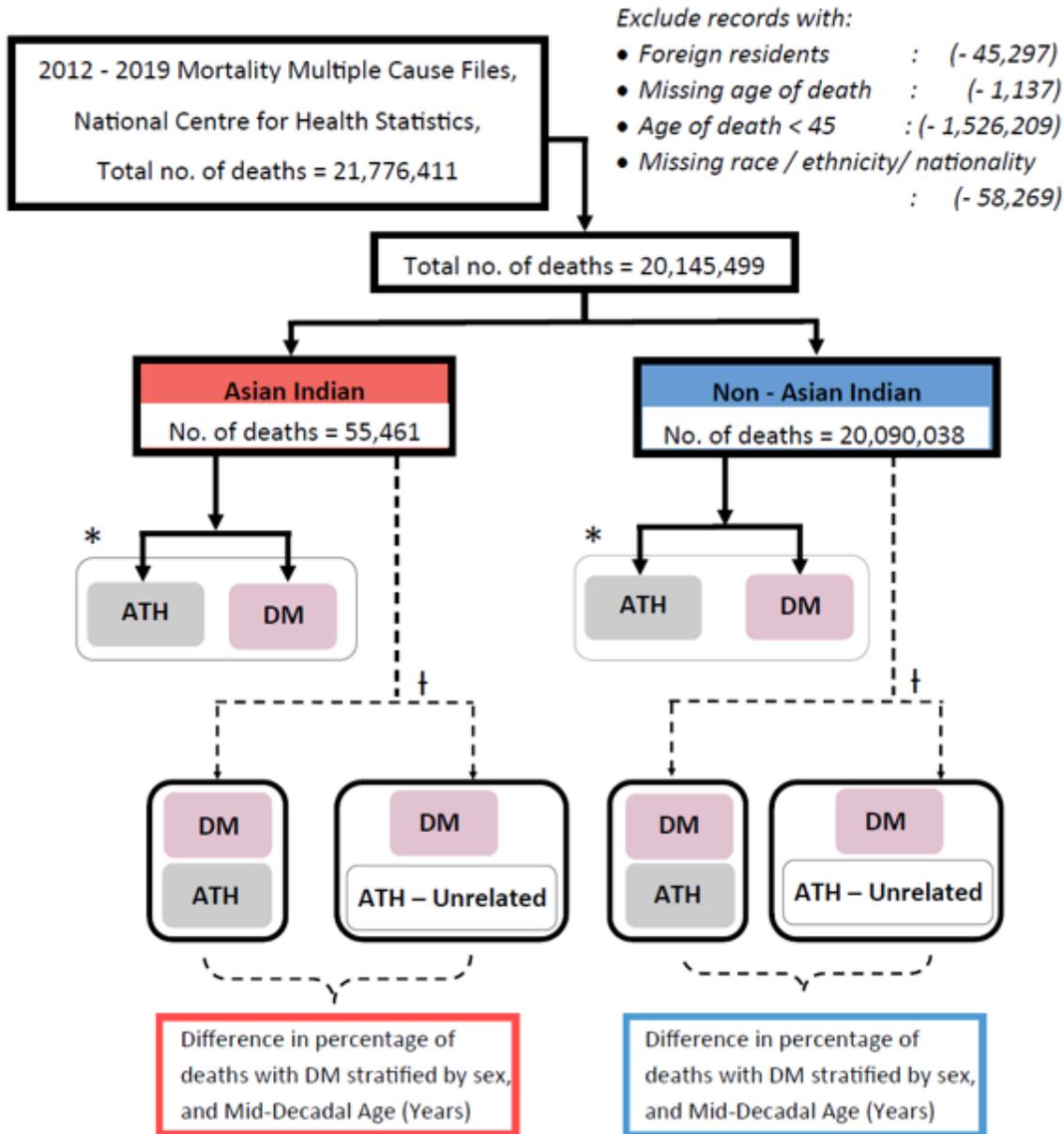


Figure 1

Flowchart showing study design and methodology. * Dichotomous tetrachoric correlation (Rho) between diabetes mellitus and atherosclerotic disease as co-occurring causes of death were identified in Asian Indian and Non-Asian Indian groups. † To examine whether this association (i.e., Rho) differed by age decade and sex, the difference in the fraction (% excess) of deaths with diabetes mellitus in those with atherosclerotic disease versus those without atherosclerotic disease, as a co-occurring cause of death, was calculated. Atherosclerotic disease (ATH): any of ischemic heart disease (ICD10 I20 – I25), ischemic stroke (ICD10 I63), or atherosclerosis (ICD10 I70), diabetes mellitus (DM) (ICD10 E10 – E14).

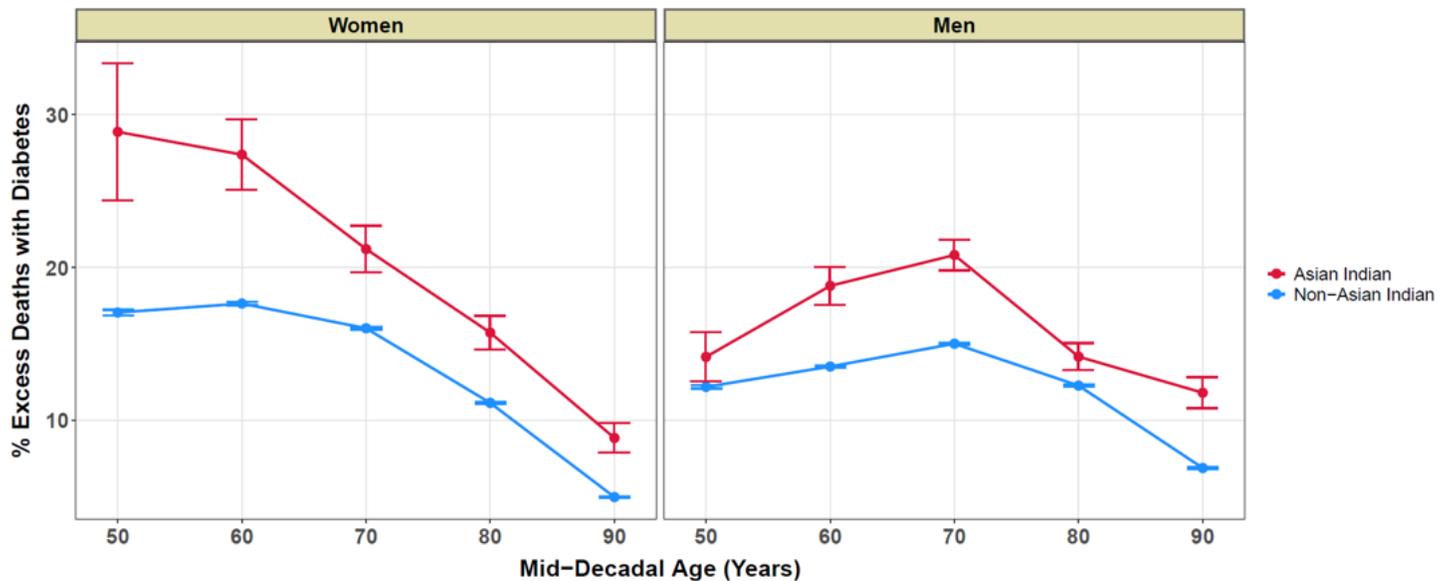


Figure 2

Excess diabetes mellitus in atherosclerotic disease-related versus atherosclerotic disease unrelated deaths – United States (2012-2019). The graph shows the difference in the percentage of deaths with diabetes stratified by sex, mid-decadal age (years), and Asian Indian national origin status.

Supplementary Files

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