Original Article

HYPERGLYCEMIA, YOUNG AGE, ALTERED SLEEP HABITS: THE THREE SHIFTING PARADIGMS OF CORONARY ARTERY DISEASE RISK STRATIFICATION

Irtiza Hasan[1], Tasnuva Rashid[1], Iffat Tasnim[2] and Mir Masudur Rhaman[3]

[1]19125 NE 65th Way, Redmond, Washington 98052, USA; [2]7920 Strawberry Street, Cheney 99004, USA; [3]Department of Community Medicine, Ibrahim Medical College, 122 Kazi Nazrul Islam Avenue, Dhaka, Bangladesh

Abstract

The study was undertaken to estimate the risk factors age, gender, race, obesity (BMI), glycemic status (prediabetes, diabetes), exercise and psychosocial factors (sleep, sadness) related to coronary artery disease (CAD). The data set for this study is the National Health Interview Survey (NHIS), which is a large scale, cross sectional, voluntary, household interview survey maintaining data on health status, health care access and progress towards achieving the national health objectives in the USA. A total of 26,965 (male/female =55.8/ 44.2%) subjects were included in the study. Of them, 79.9% were less than 65 years of age. Regarding obesity, overweight, obese and morbid obese were 34.8, 17.3 and 11.0%, respectively. Sadness of any degree was reported in 28%. Sleep duration was found < 5h/d in 8.7% and > 9h/d in 9.7%. Heart disease was reported in 4.9%. About 10% were reported to have diabetes and 4.1% prediabetes. 40% of the respondents' maintained exercise once per week and only 12.8% maintained 10 or more times per week. Logistic regression estimated that compared with the non-diabetics, the subjects with prediabetes (OR 3.27, 95% CI, 2.32-4.59) and diabetes (OR 6.44 95% CI, 5.21-7.96) had excess risk of CAD, more significant in the younger subjects (< 65y) than in the older (> 65y). The risk of CAD was found significant in both prediabetes (OR 2.47, 95% CI, 1.44-4.23) and diabetes (OR 3.03, 95% CI, 2.16-4.24) as compared with non-diabetic group who slept > 9h a day. The subjects with prediabetes or diabetes had excess risk for CAD compared with the non-diabetic subjects, which was more marked in the younger people. Again, compared with the non-diabetic people, the subjects with prediabetes or diabetes, having less sleep or excess sleep, had excess risk for CAD. Further study may confirm our findings.

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Introduction

National Institutes of Health (NIH) observed that coronary artery disease (CAD) was a leading cause of death in both male and female.[1,2] Various intermediate risk factors were the major contributors of the epidemic of heart diseases and an improvement and control of these risk factors would significantly reduce the disease burden.[3,4] One of the target risk factors would be increased blood glucose. In 2005-2008, about 11% of the US adults had diabetes as a heart disease risk factor.[5]

An increase in blood glucose may result in prediabetes and diabetes. According to the American Diabetic Association, prediabetes is a stage where the blood glucose level is higher than normal but not high enough to be diagnosed as diabetes and include impaired fasting glucose (IFG) and impaired glucose tolerance (IGT).[6] It has been estimated that the global diabetes prevalence among adults over 19 years would be 6.4%, affecting 285 million adults in 2010, and might increase to 7.7% and 439 million adults by 2030. Between 2010

Address for Correspondence:

Dr. Irtiza Hasan, 19125 NE 65th Way, Redmond, Washington 98052, USA. e-mail: mihasal@live.com

and 2030, there will be a 69% increase in numbers of adults with diabetes in developing countries and a 20% increase in developed countries.[7] The increase in the incidence of prediabetes, diabetes and heart disease is increasing in the same fashion and same distribution.[8] There are many known modifiable (eg. smoking, obesity, physical inactivity, hypertension, hyperglycemia, dyslipidemia) and non-modifiable (e.g. ageing, heredity / ethnicity) risk factors for developing atherosclerotic heart disease.[8,9] Younger aged people with diabetes were found to have enhanced atherogenesis than their non-diabetic younger counterparts.[10] Psychosocial stress, sleep disorders, mood disorders have also been found to have detrimental effect on coronary artery disease (CAD).[11-14] This study aimed to measure the risk factors for CAD like age, gender, race, obesity (BMI), glycemic status (prediabetes, diabetes), exercise and psychosocial factors (sleep, sadness). Additionally, habit of smoking and excess sugar intake was also investigated as risk factor.

Materials and Methods

The data set for this study is the National Health Interview Survey (NHIS). The NHIS is a large scale, cross sectional, voluntary, household interview survey done from 1957 so as to monitor and track the health status, health care access and progress towards achieving the national health objectives.[1] It is carried out by the National Center for Health Statistics (NCHS) with the collaboration of US Census Bureau on a statistically representative sample of the non institutionalized US civilians; but does not include those in long term care facilities, prisons, armed forces and US nationals living in foreign countries. The survey is done in computer assisted personal interviewing (CAPI) mode, has 90% response rate and contains data from 100,000 people from 40,000 households.

The NHIS data set of 2010 was used in our study.[1] The inclusion criteria included all the adults of age 18 or more who were in any of the four racial groups as Hispanics, non-Hispanic White, non-Hispanic Blacks and non-Hispanic Asians. The exclusion criteria included those who could not be classified in either of the four race groups and who were less than 18 years of age. We initially merged the dataset for adult person and family questions from core questionnaire. The merged data set had 27,157 observations from which the non-Hispanic and all other racial groups were excluded (n=192) resulting 26,965 observations.

The outcome or dependent variable for our study was coronary artery disease (CAD) which was determined by the answer to the question 'Ever been told that you had coronary heart/artery disease' in the sample adult dataset. The outcome variable was recoded into a binary yes/no variable. Our diseased group was those who answered yes to the question about heart disease. The main risk variable analyzed in this study was a composite variable "diabetes status" made up of combining the answers to two questions as 'ever been told that you have diabetes' and 'ever had prediabetes or other symptoms' in an attempt to capture both prediabetes and diabetes indicating the level of glycemia: "no diabetes" (normo-glycemia), prediabetes (mild hyperglycemia) and "diabetes" (moderate to severe hyperglycemia).

Taking CAD as an outcome variable we included age, race, gender, race, obesity (BMI), exercise, and habit of smoking and added sugar consumption as the other risk variables (covariates). For a crude assessment of psychosocial risks sadness and sleep status were included as other covariates. Education was included as a surrogate social class.

Statistical Analysis – Software (SAS) version 9.2 was used for all analyses. All the *P* values were two sided and a *P* value of less than 0.05 was considered to be statistically significant. A logistic regression model was used to assess the association between outcome variable (heart disease) and independent variable (diabetes status) before and after adjusting for the covariates. Covariates were included in the model based on bivariate analyses with outcome and exposure and a 10% change in beta rule. Some covariates which were not significant were still included based on previous literatures. We tested for effect modification by age and sleep status. We also tried to see whether the effect changes when we used weighted data developed based on design, ratio, non-response, probability of selection and post-stratification adjustments so as to represent the population from which the sample was drawn.

Results

A description of the baseline characteristic of the study population is provided in Table 1. The total sample size for the study was 26,965, of which 79.9% were less than 65 years of age with an average age of 47.8 years, with a slight female predominance (55.8% vs.

44.2% male) and 57.3% were non-Hispanic White. Regarding obesity, overweight, obese and morbid obese were 34.8%, 17.3% and 11.0%, respectively. Sadness of any degree was reported in 28%. Sleep duration was found lower than 5h/d in 8.7% and higher than 9h/d in 9.7%. Heart disease was reported in 4.9%. About 10% were reported to have diabetes and 4.1% prediabetes. 40% of the respondents used to maintain exercise for less than 1 time per week and only 12.8% maintained 10 or more times per week.

The measurement of association of risk variables with CAD are shown in Table 2. Compared with the younger subjects the elderly people had more risk (OR, 6.4; 95% CI, 5.7-7.2). Compared with the women the men had higher risk (OR, 1.7; 95% CI, 1.5-1.9). For other categorical variables, the risks of CAD were found significantly increasing with increasing obesity (BMI), hyperglycemia and sadness, and with decreasing exercise (Table 2). As regards race, compared with other groups, non-Hispanic whites had excess risk. Taking sleep duration of 6–8 h/d as normal and reference category, both lower (<5h/d) and higher (>9h/d) duration of sleep had more risk. An association was also found with smoking. Education level, marital

Table-1: *Study characteristics, National Health Interview Survey, 2010[1] (n=26,965)*

Characteristic	*n*	*%*	*Characteristic*	*n*	*%*
Age ($\bar{X}$=47.8 Y, SD=18.1)			**Coronary Artery Disease**		
Younger population, 18-<65 Y (ref.)	21535	79.9	Yes	1318	4.9
Elderly population, ≥65 Y	5430	20.1	No	25587	95.1
Gender			Excluded	60	
Female (ref.)	15051	55.8	**Sugar Consumption ($\bar{X}$=2.1 servings/day, SD=3.1)**		
Male	11914	44.2	Less than 1 serving/day (ref.)	9114	36.4
Education			1 to Less than 2 servings per day	7439	29.7
No High School (ref.)	4461	16.7	2 or more servings/day	8509	34.0
High School Grad	7106	26.6	Excluded	1903	
Some College	7972	30.0	**Diabetes Status**		
College Grad	4610	17.3	Non-diabetic (ref.)	23113	85.8
Graduate Degree	2527	9.5	Diabetic	2739	10.2
Excluded	289		Pre-diabetic	1097	4.1
Race			Excluded	16	
Hispanic	5158	19.0	**Smoking Status**		
Non-Hispanic White (ref.)	15570	57.3	Never Smoked (ref.)	16007	59.8
Non-Hispanic Black	4511	16.6	Former Smoker	5688	21.2
Non-Hispanic Asian	1726	6.4	Every/someday Smoker	5084	19.0
BMI ($\bar{X}$=27.7, SD=6.1)			Excluded	186	
16-18.5 BMI units (Underweight)	458	1.8	**Sadness Status**		
18.5-25 BMI units (Normal) (ref.)	9130	35.2	Never sad (ref.)	19301	72.0
25-30 BMI units (Overweight)	9028	34.8	Sad a little bit of the time	3832	14.3
30-35 BMI units (Obese)	4490	17.3	Sad All/Most/Some of the Time	3660	13.7
35-75 BMI Units (Morbid Obese)	2845	11.0	Excluded	172	
Excluded	1014		**Exercise Status ($\bar{X}$=4.0 times/week, SD=5.6)**		
Sleep Status ($\bar{X}$=7.2 hours/day, SD=1.4)			Less than 1 time per week (ref.)	10759	39.9
3-5 hours/day	2301	8.7	1 to Less than 5 times per week	7973	29.6
6-8 hours/day (ref.)	21717	81.7	5 to Less than 10 times per week	4791	17.8
9 or more hours/day	2568	9.7	10 or more times per week	3442	12.8
Excluded	379		**Marital Status**		
			Cohab (ref)	13083	48.52
			Not Cohab	13882	51.48

$\bar{X}$ = Mean, SD = Standard Deviation , Y = Years, BMI = Body Mass Index , Cohab = Married or living together

Table-2: *Study characteristics by Coronary Artery Disease (CAD), National Health Interview Survey, 2010*[1]

Characteristic	Total N	Coronary Artery Disease n (%)	Odds Ratio OR (95% CI)
Age			
Younger population, 18-<65 Y (ref.)	21504	546 (2.5)	1
Elderly population, ≥65 Y	5401	772 (14.3)	6.4 (5.7-7.2)
Gender			
Female (ref.)	15020	575 (3.83)	1
Male	11885	743 (6.25)	1.7 (1.5- 1.9)
Education			
No High School (ref.)	4449	305 (6.9)	1
High School Grad	7093	389 (5.5)	0.8 (0.7- 0.9)
Some College	7953	342 (4.3)	0.6 (0.5- 0.7)
College Grad	4607	167 (3.6)	0.5 (0.4- 0.6)
Graduate Degree	2521	95 (3.8)	0.5 (0.4-0.7)
Race			
Hispanic	5150	152 (3.0)	0.5 (0.4-0.6)
Non-Hispanic White (ref.)	15535	903 (5.8)	1
Non-Hispanic Black	4497	203 (4.5)	0.7 (0.6- 0.9)
Non-Hispanic Asian	1723	60 (3.5)	0.6 (0.4- 0.8)
BMI			
16-18.5 BMI units (Underweight)	458	21 (4.6)	1.1 (0.7-1.9)
18.5-25 BMI units (Normal) (ref.)	9120	319 (3.5)	1
25-30 BMI units (Overweight)	9011	466 (5.2)	1.5 (1.3- 1.8)
30-35 BMI units (Obese)	4480	266 (5.9)	1.8 (1.5- 2.1)
35-75 BMI Units (Morbid Obese)	2836	207 (7.3)	2.2 (1.8- 2.7)
Diabetes Status			
Diabetic	2718	451 (16.6)	6.1 (5.4- 7.0)
Pre-diabetic	1094	101 (9.2)	3.0 (2.4- 3.8)
Non-diabetic (ref.)	23088	765 (3.3)	1
Marital Status			
Cohab (ref.)	13067	592 (4.5)	1
No Cohab	13838	726 (5.3)	1.1 (1.0- 1.3)
Smoking Status			
Every/someday Smoker	5074	209 (4.1)	1.3 (1.1- 1.5)
Former Smoker	5668	548 (9.7)	3.0 (2.7- 3.5)
Never Smoked (ref.)	15984	546 (3.4)	1
Sadness Status			
Sad all/Most of the Time	3646	291 (8.0)	2.0 (1.7- 2.3)
Sad a little bit of the time	3825	207 (5.4)	1.3 (1.1- 1.5)
Never sad (ref.)	19270	797 (4.1)	1
Exercise Status			
Less than 1 time per week	10720	720 (6.7)	2.5 (2.0- 3.1)
1-5 times per week	7960	368 (4.6)	1.7 (1.3- 2.1)
5-10 times per week	4788	136 (2.8)	0.9 (0.8- 1.3)
More than 10 times per week (ref.)	3437	94 (2.7)	1
Sleep Status			
3-5 hours/day	2290	160 (7.0)	1.8 (1.5- 2.1)
6-8 hours/day (ref.)	21683	891 (4.1)	1
9 or more hours/day	2557	236 (9.2)	2.4 (2.0- 2.8)
Added Sugar Consumption			
Less than 1 servings/day (ref.)	9090	529 (5.8)	1
1 -2 servings/day	7429	418 (5.6)	1.0 (0.8- 1.1)
More than 2 servings/day	8495	259 (3.1)	0.5 (0.4- 0.6)

ref. = Reference, Y = Years, BMI = Body Mass Index, Cohab = married or living together

status and added sugar intake were found to have no significant effect on CAD.

The unadjusted logistic regression model for unweighted data (Table 3) showed a significant positive association of CAD with prediabetes (OR 2.97, 95% CI, 2.39- 3.69) and with diabetes (OR 5.81, 95% CI, 5.13- 6.57). When adjusted for the possible confounders, those with prediabetes were 2 times more likely and those with diabetes were 3.2 times more likely to have coronary artery disease compared to non diabetics. When weighted data was used, although the adjusted association remained significant but there was a slight increase in odds ratio and narrowing of the confidence interval possibly because the data was weighted to a larger population. We need to use special statistical techniques to correct the confidence interval and standard error which is beyond the scope of this study. As the association more or less remained similar, so we would be using unweighted data for further analysis.

The risk of CAD related to prediabetes and diabetes according to age-groups and sleep duration was shown in Table 4. The analyses included "no diabetes" as a reference category, and adjusted for gender, race, sadness status, BMI, smoking status, education level, exercise status, added sugar consumption and marital status. Compared with the subjects having no diabetes, the subjects with prediabetes (OR 3.27, 95% CI, 2.32-4.59) and diabetes (OR 6.44, 95% CI, 5.21-7.96) were proved to have excess risk of CAD, which were strongly significant in the relatively younger subjects (<65y); whereas, for the elderly subjects (>65y), the prediabetes group showed no significant risk though it was somehow significant for the diabetes group. The subjects having diabetes and used to sleep <5h a day had significant risk for CAD as compared with the non-diabetic subjects having same duration of sleep. The risk of CAD was found significant in both prediabetes (OR 2.47, 95% CI, 1.44-4.23) and diabetes (OR 3.03, 95% CI, 2.16-4.24) as compared with non-diabetic group having sleep >9h a day.

Table-3: *Crude and adjusted Odds Ratios for the Association between Diabetes and Prediabetes with Coronary Artery Disease*[1]

Models	Diabetes Status	Unweighted data			Weighted data		
		Odds Ratio	95% CI	P Value	Odds Ratio	95% CI	P Value
Model 1*	No Diabetes (reference)	1			1		
	Prediabetes	2.97	2.39, 3.69	<0.0001	3.45	3.44- 3.46	<0.0001
	Diabetes	5.81	5.13, 6.57	<0.0001	6.57	6.56- 6.58	<0.0001
Model 2†	No Diabetes (reference)	1			1		
	Prediabetes	2.00	1.57, 2.55	<0.0001	2.35	2.34, 2.36	<0.0001
	Diabetes	3.2	2.76, 3.72	<0.0001	3.47	3.46, 3.48	<0.0001

* - unadjusted model

† - adjusted for age, gender race, BMI, sleep duration, sadness, smoking, added sugar consumption, exercise, education level, marital status,

Discussion

The study investigated some known risk factors (age, sex, race, obesity, diabetes, exercise and smoking) related to coronary artery disease (CAD). Other possible risk factors like mood disorders (sadness), altered sleep habits (lack or excess) and social status (education) were also estimated to relate CAD. As Stern pointed out that diabetes and cardiovascular diseases are very much interrelated,[3] it is important to determine the quantity of association between diabetes and CAD. Thus, this study addressed important issues in quantifying some risk factors related to CAD.

The study clearly demonstrates that compared with the non-diabetics, the subjects with prediabetes and diabetes had significant risk for developing CAD though less with prediabetes in either sex. The risk was more marked in the age group below 65 years of age. Most of the studies observed that advancing age was the predictor of atherosclerotic heart disease. So, this study contradicted in this regard.[3,4] As this study compared younger diabetics with younger non-diabetics and elderly diabetics with elderly non-diabetics it could demonstrate the glycemic effect on the younger aged

Table-4: *Effect of Prediabetes and Diabetes on CAD by Age group and sleep abnormalities*[1]

Covariates	*OR**	*95% CI*	*Covariates*	*OR**	*95% CI*
Age 18 - 65 (yrs)			**Sleep < 5 h/d**		
Prediabetes v. No Diabetes	3.27	2.32, 4.59	Prediabetes v. No Diabetes	1.53	0.74, 3.16
Diabetes v. No Diabetes	6.44	5.21, 7.96	Diabetes v. No Diabetes	3.62	2.45, 5.34
Age > 65 (yrs)			**Sleep > 9 h/d**		
Prediabetes v. No Diabetes	1.31	0.94, 1.83	Prediabetes v. No Diabetes	2.47	1.44, 4.23
Diabetes v. No Diabetes	1.93	1.59, 2.33	Diabetes v. No Diabetes	3.03	2.16, 4.24

OR- Odds ratio; CI- Confidence interval; h/d- hours/day

* - adjusted for gender, race, sadness status, BMI, smoking status, education level, exercise status, added sugar consumption and marital status

people, which is consistent with other study.[10] There are plenty of publications which reported that hyperglycemia and especially metabolic syndrome has strong association with CAD.[8,10,14-18]

Altered sleep habits, either less (<5h/d) or excess (>9h/d), were found to have significant risk for developing CAD. This finding is important because either extreme of sleep abnormalities predict CAD. Other investigators also observed similar association of sleep abnormalities with hypertension, diabetes and CAD.[12-14] So, our findings also indicate the importance of early detection and intervention of sleep habit changes. Further studies may be undertaken to relate sleep with CAD.

Our study has several strengths including being nationally representative sample of non institutionalized civilians, large sample size, 90% response rate, large number of variables to compare various demographic and socioeconomic characteristics and controlling for various confounders, use of computer assisted data collection mode and trained staff all increased the accuracy and validity of the data collected. Also, using weighted data and correcting the standard errors using higher statistical techniques could have increased the strength of the study.

The cross sectional nature of the dataset limits the study to measure association only and not temporality and causality. The self reporting of diabetes status and heart disease might provide erroneous information and result in misclassification and recall bias. The sensitivity and specificity of the data could have been increased if we had medical and laboratory report which is one of the many drawbacks of the data set. We could not take into consideration income, occupational status, stress factor, use of diabetic medications, and duration of diabetes either due to unavailability of variable or large number of missing data.

Considering all the strengths and drawbacks, our study did estimate two important cardiovascular risks –sleep abnormalities and younger people with prediabetes and diabetes. However further prospective studies are needed to determine causality and special focus should be kept on the younger population in addition to the older population. The measurements of diabetes status and heart disease should be correlated with biological and laboratory measurements.

Conclusion

Hyperglycemia of any grade – mild, moderate or severe whether prediabetes or diabetes was proved to have significant risk for CAD. The diabetic subjects aged less than 65 years were more prone to develop CAD than their non-diabetic counterparts. Again, compared with the non-diabetic people, the subjects with prediabetes or diabetes, having less sleep or excess sleep, had excess risk for CAD. Further study may confirm our findings.

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