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Original Research Article

Risk Factors Associated with Myocardial Infarction in a North East Indian Study

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ABSTRACT

Background: Acute Myocardial infarction (AMI) results from multiple risk variable. There is paucity of data on the relative importance of various traditional risk factors for AMI in North East (NE) India, which represents a predominant agrarian, tribal population relatively untouched by the typical epidemiological transition of Indian subcontinent in terms of diet, lifestyle, and physical activity. Many individual studies in other parts of India have reported substantial regional variations in risk factors.
Methods: We conducted a hospital based case control study by including a total of 400 subjects (200 MI patients and 200 age and sex matched controls). We collected relevant socio-demographic and clinical data in the subjects admitted with AMI in a tertiary care hospital after confirming the diagnosis with standard criteria. The control subjects were chosen after history, administration of questionnaires and thorough objective search did not reveal coronary artery disease (CAD).
Results: The most important predictor of AMI was current smoking of cigarettes or use of tobacco products [odds ratio (OR) 5.26] followed by sedentary physical activity (OR 3.14), serum triglyceride level (OR 2.85), hypertension (OR 2.65), waist to hip ratio (OR 2.26) and diabetes (OR 1.99).
Conclusions: In North East India, consumption of tobacco and smoking is the strongest risk predictor of AMI. Attention to preventive measures and control of modifiable risk factors can contain the menace of AMI in this region.

Keywords: Myocardial infarction, risk factors, smoking, North East India.

INTRODUCTION

Worldwide, cardiovascular disease (CVD) is estimated to be the leading cause of death and loss of disability-adjusted life years. World Health Report 2002 predicted CVD to be the largest cause of death and disability in India by 2020. [(1)] Myocardial infarction (MI) constitutes a substantial chunk of the global burden of CVD, which is a complex multifactorial disorder caused by the interaction of environmental factors and hereditary predisposition. [(2,3)] Six primary risk factors have been identified with the development of atherosclerotic coronary artery disease and MI: dyslipidemia, diabetes mellitus,

hypertension, tobacco use, male gender, and family history of atherosclerotic arterial disease. The presence of any risk factor is associated with doubling the relative risk of developing atherosclerotic coronary artery disease. [4] In the INTERHEART study, nine easily measured and potentially modifiable risk factors account for an overwhelmingly large (over 90%) proportion of the risk of an initial acute myocardial infarction. [2] Much of this enormous burden is already evident in urban as well as semi-urban dwellings across India, where rapid acquisition of adverse lifestyles related to demographic transition have contributed to rising prevalence of smoking, physical inactivity, improper diet , obesity , hypertension and diabetes. [5] This has significant implications for the national productivity. There is also an increasing trend for reversal in the socio-economic gradient for CVD with the poor and disadvantaged having an equal, sometimes higher, burden of CVD and its risk factors. [6] Effective prevention needs knowledge of the importance of risk factors for cardiovascular disease in different geographic regions and among various ethnic groups. Some data suggest that risk factors for coronary heart disease vary between populations. [2,7-10]

The vast country of India , with different ethnic and geographic populations, shows a unique epidemiological transition pattern in terms of non-communicable diseases due to change from a traditionally agrarian and rural population to an industrialized and urbanized population with attendant changes in diet, lifestyle, and physical activity. [11] However, North East India, with a population of 45.78 million, constitutes a unique region with its predominant tribal population being relatively untouched by this transition. [12] So we get an opportunity to study a different model in this population to study MI. Moreover there is not much of data on the relative importance of risk factors in MI in this semi-urban and rural population.

MATERIALS AND METHODS

Study design and setting: This hospital-based age(± 5 years) and sex matched case-control study was carried out in the Intensive Cardiac Care Unit (ICCU) of Assam Medical College, Dibrugarh, India over 2 years. The study hospital is a tertiary care hospital catering to patients from the districts of upper Assam and neighbouring states of Arunachal Pradesh and Nagaland, which are basically rural and semi urban areas of NE.

Selection of participants: 200 consecutive patients with an acute myocardial infarction (AMI) were prospectively recruited as cases. Both ST-segment elevation (STEMI) and non–ST-segment elevation (NSTEMI) Myocardial infarction cases were taken as defined by the Joint European Society of Cardiology/American College of Cardiology criteria. [13] A subject was considered as a *case* of AMI if two of the three criteria (clinical symptom of typical chest pain, ECG changes, and raised troponin – I levels) were positive as per the above criteria. Patients were excluded if they had previous history of CAD, clinical evidence of liver disease, any significant chronic medical illness (e.g., untreated hyper or hypothyroidism, renal disease, or malignancy). *Controls* comprised of unrelated attendants of the *cases* from the same neighbourhood or work place of the patients or those attending the hospital for conditions unrelated to CVD or its risk factors (e.g. correction of refractive errors, general medical check-up, elective minor surgery, hemorrhoids, etc.). Those subjects were enrolled as *controls* only in whom the clinical history aided by Rose Questionnaires, [14] the objective search for evidence of CAD with ECG aided by Minnesota coding, [15] and

echocardiographic examination did not suggest the presence of CAD. Individuals with a 12-lead ECG showing pathological Q waves, ST segment deviation, T wave inversion, bundle branch or atrioventricular block, tachyarrhythmia other than isolated atrial ectopics, or chamber hypertrophy were not taken as controls.

Ethical Clearance: The study was approved by the *Institutional Ethical Committee*, and written informed consent was obtained from all subjects.

Socio-demographic and clinical variables: Structured questionnaires were administered and physical examinations were undertaken in the same manner in cases and controls. Information about demographic factors, socio economic status (education, income), lifestyle (smoking and tobacco chewing, physical activity, and dietary patterns), personal and family history of cardiovascular disease, drug history and risk factors (hypertension, diabetes mellitus) were obtained. Activity during leisure and working time was classified into sedentary, light to moderate and heavy if the subjects performed less than 150 minutes of light physical activity (PA) per week, performed more than 150 minutes of light to moderate PA per week, performed more than 150 minutes of moderate to heavy PA per week respectively. Activities were considered light if those involved activities of 3-4.5 MET (Metabolic equivalents) like walking on level, gardening etc. Activities were taken as of moderate intensity if those involved activities of 4.5 to 6 METs like climbing stairs, swimming, bicycling, and playing light outdoor game etc. Activities were considered as heavy if those involved activities > 6.5 METs like jogging, running, playing heavy outdoor games etc. If the occupation involved sitting for most of the hours for up to 6 hours in an entire day and lifting weight up to 5 kg occasionally during a day, it was considered as sedentary. If such a worker did not do additional leisure time activity he was considered as *sedentary*. Occupationally, physical activity was considered *light to moderate* if those required walking, pushing or pulling objects weighing less 20 to 30 kg, lifting objects weighing less than 20 kg and *heavy* if those involved greater than moderate intensity. We considered the above two categories of occupational physical activity as *light to moderate* and *heavy*, even without any additional leisure time physical activity. [(16,17)] Dietary patterns were classified into four patterns - vegetarian diet with regular intake of green leafy vegetables and fruits, vegetarian diet without regular intake of fruits and vegetables, non-vegetarian diet with regular intake of fruits and vegetables and non- vegetarian diet without regular intake of fruits and vegetables. Height, weight, waist and hip circumferences and body mass index (BMI) were determined by a standardized protocol. [(18)] Waist and hip circumferences were measured with a non-stretchable standard tape measure: waist measurements were obtained over the unclothed abdomen at the narrowest point between the costal margin and iliac crest, and hip circumferences over light clothing at the level of the widest diameter around the buttocks. After calculation of BMI and waist to hip ratio (WHR), subjects were classified using standard cut- offs. [(19,20)] Smokers were defined as those reporting daily smoking. Ex-smokers and occasional smokers were classified as non-smokers. Since patients were found to drink alcohol in various forms, we defined alcohol usage as consumption of at least three alcoholic drinks in a week.

Hypertension was defined, according to JNC-VII guidelines. [(21)] The known and self- reported diabetics and those with blood sugar levels consistent with a diagnosis of Diabetes Mellitus were considered as diabetic.

Biochemical and other relevant investigations: Fasting blood glucose and lipids were measured in all participants. ECG and Echocardiography was done in all the cases. Troponin-I was done in all cases except those where ECG and clinical features already clinched the diagnosis. Troponin I measurement was done at least six hours after onset of chest pain or index symptom. It was done by using commercially available kit (mini vidas bioMérieux France) and a Troponin I value above the 99th percentile with a CV (coefficient of variation) of ≤10% (> 0.11µg/L) was taken as the cut off as per Joint European/AHA/ACCF guidelines and other recommendations. [(22)] For estimation of lipid profile in *cases* fasting blood samples were collected within 24 h of onset of chest pain. Venous blood (5 ml) was collected and serum was separated. Total cholesterol (TC), triglycerides (TG), low density lipoprotein (LDL) and high-density lipoprotein (HDL), were estimated using a fully automated analyser (Siemens Dade Behring Dimension RxL Max). TC>200mg/dl, LDL>130mg/dl, HDL<40mg/dl and TG>150 mg/dl were used as risk variables. [(23)]

Statistical analysis: The sample size was calculated based on the approach described by Kelsey *et al.* and Fleiss *et al.* [(24,25)] Our sample size of 200 *cases* and 200 *controls* provided the study with 80% power to detect the risk level associated with the factor. The risk level of interest was expressed as the Odds Ratio. Taking the Odds ratio as 2 and a 20% exposure level in the controls, 173 individuals were needed in each group. Hence we decided to take a sample size of 200 cases and 200 controls. Clinical data were expressed as mean ± SD, and the differences between patients and controls were analysed by t tests for continuous variables and chi square test for categorical concomitants. $p<0.05$ was considered as significant. Odds Ratio (OR) with 95 % confidence interval and p values were calculated while analysing the association of different risk factors under study with the disease. Logistic regression analysis was carried out amongst the groups under consideration with appropriate software to find the unadjusted OR and adjusted OR of the risk factors in relation to the disease. All analysis was done in SPSS (V.19, Chicago) software.

RESULTS AND OBSERVATIONS

The present case-control study included 200 cases of AMI and 200 controls. Out of the cases, 147(73.5%) were STEMI and 53(26.5%) were NSTEMI. The clinical risk factors for CAD and Myocardial Infarction including the anthropometric and demographic characteristics were compared in the cases and the controls (Table 1). The subjects were in the 30-70 years age group. There was no statistically significant difference between the distribution of age and sex, as they were used as matching variables. In comparison it was found that obesity as measured by BMI and abdominal obesity as measured by WHR was significantly different in the *cases* compared to that of the *controls*. Similarly, there was higher presence of smokers (63.5% vs. 38%), diabetics (35% vs. 17%), subjects with hypertension (69% vs 41%) and subjects with positive family history in *cases* than *controls* (13.5% vs. 2.5%). In the comparison of the lipid profiles, total cholesterol, triglycerides, LDL-C were significantly higher for cases than for controls (p=0.001), whereas HDL-C levels were high among the controls (p=0.012). (Table 1)

Table1: Socio-demographic, clinical and biochemical characteristics of study subjects

Variables	Control (n = 200)	Case (n = 200)	p value
Age, years (Mean ± S.D.)	55.24 ± 12.23	57.01 ± 9.12	0.101
Sex Male [n (%)]	144 (72%)	157 (78.5%)	0.164
Body Mass Index, Kg/m^2 (Mean ± S.D.)	23.95 ± 3.70	25.15 ± 3.70	0.001 *
Waist hip ratio ≥0.9 (males) and ≥0.8 (females) Activity patterns : **	132(66%)	155(77.5%)	0.014 * 0.01 *
Subjects with sedentary activity *Subjects with light to moderate activity* *Subjects with heavy activity* Dietary pattern *** *Pattern 1* *Pattern 2* *Pattern 3* *Pattern 4*	60(30%) 114(57%) 26(13%) 42(21%) 109(54.5%) 28(14%) 21(10.5%)	80(40%) 108(54%) 12(6%) 35(17.5%) 109(54.5%) 22(11%) 34(17%)	 0.21
Smoker [n (%)]	76 (38%)	127 (63.5%)	0.001*
Diabetes [n (%)]	34 (17%)	70 (35%)	0.001*
Alcohol Users [n (%)]	63 (31.5%)	67 (33.5%)	0.749
Hypertensive [n (%)]	82 (41%)	138 (69%)	0.001*
Positive Family History of Ischemic Heart Disease [n (%)]	5 (2.5%)	27 (13.5%)	0.001*
HDL (mg/dl)	41.89 ±9.62	39.65±8.13	0.012*
TG (mg/dl)	140.63±59.09	168.09±52.40	0.001*
LDL (mg/dl)	99.30±20.32	116.01±25.98	0.001*
TC (mg/dl)	169.68±26.31	189.51±34.05	0.001*

*p value significant at <0.05
** Activity pattern – As described in the materials and methods section 2.03

***Pattern 1: vegetarian diet with regular intake of green leafy vegetables and fruits**,*
Pattern 2: vegetarian diet without regular intake of fruits and vegetables, pattern 3:non-vegetarian diet with regular intake of fruits and vegetables and pattern 4: non- vegetarian diet without regular intake of fruits and vegetables.
Abbreviations: HDL – High density lipoprotein; TG- Triglycerides; LDL-Low density lipoprotein; TC – Total cholesterol

TABLE 2: Risk factors for AMI: Univariate and multivariate regression analysis

Variables	Unadjusted ODDs Ratio (95% CI)	p value	Adjusted ODDs Ratio (95% CI)	p value
Hypertension	3.20 (2.12-4.83)	0.001	2.65(1.63-4.29)	0.001*
Diabetes	2.63 (1.64-4.21)	0.001	1.99(1.10-3.59)	0.023*
BMI (25-29.9)kg /m^2 vs. normal	2.75 (0.92-8.19)	0.07	-	
BMI ≥ 30kg/m ^{2} vs. normal	4.53 (1.21-16.96)	0.025*	1.53(0.29-8.06)	0.61
Smokers/tobacco users vs. non-smokers /non tobacco users	2.84 (1.89-4.26)	0.001*	5.26(3.12-4.87)	0.001*
WHR ≥0.9 in males and ≥0.8 in females vs. normal WHR	1.78(1.14-2.76)	0.011*	2.26(1.30-3.91)	0.004*
Dietary pattern **				
Dietary Pattern 2 vs. 1	1.20(0.71-2.02),	0.49	-	
Dietary Pattern 3 vs. 1	0.94(0.46-1.93)	0.87	-	
Dietary pattern 4 vs. 1	1.94(0.96-3.93)	0.06	-	
Activity pattern ***				
Light to moderate activity vs. heavy activity	1.16(0.60-2.25)	0.64	1.43(0.64-3.18)	0.378
Sedentary activity vs. Heavy activity	2.27(1.13-4.53)	0.02*	3.14(1.28-7.69)	0.012
HDL-C<40mg/dl vs. HDL-C≥40mg/dl	1.0(0.67-1.49)	1.000	0.67(0.40-1.14)	0.139
Triglyceride>150mg/dl vs. Triglyceride ≤150mg/dl	3.44(2.27-5.21)	0.001	2.85(1.66-4.91)	0.001*
LDL-C>130mg/dl vs. LDL-C ≤130mg/dl	2.78(1.52-5.08)	0.001	1.62(0.59-4.42)	0.345
Total cholesterol>200 mg/dl vs. Total cholesterol ≤200 mg/dl	3.58(2.27-5.20)	0.001	2.11(0.85-5.23)	0.107

*p value significant at <0.05
** Activity pattern – As described in the materials and methods section 2.03
*** Dietary pattern - Pattern 1: vegetarian diet with regular intake of green leafy vegetables and fruits, Pattern 2: vegetarian diet without regular intake of fruits and vegetables.
Pattern 3:non-vegetarian diet with regular intake of fruits and vegetables and Pattern 4: non- vegetarian diet without regular intake of fruits and vegetables.
Abbreviations: HDL – High density lipoprotein; TG- Triglycerides; LDL-Low density lipoprotein; TC – Total cholesterol

Variables showing statistically significant associations with CAD at p<0.05 after univariate logistic regression were simultaneously considered in a multivariate logistic regression model. Finally six risk factors were found to be strongly associated with the disease after multivariate logistic regression. Those were current smoking of cigarettes or use of tobacco products (OR 5.263, CI 3.12-8.87, p=0.001) followed by sedentary physical activity(OR 3.14, CI 1.28-7.69, p=0.012), serum triglyceride level (OR 2.85, CI 1.66 -4.91, p=0.001), hypertension (OR 2.65, CI 1.63-4.29,p=0.001), waist to hip ratio (OR 2.26, CI 1.30-3.91, p=0.004) and diabetes (OR 1.99, CI 1.10 -3.59, p=0.023). The strongest risk was seen with smoking and use of tobacco products. [Table 2]

DISCUSSION

In our study the association of hypertension with MI was strong (OR 2.65 CI 1.63- 4.29; p= 0.001). HTN is directly responsible for 24% of all coronary heart disease (CHD) deaths in India [26] and about 25 % MIs in Europe. [2] Most of the global and Indian studies have found hypertension to be a strong risk factor for MI with odds ratio ranging from 1.9 to 2.7. [2,9,27] We found diabetes to be an independent risk factor (OR 1.99, 95 % CI 1.10-3.59). Pais *et al.* found diabetes mellitus to be strongly associated with MI (OR 2.64; p = 0.004). [9] However a recent central Indian study could not find association of diabetes with MI (OR 1.04; 95%CI 0.89-1.22). [27] We found strong association (OR 2.25; 95 % CI 1.30-3.91) of waist hip ratio of ≥0.9 (males) and ≥0.8 (females) with MI. INTERHEART study showed that the odds ratio of MI was significantly higher for each successive quintile of WHR. [2] In a recently published Indian study a similar association of waist hip ratio ≥ 0.9 in males and ≥0.8 in females was seen with MI (OR 1.78; 95 % 1.06-2.99). [27] In another study, abnormal waist-hip ratio (OR 3.0; 95% CI 1.7, 5.4) was found to be independently associated with MI. [28] we found smoking to be an independent risk factor (OR 5.26; 95 % CI 3.12-8.87). Almost half (48%) of the acute myocardial infarctions have been attributed to tobacco in an Indian study. [29] An analysis of data from the INTERHEART study of risk factors for acute myocardial infarction (AMI) [2] has documented that not only cigarette smoking (OR 2.95, 95% CI 2.77-3.14) was strongly associated with MI , the risk of having an AMI associated with the use of chewing tobacco was also high (OR 2.23, 95% CI 1.41-3.52). [30] Most of the Indian studies have found that cigarette smoking and chewing of tobacco were strongly associated with MI. [27] Pais *et al.* also found that the most important predictor of AMI was current smoking [OR 3.6, p < 0.001)] of cigarettes or *beedis (*a form of tobacco). [9] We found association of serum triglycerides (OR 2.85; 95 % CI 1.66-4.91) with MI, while we could not found any association with HDL-C and LDL-C and total cholesterol. The relationship between cholesterol and ischemic heart disease has been studied by the Prospective Studies Collaboration where in total cholesterol was positively associated with ischemic heart disease mortality in both middle and old age. [31] The INTERHEART case-control study estimated that around 40% of MIs in Europe are associated with dyslipidemia. [2] In a previous Indian study, abnormal triglycerides (OR 1.7; 95% CI 0.9-3.1) showed a trend towards being associated with MI, though it was not significant. [28] Previously two other studies from India showed that total cholesterol and triglycerides were higher in individuals with IHD than in those without IHD. [32, 33] Pais *et al.* did not find any association of serum lipids with AMI. [9]

As an important finding, we noted strong association of sedentary physical activity with AMI. In our study we have considered both leisure- time and occupational physical activity together as leisure-time physical activity is less in our study subjects hailing from predominantly rural and semi-urban catchment areas. INTERHEART study [(2)] shows that mild-to-moderate PA at work and any level of PA during leisure time reduce the risk of an MI. Most of the previous studies have shown benefit from leisure time physical activity rather than occupational physical activity. [(34,35)] The lack of a protective benefit of occupational activity in developed countries may be due to the fact that the physical demands in most occupations have decreased resulting in a lack of heterogeneity. At the same time, these countries have been reporting increasing levels of leisure-time PA participation. Conversely, occupational demands in developing countries are much greater and the opportunity to participate in leisure-time PA is much less.

If we analyse mechanistic reasons of the associations found in our study, most of the reasons are well established. Studies have shown that smoking enhances platelet aggregation and adhesiveness, causes endothelial dysfunction, oxidation of LDL, and increases levels of C-reactive protein (CRP), soluble intercellular adhesion molecule -1 (ICAM-1), fibrinogen and homocysteine. [(36-38)] Changes in endothelial function and morphology are cardinal features of hypertension. [(39)] Data is also available supporting the notion that oxygen free radicals contribute to consequences of hypertension and thus act as a mechanism of MI. [(40)] we found significant association of WHR and hypertriglyceridemia with MI. WHR is a measure of abdominal obesity and a surrogate measure for visceral fat deposition. [(41)] Visceral fat leads to an increase in adipokines including leptin which may promote atherosclerosis by enhancing endothelial cell activation and migration, smooth muscle cell proliferation and vascular calcification. [(42)] Visceral fat produces more plasminogen activator inhibitor-1, an inhibitor of fibrinolysis compared with subcutaneous fat, [(43)] and is associated with other CVD risk factors such as metabolic syndrome (increased waist circumference, diabetes, hypertension, hypercholesterolemia and atherosclerosis), inflammation and oxidative stress. Defective fibrinolytic capacity appears to be common among men with myocardial infarction. Low tissue plasminogen activator (tPA) activity after high plasma levels of plasminogen activator inhibitror-1 (PAI-1) activity and, to some extent, by impaired release of tPA from the vessel wall has been a frequent finding in hypertriglyceridimic MI patients. [(44)] Hypertriglyceridemia represents pro-coagulant state involving derangements both of blood coagulation and fibrinolysis. Hypertriglyceridemic subjects have delayed clearance of postprandial lipoproteins, which may be taken up by arterial wall macrophages. [(45)]

The strengths and limitations of our study: We have included adequate number of subjects after calculating the sample size as per the approach given by Kelsey *et al.* and Fleiss *et al.* [(24,25)] Further, inclusion of hospital-based *controls* enhanced motivation of the *controls*. The hospital-based design ensured that *cases* and *controls* were similarly sensitized towards recalling exposure. Methodologically, the recruitment used in the current research ensured that *cases* and *controls* were drawn from the same catchment area and met a fundamental criterion that cases and controls were selected from the same source population. We avoided misclassification of disease status, a common source of error, [(46)] by identifying the *cases* according to

established criteria, i.e., the Joint European Society of Cardiology/American College of Cardiology criteria. [13] The study area being a medical college with qualified cardiologists, the diagnosis of MI in the *cases* was fairly accurate. Further to reduce the effect of confounding, we chose age and sex-matched *controls* and then on top of that performed multivariate analyses to adjust for other potential confounders. As to the *controls* we ensured absence of ischemic heart disease by careful subjective search through clinical history aided by Rose Questionnaires [14] and thorough objective search for evidence of CAD with ECG aided by Minnesota coding. [15] We enrolled only those subjects as *controls* in whom such objective and subjective analysis did not reveal any evidence of CAD.

Our study has some limitations. We included questions on known risk factors of the disease by administering a structured questionnaire to all study subjects. However there are still some amount of chance that some of the subjects might have selectively and differentially reported on their exposure status for various risk factors. Our case-control study employed 1-1 matching for *cases* and *controls*. A higher number of *controls* per *case* could have provided precise estimates. We included diagnosed cases of AMI in a hospital set-up. Although the hospital is a government hospital with easy physical and financial access, geographical factors may have precluded some rural patients from the remotest areas to seek care at this institution. Additionally, some cases of AMI might have resulted in deaths before the arrival of the patient to a healthcare facility. So our *cases* might not exactly represent the true picture of the population at large. Moreover the *control* subjects might not be representative of the general population as we emphasised on matching the controls with same study base of the cases and included only those subjects who had an access to the Govt. medical college for outpatient or in patient care. We had to exclude few of the *cases* as they died soon after reaching the hospital and the fasting blood samples could not be taken. We could not collect data on some of the emerging risk factors like hs CRP, Lp (a), fibrinogen, homocysteine. However as INTERHEART study [2] has shown that most of the CAD cases are due to conventional risk factors, and the current evidence for emerging risk factors are inconclusive, it might not have made much difference. Finally as our study is done in a predominantly semi- urban and rural population of North East India, our findings may not be extrapolated to other urban populations of India. One more area of limitation was that the center being a non-intervention set up, coronary angiography was not done in any of the subjects. However it did not make much influence as coronary angiography is not essential for diagnosis of AMI as per all the international guidelines and criteria. Secondly, in case of the *controls* history is quite sensitive and specific to include or exclude ischemic heart disease. [47] Further, coronary angiography is not indicated or deemed essential to exclude CAD in asymptomatic low risk subjects like the control subjects of our study. Hence coronary angiography was not done in the cases and the controls.

Novelty and implication of the study: Relative contribution of risk factors in our study shows some difference from other national and international studies as we found stronger association of smoking, physical inactivity, triglyceride level > 150 mg/dl and hypertension with MI compared to other lipid parameters and diabetes. [2, 9, 27,28] The hierarchy of the risk factors is different here. That puts faulty food habit and life style in this population as possible culprits. This has got a strategic importance as the habits like excessive salt consumption

leading to high prevalence of hypertension [(48)] and high carbohydrate diet with increased serum triglyceride can be changed with appropriate public health strategy and education. NE India has a very high prevalence of use of tobacco [(49)] and our study found smoking to be the most important cause of MI. So, the disease can be prevented to a great extent with avoidance of smoking. The population in NE is generally physically active and here in this study, 70 percent of the control subjects and 60 percent of the cases were active (Table 1). This is in sharp contrast to the finding of the Phase 1 of the ICMR-INDIAB study [(50)] conducted in other regions of India (Tamilnadu, Maharashtra, Jharkhand and Chandigarh), where physical inactivity was noted in more than 60 percent of the population in some of the regions. Now it is curious to find significant association of sedentary physical activity with MI in our study in spite of less prevalence of this habit compared to other states. The implication of this finding lies in the fact that the subjects, of this region, who are otherwise protected by a reasonable activity level, in spite of the poor life style and dietary habits, become vulnerable to MI, the moment they change to a sedentary life style from a physically active life.

CONCLUSION

Out of the traditional cardiovascular risk factors smoking showed significant strongest association with Acute Myocardial Infarction in a north-east Indian population. Hypertension, sedentary physical activity, waist to hip ratio, serum triglyceride and diabetes also showed independent association. Since most of these are modifiable risk factors, adequate preventive and treatment strategies can make great impact in north east India in terms of preventing this dreaded disease.

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REFERENCES

1. World Health Organization. The World Health Report 2002. Geneva, Switzerland: WHO.
2. Yusuf S, Hawken S, Ounpuu S, et al. Effect of potentially modifiable risk factors associated with myocardial infarction in 52 countries (the INTERHEART study): case-control study. Lancet 2004; 364: 937-52
3. Fischer M, Mayer B, Baessler A, et al. Familial aggregation of left main coronary artery disease and future risk of coronary events in asymptomatic siblings of affected patients. Eur Heart J. 2007; 28: 2432-37.
4. Cotran RS, Kumar V, Robbins SL (eds): Robbins Pathologic Basis of Disease. 5th ed. Philadelphia: WB Saunders, 1994.
5. Reddy KS. Rising burden of cardiovascular disease in Indians. In: Sethi KK, editor. Coronary artery disease in Indians. A global perspective. Mumbai; Cardiological Society of India: 1998:63-72
6. Gupta R, Gupta VP, Sarna M, et al. Serial epidemiological surveys in an urban Indian population demonstrates increasing coronary risk factors among the lower socioeconomic status. J Assoc Physicians India. 2003; 51:470-7
7. Yusuf S, Reddy S, Ounpuu S, et al. Global burden of cardiovascular diseases: part I: general considerations, the epidemiologic transition, risk factors, and impact of urbanization. Circulation 2001; 104: 2746-53.
8. Gupta R, Gupta VP. Meta-analysis of coronary heart disease prevalence in India. Indian Heart J 1996; 48: 241-5.

9. Pais P, Pogue J, Gerstein H, et al. Risk factors for acute myocardial infarction in Indians: a case-control study. Lancet. 1996; 348:358-63.
10. Yusuf S, Reddy S, Ôunpuu S, et al. Global burden of cardiovascular diseases, part II: variations in cardiovascular disease by specific ethnic groups and geographic regions and prevention strategies. Circulation 2001; 104: 2855-64.
11. Popkin BM, Horton S, Kim S, et al. Trends in diet, nutritional status, and diet-related non-communicable diseases in China and India: the economic costs of the nutrition transition. Nutr Rev. 2001;59:379-90
12. Saha S, Gupta K, Kumar S. Cardiovascular health among healthy population of Northeast region of India: a cross-sectional study comparing urban-tribal difference. J Indian Med Assoc. 2013; 111(12):810-4.
13. Alpert JS, Thygesen K, Antman E, Bassand JP. Myocardial infarction redefined--a consensus document of The Joint European Society of Cardiology/American College of Cardiology Committee for the redefinition of myocardial infarction. J Am Coll Cardiol. 2000; 36 (3):959-969. Erratum in: J Am Coll Cardiol 2001; 37 (3):973.
14. Rose GABH, Gillum RF, Prineas RJ. Cardiovascular Survey Methods. 2. Geneva: World Health Organization; 1982.
15. Prineas RJ. Crow RS. Blackburn HW. The Minnesota Code Manual of Electrocardiographic Findings: Standards and Procedures for Measurement and Classification. Boston, MA: John Wright-PSG; 1982.
16. U.S. Department of Health and Human Services Public Health Service, Centers for Disease Control and Prevention, National Center for Chronic Disease Prevention and Health Promotion, Division of Nutrition and Physical Activity. Promoting physical activity: a guide for community action. Champaign, IL: Human Kinetics, 1999.
17. Centers for Disease Control and Prevention. Steps to Wellness: A Guide to Implementing the 2008 Physical Activity Guidelines for Americans in the Workplace. Atlanta, GA: US Department of Health and Human Services; 2012 http://www.cdc.gov/nccdphp/dnpao/hwi/downloads/Steps2Wellness_BROCH14_508_Tag508.pdf.
18. Lohman TG, Roche A F, Martoreli R, editors. Anthropometric standardization references manual. Chicago: Human Kinetics, 1988.
19. World Health Organization. Obesity: Preventing and managing the global epidemic. Report of a WHO Expert Consultation. World Health Organ Tech Rep Ser. 2000;894:9.
20. Gupta R, Jain P, Kaul U, Reddy KS, Kumar A. Prevention of coronary heart disease in India: Cardiological Society of India Guidelines. South Asian J Prev Cariol. 2001;5: 45-61.
21. Chobanian A V et al. The seventh report of Joint National Committee on prevention, detection, evaluation and treatment of high blood pressure: The J N C 7 report. JAMA 2003;289 (19): 2560-72
22. Thygesen K, Alpert J S, White H D on behalf of the Joint ESC/ACCF/AHA/ WHF Task force for the redefinition of Myocardial Infarction. Universal Definition of Myocardial Infarction. Circulation. 2007; 116(22): 2634-53.
23. Expert Panel on Detection, Evaluation and Treatment of High Blood Cholesterol in Adults (Adult Treatment Panel III). Executive Summary of the Third Report of the National Cholesterol Education Program (NCEP). JAMA 2001; 285:2486-97.
24. Kelsey JL, Whittemore AS, Evans AS, Thompson WD. Methods in Observational Epidemiology. 2nd edition. New York: Oxford University Press, 1996.

25. Fleiss JL. Statistical Methods for Rates and Proportions. 2nd edition. New York. John Wiley & Sons, 1981
26. Gupta R. Trends in hypertension epidemiology in India. J Hum Hypertens. 2004; 18:73-78.
27. Zodpey S P, Shrikhande S N, Negandhi H N, et al. Risk Factors for Acute Myocardial Infarction in Central India: A Case-Control Study. Indian Journal of Community Medicine : Official Publication of Indian Association of Preventive & Social Medicine. 1915; 40(1), 19-26.
28. Patil SS, Joshi R, Gupta G, et al. Risk factors for acute myocardial infarction in a rural population of central India: a hospital-based case-control study. Natl Med J India. 2004; 17(4):189-94.
29. Shah B, Kumar N, Menon G et al. Assessment of burden of non-communicable diseases. Indian Council of Medical Research, New Delhi, 2006. Available from: http://www.whoindia.org/EN/Section20/Section306_1025.htm (Accessed July 2015)
30. Teo KK, Ounpuu S, Hawken S, et al. Tobacco use and risk of myocardial infarction in 52 countries in the INTERHEART study: a case control study. Lancet 2006; 368(9536):647-58.
31. Prospective Studies Collaboration, Lewington S, Whitlock G, Clarke R, et al. Blood cholesterol and vascular mortality by age, sex, and blood pressure: a meta-analysis of individual data from 61 prospective studies with 55,000 vascular deaths. Lancet. 2007; 370 (9602):1829-39. Review. Erratum in: Lancet. 2008 26; 372 (9635):292.
32. Chadha SL, Gopinath N, Ramachandran K. Epidemiological study of coronary heart disease in Gujeratis in Delhi (India). Indian J Med Res.1992; 96: 115-21.
33. Dhawan J, Bray CL, Bennet DH, et al. Lipid abnormalities in British Asian and white patients and in Asian patients in India with coronary artery disease. Br Heart J. 1991; 66: 81.
34. Erlichman J, Kerbey AL, James WP. Physical activity and its impact on health outcomes. Paper 1: The impact of physical activity on cardiovascular disease and all-cause mortality: an historical perspective. Obes Rev. 2002; 3: 257-71.
35. Hu G, Tuomilehto J, Silventoinen K, et al. The effects of physical activity and body mass index on cardiovascular, cancer and all-cause mortality among 47 212 middle-aged Finnish men and women. Int J Obes (Lond) 2005; 29:894-902.
36. Nowak J Anderson K, Bemthin G, et al. Effect of Nicotine infusion in humans on platelet aggregation and urinary excretion of a major thromboxane metabolite. Acta Physiol Scand 1996; 157: 101-107
37. Lekakis J, Papamichael C , Vemmos C et al. Effects of Acute Cigarette Smoking on endothelium-dependent arterial dilatation in normal subjects. Am J Cardiol. 1998; 81(4): 1225-28.
38. Ridker P M, Libby P, Buring J E. Risk Markers and the primary prevention of cardiovascular disease In: Libby P, Bonow RO, Mann DL, Zipes DP, Braunwald E. Braunwald's Heart Disease: A Textbook of Cardiovascular Medicine 10th Edition. Philadelphia. WB Saunders, 2015; 891-930.
39. Todd ME. Hypertensive structural changes in blood vessels: do endothelial cells hold the key? Can J Physiol Pharmacol. 1992; 70: 536-51.
40. Zhang X-M, Ellis EF. Superoxide dismutase decreases mortality, blood pressure, and cerebral blood flow responses induced by acute hypertension in rats. Stroke. 1991;22:489-494
41. Kvist H, Chowdury B, Grangard V, et al. Total and visceral adipose tissue volumes derived from measurements with computed tomography in adult men and women: predictive equations. Am J Clin Nutr. 1988; 48: 1351-61.

42. Yamagishi SI, Edelstein D, Du XL, et al. Leptin induces mitochondrial superoxide production and monocyte chemoattractant protein-1 expression in aortic endothelial cells by increasing fatty acid oxidation via protein kinase A. J Biol Chem. 2001;276:25096-25100
43. Alessi MC, Peiretti F, Morange P, et al. Production of plasminogen activator inhibitor 1 by human adipose tissue: possible link between visceral fat accumulation and vascular disease. Diabetes. 1997; 46: 860-867.
44. Hamsten A, Wiman B, de Faire U, et al .Increased plasma levels of a rapid inhibitor of tissue plasminogen activator in young survivors of myocardial infarction. N Engl J Med 1985; 313: 1557-63.
45. Hamsten A. Myocardial infarction at a young age: mechanisms and management. *Vasc Med Rev 1991; 2: 45-60*
46. Jajoo UN, Vitthalrao KP, et al. False positive ECG and coronary heart disease. J Assoc Physicians India 1993; 41: 205–07.
47. Pryor DB, Shaw L, McCants CB, et al. Value of the History and Physical in Identifying Patients at Increased Risk for Coronary Artery Disease. Ann Intern Med. 1993;118: 81-90.
48. Hazarika NC, Narain K, Biswas D, et al. Hypertension in the native rural population of Assam. Natl Med J India. 2004; 17(6):300-4.
49. Subramanian SV, Nandy S, Kelly M, et al. Patterns and distribution of tobacco consumption in India: cross sectional multilevel evidence from the 1998-9 national family health survey. BMJ 2004; 328:801-6
50. Anjana RM, Pradeepa R, Das AK, et al. Physical activity and inactivity patterns in Indian-results from the ICMR-INDIAB study (Phase-1) [ICMR-INDIAB-5]. The International Journal of Behavioral Nutrition and Physical Activity. 2014; 11:26.

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