Original Article

# Risk Factors for Acute Myocardial Infarction in Central India: A Case-Control Study

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## ABSTRACT

**Background:** Atherosclerosis is a multi-factorial disease involving the interplay of genetic and environmental factors. Studies highlighting the public health importance of risk factors like chronic infections causing acute myocardial infarction (AMI) in the Indian context are scarce. This study was undertaken to study the association of socio-demographic and life-style factors with acute myocardial infarction in central India. **Materials and Methods:** The cases and controls were group-matched for age, gender, and socio-economic status. A blinded research associate administered the study questionnaire. We performed an unconditional multiple logistic regression analysis. **Results:** The case-control study included 265 cases of AMI and 265 controls. The results of final model of logistic regression analysis for risk factors of AMI included 11 risk factors at $\alpha = 0.05$. They were waist hip ratio, body mass index, stress at home in last 1 year, hypertension, family history of CHD, past history of gingival sepsis, tobacco smoking, raised total serum cholesterol, *Chlamydia pneumoniae*, *Helicobacter pylori* and raised C-reactive protein. **Conclusion:** The findings confirm the role of conventional risk factors for cardiac disease and highlight need for research into the association between chronic infections with AMI.

**Keywords:** Atherosclerosis, acute myocardial infarction, risk factors

## Introduction

The global estimates for the burden of cardiovascular diseases (CVD) for 1998 released by the World Health Organization estimated that CVDs were responsible for 30.9% of all deaths and 10.3% of the total burden of disease in terms of disability-adjusted life years (DALYs).[1] The World Health Report also estimated that 78% of the non-communicable disease (NCD) burden and 85% of the cardiovascular burden was borne by the low and middle-income countries including India.[1] A cross-sectional population-based study in a developed country has suggested that participants from most deprived socio-economic areas had unhealthier ultrasound markers of atherosclerosis,[2] suggesting that socio-economically deprived groups share a disproportionately higher share of the disease. A similar socio-economic disadvantage could be expected to exist in India and other developing countries.

Atherosclerosis is a multi-factorial disease involving the interplay of genetic and environmental factors.[3] The causation of atherosclerosis in humans is an active area of research that has culminated in the discovery of several new risk factors over the last two decades. These include biochemical factors like lipid peroxidation[4] and socio-economic deprivation.[2] Infectious agents like *Helicobacter pylori*, *Chlamydia pneumoniae* and Cytomegalovirus have also been implicated in the causation of coronary heart disease.[5] The importance of the classical risk factors for heart disease was examined in the INTERHEART

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study,[6] which is a large, international, standardized, case-control study from 262 centers in 52 countries from Asia, Europe, the Middle East, Africa, Australia, North America, and South America. All these classical and novel risk factors for cardiovascular disease would be expected to have varying relative contributions to the disease outcome in different populations. Although, thrombus formation is the proximate cause of acute myocardial infarction (AMI), atherosclerosis, the chief underlying cause, is a chronic progressive disease.[7] Studies highlighting the public health importance of risk factors like chronic infections causing acute myocardial infarction (AMI) in the Indian context are scarce. We have explored the role of chronic infections in the causation of AMI using a hospital-based case-control design in a central Indian city. The study results examining the association between various socio-demographic and life-style factors and AMI could help prioritize primary prevention measures for AMI in the community.

## Materials and Methods

### Study design and setting

This group-matched hospital-based case-control study was carried out in the Intensive Cardiac Care Unit (ICCU) of Government Medical College, Nagpur, India over 2 years. The study hospital is a tertiary care hospital catering to patients from Central India.

### Selection of Participants

*Eligibility criteria for cases*

All consecutive patients admitted to the ICCU, or equivalent cardiology ward of the study hospital that screened positive for incident AMI were eligible for inclusion as cases. Patients with only angina were excluded. Cases with cardiogenic shock, any significant chronic medical illness (e.g., untreated hyper or hypothyroidism, renal disease, or malignancy) or pregnancy were excluded. Consenting eligible cases were identified and enrolled within 24 hours of onset of symptoms.

### Case ascertainment

A patient was considered an incident case of AMI if two of the three criteria (clinical symptoms, ECG changes, and raised enzyme levels) were positive on admission.

### Selection of controls

The cases and controls were group-matched for age (± 2 years), gender and socio-economic status and they were selected from patients admitted in hospital for other conditions not related to CHD or its risk factors. We have employed group matching which consists of selecting controls in such a manner that the proportion of controls with a certain characteristic is identical to the proportion of cases with the same characteristic.[8] This ensured that the controls were from the same study base as the cases (location, age, factors influencing access to health care at the study institution). Patients attending the hospital for correction of refractive errors, routine Pap smear, elective minor surgery, hemorrhoids, or hernia surgery, minor dermatological disorders were preferred as controls. Controls with no prior history of heart disease or exertional chest pain were included.

### Rationale for selection of cases and controls

Inclusion of hospital-based controls enhanced motivation of the controls and improved the study feasibility. A potential disadvantage was that this control population might not be representative of the general population. Methodologically, the recruitment used in the current research ensured that cases and controls were drawn from the same area, and met a fundamental criterion that cases and controls were selected from the same source population.

### Variables

Table 1 shows the classification criteria used for individual study factors.

**Table 1: Classification criteria for individual study factors**

| Factor | Classification | Code |
|---|---|---|
| Socioeconomic status[9] | Lower (SES Score <5) | 5 |
| | Upper Lower (SES Score 5-10) | 4 |
| | Lower Middle (SES Score 11-15) | 3 |
| | Upper Middle (SES Score 16-25) | 2 |
| | Upper (SES Score 26-29) | 1 |
| Waist-hip Ratio[10] | <0.9 (Men), <0.8 (Women) | 0 |
| | ≥0.9 (Men), ≥0.8 (Women) | 1 |
| Body Mass Index[11] | 18.5-24. 9 kg/m$^2$ | 0 |
| | ≥25 kg/m$^2$ | 1 |
| Stress in past 1 year | No | 0 |
| | Mild stress | 1 |
| | Moderate stress | 2 |
| | Heavy stress | 3 |
| Stress at work place in last 1 year | Never experienced stress | 0 |
| | Some period of stress | 1 |
| | Several period of stress | 2 |
| | Permanent stress | 3 |
| Stress at home in last 1 year | Never experienced stress | 0 |
| | Some period of stress | 1 |
| | Several period of stress | 2 |
| | Permanent stress | 3 |
| Financial stress | Little/none | 0 |
| | Moderate | 1 |
| | High/severe | 2 |
| Hypertension[12] | No | 0 |
| | Yes | 1 |
| Diabetes Mellitus[13] | No | 0 |
| | Yes | 1 |
| Family History of CHD | No | 0 |
| | Yes | 1 |
| Past history of gingival sepsis (painful teeth, painful gums, lost teeth) | No | 0 |
| | Yes | 1 |

*(Continued)*

**Table 1: (Continued)**

| Factor | Classification | Code |
|---|---|---|
| Past history of oral contraceptive use | No | 0 |
| | Yes | 1 |
| Past history of female hormone replacement | No | 0 |
| | Yes | 1 |
| Tobacco Smoking (smoking index)[14] | Non-smoker | 0 |
| | Smoking Index <100 | 1 |
| | Smoking Index 100-300 | 2 |
| | Smoking Index >300 | 3 |
| Passive smoking (spouse regularly smokes in subject's presence) | No | 0 |
| | Yes | 1 |
| Past history of tobacco smoking (ex-smoker)[14] | No | 0 |
| | Yes | 1 |
| Snoring | Never | 0 |
| | A few times | 1 |
| | Sometimes | 2 |
| | Often | 3 |
| | Always or almost always | 4 |
| | Do not know | 99 |
| Activity at work | Heavy physical work | 0 |
| | Mainly walking, climbing stairs, walking uphill, lifting heavy objects | 1 |
| | Predominantly walking on one level, no heavy lifting | 2 |
| | Mainly sedentary | 3 |
| | Subject does not work at all | 4 |
| Activity during leisure time | Strenuous exercise | 0 |
| | Moderate exercise | 1 |
| | Mild exercise | 2 |
| | Mainly sedentary | 3 |
| Playing sports during leisure time | No | 0 |
| | Yes | 1 |
| Alcohol intake[15] | No | 0 |
| | Yes | 1 |
| Alcohol intake frequency | No intake | 0 |
| | Rarely (<1 per month) | 1 |
| | <1 time per week | 2 |
| | 1-2 times per week | 3 |
| | 3-4 times per week | 4 |
| | 5-6 times per week | 5 |
| | Everyday | 6 |
| Food | Vegetarian | 0 |
| | Non-vegetarian | 1 |
| Total Serum Cholesterol[16] | Within normal range | 0 |
| | Raised | 1 |
| *C. pneumoniae* (IgG antibodies) | Negative (EIU ≤45) | 0 |
| | Positive (EIU >45) | 1 |
| *H. pylori* (IgG Antibodies) | Absent (≤20 U/ml) | 0 |
| | Present (>20 U/ml) | 1 |
| C-reactive protein | ≤0.5 mg/dl | 0 |
| | >0.5 mg/dl | 1 |

Genix HP IgG EIA test kit (sensitivity 99%, specificity 97%) was used for the quantitative determination of IgG antibodies to *H. pylori* in human serum. Ani Labsystems' Chlamydia pneumoniae IgG test (sensitivity 96%, specificity 99%) was used for the detection of IgG antibodies specific to *C. pneumoniae* infection. The measurement of IgG antibodies was carried out in Department of Microbiology and levels of C-reactive proteins were measured in Department of Biochemistry, Government Medical College, Nagpur.

The study participants subjectively reported stress in past one year as mild, moderate or severe. Tobacco smoking was quantified by calculating the smoking index for smokers. Smoking index for an individual was equal to multiplication of the average number of cigarettes/bidis smoked per day and duration (in years) of tobacco smoking. Further, smokers were classified in three categories of exposure level based on the smoking index. The research study had ethics approval from the institutional ethics committee at Government Medical College, Nagpur.

The study questionnaire was designed to acquire information on participants' risk factors for AMI. The validation was performed in a total of 60 subjects who were not part of the original study; 38 subjects with proven AMI and 22 subjects admitted in other hospital wards. All the 60 subjects were required to complete the questionnaire to assess acceptability and feasibility. The reproducibility of the questionnaire was assessed in 25 subjects who were required to complete a second questionnaire after a 2-week interval. Consistency of the questionnaire was assessed on the basis of an interview and access to hospital records by using kappa-statistics. A single trained research associate who was blinded to the study hypothesis administered a pre-validated study questionnaire designed to acquire information on participants' risk factors for AMI. It was administered preferably within 24 hours of admission and before the patient was discharged from the hospital. A similar process was followed for administering the questionnaire to cases and controls. The time required for completing the interview of each case and control was also recorded. As the research associate was blinded to the study hypothesis, it was assumed that cases and controls were probed equally about the presence of risk factors of AMI. However, it was not confirmed if the research associate was blinded to the study hypothesis at the end of data collection.

The sample size was calculated based on the information available in the literature. The sample size of 265 cases and equal number of controls was required for attaining 80% power. The sample size was calculated using Schesselmen's approach and it was checked by using the

two sample proportion formula. The risk level of interest was expressed as the Odds Ratio. A one-sided μ was assumed as the lack of risk is not of interest. The sample size provided the study with 80% power to detect the risk level associated with the factor. It was assumed that the prevalence of the risk factors in the general population, represented by the controls will be not less than 10% and not more than 25%. It was assumed that a level less than 10% will not be of interest for mass intervention. If the level is higher than 25% the power will not be affected. Taking the Odds ratio as 2 and a 10% exposure level in the controls, 250 individuals are needed in each group.

Descriptive analysis was carried out to present the summary statistics. Bi-variate analysis was carried out as per the method described by Greenberg and Ibrahim.[17] Crude odds ratio (OR) and their 95% confidence intervals (CI) and Pearson's Chi-square was calculated for all the risk factors. Unconditional multiple logistic regression (MLR) analysis was performed using STATA 7.0 (2001) as this is a group matched case-control study. Risk factors which were significant at α (level of significance) = 0.2 in the full model were included in the reduced full model. Final model included those risk factors which were significant at α (level of significance) = 0.05 in the reduced full model. Final model used α (level of significance) = 0.05 for judging the significance of risk factors. Attributable risk percent (ARP) and population attributable risk percent (PARP) and their 95% CI were estimated for significant risk factors.

## Results

The present case-control study included 265 cases of AMI and 265 controls. Table 2 shows the distribution of study subjects by matching factors. Majority of subjects were in the 41-70 years age group. The study included 70% males and 30% females. Sixty-seven percent subjects belonged to upper lower class of socioeconomic status. There was no statistically significant difference between the distribution of age, sex, and socioeconomic status of cases and controls, as they were used as matching variables.

**Table 2: Distribution of study subjects by matching factors**

| Factor | Cases (*n* = 265) *N* % | Controls (*n* = 265) *N* % |
|---|---|---|
| Age (years) | | |
| ≤30 | 05 (01.89) | 04 (01.51) |
| 31-40 | 21 (07.92) | 22 (08.30) |
| 41-50 | 61 (23.02) | 57 (21.51) |
| 51-60 | 78 (29.43) | 89 (33.58) |
| 61-70 | 82 (30.94) | 76 (28.68) |
| >70 | 18 (06.79) | 17 (06.42) |
| Sex | | |
| Male | 186 (70.19) | 186 (70.19) |
| Female | 079 (29.81) | 079 (29.81) |
| Socio-economic Status | | |
| Upper | 02 (00.75) | 02 (00.75) |
| Upper Middle | 44 (16.60) | 44 (16.60) |
| Lower Middle | 40 (15.09) | 40 (15.09) |
| Upper Lower | 178 (67.17) | 178 (67.17) |
| Lower | 01 (00.38) | 01 (00.38) |

Table 3 shows the results of bi-variate analysis according to risk factors for AMI along with the unadjusted and adjusted odds ratios with their 95% CI. The study extracted data on 26 risk factors for AMI. Of these 26 risk factors, 14 were found to have significantly higher proportion in cases as compared to controls (as reflected from their Chi-square values). The significant factors included waist hip ratio (≥0.9 (Men), ≥0.8 (Women)), body mass index (≥25 kg/m$^2$), stress in past 1 year, stress at home in last 1 year, financial stress, hypertension family history of CHD, past history of gingival sepsis (painful teeth, painful gums, lost teeth), tobacco smoking, snoring, raised total serum cholesterol, *Chlamydia pneumoniae* (IgG antibodies positivity), *Helicobacter pylori* (IgG Antibodies positivity) and raised C-reactive protein.

The results of unconditional multiple logistic regression analysis are also depicted in Table 3. The full model of logistic regression included 23 risk factors. Past history of oral contraceptive use, alcohol intake frequency and activity during leisure time are dropped from the model due to co-linearity. Of the 23 risk factors included in the model, 13 risk factors were significant at α (level of significance) = 0.2. These risk factors are waist-hip ratio (≥0.9 (Men), ≥0.8 (Women)), body mass index (≥25 kg/m$^2$), stress at work in last 1 year, stress at home in last 1 year, financial stress, hypertension, family history of CHD, past history of gingival sepsis (painful teeth, painful gums, lost teeth), tobacco smoking, raised total serum cholesterol, *C. pneumoniae* (IgG antibodies positivity), *H. pylori* (IgG Antibodies positivity) and raised C-reactive protein.

Table 4 depicts the reduced full model of logistic regression analysis for risk factors of AMI. This model included waist-hip ratio (≥0.9 (Men), ≥0.8 (Women)), body mass index (≥25 kg/m$^2$), stress at work in last 1 year, stress at home in last 1 year, financial stress, hypertension, family history of CHD, past history of gingival sepsis (painful teeth, painful gums, lost teeth), tobacco smoking, raised total serum cholesterol, *C. pneumoniae* (IgG antibodies positivity), *H. pylori* (IgG Antibodies positivity) and raised C-reactive protein. These risk factors were significant in the full model at α = 0.2. Of the 13 risk factors included in this model, except stress of work at work place in last one year and financial stress, all other 11 risk factors were significantly associated with AMI at α = 0.05. This is reflected from the estimates of odds ratios and their 95% CI.

**Table 3: Risk factors for AMI - bivariate analysis, unadjusted and adjusted OR with 95% CI**

| Risk Factors | Code/ Characteristic[##] | Controls | Cases | Unadjusted OR Odds ratio (95% CI) | Full model-adjusted OR (95% CI) |
|---|---|---|---|---|---|
| Behaviors | | | | | |
| Stress in past 1 year | 0 | 185 | 143 | 1.00 | 1.06 |
| | 1 | 61 | 84 | 1.78 (1.18-2.70) | (0.70-1.61) |
| | 2+3 | 19 | 38 | 2.59 (1.38-4.95) | |
| Stress at work place in last 1 year | 0 | 229 | 216 | 1.00 | 1.53 |
| | 1 | 34 | 41 | 1.28 (0.76-2.16) | (0.84-2.79) |
| | 2 | 2 | 8 | 4.24 (0.83-41.31) | |
| Stress at home in last 1 year | 0 | 180 | 130 | 1.00 | 1.50 |
| | 1 | 67 | 97 | 2.00 (1.34-3.00) | (0.94-2.39) |
| | 2+3 | 18 | 38 | 2.92 (1.54-5.68) | |
| Financial stress | 0 | 98 | 113 | 1.00 | 0.74 |
| | 1 | 163 | 139 | 0.74 (0.51-1.07) | (0.48-1.16) |
| | 2 | 4 | 13 | 2.82 (0.83-12.20) | |
| Tobacco smoking (smoking index) [‡] | 0 | 115 | 84 | 1.00 | 1.30 |
| | 1 | 12 | 19 | 2.17 (0.94-5.17) | (1.04-1.61) |
| | 2 | 11 | 12 | 1.49 (0.57-2.93) | |
| | 3 | 48 | 71 | 2.02 (1.24-3.30) | |
| Passive smoking (Spouse regularly smokes in subject's presence) | 0 | 258 | 251 | 1.00 | 1.92 |
| | 1 | 7 | 14 | 2.06 (0.76-6.11) | (0.56-6.59) |
| Past history of tobacco smoking (ex-smoker) [‡] | 0 | 137 | 134 | 1.00 | 0.79 |
| | 1 | 49 | 52 | 1.08 (0.67-1.76) | (0.40-1.55) |
| Snoring[†] | 0 | 168 | 117 | 1.00 | 0.99 |
| | 1 | 27 | 30 | 1.59 (0.87-2.94) | (0.97-1.01) |
| | 2 | 29 | 28 | 1.39 (0.75-2.55) | |
| | 3 | 24 | 49 | 2.93 (1.65-5.28) | |
| | 4 | 14 | 37 | 3.79 (1.89-7.92) | |
| Activity at work | 0 | 44 | 26 | 1.00 | 1.06 |
| | 1 | 41 | 32 | 1.32 (0.64-2.75) | (0.88-1.27) |
| | 2 | 46 | 57 | 2.10 (1.08-4.10) | |
| | 3 | 43 | 43 | 1.69 (0.85-3.39) | |
| | 4 | 91 | 107 | 1.99 (1.10-2.64) | |
| Activity during leisure time* | 0+1 | 7 | 13 | 1.00 | NA |
| | 2 | 35 | 46 | 0.71 (0.22-2.16) | |
| | 3 | 223 | 206 | 0.50 (0.16-1.37) | |
| Playing sports during leisure time | 0 | 245 | 236 | 1.00 | 1.03 |
| | 1 | 20 | 29 | 1.51 (0.80-2.88) | (0.93-1.15) |
| Alcohol intake[‡] | | 113 | 104 | 1.00 | 0.89 |
| | | 73 | 82 | 1.22 (0.80-1.88) | (0.49-1.64) |
| Alcohol intake frequency[‡,§] | 0 | 113 | 104 | 1.00 | NA |
| | 1+2 | 32 | 32 | 1.00 (0.55-1.82) | |
| | 3+4 | 27 | 31 | 1.22 (0.66-2.29) | |
| | 5+6 | 14 | 19 | 1.45 (0.65-3.29) | |
| Non-vegetarian food consumption | 0 | 78 | 68 | 1.00 | 1.16 |
| | 1 | 187 | 197 | 1.21 (0.81-1.81) | (0.68-1.98) |
| Clinical Measures and history | | | | | |
| Waist-Hip Ratio ≥0.9 (Men), ≥0.8 (Women) | 0 | 84 | 47 | 1.00 | 1.72 |
| | 1 | 181 | 218 | 2.15 (1.41-3.31) | (0.98-3.02) |
| Body mass index ≥25 kg/m$^2$ | 0 | 251 | 216 | 1.00 | 4.07 |
| | 1 | 14 | 49 | 4.07 (2.13-8.19) | (1.89-8.75) |
| Hypertension | 0 | 232 | 161 | 1.00 | 2.72 |
| | 1 | 33 | 104 | 4.54 (2.87-7.28) | (1.55-4.78) |
| Family history of CHD | 0 | 259 | 220 | 1.00 | 4.72 |
| | 1 | 6 | 45 | 8.83 (3.65-25.72) | (1.61-13.89) |

*(Continued)*

**Table 3: (Continued)**

| Risk Factors | Code/ Characteristic## | Controls | Cases | Unadjusted OR Odds ratio (95% CI) | Full model-adjusted OR (95% CI) |
|---|---|---|---|---|---|
| Past history of gingival sepsis (painful teeth, painful gums, lost teeth) | 0 | 215 | 161 | 1.00 | 2.79 |
| | 1 | 50 | 104 | 2.78 (1.84-4.21) | (1.67-4.66) |
| Past history of oral contraceptive use` | 0 | 76 | 74 | 1.00 | NA |
| | 1 | 6 | 5 | 0.82 (0.19-3.39) | |
| Past history of female hormone replacement* | 0 | 73 | 76 | 1.00 | 1.00 |
| | 1 | 6 | 3 | 0.48 (0.08-2.36) | (0.99-1.01) |
| Biochemistry | | | | | |
| Diabetes mellitus | 0 | 238 | 221 | 1.00 | 1.04 |
| | 1 | 27 | 44 | 1.75 (1.02-3.05) | (0.89-1.22) |
| Raised total Serum cholesterol | 0 | 199 | 135 | 1.00 | 3.84 |
| | 1 | 66 | 130 | 2.90 (1.98-4.27) | (2.37-6.22) |
| *C. pneumoniae* (IgG antibodies) | 0 | 116 | 63 | 1.00 | 2.01 |
| | 1 | 148 | 201 | 2.50 (1.69-3.70) | (1.22-3.29) |
| *H. pylori* (IgG Antibodies) | 0 | 131 | 75 | 1.00 | 2.98 |
| | 1 | 130 | 186 | 2.50 (1.71-3.65) | (1.82-4.88) |
| C-reactive protein | 0 | 217 | 144 | 1.00 | 3.40 |
| | 1 | 47 | 120 | 3.85 (2.54-5.87) | (2.09-5.54) |

**Derived from Table 1, *Data for females only, †Three cases and four controls excluded from analysis as they did not know about snoring, ‡Data for males only, §Excluded from full model due to co-linearity

**Table 4: Risk factors for AMI by unconditional logistic regression analysis-reduced full model, final full model (OR with 95% CI), ARP and PARP (with 95% CI)**

| Risk Factors | Reduced full model OR (95% CI) | Final full model OR (95% CI) | ARP (95%CI) | PARP (95% CI) |
|---|---|---|---|---|
| Behaviors | | | | |
| Stress at work place in last 1 year | 1.38 (0.78-2.43) | NA | NA | NA |
| Stress at home in last 1 year | 1.60 (1.10-2.27) | 1.59 (1.14-2.22) | 37.11 (12.28-55.16) | 12.98 (03.42-23.72) |
| Financial stress | 0.77 (0.50-1.18) | NA | NA | NA |
| Tobacco smoking | 1.23 (1.02-1.48) | 1.23 (1.03-1.48) | 18.70 (02.91-32.43) | 08.07 (01.13-15.48) |
| Clinical Measures and History | | | | |
| Waist-Hip Ratio ≥0.9 (Men), ≥0.8 (Women) | 1.81 (1.07-3.05) | 1.78 (1.06-2.99) | 43.82 (05.66-66.56) | 34.76 (03.94-57.61) |
| Body Mass Index ≥25 kg/m$^2$ | 4.27 (2.01-9.05) | 4.39 (2.08-9.29) | 77.22 (51.92-89.24) | 15.18 (05.39-30.45) |
| Hypertension | 2.96 (1.72-5.08) | 2.91 (1.70-4.98) | 65.64 (41.18-79.92) | 19.21 (08.02-33.13) |
| Family history of CHD | 4.86 (1.69-13.93) | 5.01 (1.75-14.37) | 80.04 (42.86-93.05) | 08.31 (01.67-23.22) |
| Past history of gingival sepsis (painful teeth, painful gums, lost teeth) | 2.88 (1.75-4.76) | 2.88 (1.75-4.74) | 65.28 (42.86-78.90) | 26.18 (12.39-41.36) |
| Biochemistry | | | | |
| Raised Total Serum Cholesterol | 3.77 (2.35-6.07) | 3.70 (2.31-5.94) | 72.97 (56.71-83.16) | 40.21 (24.60-55.17) |
| *C. pneumoniae* (IgG antibodies positivity) | 1.95 (1.21-3.14) | 1.97 (1.22-3.17) | 49.24 (18.03-68.45) | 35.14 (10.94-54.79) |
| *H. pylori* (IgG Antibodies positivity) | 2.98 (1.85-4.82) | 2.80 (1.75-4.47) | 64.29 (42.86-77.63) | 44.90 (26.90-63.00) |
| Raised C-reactive protein | 3.37 (2.08-5.45) | 3.40 (2.10-5.49) | 70.59 (52.38-81.79) | 29.85 (16.32-44.32) |

The results of final model of logistic regression analysis for risk factors of AMI included waist hip ratio (≥0.9 (Men), ≥0.8 (Women)), body mass index (≥25 kg/m$^2$), stress at home in last 1 year, hypertension, family history of CHD, past history of gingival sepsis (painful teeth, painful gums, lost teeth), tobacco smoking, raised total serum cholesterol, *C. pneumoniae* (IgG antibodies positivity), *H. pylori* (IgG Antibodies positivity) and raised C-reactive protein. These risk factors were significant in the reduced full model at α (level of significance) = 0.05. Final model confirmed the significance of these 11 risk factors at α (level of significance) = 0.05. ARP and PARP estimates for the significant risk factors are also depicted in Table 4.

## Discussion

A substantial proportion of patients with coronary artery disease do not have traditional risk factors[18] of the disease. The common risk factors of atherosclerosis explain disease occurrence in only half of the diagnosed cases. In only 40% patients, risk factors modification inhibits the progression of atherosclerosis. This necessitates a context-specific and holistic model to explain the occurrence of AMI, including searching for new risk factors of atherosclerosis.[19] The present study identified 11 significant risk factors of AMI in the final model. These include conventional risk factors

for coronary artery disease like obesity (estimated through waist-hip ratio and BMI), stress, hypertension, family history of CHD, tobacco smoking, raised total serum cholesterol, and past history of gingival sepsis. The INTERHEART study identified abnormal lipids, smoking, hypertension, diabetes, abdominal obesity, psychosocial factors, consumption of fruits, vegetables, and alcohol, and regular physical activity account for most of the risk of myocardial infarction world-wide.[6] The relationship between cholesterol and ischemic heart disease has been studied by the Prospective Studies Collaboration[20] wherein total cholesterol was positively associated with ischemic heart disease mortality in both middle and old age and at all blood pressure levels. The age-specific relevance of usual blood pressure to vascular mortality has been examined in a meta-analysis[21] wherein a meta-analysis of individual data for one million adults in 61 prospective studies was performed. The meta-analysis concluded that throughout middle and old age, usual blood pressure is strongly and directly related to vascular (and overall) mortality, without any evidence of a threshold down to at least 115/75 mmHg.[21]

Additionally, our study also identified infection with *C. pneumoniae* and *H. pylori* infection and raised levels of C-reactive proteins as significant risk factors in the outcome of AMI. An association between CHD and H. pylori may be accounted for by residual confounding from risk factors among a predominantly western population.[22] Although, currently the association between *H. pylori* infection and chronic disease is viewed with skepticism, a significant odds ratio of 2.80 (CI 1.75-4.47) suggests the need for further work to explore the association between them in the developing countries.

The pathophysiology of conventional risk factors of AMI is well understood. However, information on association of markers of infection and inflammation with AMI is sparse in this country. A wide variation in the prevalence of these microbial agents in different parts of the country; patient age and their level of immunity may modify this prevalence. Additionally, the extent of antibiotic usage in the treatment of other incidental infections may also alter this prevalence estimate. Consequently, we can expect a wide variation in the national prevalence of these infections among adults. If similar association between these agents and AMI is observed in other population groups in this country, this will have for reaching implications for the prevention and treatment of AMI.[23]

The three largest effect sizes reported in the final model include family history of CHD, high BMI and raised total serum cholesterol. However, the former have wide confidence intervals around the point estimate. The ARP and PARP estimates obtained as a part of this study are India specific and could directly guide program managers into developing a prevention strategy for AMI.

## Limitations

Our study was a group-matched case control study design where we interviewed cases and controls about their prior exposure to risk factors of the disease. We included questions on known risk factors of the disease. Although the research associate was blinded to the study hypothesis and administered a structured questionnaire to all study subjects, we could still expect cases to selectively and differentially report on their exposure status for various risk factors. This could result in a differential misclassification and bias the effect estimate away from the null value. We subjectively assessed the level of stress in individuals. The use of a specialized tool could have yielded precise results, but was not pursued to limit the size of the study questionnaire. We expect this to cause a non-differential misclassification in the effect estimates. Our case-control study employed 1-1 matching for cases and controls. A higher number of controls per case could have provided precise estimates; but was not pursued for lack of resources for a study larger than 530 participants. 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 rural patients from seeking care at this institution. Additionally, some cases of severe AMI may result in deaths before the arrival of the patient to a healthcare facility. Our study design limited our data collection to only hospitalized cases of AMI. Our study results are generalizeable to tertiary care public health services across central India. The research findings confirm the role of conventional risk factors causing cardiovascular disease in the Indian population. It introduces an intriguing probability of a further element of infection in our population that is undergoing an epidemiological transition. If these associations are causal, the high ARP and PARP values connote an urgency to examine the possible role of these risk factors in different settings across India using further prospective observational and interventional research.

## Declarations

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