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Serum Homocysteine and Vitamin D as Determinants of Angiographic Severity in Young Myocardial Infarction: A Case–Control Study

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ABSTRACT

Background: Myocardial infarction (MI) in young adults (<45 years) is an emerging public health concern. Early coronary atherosclerosis results from multiple interacting risk factors. Among traditional determinants, dyslipidaemia shows the strongest association, while smoking is the most critical behavioural contributor. Other modifiable risks—hypertension, diabetes mellitus, obesity, sedentary lifestyle, and depression—further accelerate vascular injury. Emerging evidence also implicates elevated homocysteine and vitamin D deficiency in advanced atherosclerosis. This study aimed to evaluate the relative impact of conventional and behavioural risk factors and to examine the association of angiographic severity with serum homocysteine and vitamin D levels.

Aim: To identify risk factors for MI in young adults (<45 years) and assess the association of vitamin D and homocysteine levels with coronary angiographic severity.

Methodology: A case control study was conducted involving 112 young patients admitted with MI (STEMI and NSTEMI) and 112 age and sex matched controls. Standard clinical evaluation and management protocols were followed. Laboratory investigations included blood sugar, lipid profile, homocysteine, and vitamin D estimation. Coronary angiography was performed, and patients were categorised into single , double , or triple vessel disease groups. Statistical analysis determined the strength of association between risk factors and angiographic findings.

Results: The study population was predominantly male (91.9%) and urban (73.2%). STEMI accounted for 69.6% of cases. Dyslipidaemia (75%) showed the strongest association with MI, followed by hypertension (56.3%) and diabetes (39.3%). Compared with controls, dyslipidaemia conferred a ten fold risk, while hypertension

and diabetes each tripled the risk. Elevated homocysteine and vitamin D deficiency were significantly correlated with greater angiographic severity.
Conclusion: The rising incidence of MI in young adults underscores the need for preventive strategies targeting modifiable risk factors. Dyslipidaemia and smoking remain major concerns, while vitamin D deficiency and hyperhomocysteinaemia emerge as important markers of advanced atherogenesis, significantly associated with coronary artery involvement.

Keywords*:* Myocardial infarction, Young Adults (<45 years), Coronary Artery Disease, Homocysteine, Vitamin D deficiency.

INTRODUCTION

Myocardial infarction (MI) has been defined in the 2018 Fourth Universal Definition by the European Society of Cardiology, the American College of Cardiology, the American Heart Association, and the World Heart Federation. The consensus classified myocardial infarction and guided the management strategy.[1]

MI in the young is defined as occurring at an age less than 45 years and being significantly associated with risk factors. MI in young is divided into four subtypes: atheromatous coronary artery, non-atheromatous coronary artery, hypercoagulable state, and substance abuse.[2]

The INTERHEART study showed the contributions of several risk factors to the increased prevalence of coronary artery disease (CAD) in young individuals. Traditional risk factors like dyslipidaemia, hypertension (HTN), diabetes mellitus, obesity, sedentary lifestyle, and a positive family history are coupled with behavioural risk factors like smoking, alcohol consumption, and atherogenic dietary habits, such as diets rich in saturated fats, trans fats, and refined carbohydrates.[3]

Psychological risk factors also play a significant role, such as depression, financial stress, workplace anxiety, and family conflicts.[4] Among all the risk factors, smoking and abnormal lipid profile have the strongest association.[5]

MI in young individuals leading to death is a major health crisis.[6] Recent studies concerning younger individuals with MI found smoking to be the most common risk factor (70%), followed by dyslipidaemia as the second most common risk factor (36.7%). The third important risk factor is diabetes mellitus (20%), and in 10 % of cases, diabetes is diagnosed at the time of MI presentation.[7]

Contemporary studies have revealed new emerging risk factors for MI in young individuals, among which hyperhomocystinemia, hypovitaminosis D, and elevated lipoprotein(a) are important.[8] Indians and Asians, in particular, are at an increased risk of MI at a younger age (<45 years), and studies have documented elevated homocysteine levels and raised lipoprotein(a) as the top contributors of risk factors among Indians. Metabolic syndrome and insulin resistance are found in two-thirds of such cases.[9,10]

Homocysteine is an independent risk factor for atherosclerosis. Several cross-sectional and case-control studies have shown a clear correlation between elevated serum homocysteine and the incidence of coronary, carotid, and peripheral artery disease. The severity of coronary artery involvement, as assessed by angiography and categorised as single-vessel disease (SVD), double-vessel disease (DVD), and triple-vessel disease (TVD), reflects the extent of underlying atherosclerosis, in which hyperhomocysteinemia and dyslipidaemia are key contributors to disease progression.[11]

Homocysteine mediates vascular disease through adverse effects on the vascular endothelium and smooth muscle cells, leading to smooth muscle cell proliferation, endothelial dysfunction, and reduced arterial wall elasticity. Hyperhomocysteinemia causes oxidative stress, reduces nitric oxide bioavailability, and enhances thrombosis, leading to accelerated atherosclerosis.[12,13]

A study conducted in Northeast India for evaluating risk factors among patients with myocardial infarction found a significant association with smoking and dyslipidaemia, where dyslipidaemia was found to have the strongest association, followed by hypertension. Diabetes mellitus was the next most common risk factor. The study highlighted that smokers with vitamin D deficiency have an increased risk of developing MI.[14]

New evidence suggests that vitamin D plays a role in multiple cardiovascular diseases, particularly hypertension, metabolic syndrome, and type II DM. These findings support the notion that vitamin D deficiency is involved in cardiovascular risk development, ultimately leading to an increased burden of CAD.[15]

Vitamin D deficiency causes endothelial dysfunction, increases vascular inflammation, and activates the renin-angiotensin system, leading to hypertension. It promotes insulin resistance, vascular smooth muscle cell proliferation, and accelerates atherosclerosis, thereby increasing the risk of CAD.[16,17]

The synergistic effect of hyperhomocysteinemia and vitamin D deficiency impairs endothelial nitric oxide synthase and promotes the production of pro-inflammatory cytokines, resulting in severe endothelial dysfunction, increased LDL permeability, and initiation of atherogenesis. Inflammatory amplification leads to intimal hyperplasia and luminal narrowing. A pro-thrombotic milieu occurs in which homocysteine increases platelet activation and vitamin D deficiency promotes a procoagulant tendency. Consequently, there is resultant atheroma formation with a higher risk of plaque rupture and superimposed thrombosis.[18-20]

The incidence of MI in young individuals (<45 years) is rising in our state, and there is a need to identify both traditional and emerging risk factors to initiate preventive approaches. The aim of the study is to estimate the strength of association between traditional risk factors and to determine the association between elevated homocysteine levels and vitamin D deficiency and the severity of coronary atherosclerosis, as judged by angiography.

AIM & OBJECTIVES

1. To estimate the risk factors of MI in young individuals (<45 years of age)
2. To determine the association of vitamin D & serum homocysteine level with Coronary angiographic severity in young adults with MI

METHODOLOGY

The study was conducted at a tertiary care hospital in Tripura over a period of 1.5 years. The study was an age, gender and ethnicity-matched (1:1) case-control study, where 112 individuals less than 45 years of age admitted with myocardial infarction were enrolled as cases. An equal number of apparently healthy individuals without a history of MI, matched for age, gender and ethnicity, were recruited as controls to compare the exposure levels of selected risk factors.

The study was conducted after due permission from the Institutional Research Committee and the Institutional Ethics Committee.

Cases were recruited using a consecutive sampling method. All eligible patients aged <45 years admitted with confirmed myocardial infarction during the study period were enrolled as cases (n=112). Controls were selected using matched sampling and recruited to correspond to each case by age, gender, and ethnicity. They were hospital attendees who did not have evidence of coronary artery disease.

Inclusion criteria:

Individuals aged 18 to 45 years, with a first episode of confirmed diagnosis of MI

Exclusion criteria:

1. Individuals with subsequent MI
2. Individuals with a previous history of chronic renal & liver disorder

All patients were physically examined, and BMI was calculated. Venous blood samples were collected for fasting and 2 hours post-prandial blood glucose, glycated haemoglobin (HbA_{1c}) and fasting lipid profile. The parameters studied in the lipid profile are total cholesterol, triglycerides, high-density lipoprotein, low-density lipoprotein, and very low-density lipoprotein. Other parameters studied are the kidney function test, the liver function test and the complete blood count. The important biochemical parameters studied were serum homocysteine level and Vitamin D.

A 12-lead electrocardiogram was obtained from all the patients at the time of presentation. MI was categorised as ST-segment elevation MI (STEMI) or Non-ST-segment elevation MI (NSTEMI) according to the Fourth Universal Definition of MI. Accordingly, cardiac biomarker-Troponin was measured.

Coronary angiography was done in all 112 patients. The extent of coronary artery involvement (SVD, DVD & TVD) was analysed, and its association with Vitamin D and homocysteine levels was determined.

Data were statistically analysed using the Statistical Package for the Social Sciences (SPSS) software 21.0. The relationships between variables were assessed using Pearson's correlation test, and Fisher's exact test was applied to compare categorical variables. P-value< 0.05 has been considered statistically significant.

RESULTS

In the present study, 112 participants were enrolled; the majority were Bengali (75%, n=85), and the remaining 25% (n=27) were from tribal communities. A clear male predominance was noted, with 91.1% (n=102) of the study population being males compared to 8.9% (n=10) females. Within the Bengali group, 79 were male, and 6 were female, whereas among the tribal group, 23 were male and 4 were female (Table 1).

Table 1: Demographic profile of the population under study

Ethnicity	Frequency	Gender distribution	Percent

Bengali	85	Male	Female	75%
		79	06	
Tribal	27	Male	Female	25%
		23	04	
Total	112	102 (91.1%)	10 (8.9%)	100%

The age distribution revealed that all participants were over 30 years of age, with no cases recorded in the <20 or 21–30-year groups. The majority of individuals (72.4%, n=81) were in the 41–45-year age bracket, while the remaining 27.6% (n=31) were in the 31–40-year age bracket. This pattern indicates that myocardial infarction in young adults was most prevalent in the early forties, suggesting that the risk of coronary events begins to rise significantly after the age of 30 and peaks between 41 and 45 years (Table 2).

Table 2: Age group division of the study population

Age Group in years	Frequency	Percent
<20	Nil	0
21-30	Nil	0
31-40	31	27.6%
41-45	81	72.4%

In the present study, the occupational and residential distribution of the 112 participants revealed that the majority were urban dwellers (73.2%, n=82), while a smaller proportion resided in rural areas (26.8%, n=30). Among the occupational categories, employed individuals formed the largest group (28.5%, n=32), with most residing in urban areas (26) and only a few in rural settings (6). Businessmen accounted for 24.0% (n=27), again predominantly urban (25) compared to rural (2). Daily labourers represented 17.0% (n=19), with 12 from urban and 7 from rural areas, while unemployed participants also comprised 17.0% (n=19), mostly urban (16) and only 3 rural. The smallest group was farmers and others (13.5%, n=15), with a reverse trend—the majority from rural areas (12) and only 3 from urban areas (Table 3).

Table 3: Place of residence division with occupation status of the study population

Occupation	Frequency	Place of residence		Percent
		Urban	Rural	
Employed	32	26	06	28.5
Unemployed	19	16	03	17.0
Businessman	27	25	02	24.0
Daily labourer	19	12	07	17.0
Farming & others	15	03	12	13.5
Total	112	82	30	100

The obesity profile of the study population showed that none of the participants was underweight. About one-third (31.2%, n=35) had a normal BMI (18.5–24.9 kg/m²), while a slightly higher proportion were overweight (33.0%, n=37). The largest group comprised obese individuals (35.8%, n=40), indicating that excess body weight was common among the study participants (Table 4).

Table 4: Obesity category of the study population

Obesity category	Frequency	Percent
Underweight BMI < 18.5	0	0
Normal weight BMI= 18.5-24.9	35	31.2
Overweight BMI=25-29.9	37	33.0
Obese BMI>30	40	35.8

The frequency distribution of cardiovascular risk factors in the study population showed that 33.9% (n=38) were diabetic, while the majority, 66.1% (n=74), were non-diabetic. Dyslipidaemia was highly prevalent, affecting 75% (n=84) of participants compared to only 25% (n=28) who were normolipidaemic. Hypertension was present in 56.3% (n=63), whereas 43.7% (n=37) were normotensive (Table 5).

Table 5: frequency distribution of selected cardiovascular risk factors in the study population

Parameter	Diabetic	Non diabetic	Dyslipidemic	Normo lipidemic	Hypertension	Normotensive

Frequency	38 (33.9%)	74 (66.1%)	84 (75%)	28 (25%)	63 (56.3%)	37 (43.7%)
Total	112		112		112	

In the control group of 112 participants, the majority were non-diabetic (86.6%, n=97) compared to 13.4% (n=15) who were diabetic. Dyslipidaemia was present in 23.2% (n=26), while most controls were normolipidaemic (76.8%, n=86). Hypertension was observed in 27.7% (n=31), whereas 72.3% (n=81) were normotensive (Table 6).

Table 6: frequency distribution of selected cardiovascular risk factors in control

Parameter	Diabetic	Non diabetic	Dyslipidemic	Normo lipidemic	Hyper tension	Normotensive
Frequency	15	97	26	86	31	81
Total	112		112		112	

In the study population of 112 young adults with myocardial infarction, behavioural risk factors were highly prevalent. Smoking was reported in 61.6% (n=69), while 38.4% (n=43) were non-smokers. Alcohol consumption was even more common, with 71.4% (n=80) identified as alcohol users compared to 28.6% (n=32) non-alcoholics. Substance abuse was rare, with only 1.8% (n=2) reporting cocaine use, while the overwhelming majority (98.2%, n=110) were non-users (Table 7).

Table 7: frequency distribution of selected cardiovascular risk factors in the study population

Parameter	Smoker	Non smoker	Alcoholic	Non alcoholic	Cocaine abuser	Non user of cocaine
Frequency	69	43	80	32	2	110
Total	112		112		112	

In the control group of 112 participants, behavioural risk factors were far less common compared to the case population. Only 11.6% (n=13) were smokers, while the vast majority, 88.4% (n=99), were non-smokers. Alcohol use was reported in 31.3% (n=35), whereas 68.7% (n=77) were non-alcoholic. Importantly, none of the controls reported cocaine abuse, with all participants (100%, n=112) identified as non-users (Table 8).

Table 8: frequency distribution of selected cardiovascular risk factors among controls

Parameter	Smoker	Non smoker	Alcoholic	Non alcoholic	Cocaine abuse	Non user of cocaine
Frequency	13	99	35	77	0`	112
Total	112		112		112	

Table 9 shows that among the 112 study subjects evaluated by electrocardiography, the majority were diagnosed with STEMI (69.6%; n=78), while the remaining 30.4% (n=34) had NSTEMI.

Table 9: frequency distribution of study subjects based on ECG findings

Electrocardiographic finding	Frequency	Percentage
STEMI	78	69.6
NSTEMI	34	30.4

Table 10 indicates that coronary angiographic evaluation of the 112 study subjects revealed varying degrees of vessel involvement. A normal study was observed in 25% (n=28) of cases, while the majority showed evidence of coronary artery disease. SVD was the most frequent finding, present in 41% (n=46) of patients. DVD was identified in 24.1% (n=27), and TVD in 9.9% (n=11).

Table 10: frequency distribution of study subjects based on coronary angiographic findings

Coronary angiographic finding	Frequency	Percentage
Normal study	28	25
SVD	46	41
DVD	27	24.1
TVD	11	9.9

Table 11 shows that serum biomarker analysis in the study population revealed that 64.3% (n=72) had elevated homocysteine levels (>15 mmol/ml), while only 35.7% (n=40) were within the normal range (5–15 mmol/ml). Similarly, vitamin D status showed a high prevalence of deficiency, with 64.3% (n=72) classified as having low levels (<20 ng/ml). An additional 13.4% (n=15) had insufficient levels (20–29 ng/ml), and only 22.3% (n=25) demonstrated sufficient vitamin D status (30–100 ng/ml).

Table 11: frequency distribution of study subjects based on serum homocysteine level & vitamin D

Variables	**Frequency**	**Percentage**
Serum Homocysteine level: Normal: 5-15 mmol/ml High: > 15 mmol/ml	 40 72	 35.7 64.3
Vitamin D level: Low < 20 ng/ml Insufficient: 20-29 ng/ml Sufficient: 30-100 ng/ml	 72 15 25	 64.3 13.4 22.3

Analysis of serum homocysteine levels in relation to coronary angiographic findings demonstrated a significant association (p=0.001). Among patients with SVD, the majority (31 cases) had elevated homocysteine levels, while only 15 were within the normal range. Similarly, in the DVD, 25 patients had high homocysteine levels compared with just 2 with normal levels. In TVD, 10 cases had elevated levels, whereas only 1 was normal. Conversely, in the normal angiographic group, most cases (23) had normal homocysteine levels, with only 5 showing elevated values (Table 12).

Table 12: Study of the association of homocysteine level with CAG finding

Coronary angiography finding	**Serum Homocysteine level**		**P value**
	Normal 5-15 mmol/ml	High >15 mmol/ml	
Single vessel disease	15	31	0.001
Double vessel disease	2	25	
Triple vessel disease	1	10	
Normal study	23	5	

The analysis of vitamin D levels in relation to coronary angiographic findings showed a statistically significant association (p=0.03). Among patients with SVD, the majority (29 cases) had low vitamin D levels, while 6 had insufficient levels and 11 had sufficient levels. In the DVD, 16 patients had low levels, 7 had insufficient levels, and only 4 had sufficient levels. For TVD, 10 cases were deficient, none were insufficient, and only 1 had sufficient levels. In contrast, among those with a normal angiographic study, 17 participants had low vitamin D, 2 had insufficient levels, and 9 had sufficient levels (Table 13).

Table 13: Study of the association of vitamin D with CAG finding

Coronary angiography finding	**Vitamin D level**			**P value**
	Low (< 20 ng/ml)	Insufficient (20-29 ng/ml)	Sufficient (30-100 ng/ml)	
Single vessel disease	29	6	11	0.03
Double vessel disease	16	7	4	
Triple vessel disease	10	0	1	
Normal study	17	2	9	

Table 14 shows that the association of traditional cardiovascular risk factors with myocardial infarction in young adults showed statistically significant differences between cases and controls. Diabetes was present in 33.9% (n=38) of cases compared to 13.4% (n=15) of controls, conferring an odds ratio (OR) of 3.32 (p<0.01). Dyslipidaemia was the most prominent factor, observed in 75% (n=84) of cases versus 23.2% (n=26) of controls, with a markedly elevated OR of 9.92 (p<0.001). Hypertension was also significantly associated, affecting 56.3% (n=63) of cases compared to 27.7% (n=31) of controls, yielding an OR of 3.36 (p<0.001).

Table 14: Association of traditional cardiovascular risk factors with young-aged MI

Risk factor	Cases n=112	Controls n=112	OR	P value
Diabetes	38(33.9%)	15(13.4%)	3.32	P<0.01
Dyslipidaemia	84(75%)	26(23.2%)	9.92	P<0.001
Hypertension	63(56.3%)	31(27.7%)	3.36	P<0.001

Table 15 indicates that the association of behavioural cardiovascular risk factors with myocardial infarction in young adults revealed highly significant differences between cases and controls. Smoking was reported in 61.6% (n=69) of cases compared to only 11.6% (n=13) of controls, yielding an OR of 12.2 (p<0.001), indicating a very strong association. Similarly, alcohol abuse was present in 71.4% (n=80) of cases versus 31.3% (n=35) of controls, with an OR of 5.50 (p<0.001).

Table 15: Association of Cardiovascular Behavioural risk factors with young-aged MI

Risk factor	Cases n=112	Controls n=112	OR	P value
Smoking	69(61.6%)	13(11.6%)	12.2	P<0.001
Alcohol abuse	80(71.4%)	35(31.3%)	5.50	P<0.001

DISCUSSION

This case–control study demonstrates that MI in young adults (<45 years) is strongly associated with both traditional and behavioural risk factors, while emerging biomarkers such as serum homocysteine and vitamin D deficiency show significant correlations with angiographic severity. MI is defined according to the Fourth Universal Definition, which provides standardised diagnostic criteria and classification.[1]

The majority of cases clustered in the 40–45 year age group, consistent with earlier reports that coronary events in young adults typically manifest after the third decade of life.[21] Male predominance was striking, with over 90% of cases being men, a finding in line with prior studies that identified male sex as a major determinant of premature coronary artery disease.[22]

Traditional cardiovascular risk factors were highly prevalent. Dyslipidaemia emerged as the strongest predictor, conferring nearly a tenfold higher risk compared to controls. This observation mirrors the INTERHEART study, which identified an abnormal lipid profile as the strongest determinant of MI worldwide.[23] Hypertension and diabetes also showed significant associations, each tripling the risk, supporting evidence that metabolic syndrome and insulin resistance accelerate vascular injury in younger populations.[24,25]

Behavioural risk factors played a critical role. Smoking was present in over 60% of cases, conferring twelvefold higher odds of MI, making it the most potent behavioural determinant. This finding is consistent with earlier studies that identified smoking as the leading cause of MI in young adults.[26] Alcohol abuse was also significantly associated with a fivefold increased risk, underscoring the contribution of lifestyle behaviours to early atherogenesis.[27]

Emerging biomarkers provided additional insights. Elevated serum homocysteine levels were significantly associated with multi-vessel disease, supporting prior evidence that hyperhomocysteinaemia promotes endothelial dysfunction, oxidative stress, and thrombosis, thereby accelerating atherosclerosis.[28-30] Similarly, vitamin D deficiency was linked to greater coronary involvement, consistent with studies showing its role in endothelial dysfunction, vascular inflammation, and activation of the renin-angiotensin system.[31-33] The synergistic effect of hyperhomocysteinaemia and vitamin D deficiency may further amplify vascular injury, leading to plaque instability and thrombosis.[34-36]

Taken together, these findings highlight that while traditional and behavioural risk factors remain central to the pathogenesis of young-aged MI, emerging markers such as homocysteine and vitamin D deficiency provide valuable prognostic information regarding disease severity. Preventive strategies must therefore address both conventional risk factors and novel biochemical determinants to reduce the burden of premature coronary artery disease.

CONCLUSION

This case–control study establishes that myocardial infarction in young adults (<45 years) is strongly driven by modifiable risk factors. Dyslipidaemia was the most significant traditional determinant, while hypertension and diabetes also conferred notable risk. Behavioural exposures, particularly smoking and alcohol use, showed even stronger associations, underscoring the critical role of lifestyle modification.

Emerging biomarkers added prognostic value: elevated serum homocysteine and vitamin D deficiency were significantly correlated with multi-vessel coronary artery disease, highlighting their role in advanced atherogenesis. Together, these findings emphasise that early identification and management of conventional risk factors, combined with monitoring of novel biochemical markers, are essential strategies to reduce the burden of premature coronary artery disease in young adults.

Study Limitations

This study was limited by its single-centre design and restricted geographic scope, which may affect generalisability. Risk factor assessment relied on self-reported behaviours, introducing potential recall and social desirability bias. The cross-sectional nature precluded evaluation of long-term outcomes. Laboratory and angiographic findings were based on available infrastructure, and emerging biomarkers were assessed only once, limiting temporal interpretation.

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