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Original Article

Prevalence of Conventional Risk Factors in Acute Coronary Syndrome Patients in Eastern Part of Nepal

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Abstract

Background

Smoking, diabetes mellitus, hypertension and dyslipidemia are known as conventional risk factors of coronary artery disease (CAD) and the prevalence of it varies across populations. There is paucity of data in our country about the prevalence of risk factors for acute coronary syndrome (ACS). This study aims to assess the prevalence of these conventional risk factors in patients who were admitted in Nobel medical college, with the diagnosis of ACS.

Material & Methods

In this observational study, we enrolled 102 patients diagnosed as ACS with stenosis $\geq 50\%$ of any epicardial arteries as shown on angiography admitted in Nobel Medical College between September 2015 to March 2017 and evaluate the prevalence of conventional risk factors. In addition, we analyzed the lipid profiles within 24 hour of the event.

Results

Mean age of the patients was 59 years. Two third (66.7%) of the patients were male. Left anterior descending artery (43.13%) was the most common culprit lesion followed by RCA in 35.29%. Dyslipidemia was present in 73.5%, hypertension in 46.1%, smoking in 38.2% and diabetes in 37.3%. Prevalence of hypertension, diabetes and dyslipidemia was similar among male and female. Smoking (44.1% vs 26.5%) was more common in male ($P < 0.05$). TG ≥ 150 mg/dl was seen in 52% study population and higher level of TG was seen in younger population ≤ 45 years compared to ≥ 45 years old ($p = 0.013$).

Conclusion

Present study showed high prevalence of hypertension, smoking, diabetes and dyslipidemia in patients with ACS, suggesting the need of aggressive risk factor reduction in general population.

Keywords: Acute coronary syndrome, Diabetes, Dyslipidemia, Hypertension, Smoking.

Introduction

Coronary artery disease (CAD) is a leading cause of morbidity and mortality in both developing and developed countries [1]. Epidemiological studies have established cigarette smoking [2], diabetes mellitus

(DM) [3], hypertension (HTN) [4], and dyslipidemia [5] as independent risk factors for CAD and have been labeled as conventional risk factors [6]. Acute coronary syndrome includes unstable angina (UA), Non-ST elevation myocardial

infarction (NSTEMI) and ST elevation myocardial infarction (STEMI), which needs urgent or emergency care to reduce mortality or morbidity. Reduction of these risk factors has been convincingly shown to reduce the risk of future events [2,7]. Prevalence of these risk factors may vary across populations [8]. Our study aims to assess the prevalence of conventional risk factors in patients who were admitted with diagnosis of ACS in Nobel medical college.

Material & Methods

It is an observational, cross-sectional, single center study conducted in Nobel Medical College Biratnagar Nepal. A total of 102 patients admitted with the diagnosis of ACS (Unstable angina, NSTEMI, and STEMI) were enrolled for the study in between September 2015 to march 2017. Performa was designed to collect patient information, which included; age, gender, diabetes, dyslipidemia, hypertension and smoking.

Coronary angiography was done in all patients. Significant CAD was defined as the presence of >50% stenosis of any of the epicardial vessels. Patients only with significant CAD were included in the study. Patients with normal coronary angiography or mild disease, defined as <50% stenosis in any of the epicardial vessels, were excluded, as were patients in whom ACS was considered to be secondary to coronary embolism, arteritis, spontaneous dissection, muscular bridges, or an anomalous origin of the coronary artery. Stable angina patients were also excluded.

Cardiovascular risk factors were defined as follows

- a Smoking: History of cigarette smoking (regularly smokes one or more cigarettes per day)
- b Dyslipidemia: any of the following values in fasting sample taken within 24 hours of the event: TC \geq 200 mg/dL, LDL-C \geq 130 mg/dL, TG \geq 150

- mg/dL and HDL-C \leq 40 mg/dL or patient already on medication for dyslipidemia.
- c Hypertension: systolic blood pressure \geq 140 mm Hg or diastolic blood pressure \geq 90 mm Hg and/or concomitant use of antihypertensive medications.
- d Diabetes Mellitus: fasting plasma glucose \geq 126mg/dL or postprandial glucose \geq 200 mg/dL or patient being treated for diabetes.

Statistical analysis: Continuous variables were expressed as mean with range and categorical variables as count with percentage. Groups were compared using Chi Square test (cross tabulation method) for categorical variables. P value less than 0.05 was considered statistically significant with 95% confidence interval. Data were analyzed using the Statistical Package for the Social Sciences (SPSS) version 17.0 for Windows (SPSS, Inc., Chicago, Illinois, and USA).

Result

1. Demographic and study characteristics

During the study period, we identified 158 patients with acute coronary syndrome of which 102 patients were finally selected by excluding patients with (1) no angiographic study or refused to do, (2) with incomplete lipid profile at admission and (3) patients with normal coronaries and/or non-significant lesion. Mean age of the study population was 58.74 ranging from 30-84 years, among which 68 (66.7%) were male. The participants were further divided into two groups on the basis of their age as \leq 45 years and \geq 45 years among which 85.3 % were \geq 45 years. Mean value for total cholesterol (TC) was 201.03 mg/dl, which ranged from 117 mg/dl to 319 mg/dl.

Mean value for low-density lipoprotein-cholesterol (LDL-C) was 122.87 mg/dl, which ranged from 71 mg/dl to 188 mg/dl. Mean value for Triglyceride (TG) was

167.29 mg/dl, which ranged from 79 mg/dl to 400 mg/dl. Mean value for High-density lipoprotein-cholesterol (HDL-C) was 39.14 mg/dl, which ranged from 19 mg/dl to 98 mg/dl. Anterior wall myocardium was the most commonly involved (43.13%) territory followed by inferior wall myocardium (35.29%)(Table.1).

Table.1 Demographic and study characteristics

Demographic and lipid profile	N= 102
Age	58.74(30-84)
Less than 45 years	15%
More than 45 years	85%
Male	67%
Female	33%
Total cholesterol (mg/dL)	188 ± 46.34
LDL-C (mg/dL)	119 ± 30.41
HDL-C (mg/dL)	39 ± 10.57
Triglyceride (mg/dL)	167 ± 71.25

2. Prevalence of risk factors according to sex

The prevalence of CVD risk factors among the study population is summarized in Table 2. Hypertension was present in 45.6% of male and 47.1% of female was the most frequently observed risk factors in Myocardial infarction and unstable angina groups with (P=0.888), whereas prevalence of smoking was seen in 44.1% male vs 26.5% in female (P<0.05). Among the risk factors T2DM was present in 38.2% in male vs 35.3% in female with (P=0.77), respectively among 102 study populations.

Table.2. Prevalence of risk factors according to sex

Risk factors	All patients N= 102(%)	Male N= 68(%)	Female N= 34(%)	P value
Smoking	39	30(44.1)	9(26.5)	<0.05
Hypertension	47	31(45.6)	16(47.1)	.888
Diabetes	38	26(38.2)	12(35.6)	.077

3. Prevalence of risk factors by age

The prevalence of CVD risk factors among the study population by age is summarized in Table 3. Similar to the prevalence by sex HTN is by far the most common observed risk factor 49.4% in age ≥45 vs 26.7% in age ≤45 years, smoking was seen in 36.8% age ≥ 45 years and higher rate of prevalence 46.7% in age ≤ 45 years and. Among the risk factors T2DM was present in 36.8% with age ≥45 years vs as 40.0% in age ≤45 years, All of the conventional risk factors were non significant with P value ≥0.05 with acute coronary syndrome among 102 study populations.

Table.3 Prevalence of risk factors by age

Risk factors	All patients N= 102	Age >45years N= 87(%)	Age <45 years N= 15(%)	P value
Smoking	39	32(36.8)	7(46.7)	0.46
Hypertension	47	43(49.4)	4(26.7)	0.10
Diabetes	38	32(36.8)	6(40.0)	0.81

4. Lipid profile study

The blood lipid analysis showed that the mean level of total cholesterol was 201.03 mg/dl (IQR 117-319mg/dl), LDL-C was 122.87 mg/dl (IQR, 71-188 mg/dl), HDL-C was 39.14 mg/dl (IQR, 19-98) and Triglyceride was 167.29 mg/dl (IQR, 79-

400 mg/dl). **Table 4.** TC, LDL-C and TG all three levels were higher in women than men and HDL-C was seen higher in men compared to women though the difference were non-significant ($p \geq 0.05$).

When the lipid profile was differentiated by age, older patient have higher percentage of LDL-C ≤ 130 mg/dl, TC ≤ 200 mg/dl as compared to age ≤ 45 years old.

Table 5. Whereas HDL-C level ≤ 40 mg/dl is decreased in older patients compared to younger. This result could be due to decrease in physical activity and exercise

in older patients as aerobic exercise/physical activity increases HDL-C level (Table.5). TG ≥ 150 mg/dl was seen in 52% study population. Higher level of TG was seen in younger population ≤ 45 years compared to ≥ 45 years old which was statistically significant ($p = 0.01$).

As shown in **Table 7.** 10.7% are without any conventional risk factors for ACS, which is negligible compared to 89% patients with at least one or more risk factors for cardiovascular disease.

Table 4. Pattern of Lipid profiles in study populations by sex

	All patients(n=102)	Men(n=68)	women(n=34)	P value
TC (IQR)(mg/dl)	201.03(117-319)	199.90(117-319)	203.29 (118-302)	0.32
TC ≥ 200 mg/dl(%)	43.1	39.7	50	
TC ≤ 200 mg/dl(%)	56.9	60.3	50	
LDL-C (IQR)(mg/dl)	122.87(71-188)	120.74(44-188)	127.15(47-259)	0.77
LDL-C ≥ 130 mg/dl(%)	36.3	35.3	38.2	
LDL-C ≤ 130 mg/dl(%)	63.7	64.7	61.8	
HDL-C (IQR)(mg/dl)	39.14 (19-98)	39.97(19-99)	37.47(19-98)	0.67
HDL-C ≥ 40 mg/dl(%)	47.1	48.5	44.1	
HDL-C ≤ 40 mg/dl(%)	52.9	51.5	55.9	
TG (IQR)(mg/dl)	167.29(79-400)	166.19(79-340)	169.50(84-400)	0.48
TG ≥ 150 mg/dl(%)	52.0	54.4	47.1	
TG ≤ 150 mg/dl(%)	48.0	45.6	52.9	

Table 5. Lipid profile characteristics by age

AGE	LDL-C		TC		HDL-C		TG	
	≥ 130	≤ 130	≤ 200	≥ 200	≥ 40	≤ 40	≥ 150	≤ 150
≤ 45 (%)	53.3	46.7	40.0	60	40.0	60	53.3	46.7
≥ 45 (%)	33.3	66.7	59.8	40.2	48.3	51.7	51.7	48.3
TOTAL(%)	36.3	63.7	56.9	43.1	47.1	52.9	52	48.0
P value	0.13		0.15		0.55		0.01	

Table 6. Distribution of dyslipidemia by sex

		No dyslipidemia	Dyslipidemia	Total	P value
Sex	F	8 23.5%	26 76.5%	34 100.0%	0.63
	M	19 27.9%	49 72.1%	68 100.0%	
Total		27 26.5%	75 73.5%	102 100.0%	

Table 7. Distribution of cardiovascular risk factor burden

Risk factors	n=102	%
None	11	10.78
One	21	20.5
Two	38	37.25
Three	30	29.41
Four	2	1.96

Discussion

Mean age of the patients was 58.74 years in our study. Younger patients (age less than 45 years) with ACS event were 14.7%. In a study done by Adhikari et.al [9] similar results were found where mean age of the patients were 57 years and younger patient population was 12.6%. It is a matter of concern that younger patients percentage is increasing for ACS event. In this study one third (33%) of the patients were female. The incidence of acute coronary syndrome (ACS) is lower in women than men in all age group[10], which is consistent with our study , having lower percentage 33.3% of total population. The finding that ACS event is more common in male patients is consistent with report from multinational

observational Global Registry of Acute Coronary Events (GRACE)[11].

We found high prevalence of Dyslipidemia (73.5%), Hypertension (46.1%), Smoking (38.2%), Diabetes (37.3%) in our study population. In study done by Adhikari et al [9] have lower prevalence of dyslipidemia 45.5% compared to our 73.5% which is much higher, it is s because we included TG in the definition of dyslipidemia[12].

Cigarette smoking plays a critical role in the development of CHD (Coronary heart disease). Smoking is considered one of the most important modifiable risk factors for increasing cardiovascular disease. In our study, the prevalence of current smoking was 44.1% in male and 26.5% in female. Smoking was significantly higher in male population in overall as well as among all age group in our study. These results are

similar to other recent studies. It was the second most frequently encountered conventional risk factor with acute STEMI living in Turkish study population [13]. Though our study showed non-significant risk estimation with acute coronary Syndrome, it could be cause of smaller sample size of population in our study. DM (Diabetes mellitus) is a major health challenge in many Asian populations. However its prevalence is somewhat lower than that observed in developed countries[14], it is significant among South Asians, having 2% prevalence in rural South Asia but approaching 20% prevalence in urban South Asia and amongst immigrant South Asians[15-17]. In our study it is 3rd common among the conventional risk factors only after Hypertension and Smoking. Prevalence of DM in INTER HEART study was 26% in women, 16% in men[8]. The higher prevalence of diabetes in women than in men is not consistent in our study (F 35.3% vs M 38.2%) with other studies that have shown that diabetes is a powerful risk factors in women, though our study did not show any sex disparity in prevalence which were non-significant and also one of the factors effecting the ratio could be higher number of subject for ACS being male. Hypertension is one of the main factors leading to atherogenesis and the development of vulnerable plaques whose instability or rupture are responsible for the development of acute coronary syndrome (ACS). In general population, the prevalence of hypertension rises progressively with age in both male and female. In GUSTO -1 trial which enrolled 41021 STEMI patients prevalence of a history of previous hypertension was 38.1 % (15544 of 41021) [18]. Similarly, In GISSI-2 with 20491 STEMI patients, history of HTN was present in about 35% of the whole population [19]. In epidemiological studies performed in N-

STEMI patients, chronic HTN is the most prevalent risk factors [20]. Similar to this studies prevalence of HTN in-patient presented with ACS at our center was 46.1%. From all the registries and the data available up to now [18, 19, 21-23], ACS patients with hypertension are more likely to be female, older ages similar to that of our study with HTN in Female being 47.1% with age \geq 45 years being 49.4%.

An Observational study has shown untreated dyslipidemia as a strong predictor of in-hospital mortality [24]. Clinically significant changes in lipid occur after an ACS event[25]. From the Time of admission to next morning, TC and LDL-C level can undergo a change of 7% and 10% respectively, in patients with MI and 5% and 6% in those with unstable angina [29]. Our study showed 73.5% had at least one alteration in lipid levels. On other hand, these results could be due to an underestimation of the true prevalence of dyslipidemia as risk factors for Nepalese population.

In previous observational study [26], every 1 mg/dl increment in HDL-C was reported to be associated with 2%-3% decrease risk of CVD in adult. In our study 52.9% of population has HDL-C \leq 40 mg/dl, which co-relates that HDL-C level is strong biomarker and one of the conventional and important risk factors for ACS.

Elevated levels of TG are independent risk factors for CHD [27]. Even our study demonstrated that TG level \geq 150 are statistically significant (P=0.013) risk factors for ACS. For a reduction of 1% in TC has been shown to reduce the risk for coronary artery disease[28] assuming that reverse is true, our study does not correlates to previous studies as our study 57% of population have TC level \leq 200 mg/dl, and suffered acute coronary syndrome event. LDL-C \geq 130 mg/dl is seen in smaller percentage of 36.3% compared to 63.7% of LDL-C \leq 130 mg/dl.

This may point out that even lower level of LDL-C can be a risk factor for ACS event [29, 30] and future study needs to validate more accurate event. Our study clearly shows that conventional risk factors occur in most of the ACS patients in cluster. Adhikari CM et.al [9] Study showed that 70% population had more than 2 risk factors which is same in our study too. All the above data from studies shows that most of the ACS patients have cluster of conventional risk factors and primary prevention against all of the four conventional cardiovascular risk factors should be address by education, diet, exercise and pharmacologically.

Conclusion

Present study showed high prevalence of hypertension, smoking, diabetes and dyslipidemia in patients with ACS, suggesting the need of aggressive risk factor reduction in general population.

Limitations

This study has some limitations, such as its observational design and small sample size. Doses of atorvastatin taken by patient vary and many are not documented and Lipid profile was taken at variable time within 24 hours. Factors that can impact the cardiovascular risk (eg, obesity, Inactivity, familial history) were not evaluated separately which might change the results if taken into consideration.

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Reference

- [1] Lopez AD, Murray CC, The global burden of disease, 1990-2020, Nat Med. 4:11(1998) 1241-3.
- [2] Samet JM, The 1990 Report of the Surgeon General: The Health Benefits of Smoking Cessation, Am Rev Respir Dis.142:5(1990) 993-4.
- [3] Stamler J, Vaccaro O, Neaton JD, Wentworth D. Diabetes, other risk factors, and 12-yr cardiovascular mortality for men screened in the Multiple Risk Factor Intervention Trial, Diabetes Care.16:2(1993) 434-44.
- [4] MacMahon S, Peto R, Cutler J, Collins R, Sorlie P, Neaton J, et al, Blood pressure, stroke, and coronary heart disease, Part 1, Prolonged differences in blood pressure: prospective observational studies corrected for the regression dilution bias, Lancet.335(1990) 765-74.
- [5] Verschuren WM, Jacobs DR, Bloemberg BP, Kromhout D, Menotti A, Aravanis C, et al, Serum total cholesterol and long-term coronary heart disease mortality in different cultures, Twenty-five-year follow-up of the seven countries study, JAMA. 274:2 (1995) 131-6.
- [6] Khot UN, Khot MB, Bajzer CT, Sapp SK, Ohman EM, Brener SJ, et al, Prevalence of conventional risk factors in patients with coronary heart disease, JAMA. 290 (2003)898-904.
- [7] Collins R, Peto R, MacMahon S, Hebert P, Fiebich NH, Eberlein KA, et al, Blood pressure, stroke, and coronary heart disease, Part 2, Short-term reductions in blood pressure: overview of randomised drug trials in their epidemiological context, Lancet. 335 (1990) 827-38.
- [8] Yusuf S, Hawken S, Ounpuu S, Dans T, Avezum A, Lanas F, et al, Effect of potentially modifiable risk factors associated with myocardial infarction in 52 countries (the INTERHEART study): case-control study, Lancet. 364 (2004) 937-52.
- [9] Adhikari CM, Prajapati D, Baniya B, Regmi S, Bogati A, Thapaliya S, Prevalence of Conventional Risk Factors in ST Segment Elevation Myocardial Infarction Patients in ShahidGangalal National Heart Centre, Nepal, JNMA J Nepal Med Assoc. 52:195 (2014) 914-9.
- [10] Andreotti F, Rio T, Gianmarinaro M, Navarese EP, Marchese N, Crea F, Pathophysiology of ischemic heart disease in women, G ItalCardiol (Rome).13:6(2012) 396-400.
- [11] Carruthers KF, Dabbous OH, Flather MD, Starkey I, Jacob A, Macleod D, et

- al, Contemporary management of acute coronary syndromes: does the practice match the evidence? The global registry of acute coronary events (GRACE), *Heart*.91:3 (2005) 290-8.
- [12] Gonzalez-Pacheco H, Vargas-Barron J, Vallejo M, Pina-Reyna Y, Altamirano-Castillo A, Sanchez-Tapia P, et al, Prevalence of conventional risk factors and lipid profiles in patients with acute coronary syndrome and significant coronary disease, *Ther Clin Risk Manag*. 10 (2014) 815-23.
- [13] Sonmez K, Akcay A, Akcakoyun M, Demir D, Elonu OH, Pala S, et al, Distribution of risk factors and prophylactic drug usage in Turkish patients with angiographically established coronary artery disease, *J Cardiovasc Risk*.4(2002) 199-205.
- [14] King H, Aubert RE, Herman WH. Global burden of diabetes, 1995-2025: prevalence, numerical estimates, and projections. *Diabetes Care*.21:9(1998) 1414-31.
- [15] Anand SS, Yusuf S, Vuksan V, Devanesen S, Teo KK, Montague PA, et al, Differences in risk factors, atherosclerosis, and cardiovascular disease between ethnic groups in Canada: the Study of Health Assessment and Risk in Ethnic groups (SHARE), *Lancet*. 356 (2000) 279-84.
- [16] Riste L, Khan F, Cruickshank K, High prevalence of type 2 diabetes in all ethnic groups, including Europeans, in a British inner city: relative poverty, history, inactivity, or 21st century Europe? *Diabetes Care*. 24:8 (2001) 1377- 83.
- [17] Venkataraman R, Nanda NC, Baweja G, Parikh N, Bhatia V, Prevalence of diabetes mellitus and related conditions in Asian Indians living in the United States, *Am J Cardiol*. 94 (2004) 977-80.
- [18] An international randomized trial comparing four thrombolytic strategies for acute myocardial infarction. *N Engl J Med*. 329:10 (1993) 673-82.
- [19] Fresco C, Avanzini F, Bosi S, Franzosi MG, Maggioni AP, Santoro L, et al, Prognostic value of a history of hypertension in 11,483 patients with acute myocardial infarction treated with thrombolysis, GISSI-2 Investigators, *Gruppo Italiano per lo Studio della Sopravvivenza nell'Infarto Miocardico*, *J Hypertens*. 14:6 (1996) 743-50.
- [20] Hasdai D, Behar S, Wallentin L, Danchin N, Gitt AK, Boersma E, et al, A prospective survey of the characteristics, treatments and outcomes of patients with acute coronary syndromes in Europe and the Mediterranean basin; the Euro HeartSurvey of Acute Coronary Syndromes (Euro Heart Survey ACS), *Eur Heart J*. 23(2002) 1190-201.
- [21] Burt VL, Whelton P, Roccella EJ, Brown C, Cutler JA, Higgins M, et al, Prevalence of hypertension in the US adult population, Results from the Third National Health and Nutrition Examination Survey, 1988-1991. *Hypertension*. 25:3 (1995) 305-13.
- [22] Wolf-Maier K, Cooper RS, Banegas JR, Giampaoli S, Hense HW, Joffres M, et al, Hypertension prevalence and blood pressure levels in 6 European countries, Canada, and the United States, *JAMA*. 289 (2003) 2363-9.
- [23] Ali WM, Zubaid M, El-Menyar A, Al Mahmeed W, Al-Lawati J, Singh R, et al, The prevalence and outcome of hypertension in patients with acute coronary syndrome in six Middle-Eastern countries, *Blood Press*. 20:1 (2011) 20-6.
- [24] Montalescot G, Dallongeville J, Van Belle E, Rouanet S, Baulac C, Degrandt A, et al, STEMI and NSTEMI: are they so different? 1 year outcomes in acute myocardial infarction as defined by the ESC/ACC definition (the OPERA registry), *Eur Heart J*. 28 (2007) 1409-17.
- [25] Rosenson RS, Myocardial injury: the acute phase response and lipoprotein metabolism, *J Am Coll Cardiol*. 22:3 (1993) 933-40.
- [26] Maron DJ, The epidemiology of low levels of high-density lipoprotein cholesterol in patients with and without coronary artery disease, *Am J Cardiol*. 86:12a(2000)111-41.
- [27] Austin MA, Hokanson JE, Edwards KL, Hypertriglyceridemia as a cardiovascular risk factor, *Am J Cardiol*.81:4A (1998)7B-12B.
- [28] Consensus conference, Lowering blood cholesterol to prevent heart disease, *JAMA*.253:14 (1985) 2080-6.
- [29] Kostev K, Parhofer KG, Dippel FW, Prevalence of high-risk cardiovascular patients with therapy-resistant hypercholesterolemia, *Cardiovasc Endocrinol*. 6:2 (2017) 81-5.
- [30] O'Brien EC, Simon DN, Roe MT, Wang TY, Peterson ED, Alexander KP, Statin Treatment by Low-Density Lipoprotein Cholesterol Levels in Patients With Non-ST-Segment Elevation Myocardial Infarction/Unstable Angina Pectoris (from the CRUSADE Registry), *Am J Cardiol*. 115.