A study on spectrum of conventional risk factors in acute coronary syndrome in NGMCTH, Nepal

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ABSTRACT

BACKGROUND

ACS is one of the medical emergencies encountered in clinical practice. Risk factors for any disease conditions are a gesture for its futuristic impact. Surprisingly the prevalence of cardiovascular diseases, especially CAD is rising in developing countries. The presence of CAD embarks physical, psychosocial and economic burden to the individuals, family, society and nation. Conventional risk factors are one of the causal risk factors for CAD. The aim of this research was to study the following risk factors in ACS: Age, Smoking, HTN, DM, Dyslipidemia, Gender and Family history of CAD.

METHODS

This was a Single Center Hospital Based Observational Prospective Cross-sectional Study conducted at Nepalgunj Medical College Teaching Hospital (NGMCTH). All diagnosed cases of ACS with total of 100 subjects were included from Emergency department, Medical wards, Coronary Care Unit (CCU) and OPD. Duration of study was one year from March 2016 to march 2017 after approval from IRC in April. Clinical data was obtained by questionnaire and later entered into Excell and further analysis was done with SPSS software version 20.0. All categorical variables were expressed using percentage and continuous variables as mean and standard deviations and association was calculated using Chi-square test.

RESULTS

Out of 100 subjects 71% were male and 29% females. The age range was between 23 to 91 years and the mean age was 69.9±12.83. This study showed 45% subjects had STEMI, 27% were having NSTEMI and 28% were suffering from Unstable angina (UA). Hypertension was found in 73%, Male gender was seen in 71%, Family History of CAD was found in 13%, Smoking was found in 69%, DM was found in 63% and 56% were having Dyslipidemia.

CONCLUSIONS

Out of total 100 subjects enrolled hypertension was the most common conventional risk factor (73%). It was statistically significant (p value=0.02). Out of total patients 73% had at least one risk factor for ACS. Male gender was the second common risk factor (71%). STEMI was the most common ACS (45%).

KEY WORDS

Acute Coronary Syndrome (ACS), Hypertension, STEMI, UA, NSTEMI.

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INTRODUCTION

Risk factor is a characteristic feature of an individual or population that is present early in life and is associated with an increased risk of developing future disease. Coronary risk factors refer to conditions that have been demonstrated by statistical methods indicating increase in morbidity and mortality.(1)

Risk factors have been grouped into conventional and non-conventional. The Conventional risk factors have been further divided into: Modifiable and Non-modifiable. The non-modifiable risk factors for ACS are Age more than 55 years, Family History of CAD, Male gender and Ethnicity. Some Modifiable risk factors are: Smoking, Dyslipidemia, Hypertension, Physical inactivity, Obesity, Diabetes, Fatty diet and Psychosocial stress. Dyslipidemia has been the main predictor of CAD due to elevation of LDL. Non- conventional risk factors associated with cardiovascular diseases are: Chronic inflammation and its markers like CRP, Homocysteine, Oxidative stress or endothelial dysfunction, Lp(a), Psychosocial factors such as environmental stress and responsiveness to stress, plasma insulin level and activation of RAAS.(2)

According to Sadeghian et al conventional risk factors for CHD include: (i) Diabetes mellitus, defined as a past history of diabetes, or fasting plasma glucose ≥ 7mmol/L, or two hours post glucose load >or =11mmol/l (ii) Hypertension (past history of hypertension, or systolic blood pressure ≥ 140 mmHg or diastolic blood pressure ≥ 90 mmHg);(iii)Hyperlipidemia (total cholesterol> 6.5 mmol/L, LDL > 4.2 mmol/L or if on lipid-lowering therapy; (iv) Smoking regularly using tobacco for the last 6 months.(3)

Diabetes: Diabetes mellitus is a metabolic disorder principally characterized by elevated blood glucose levels and by microvascular and macrovascular complications that considerably increase the morbidity and mortality related to the disease.(4)

Hypertension: Arterial hypertension is among the most prevalent risk factor of cardiac and cerebrovascular disease such as MI, stroke and death. The risk increases progressively with every increment in blood pressure. (5)

Hyperlipidemia: Atherosclerosis results in thickening and plaque formation in the artery lumen that impedes blood flow. Atherosclerosis of one or more coronary arteries decreases the cardiac blood supply resulting in angina pectoris, while complete blockage may cause Ischemic Heart Disease. (6)(7)

Smoking: According to Rehill et al. (2006), smoking a single cigarette produces an acute increase in arterial stiffness in chronic smokers and nonsmokers, and that chronic tobacco smoking is associated with endothelial dysfunction and increased augmentation index in subjects of a wide age range free from additional cardiovascular risk factors. (8)

Acute coronary syndrome: ACS include patients with acute MI with STEMI on their presenting ECG and those with NSTE-ACS. The later include patients with non STEMI who by definition have evidence of myocyte necrosis and those with Unstable Angina (UA), who do not.

Diagnosis: Clinical presentation of NSTEMI: At least one of 3 features:

1. It occurs at rest (or with minimal exertion lasting >10minutes)

2. It is of relatively recent onset (i.e. within the prior two weeks); and or

3. It occurs with a crescendo pattern (i.e. distinctly more severe, prolonged or frequent than previous episodes)

The diagnosis of STEMI is established if a patient with these clinical features develops evidence of myocardial necrosis as reflected in abnormally elevated levels of biomarkers of cardiac necrosis. Patients with NSTEMI have elevated biomarkers of necrosis, such as troponin I or T, which are specific, sensitive and the preferred markers of myocardial necrosis. Elevated levels of these biomarkers distinguish patients with NSTEMI from those with unstable angina. Clinical presentation of STEMI: The 12 lead ECG is a pivotal in diagnostic and triage tool because it is at the center of decision pathway for management: It permits distinction of those with patients presenting with ST-segment elevation from those presenting without ST-segment elevation. Serum biomarkers are obtained to distinguish between unstable anginas from STEMI and to access the magnitude of an STEMI. (9)

Study on the four conventional risk factors: Smoking, Diabetes, Dyslipidemia, and Hypertension in population of patients at NGMC was needed so that patients and physicians can better understand the impact of preventing or modifying these specific risk factors on the risk of future ACS. Study on conventional risk factors in ACS is not done in our hospital before, so it is essential to study those risk factors and help the target groups. In the light of projection of large increase in IHD throughout the world, IHD is likely to become the most common cause of death worldwide by 2020. Obesity, insulin resistance and diabetes are increasing and are powerful risk factors for IHD. Population groups that appear to be particularly affected are men in south Asian countries, especially India and the middle east. (9)

Some studies done by Vita JA et al. and Celermajer DS et al indicated that the risk to develop endothelial dysfunction increases with the number of risk factors present in an individual. These studies also emphasized on presence of endothelial inflammation that is further associated with atherosclerosis and hence leading to different coronary syndromes. (10)(11)

In a study in 2002 to 2003 it was found that at least one of the four conventional risk factors was present in 84.6% women and 80.6% men. In younger patients (men ≤55 years and women ≤65 years) and most patients presenting either with unstable angina or for percutaneous coronary intervention, only 10% to 15% of patients lacked any of the 4 conventional risk. (12)

A study on conventional risk factors had been done in Albania, Tirana in 2003 to 2006family history of coronary heart disease was found to be a strong predictor of acute coronary syndrome in both men and women. In men, but not in women, there was a significant association with hypertension and current smoking (P = 0.011 and P<0.001, respectively. (13)

In a an observational, single-center, study from January 2010 to December 2011 on 10450 consecutive patients visiting a tertiary care center India who presented with complaints related to CAD, it was found that 6867 patients had coronary artery disease (CAD) as confirmed by angiographic investigation; 5678 were males, and 1189 were females with similar mean age. As compared to males, females had higher prevalence of hypertension, diabetes and obesity while males had higher prevalence of smoking. Depression was observed in 39.8% of acute coronary syndrome patients (n = 1648) as assessed by MARDS scale. It was higher in female patients and in low socioeconomic strata ($p < 0.001$). A study showed At 12 and 36 months, rates of revascularization ($p < 0.001$) and mortality ($p < 0.005$) were higher with poor quality of life (P<0.001) in CAD patient that suffered from depression.(14)

So far only few studies on conventional risk factor had been conducted in patient attending our hospital hence it is really an essence to do so and help adopt preventive measures beforehand to decrease future risk of acute coronary syndrome. There have been many noninvasive biochemical measures used to predict cardiovascular risk, such as lipid and lipoprotein metabolism, inflammation, and oxidative stress. (15)

Cigarette smoking is a risk factor for the development of CVD. Since the 1950s, studies have shown that prolonged smoking causes premature death and disability. The number of smokers is estimated to rise from 1.25 billion to 1.64 billion by 2025 with two-thirds of smokers living in developing countries. About half of these deaths will occur among middle-aged adults (35–69years old), who will lose on average 22 years of life. In the year 2000, about 4.83 million of adults died prematurely from smoking. Leading causes of death attributable to smoking were CVD's, chronic obstructive pulmonary disease, and lung cancer (71% of lung cancers were smoking related). Smoking related deaths in men were about three times more common than women in industrial countries, and about 7 times more common in developing countries. Currently, most tobacco-related deaths occur among men, but female mortality from tobacco is expected to increase substantially as a result of large increases in smoking among women in many developed countries, and high rates of use of non-smoking tobacco, especially in women, in several developing countries. (16),(17)

Conventional cardiovascular risk factors, such as hypertension, diabetes, smoking, and dyslipidemia, increase the risk of developing coronary artery disease (CAD). (17),(18)

Several preventive studies have shown that the early detection and aggressive treatment of risk factors prevent cardiovascular events. (19)(20)

Similarly, the INTERHEART study was designed to assess the relevance of different risk factors on development of myocardial infarction worldwide.(21)

AIMS AND OBJECTIVES

General objective:

To Study Association of Conventional Risk Factors with Acute Coronary Syndrome in NGMCTH.

Specific objective:

To illustrate types of Acute Coronary Syndrome.

METHODS

This was Hospital based observational Cross -sectional study conducted in NGMCTH. The Sample size was 100 with duration of study as one year after acceptance of protocol and approval by IRC.

nclusion criteria: All diagnosed cases of unstable angina, STEMI and NSTEMI having age ≥18 years of age.

Exclusion criteria:

1. Age <18 years
2. Patients who refuse to give consent.
3. Chronic renal failure patients.
4. Acute heart failure subject
5. Stable Angina

Sample size calculation:

Considering the prevalence(p) of conventional risk factors in ACS of 0.7 from the INTERHEART study conducted in 1999, following sample size is derived. (21)

Formula: Sample Size (N)= Z2pq/r2: Where Z=1.96, p=prevalence=7%, q=1-p, r=margin of error=5%; Calculated Sample size=100.34 which was considered approximately 100. ACS were diagnosed based on Clinical Evaluation, ECG changes and cardiac markers. As per AHA 2014.

Criteria for considering the risk factors were as follows:

1. Smoker: Person smoking before cardiac events for more than 6 months as per CDC 2010.
2. Diabetes: According to ADA 2014 classification and those under OHA or insulin.
3. Hypertension: Patient under antihypertensive medication and whose BP is more than 140/90mmhg (JNC-7).
4. Dyslipidemia: Triglycerides (TG): ≥ 1.695 mmol/L and high-density lipoprotein cholesterol (HDL-C) ≤ 0.9 mmol/L (M), ≤ 1.0 mmol/L (F) as per ATP=III classification.
5. Family History of ACS.(22)

Data collection was done in the form of questionnaire and History taken only once at the time of admission of the patient. Statistical analysis was done by help of Microsoft office excell and SPSS Software version 20.0.0

ETHICAL CONSIDERATION: Before starting the study, ethical approval was obtained from Intuitional Research Committee (IRC) of NGMC. Every participant's willingness was considered before including them in the study. Personal harm to the subjects and respondent was guarded and also the privacy of the subject was maintained.

RESULTS

Out of total 100 subjects enrolled in the study 71% were male and 29% female. The mean age was 69.9±12.83 years, median age was 70.5 years. The minimum age of the patient was 23 years and maximum was 91 years. (Table 1).

Table 1. Demographic profile of the study population (N=100).

Variables	Frequency
Age (years) (mean ± SD)	69.9 ± 12.83
Age (years)(median)	70.5
Minimum age	23 years
Maximum age	91 years
Male	71 (71%)
Female	29 (29%)
Age≤40 years	2 (2%)
Age 40 to 50 years	7(7%)
Age 50 to 60 years	8 (8%)
Age 60 to 70 years	30 (30%)
Age ≥70 years	53 (53%)

Table 2: Gender distribution of the population.

Gender	Percentage
Male	71
Female	29
Total	100

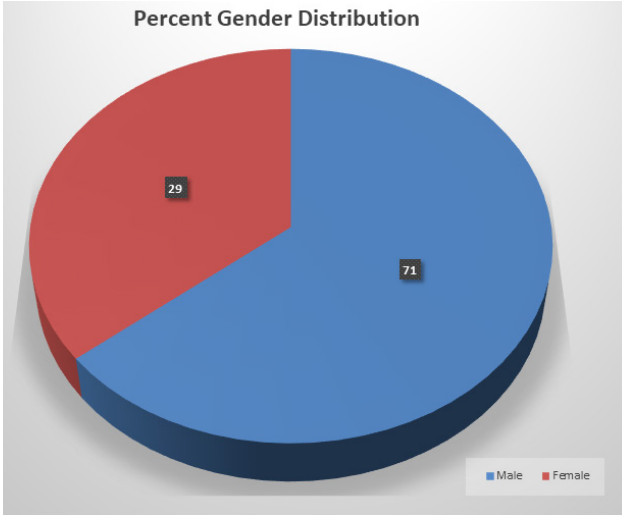

Figure 1: Showing Gender distribution of the study Population.

Table 3. Table showing distribution of ACS in the study population (N=100)

Types of ACS	Percentage
NSTEM	27
STEMI	45
Unstable Angina	28
Total	100

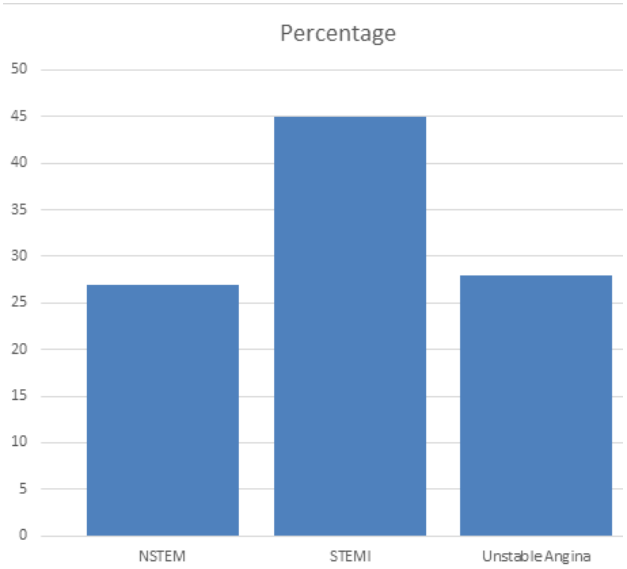

Figure 2: The figure showing percentage distribution of ACS in the study.

Table 4: Association between Types of ACS and Age group (N=100).

Types of ACS	Age ≤40 years	Age 41 to 49	Age 50 to 60	Age 61 to 69	Age ≥70
NSTEMI	0	1	1	8	17
STEMI	2	5	6	13	19
UA	0	0	1	9	18
Total	2	6	8	30	54

The table shows there is no statistically significant between age group and types of ACS (P value= 0.5).

Table 5: Table showing association between Gender and Types of ACS (N=100).

Types of ACS	Male	Female
NSTEMI	14	13
STEMI	35	10
UA	22	6
Total	71	29

Chi-square = 6.5912, P Value =0.05 The table shows there was statistical significance between gender and types of ACS. STEMI was found in 35% males and 10% females. NSTEMI was present in 14% males and 13% females while 22% males and 6% females had Unstable angina.

Table 6: Distribution of Family history of Coronary Artery Disease (N=100)

Family History of CAD	Percentage
Present	13%
Absent	87%

The data shows most (87%) subjects in this study had no family history of CAD.

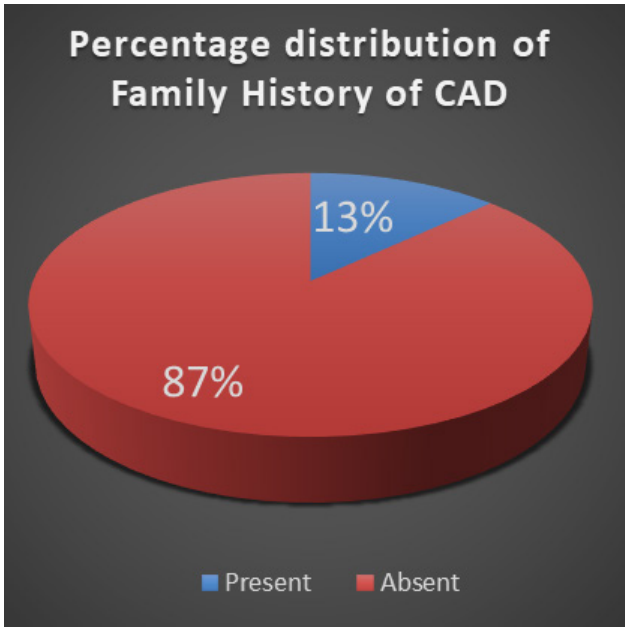

Figure 3: Shows the distribution of Percentage Family History of CAD. There was family history of CAD in 13% patients only.

Table 7: Frequency distribution of Smoking in the study population (N=100)

Smoking	Percentage
Yes	69%
No	31%

The table shows 69% of subjects were smokers while rest were non- smoker.

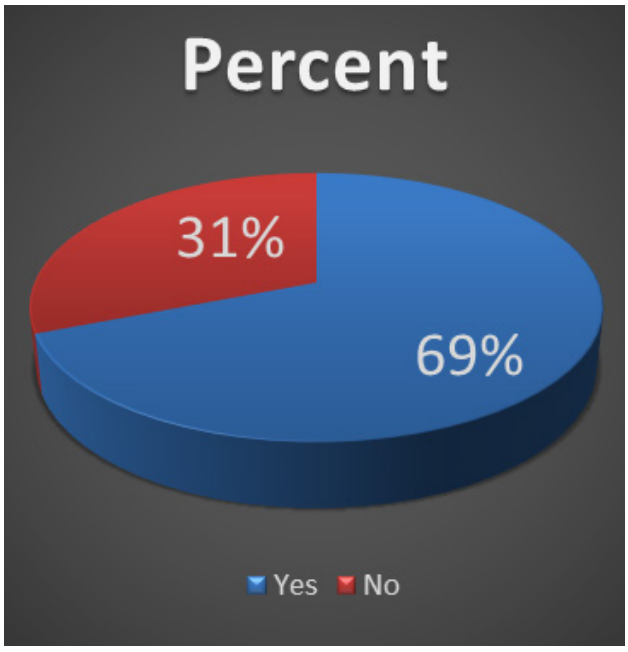

Figure 4: Figure shows the smoking status where 69% were smokers.

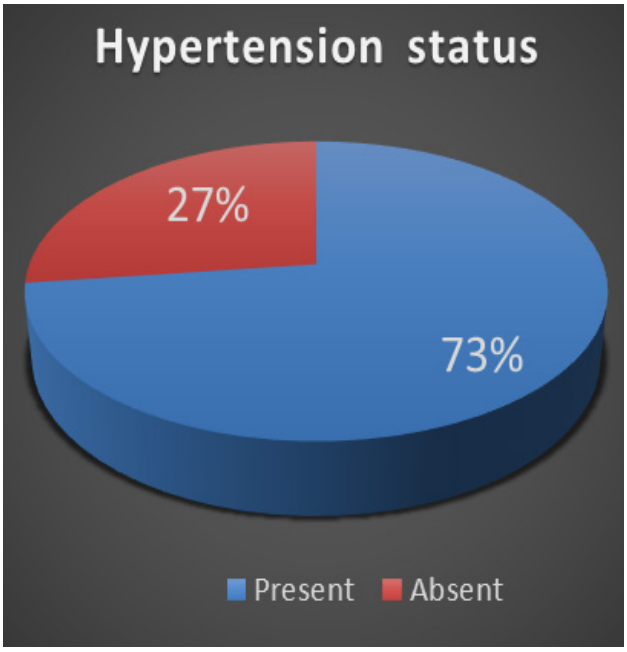

Figure 5 Shows 73% were Hypertensive and 27% were Normotensive.

Table 8: Association between Smoking and Types ACS (N=100)

Types of ACS	Smoking status		Total	X^2	P value
	Yes	No			
NSTEMI	14	13	27	7.6795	P<0.05
STEMI	37	8	45		
Unstable Angina	18	10	28		
Total	69	31	100		

X= Chi square

The above mentioned table 7 illustrates that the association between Smoking and Types of ACS is statistically significant (P value<0.05). It means that smoking influences occurrence of ACS.

Table 9: Frequency distribution of Hypertension in the study patients (N=100).

Hypertension	Percentage
Present	73%
Absent	27%

Table 10: Association between Hypertension and Types of ACS (N=100).

Types of ACS	Hypertension		Total	X^2	P value
	Yes	No			
NSTEMI	15	12	27	8.8066	P<0.02
STEMI	39	6	45		
Unstable Angina	19	9	28		
Total	73	27	100		

The table no 10 shows association between types of ACS and Hypertension was statistically significant, Chi-square (X2) = 8.8066, (P Value < 0.02)

Table 11: Frequency distribution of Diabetes in the study population (N=100).

Diabetes	Percentage
Yes	63%
No	37%

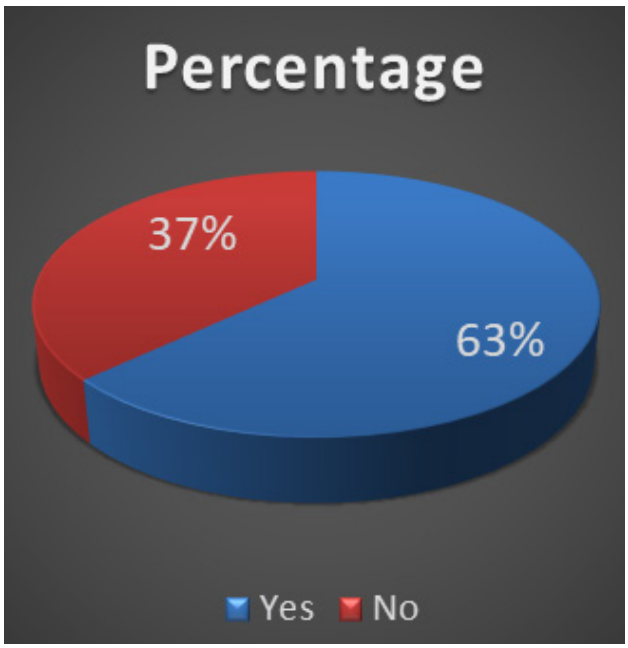

Figure 6: shows there were 63 % diabetics and 37% were non-diabetics.

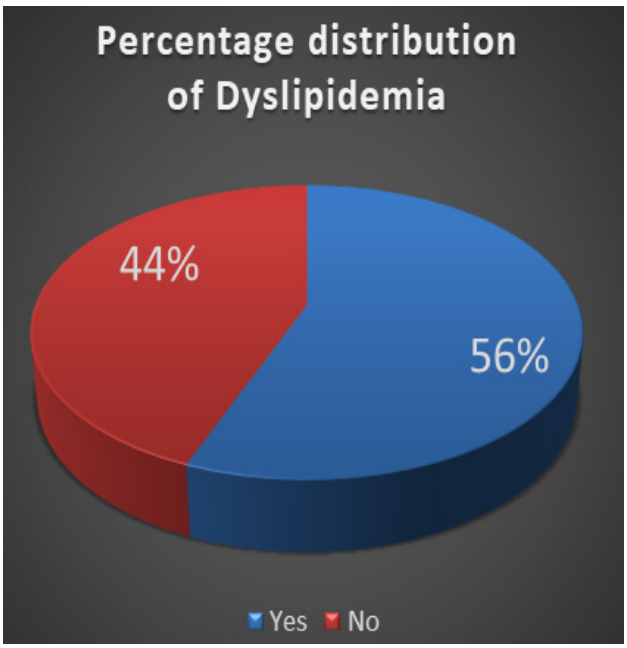

Figure 7 shows 56% of the population had dyslipidemia and 44% had normal lipid status.

Table 12: Association between Diabetes and Types of ACS

Types of ACS	Diabetes		Total	X^2	P value
	Yes	No			
NSTEMI	15	12	27	1.1401	P<0.50
STEMI	28	17	45		
Unstable Angina	20	8	28		
Total	63	37	100		

The above table shows the association between Diabetes and types of ACS was not statistically significant (Chi-square=1.1401, P Value>0.5).

Table14: Association between Dyslipidemia and Types of ACS in the study population (N=100).

Types of ACS	Dyslipidemia		Total	X^2	P value
	Yes	No			
NSTEMI	18	9	27	1.7499	P<0.05
STEMI	23	22	45		
Unstable Angina	15	13	28		
Total	56	44	100		

The table shows association between Dyslipidemia and types of ACS was not statistically significant (Chi-square=1.7499, P value>0.05).

Table 13: Distribution of Dyslipidemia in the study population (N=100).

Dyslipidemia	Percentage
Yes	56%
No	44%

DISCUSSION

Out of total 100 subjects enrolled, mean age was 69.9 ±12.83 years, youngest age was 23 years and eldest was 89 years old. Majority of the population was in the age group ≥ 70 years with only 2% in age group ≤ 40 years. Most common conventional risk factor was Hypertension (73%).

Age and gender: Conventional risk factors are more common in males in this study probably for the reason that they seek more medical facility than female counterparts. Age wise

this study shows consistent rise in prevalence of ACS in age group 20 to 70 years (2% to 54%). Several studies have emphasized significance of age and gender as risk factor of ACS. Ranjit N et al in a similar study have mentioned mean age of 54.69 years with 67 males.(23)

Study conducted by Nanjappa V et al in 2016, mean age of subjects was 60 years, minimum age being 30 years and maximum 87 years.(24)

Family History: Family history doses not seem to be a risk factor in our current study, however, family history in ACS carries causal relationship. This is pointed out by Hoseini K et al in his study of 6399 patients of ACS where he reported that 14.9 % had family history of CAD. 14.9% had verified positive family history and 20.2% and 22.5% had paternal and maternal family history respectively. Therefore, they concluded that positive family history is an important risk factor for ACS.(25)

A study conducted in Nepal by Dali B et al also reported family history in 57% of their study population.(26)

Smoking: Smoking was found in 69% subjects in this study. Occurrence of this risk factor have been stressed by many investigators. Hammoudeh A et al showed the significance of smoking where among patients with ACS, 40% males and 30% females were smokers. In patients without ACS the figure was 11% and 7% respectively and this difference was statistically significant.(27)

Adhikari C et al in 2008 also reported history of smoking in 70% subjects of ACS, however sample size was smaller than our study.(28)

Selim S et al in 2013 also reported smoking to be found in 70% patients of ACS. Our study had statistically significant association between smoking and ACS (P value < 0.05).(21)

Hypertension, Diabetes and Dyslipidemia: In many subjects of ACS, Hypertension, DM and Dyslipidemia occur together as common risk factors. In our present study 73% were Hypertensive, 63% were Diabetic and 56% were dyslipidemic. Association of hypertension with ACS was statistically significant (P value <0.02). Goel P et al in their study of 2656 patients of ACS have demonstrated prevalence of these risk factors but statistical significance was not reached.(29)

Similarly, Hoff J et al in 2003 studied conventional risk factors like HTN, DM and lipid profile in patients of ACS and found statistically significant association as mentioned in our study too.(30)

Hammoudeh A et al in their study had demonstrated Hypertension in 38% and hypercholesterolemia in 19% subjects. Diabetes was prevalent in 64% men and 24% women.(27)

A metanalysis by Dong et al has stressed greater role of Diabetes as risk factor of ACS. They included 19 studies with data for 1085279 individuals and at least 106703 fatal and non- fatal ACS events. In diabetic men and women ACS was relatively higher.(31)

Trivedi et al also reported that hypertension was significant risk factor in ACS in 53% study population. A total of 100 patients were studied out of which 75 were males. Mean age of presentation was 63.12±14.10 years. Smoking, Dyslipidemia and obesity were major risk factors studied. The prevalence of Hypertension, DM and Dyslipidemia was 53%, 24% and 69% respectively.(32)

The role of these conventional risk factors in pathogenesis of CAD clinically reflected in ACS have also been stressed by Nanjappa V et al. The mean age was 64.4±11 years. Diabetes was found in 58.3% in NSTEMI, 65.1% STEMI and 57.1% UA. Hypertension was found in 75% subjects of NSTEMI, 60.2% of STEMI and 71.1% UA.(24)

A study by Adam AM et al in 2017, most frequent risk factor was dyslipidemia (91.2%) followed by hypertension (70.1%), Diabetes was found in 51.2%, family History of CAD was found in 40% and smoking was found in 29.2%.(33)

In the present study 73% of ACS patients had Hypertension, 13% had family History of CAD, 69% were smokers, 60% were diabetics and Dyslipidemia was found in 56%. The prevalent rate of these risk factors vary from the prevalence of those conventional risk factors in the available medical literature as discussed. The discrepancy might be due to study design and various genetic differences.

CONCLUSION

There were 100 patients in the study with mean age of 69.9±12,89 years. Age group ≥70 years had highest percentage of ACS (54%) with lowest in age group ≤ 40 years. Male Hypertension was the most common risk factor for ACS with statistically significant association (P value < 0.02). Male gender (71%) followed by smoking (69%) were other significant risk factors noted along with other comorbid conditions like diabetes, and dyslipidemia. STEMI was found in 45% which was the most common ACS. Considering the significant percentage of modifiable risk factors like HTN, Diabetes, Smoking and Dyslipidemia in ACS, coronary artery disease can be prevented by early intervention and applying various mode of prevention strategies.

LIMITATIONS

This was Uncontrolled Hospital based study conducted in a single center and may not have represented the sample from all parts of local demography. Therefore, result of this study might not be generalized.

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