Cardiovascular risk factors and clinical pattern in young Nepalese population with acute coronary syndrome presenting to a tertiary care center of Nepal

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Abstract

Background and objectives: Cardiovascular disease is a major health problem reaching epidemic proportions. Although Acute Coronary Syndrome (ACS) is an uncommon entity in the young, it constitutes a rising burden in the socioeconomic status of the country because of its impact on the economically productive age group. Early identification and control of the cardiovascular risk factors helps to prevent cases of Myocardial Infarction (MI) in young resulting in reduced health burden. Therefore, we aimed to assess clinical pattern and the prevalence of cardiovascular risk factors in the young and economically productive population of an underdeveloped country to lower the socioeconomic burden.

Methods: A total of 60 patients presenting at the cardiology department of Mannmohan Cardiothoracic Vascular and Transplant Center were included in our study after fulfilling the inclusion criteria. ACS was diagnosed by cardiac enzymes, electrocardiography, and echocardiography and coronary intervention was done in the cardiac catheterization room. Patients were followed up at 1 and 3-months and reassessed clinically and by echocardiography.

Results: Mean age of presentation was 38.55 ± 4.98 (SD) years. Over three-fourth of the patients were male (80%) and nearly three-quarter experienced ST-elevated MI (73%). Smoking was the most prevalent risk factor (67%), followed by dyslipidemia (40%), diabetes (32%), hypertension (30%), and obesity (13%). Most of the patients presented with single-vessel disease (65%), followed by double-vessel disease (18%), triple-vessel disease (12%), left main disease (3%), and minor coronary artery disease (2%).

Conclusions: ACS in underdeveloped country is more common in male and single-vessel disease is the most common clinical pattern of ACS and smoking the most prevalent risk factor.

Introduction

Cardiovascular disease is a major health problem reaching epidemic proportions. The Global Burden of Disease (GBD) study done in 2010 reported that Coronary Artery Disease (CAD) deaths have drastically increased in South Asia by 87% between 1990 to 2010 second only to East Asia which has been predicted to increase a further 50% by 2030[1–3]. Coronary Heart Disease (CHD) related deaths in Nepal reached 34,167 (21% of total deaths) according to 2018 WHO published data,
positioning Nepal at 38th position as per the Age-Standardized Death Rate (184.95 per 100,000 population) [4].

Although Acute Coronary Syndrome (ACS) is an uncommon entity in the young, 5-10% of Myocardial Infarctions (MI) occur in patients <45 years old [5-7]. The occurrence of ACS in young constitutes an important problem for the patients and their treating physicians because of its devastating effect on their more active lifestyle. This also leads to early morbidity and mortality in what should be the most productive years of life. Previous studies have found a high prevalence of smoking, obesity, hyperlipidemia, and a positive family history among young MI patients [5-8].

Most of the existing studies on young ACS patients are from the developed nations and presently there is no contemporary data on the prevalence, risk factors and clinical patterns of such patients in the underdeveloped countries. The young population constitutes the economically active age-group which in turn significantly influences the country’s economy, especially in underdeveloped countries. Population of the 16-45 years age group is considered as the youth population in Nepal as per the Ministry of Youth and Sports. The aim of this study was to assess the prevalence, risk-factors, and clinical patterns in ACS patients <45 years of age from Nepal.

Methods

This study which was carried out at Manmohan Cardiothoracic Vascular and Transplant Center (MCVTC), a tertiary referral hospital in Nepal, from 1st May 2018 to 30th April 2019. Sixty patients who presented to Cardiology Department of MCVTC in the above time period with first episode of ACS or were undergoing coronary angiography, were studied. All the patients provided written informed consent at study entry. The study was approved by Institutional review board. The following pre-specified inclusion and exclusion criteria were applied:

**Inclusion criteria**

- Patient aged <45 years with ACS presenting at Emergency or Outpatient department.

**Exclusion criteria**

- Patient's aged ≥45 years.
- Patient previously diagnosed with ACS.
- Patient with previous history of percutaneous transluminal angioplasty (PTCA) and (coronary artery bypass graft) CABG surgery.
- Patient who did not give written consent for the study.

Dyslipidemia & premature CAD was defined as per ATP III guideline [9], HTN as per JNC 7 guideline [10], diabetes as per ADA guideline [11] and obesity as per Asia Pacific guidelines [12]. Normal vessels were defined as the complete absence of any disease in the Left Main Coronary Artery (LMCA), Left Anterior Descending Artery (LAD), Right Coronary Artery (RCA) and Left Circumflex Artery (LCX) while significant CAD was defined as a diameter stenosis >50% in each major epicardial artery.

**Statistical analysis**

The results are reported as mean (SD) for the quantitative variables and number (%) for the categorical variables. The groups were compared using the Student’s t-test for the continuous variables and the Chi-square test for the dichotomous variables. P-value <0.05 were considered as statistically significant. All the statistical analyses were carried out via Statistical Package for Social Sciences version 20 (SPSS, IL, Chicago Inc., USA).

**Results**

The study included total of 60 young ACS patients, among which majority were male 48 (80%) and 12 (20%) were female. The mean age of presentation was 38.55 (4.98) years. Mean age of male and female patients were 38.08 (5.06) and 40.42 (4.31) years respectively, 46% of patients were around 41-44 years of age and 2 % were around 21-25 years of age. Most common presentation in ACS was ST elevated myocardial infarction (STEMI) in 44 (73%) patients followed by non-ST elevated myocardial infarction (NSTEMI) in 10 (17%) and unstable angina (UA) in 6 (10%). Baseline characteristics are mentioned in Table I.

**Table 1:** Baseline characteristics of the study population (N = 60).

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Mean</th>
<th>Std. Deviation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>38.55</td>
<td>4.98</td>
</tr>
<tr>
<td>Fasting blood sugar (mg/dl)</td>
<td>129.2</td>
<td>44.95</td>
</tr>
<tr>
<td>HbA1C</td>
<td>5.9</td>
<td>1.41</td>
</tr>
<tr>
<td>Creatinine (mg/dl)</td>
<td>0.83</td>
<td>0.17</td>
</tr>
<tr>
<td>Triglyceride</td>
<td>152.4</td>
<td>93.8</td>
</tr>
<tr>
<td>Total cholesterol</td>
<td>158.43</td>
<td>40.69</td>
</tr>
<tr>
<td>HDL</td>
<td>35.0</td>
<td>7.87</td>
</tr>
<tr>
<td>LDL</td>
<td>106.5</td>
<td>34.0</td>
</tr>
</tbody>
</table>

**Risk factors analysis**

A total of 19 (32%) patients were diabetic and 18 (30 %) patients were hypertensive. Smoking was the most prevalent risk factor found in 40 (67%) patients. Dyslipidemia was present in 24 (40%) patients. Family history of premature CAD was present in 4 (7%) of patients. Three (5%) patients had hypercoaguable state in which 1 had protein S deficiency, 1 had protein S & C deficiency, and 1 had protein S deficiency along with hyperhomocystenemia. One (2%) patient had coronary artery anomaly i.e. ectasia of proximal LAD. One (2%) had rheumatoid arthritis and 1 (2%) patient had HIV infection and was taking Anti-Retroviral Therapy (ART) (Table II).

Smoking was significantly higher in male population (75%) compared to female (33%) (p=0.006). Of all the patients that smoked, 9 (23%) had history of smoking >10 packs per year. Dyslipidemia was seen higher in male population 42%
compared to female 33%. Eight patients fulfilled the criteria for obesity as per Asia-Pacific guidelines. There was no significant gender difference in prevalence of dyslipidemia, hypertension, premature CAD & diabetes (Table III).

<table>
<thead>
<tr>
<th>Clinical Risk factors</th>
<th>Frequency</th>
<th>Percent (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Smoking</td>
<td>40</td>
<td>66.7</td>
</tr>
<tr>
<td>Diabetes Mellitus</td>
<td>19</td>
<td>31.7</td>
</tr>
<tr>
<td>Hypertension</td>
<td>18</td>
<td>30.0</td>
</tr>
<tr>
<td>Dyslipidemia</td>
<td>24</td>
<td>40.0</td>
</tr>
<tr>
<td>Family h/o Premature CAD</td>
<td>4</td>
<td>6.7</td>
</tr>
<tr>
<td>Obesity</td>
<td>8</td>
<td>13.3</td>
</tr>
<tr>
<td>Hypercoaguable state</td>
<td>3</td>
<td>5.0</td>
</tr>
<tr>
<td>Coronary artery anomaly</td>
<td>1</td>
<td>1.6</td>
</tr>
<tr>
<td>Connective tissue disorder</td>
<td>1</td>
<td>1.6</td>
</tr>
<tr>
<td>HIV patient</td>
<td>1</td>
<td>1.6</td>
</tr>
</tbody>
</table>

Of 48 male patients, 35 (73%) were STEMI, 9 (19%) were NSTEMI and 4 (8%) were UA. Whereas in 12 female patients 9 (75%) were STEMI, 1 (8%) NSTEMI and 2 (17%) were UA. There was no gender difference in the presentation of ACS and in the number of vessels involved.

**Table III:** Comparison between males and females with risk factors.

<table>
<thead>
<tr>
<th>Risk factors</th>
<th>Male</th>
<th>Female</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Smoking</td>
<td>36</td>
<td>4</td>
<td>0.006</td>
</tr>
<tr>
<td>Dyslipidemia</td>
<td>20</td>
<td>4</td>
<td>0.59</td>
</tr>
<tr>
<td>Diabetes</td>
<td>15</td>
<td>4</td>
<td>0.89</td>
</tr>
<tr>
<td>Hypertension</td>
<td>13</td>
<td>5</td>
<td>0.32</td>
</tr>
<tr>
<td>Premature CAD</td>
<td>4</td>
<td>0</td>
<td>0.30</td>
</tr>
</tbody>
</table>

**Electrocardiography findings**

In this study anterior wall electrocardiogram (ECG) changes (45%) was the most common ECG finding in patients with acute STEMI, followed by inferior wall (28%). Approximately one-third of patients had others changes like ST depression or normal ECG.

**Echocardiographic profile**

During admission, assessment of left ventricle systolic function was done by echocardiography of which 19 (32%) had normal ejection fraction, 16 (27%) had mild left ventricular systolic dysfunction, 23 (38%) had moderate left ventricular systolic dysfunction and 2 (3%) had severe left ventricular systolic dysfunction (Figure 1).

**Angiographic profile**

Out of 60 patients, single vessel disease (SVD) was seen in 39 (65%), double vessel disease (DVD) in 11 (18%), triple vessel disease (TVD) in 7 (12%), left main disease in 2 (3%), and minor lesion was seen in 1 (2%) (Figure 2).

In STEMI, SVD was seen in 32 (72%), DVD in 8 (18%), TVD in 2 (5%), and Left Main disease in 2 (5%). In NSTEMI, SVD was seen in 5 (50%), DVD in 2 (20%), TVD in 2 (20%) and minor lesion in 1 (10%). In UA, SVD was seen in 2 (33%), DVD in 1 (17%) and TVD in 3 (50%) (Figure 3).

Of 48 male patients, 35 (73%) were STEMI, 9 (19%) were NSTEMI and 4 (8%) were UA. Whereas in 12 female patients 9 (75%) were STEMI, 1 (8%) NSTEMI and 2 (17%) were UA. There was no gender difference in the presentation of ACS and in the number of vessels involved.

Of all the risk factors, diabetes was significantly associated
with multi vessel lesion compared to non-multivessel lesion (53% vs 24%; p = 0.03) (Table IV).

On analyzing culprit artery, LAD was found to be the most commonly involved (60%) followed by RCA (23%) and LCX (17%).

**Treatment modalities used in ACS patients**

**Figure 4:** Out of total 44 STEMI patients, of which 36 patients presented within window period and underwent primary intervention. Among those 36 patients, stents were deployed in 32 while POBA was done in 4. In these 4 patients who had undergone POBA 1 was later referred to cardiac surgery for CABG while other 3 were managed medically. Other 8 STEMI patients presented beyond window period of which 5 underwent routine PCI, 2 patients were referred to cardiac surgery for CABG and 1 was was managed medically. Remaining 16 patients of NSTEMI & UA beside 1 all underwent routine PCI during hospital admission.

**Complications**

8% patients developed cardiogenic shock requiring inotropes, while 3% developed venous thromboembolism of which 1 patient underwent emergency embolectomy, 5% developed heart failure which was managed with diuretics and inotropes, 2% had complete heart block requiring temporary and then permanent pacemaker insertion, 2% had significant arrhythmia, 2% developed CIN, 7% developed acute pericarditis which was managed with high dose aspirin and colchicine. There was two mortality (3%) during hospital admission, both of them were female, diagnosed as extensive anterior wall MI in cardiogenic shock (Figure 5).

**Follow up**

During 1 month follow 23 (38%) had Normal left ventricular ejection fraction (LVEF), 12 (20%) had mild left ventricular systolic dysfunction (LVSD), 19 (32%) had Moderate LVSD, 12 (21%) had severe LVSD and 5 (8%) patients were lost to follow up. During 3 months follow up 27 (45%) had Normal LVEF, 16 (28%) had Mild LVSD, 9 (15%) had Moderate LVSD & 1 (2%) had severe LVSD. Further 2 patients were lost to follow up making a total of 7 (12%) (Figure 6).

**Re-admission**

Two patients were readmitted within 3 months duration of which 1 was a case of inferior wall MI with right ventricular extension with moderate LVSD and right ventricular dysfunction, who presented due to Acute Decompensated Heart Failure (ADHF) and was managed with inotropes and diuretics; and the other one was the case of extensive anterior wall MI with HIV undergoing ART, who presented because of late stent thrombosis and was managed by Plain Old Balloon Angioplasty (POBA).

**Discussion**

This is an observational prospective study of 60 patients aged 44 and below admitted with a diagnosis of ACS at the Department of Cardiology, MCVTC. The mean age of patients presenting with ACS was 38.55 ± 4.98 with male predominance which was similar to the study conducted by E. Incalcaterra [13]. In young ACS patients the most common risk factor was found to be smoking (66%) with male predominance (75%) which was also similar in the study done by Zimmerman, et al. where 73% had a history of smoking [13]. Haque, et al. also stated that smoking was most common risk factor (64%) with male preponderance (77%) [14]. So, there’s no doubt that either in old or young smoking is hazardous to health.

**Figure 4:** Treatment modalities in young ACS patients.

<table>
<thead>
<tr>
<th>Risk factors</th>
<th>Multivessel</th>
<th>Non multivessel</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Smoking</td>
<td>14</td>
<td>26</td>
<td>0.69</td>
</tr>
<tr>
<td>Dyslipidemia</td>
<td>10</td>
<td>14</td>
<td>0.26</td>
</tr>
<tr>
<td>Diabetes</td>
<td>10</td>
<td>9</td>
<td>0.03</td>
</tr>
<tr>
<td>Hypertension</td>
<td>9</td>
<td>9</td>
<td>0.07</td>
</tr>
<tr>
<td>Premature CAD</td>
<td>2</td>
<td>2</td>
<td>0.46</td>
</tr>
</tbody>
</table>
The other risk factors besides smoking are diet rich in cholesterol, sedentary lifestyle, diabetes, hypertension, and paternal history of cardiovascular disease [15,16]. This illustrates the need to increase awareness among the young population and evaluate the risk factors among those with family history or those at high-risk. These simple measures can make a large difference in preventing the occurrence of MI in young.

In 40% of young ACS patients dyslipidemia was present which was comparable to other existing studies which showed a similar prevalence of 47% (Moccetti and Malacrida, et al. 1997), 42% (Dwiwedi, et al. 2000), and 42% (Dani, et al. 2003) [17–19].

Another risk factor, obesity was present in 13 % of our cases which is similar to that reported by Siwach, et al. (14%) and Singh, et al. (16%) [20,21]. The disproportionate rise in the prevalence of heart disease among certain ethnic groups like people of Asian Indian origin has become a study of great interest. These people in very young age tends to get ACS and more complex coronary artery abnormalities probably due to proliferation of vascular endothelial cells and activation of inflammatory response promoting with endothelial dysfunction and atherosclerosis [22–25].

Diabetes and hypertension were also found to be higher (32% and 30% respectively) in younger generation of our population and diabetes was significantly associated with multivessel disease. In the study done by Paudel, et al. 45% were hypertensive with 16 % diabetic and diabetes was associated with multivessel disease and poor prognosis [26]. Many other studies have reported hypertension in 30–50% and diabetes in 20–30% of individuals with young ACS [27–32].

The family history of CAD is associated with increased risk of young ACS and strengthened the belief of important risk factor for CAD. In patients with positive family history it had been reported that risk of developing ACS was more than a decade earlier compared to those without a family history of CAD [33]. In our study, 7 % of the young ACS presented with a positive family history of CAD. There are many genomic studies suggesting different chromosomal abnormalities contributing to the onset of ACS in young [34].

Apart from the classical risk factors for CAD, young patients are likely to have other risk factors like coagulation abnormalities (thrombophilia, Protein C and S deficiency) and vasculitis. In our study only 3 patients (5%) had hypercoagulable state and 1 (2%) had connective tissue disorder whereas in the study conducted in Nepal by Laudari, et al. 5 patients (13%) were found to have coagulation abnormalities [35].

Angiographic pattern has been analyzed in different studies and in our study, SVD was the most common angiographic finding (65%), while LAD was the most common infarct-related artery (60%). In a study done by Tambyah, et al. on MI in young, all patients had evidence of atherosclerotic disease, majority had single vessel disease and LAD was the most common infarct related artery [36]. Similarly, in the study of Colkesen, et al. involving young STEMI patients it was found that LAD was the most common vessel involved followed by RCA and LCX [37].

In our study anterior wall STEMI was about 45% followed by 28% inferior wall STEMI, and 27 % of patients had no ECG changes. Alappat, et al. (56% anterior wall, 38% inferior wall and 6% others) and Tambyah, et al. both studies demonstrated that anterior wall MI (AWMI) was the most common STEMI in young patients [36,38].

AWMI with severe LV systolic dysfunction was the antecedent cause of death in 3% in our study during admission period. Stone, et al. quoted that young patients with anterior infarction had a substantially worse in-hospital and follow-up clinical course evidenced by a larger infarct size, higher incidence of heart failure, LV dysfunction and ventricular arrhythmia [38].

The prognosis of young ACS depends not only on diagnosing early and treating adequately but also on identifying, preventing and treating the risk factors at primary and secondary level. Heart failure is a most common and serious complication after MI which was found in 14%, 18%, and 9% in the series of Sarr, et al. Al–Khadra, et al. and Kanitz, et al. respectively [40–42]. However, in our study only 5% had heart failure. A relationship between age and heart failure has been reported by Magid et al with a greater frequency of occurrence in the elderly compared to young subjects [43].

Limitations

This study has effectively highlighted the clinical profile of young MI patients, but there were few limitations. It was conducted in a single center, which may not be representative of whole population. As no control group was used, the risk of each factor could not be analyzed statistically. Larger studies involving multiple centers are required focusing on the risk factors and management of young MI.

Conclusion

From this study we observed that CAD is a major health challenge. Young patients diagnosed with ACS have some important differences that should be appreciated. The most important modifiable risk factor is smoking and dyslipidemia. In our study population, there was male preponderance. STEMI was the most common presentation of ACS. Single vessel disease was the most common CAG finding irrespective of type of ACS and LAD was found to be most commonly involved artery. Diabetic patients had more multivessel CAD compared to non-diabetics.

A careful search for other contributing risk factors is necessary as progressive atherosclerosis may not always be the underlying pathophysiology. If timely managed, young patients with AMI have promising inhospital prognosis. In order to decrease long-term morbidity and mortality from CAD, young patients should be concerned on preventive measures like knowledge about risk factors, physical exercise and healthy diet.
Acknowledgement

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References


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