A study of clinical profile of low risk Acute Coronary syndrome in a teaching tertiary care hospital - A prospective observational study

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Abstract
The study is chosen to help understand the current state of knowledge regarding the clinical profile of low risk Acute Coronary Syndrome (ACS) and to generate data for future recommendations. 100 patients presenting to the Emergency Department (ED) with acute onset chest pain with normal electrocardiogram (ECG) and negative cardiac biomarkers and with alternative diagnosis less likely were enrolled for a prospective observation and evaluation. All the patients underwent periodic biomarkers and serial ECGs. Endpoint of the study was either the diagnosis of ACS or a cardiologist examination confirming a low risk ACS. Out of 100 patients 4 patients subsequently were diagnosed with ACS and managed accordingly. Factors such as age < 40 years (sensitivity 100% with CI 94.48%-100%, specificity 11.43%, PPV 67.71%, NPV 100%, accuracy 69%), female sex (sensitivity 66.67% with CI 56.31%-75.96%, specificity 25%, PPV 95.52%, NPV 3%, accuracy 65%), sharp nature of pain (sensitivity 9.38% with CI 4.38%-17.05%, specificity 100%, PPV 100%, NPV 4.4%, accuracy 13%) and pain defined as slightly suspicious by the examining physician (sensitivity 91.67% with CI 84.24%-96.33%, specificity 100%, PPV 100%, NPV 33.33%, accuracy 13%) were associated with high likelihood of low risk ACS. Pulse, respiration and saturation of all the patients were well maintained. Although heart rate has been positively correlated with ACS in previous studies our study showed that it has little correlation in low risk ACS cases. Only variable which had variance was systolic blood pressure with a standard deviation of 16. The mean systolic blood pressure was 127.62 mm of Hg.

Keywords: low risk, low probability acute coronary syndrome, clinical profile.

Introduction
Acute Coronary Syndrome (ACS) is one of the most common presentations to the emergency departments. Given that Indians have a mean onset of coronary artery disease (CAD) 5–10 years earlier than the western world, the burden of chest pain visits to EDs in India is likely much higher. The mean age of presentation of acute myocardial infarction in Indians is 50 years. As per the WHO factsheet 2017 Ischemic heart disease and stroke are the world’s biggest killers, accounting for a combined 15 million deaths in 2015. These diseases have remained the leading causes of death globally in the last 15 years. Approximately 10% of patients presenting to the ED with chest pain are ultimately diagnosed with ACS. In the resource constraint Indian scenario the biggest dilemma of emergency physicians is to
successfully rule in patients without high probability ACS. Although guidelines for management of low risk chest pain have been issued in 2017, these are largely limited by the lack of validation studies and paucity of data related to the Indian patients.\(^4\)

By comparing the demographic characters, history, electrocardiogram, cardiac enzyme levels, 2D ECHO findings and if possible coronary angiogram and treadmill findings the study will help the emergency physician to better risk-stratify the patients, and determine which patients may require further diagnostic studies, focused management, and who may be safely discharged home.

Amsterdam et al., defines patients at low risk for ACS as “those with no hemodynamic derangements or arrhythmias, a normal or near normal ECG, negative initial cardiac injury markers, and low likelihood of signs and symptoms suggestive of ACS.”\(^5\)

As with the western studies, even the Indian studies point that increasing age is a definite risk factor for developing acute coronary syndromes.\(^6\)\(^-\)\(^8\) It may be construed that younger age group may be taken as significant attribute in the low risk ACS group. Similarly because of the inherent protection provided by estrogen to female and the lower incidence of risk factors (smoking, alcoholism, etc), females are generally at low risk in acute coronary syndromes.\(^9\)

Serial testing of serum biomarkers of acute myocardial damage is essential to confirm the diagnosis of myocardial infarction. In a multicenter evaluation, it was demonstrated that a 0-hour and 3-hour hsTnT assay using less than 6 ng/L provides a safe and early rule-out for AMI and identified a large cohort of patients with suspected ACS at very low risk of 30-day acute coronary event.\(^10\)

But this test has not been done universally and in a resource constraint scenario like India the availability is scarce.

**Material and Methods**

A prospective observational study to evaluate the clinical profile of patients presenting to emergency department with low risk ACS at a tertiary health care center is done. IEC clearance for the study was obtained before the start of study.

**Inclusion Criteria**

All Adult patients (above 18 years of age), with acute onset anginal chest pain and Electrocardigrams normal or with non characteristic changes and with low probability by biomarkers or history and clinical examinations and patients willing to undergo 2D Echocardiography and further testing are included.

**Exclusion Criteria**

Trauma cases, patients with obvious other diagnosis like musculoskeletal, gastritis, etc and with other acute co-morbidities like Fever, Stroke, Deep Venous Thrombosis, Pulmonary Embolism, Renal failure and Intubated and ventilated patients are excluded.

**Statistical Methods**

The data was entered and analyzed in Microsoft excel. Continuous variables were depicted with arithmetic mean and standard deviation, for normally distributed data. Median was used for non-normally distributed data, while categorical variables such as age groups, sex, etc were expressed as frequencies and percentages.

**Material**

All the routine equipment available in emergency department along with 2D ECHO, Biomarker analyzer, CT angiogram, Treadmill, etc was utilized. As this was a completely observational study the normal course of treatment of patients was studied. All the costs regarding the treatment were born by patients themselves.

**Limitations**

a. The small sample size was the major limitation of the study.

b. Owing to the financial constraints a lot of patients were not enrolled in the study as the patient considered the condition to be of lower priority

c. This study was limited to one study center.

d. Long term follow-up of the patients was not done being an ED centric study.
Results

The majority of the patients attending to emergency department with chest pain and categorized as having low risk acute coronary syndrome consisted of the age group 21 to 30 years (37%). The median age was 35 years with a SD of 13.21. 4 patients turned out to be of acute coronary syndrome later in the study. Age above 40 years included these patients. Grouping the patients in age group of less than 40 years and age above 40 years clearly delineates the at risk group. Age < 40 years had a sensitivity of 100% with CI 94.48%-100%, specificity 11.43%, PPV 67.71%, NPV 100%, accuracy 69% for predicting low risk ACS. 67 patients were male and 33 patients were female indicating male patients were more likely to present with chest pain to the emergency department (sensitivity 66.67% with CI 56.31%-75.96%, specificity 25%, PPV 95.52%, NPV 3%, accuracy 65%). Also the prevalence of cardiovascular disease is more among the male patients due to the presence of risk factors more common in them. Occupation wise the majority of the female presenting with chest pain and low probability acute coronary syndromes were housewives. This finding is consistent with the local demographics of the area as families consisted of nonworking housewives. Laborer men were the majority among men and consisted 24 % of the total sample of study. In the young age group students predominated the scene with 17 % of the total sample. 42% of the patients were thin built and 46% were of moderate built. 12% of the patients were obese. Out of the 100 patients 21 were smokers and 20 were current tobacco chewers.

The average duration of presentation of chest pain was 15.23 hours with standard deviation of 19.85 hours. 91 patients in the study complained of dull aching type of chest pain while 9 patients complained of sharp pain. Most of the patients (93) had left sided chest pain. 5 patients complained of right sided pain and 2 complained of central chest pain. 68 patients had moderate severity pain. 27 patients had mild pain and 5 complained of severe chest pain. 91 patients complained of pain increasing with exertion. According to the presentation of the patient they were categorized on the suspicion of the pain into slightly suspicious, moderately suspicious and highly suspicious. 88 patients were having pain which was slightly suspicious of ACS, 7 had moderately suspicious pain and 5 had highly suspicious nature of pain. Sharp pain had a sensitivity of 9.38% with CI 4.38%-17.05%, specificity 100%, PPV 100%, NPV 4.4%, accuracy 13%. Pain defined as slightly suspicious by the examining physician had a of sensitivity 91.67% with CI 84.24%-96.33%, specificity 100%, PPV 100%, NPV 33.33%, accuracy 13% for low risk ACS. In the patients diagnosed with acute coronary syndrome on prospective evaluation the only vital which correlated with ACS was the blood pressure. Both the systolic and diastolic blood pressure was high in these patients. 83% of the patients had normal ECG. 11% of the patients had non-specific ST-T changes and 6% of patients had ST depressions. A normal 2DECHO was defined as no evidence of ischemic changes and no acute changes. Abnormal 2DECHO was defined as wall motion abnormalities suggestive of ischemic changes. Trivial and chronic abnormalities were considered as normal. Out of the 100 patients 98 patients had normal 2DECHO. One patient had inferior wall hypokinesia and the other had antero-septal wall hypokinesia. Both the patients were later diagnosed as NSTEMI. Other two patients who were later diagnosed as ACS had normal 2DECHO.

Discussion

A cross sectional observation study was done with a sample size of 100 patients presenting with low risk ACS to an ED of a teaching tertiary care centre in an urban area. Patients selected for enrollment in the study included those with chest pain and negative initial ECG and biomarkers. They were studied with serial ECGs and biomarkers to rule out ACS. Patients with non-cardiac chest pain were excluded from the study.

Age was the most significant non-modifiable risk attribute in our patients. Age less than 40 years has
100% sensitivity for ruling in low risk acute coronary syndrome. All the patients in the study less than 40 years of age were not diagnosed as acute coronary syndrome later during the evaluation in hospital. Our findings correlate well with other studies used to rule out acute coronary syndromes (6,8).

As per the previous studies male sex conferred an increased risk of cardiovascular disease. Our study also presents similar figures with 67% patients presenting with chest pain being male. They also had more risk factors as smoking and tobacco use and also had more co-morbidity. 3 of the four patients who were later diagnosed with ACS were males. It can be easily inferred that male sex gives a higher probability of acute coronary syndromes and also in the low risk group they form the majority. (9)

The mean duration of pain was 15.23 hours. Duration of pain had no correlation with diagnosis of ACS later during the stay in hospital. All the patients who were later diagnosed with ACS had their Troponin raised on the repeated blood samples taken after 6 hours irrespective of the time of onset of pain. Sharp nature of pain however had 100% specificity for low risk ACS. The sensitivity was low around 9% and a PPV of 100% with accuracy of 13%. All other characters of pain showed no significance with probability of ACS. As all the patients had varied presentation and the site, severity association with exertion were could not be correlated well with low risk ACS turning into ACS. This is in contrast to previous findings as in one study conducted by Holmberg et al and reported in BMC Cardiovascular Disorders; severity of chest pain was directly proportional to the diagnosis of ACS. (11)

As the sample size was small in our study we need more number of patients to comment on such correlation.

| Parameter                        | N  | %  |
|----------------------------------|----|----|
| Age                              |    |    |
| Age <40 years                    | 65 | 65 |
| Age >40 years                    | 35 | 35 |
| Sex                              |    |    |
| Male sex                         | 67 | 67 |
| Female sex                       | 33 | 33 |
| Occupation                       |    |    |
| Housewife                        | 27 | 27 |
| Driver                           | 7  | 7  |
| Office                           | 13 | 13 |
| Laborer                         | 24 | 24 |
| Student                          | 17 | 17 |
| Cook                             | 2  | 2  |
| Plumber                          | 1  | 1  |
| Nurse                            | 1  | 1  |
| Farmer                           | 1  | 1  |
| Guard                            | 3  | 3  |
| Mechanic                         | 1  | 1  |
| Retired                          | 3  | 3  |
| Smoking                          |    |    |
| Yes                              | 21 | 21 |
| No                               | 79 | 79 |
| Built                            |    |    |
| Thin                             | 42 | 42 |
| Moderate                         | 46 | 46 |
| Obese                            | 12 | 12 |
| Duration of pain                 |    |    |
| 3                                | 15 | 15 |
| 6                                | 36 | 36 |
| 12                               | 25 | 25 |
| 24                               | 7  | 7  |
| 36                               | 4  | 4  |
| 48                               | 6  | 6  |
| 72                               | 7  | 7  |
| Quality of pain                  |    |    |
| Dull                             | 91 | 91 |
| Sharp                            | 9  | 9  |
| Location of pain                 |    |    |
| Left sided                       | 5  | 5  |
| Right sided                      | 93 | 93 |
| Central                          | 2  | 2  |
| Severity of pain                 |    |    |
| Mild                             | 27 | 27 |
| Moderate                         | 68 | 68 |
| Severe                           | 5  | 5  |
| Associated with exertion         |    |    |
| Yes                              | 9  | 9  |
| No                               | 91 | 91 |
| Suspicousness of pain            |    |    |
| Slightly                         | 88 | 88 |
| Moderately                       | 7  | 7  |
| Highly                           | 5  | 5  |
| ECG changes                      |    |    |
| Normal                           | 83 | 83 |
| Non-specific                     | 11 | 11 |
| ST depression                    | 6  | 6  |
| 2DECHO                           |    |    |
| Normal                           | 98 | 98 |
| Abnormal                         | 2  | 2  |

Table 1: Shows Baseline Characteristics of the study population
Table 2: Statistical data of clinical profile of patients with low risk ACS presenting to ED

| Variable                        | Sensitivity (95% CI) | Specificity (95% CI) | PPV (95% CI) | NPV (95% CI) | LR+ (95% CI) | LR- (95% CI) |
|---------------------------------|----------------------|----------------------|--------------|--------------|--------------|--------------|
| Age less than 40 years          | 100.00% (94.48% - 100%) | 11.43% (3.2% - 26.74%) | 67.71% (65.05% - 70.25%) | 100% | 1.13 (1.1-1.27) | 0 |
| Male sex                        | 66.67% (56.31 - 75.96%) | 25% (0.63% - 80.59%) | 95.52% (92.25% to 97.45%) | 3.03% (0.56% to 14.87%) | 0.89 (0.50 to 1.59) | 1.33 (0.24 - 7.45) |
| Dull pain                       | 90.62% (82.95% to 95.62%) | 0% (0.00% to 60.24%) | 95.60% (95.33% to 95.87%) | 0 | 0.91 (0.85 - 0.97) | 0 |
| Sharp pain                      | 9.38% (4.38% - 17.05%) | 100% (39.76% - 100%) | 100% | 4.4% (4.13% - 4.67%) | 0 | 0.91 (0.85 - 0.97) |
| Slightly suspicious pain        | 91.67% (84.24% - 96.33%) | 100% (39.76% - 100%) | 100% | 33.33 (20.48% - 49.26%) | 0 | 0.08 (0.04 - 0.16) |

Table 3: Mean and SD of vitals of patients

| Vitals | Mean | SD |
|--------|------|----|
| Temp   | 97.22 | 0.612661 |
| Pulse  | 80.76 | 11.5742 |
| SBP    | 127.62 | 16.0068 |
| DBP    | 82.2 | 8.969083 |
| RR     | 16.9 | 2.236068 |
| SpO2   | 98.19 | 1.709717 |

Fig 1. Distribution of patients as per the ECG changes

Fig 2. Distribution of patients as per their age groups

Fig 3. Distribution of patients as per their Occupation
Suspiciousness of pain as per the clinical gestalt of the treating physician did show correlation of finding patients with low risk ACS. With slightly suspicious pain taken as a marker of low risk ACS, the sensitivity comes to 91.7% and is 100% specific. Pulse, respiration and saturation of all the patients were well maintained. Although heart rate has been positively correlated with ACS in previous study our study showed that it has little correlation in low risk ACS cases. The mean heart rate was 80.76 and the SD was 11.57. Only variable which had variance been the systolic blood pressure with a standard deviation of 16. The mean systolic blood pressure was 127.62. All the 4 patients who were later diagnosed with ACS were having systolic blood pressure of more than or equal to 140. They also had a higher diastolic blood pressure. These results are in accordance with previous studies. In a review article presented by Rajeev Gupta, et al 2018 the most important risk factor for cardiovascular disease in India was hypertension. The study was based on the statistics provided by Government of India and Registrar General of India and was based on Census of India.

Conclusions
Age was the most significant non-modifiable risk attribute in our patients. The sensitivity of age criteria less than 40 years is 100% with 11.43% specificity for patients with normal ECG and negative cardiac markers in patients considered to be low risk acute coronary syndrome. Sex is also a major determinant for cardiovascular disease. Considering the time required to detection of biomarkers in blood (troponin I), and all the patients who turned out to be having acute coronary syndrome with positive tests after 6 hours of admission it may be construed that all patients regardless of duration of pain should undergo a second marker assay to completely rule out acute coronary syndrome. As per our study sharp character can easily rule out ACS in patients with negative biomarkers and normal initial ECG. Patients with slightly suspicious pain can be characterized as low risk in presence of no characteristic ECG changes and negative cardiac markers.

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Conflict of Interests
None declared.

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