

**ADDIS ABABA UNIVERSITY
COLLEGE OF HEALTH SCIENCE
SCHOOL OF MEDICINE**



**DEPARTMENT OF EMERGENCY MEDICINE
RESEARCH THESIS ON
ASSESEMENT OF CLINICAL PROFILE AND OUTCOME OF PATIENTS
WITH ACUTE CORONARY SYNDROME IN TIKUR ANBESSA AND
AaBET HOSPITALS, ADDIS ABEBA, ETHIOPIA.**

**BY
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JULY, 2018

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Declaration

I, the undersigned, declare that this is my original work and that all sources of materials used for this thesis are duly acknowledged.

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TABLE OF CONTENTS

LIST OF TABLES	VII
LIST OF FIGURES	VIII
LIST OF ABBREVIATIONS AND ACCRONOMYS	IX
ABSTRACT	X
1.INTRODUCTION	1
1.1Background	1
1.2Statement of the problem	2
1.3Significance of the study	3
2.LITERATURE REVIEW	4
2.1 Burden of disease	4
2.2 Socio demographic data	4
2.4 Clinical presentation	6
2.5 Class of ACS	6
2.5 In-hospital mortality	7
2.6 Predictors of in-hospital mortality	7
3.OBJECTIVES	8
3.1 General objective	8
3.2 Specific objective	8
4.METHODOLOGY	9
4.1 Study Area and Period	9
4.2 Study design	9
4.3 Source Population	10
4.4 Study Population	10
4.5 Inclusion and Exclusion criteria	10
4.6 Sample size determination	10
4.7 Methods of Data Collection	10
4.8 Variables	11
4.8.1 Dependent variables	11
4.8.2 Independent variables	11
4.9 Data Collection	11
4.10Data Quality Control	11

4.11 Data Analysis and interpretation	12
4.12 Ethical considerations	12
4.13 Dissemination of the result	12
4.14 Operational definitions	13
5. RESULTS	15
5.1 Socio-demographic characteristics	15
5.2 Clinical presentation	15
5.3 Duration of symptom from onset to presentation to the hospital	16
5.4 Risk Factors	17
5.5 Class of diagnosis	18
5.6 Initial assessment and investigations	19
5.7 Treatment commenced during hospitalization	21
5.8 Treatment outcome and major in-hospital events	22
5.9 Predictors of in-hospital mortality	23
6. DISCUSSION	25
7. LIMITATION OF THE STUDY	28
8. CONCLUSION	29
9.RECOMMENDATION	30
REFERENCES	31
ANNEX	35

LIST OF TABLES

Table 1: Duration from onset of symptoms to Emergency visit in relation to type of ACS in Tikur Anbessa and AaBET hospitals, Addis Ababa Ethiopia, 2016-2018	17
Table 2: Identified Risk factors for Acute Coronary Syndrome on ACS patients admitted to Tikur Anbessa and AaBET hospitals Addis Ababa Ethiopia, 2016-2018	18
Table 3: Intial assement ,class of kliip and laboratory investigation for ACS patients admitted in Tikur Anbessa and AaBET Hospitals, Addis Ababa ,Ethiopia, 2016-2018.....	21
Table 4: Medical treatment commenced during hospital stay for Acute Coronary Syndrome patients in Tikur Anbessa and AaBET Hospitals Addis Ababa, Ethiopia, 2016-2018	22
Table 5: Predictors of in-hospital mortality for Acute Coronary Syndrome patients admitted in Tikur Anbessa and AaBET hospitals, Addis Ababa Ethiopia, 2016-2018.....	24

LIST OF FIGURES

Figure 1 Frequency distribution of acute coronary syndrome symptoms of patients with ACS in Tikur Anbessa and AaBET hospitals, Addis Ababa Ethiopia, 2016-2018.....	16
Figure 2 Class of diagnosis for Acute Coronary Syndrome patients in patients admitted with ACS Tikur Anbessa and AaBET hospitals, Addis Ababa Ethiopia, 2016-2018	19
Figure 3 In-hospital mortality of Acute Coronary Syndrome patients admitted in in Tikur Anbessa and AaBET Hospitals, Addis Ababa, Ethiopia, 2016-2018	23

LIST OF ABBREVIATIONS AND ACCRONOMYS

A.A: Addis Ababa

AAU: Addis Ababa University

AHA: American Heart Association

CAD: Coronary Artery Disease

ACS: Acute Coronary Syndrome

STEMI: ST Segment Elevated Myocardial Infarction

NSTEMI: Non ST Segment Elevated Myocardial Infarction

UA: Unstable Angina

SPSS: Statistical Package for Social Science

CABG: Coronary Artery Bypasses Graft

PCI: Percutaneous Coronary Intervention

Tpa: Tissue Plasminogen Activator

LMWH: Low Molecular Weight Heparin

UFH: Unfractionated Heparin

TASH: Tikur Anbessa Specialized Hospital

WHO: World Health Organization

ABSTRACT

Background: Coronary artery disease (CAD) is the leading cause of mortality and morbidity in the world. Although no countrywide study has been done on cardiovascular disease (CVD) in Ethiopia some hospital based studies have shown the incidence of CVD is progressively increasing.

Methodology: A retrospective cross sectional study was conducted on the clinical profile of patients with Acute Coronary Syndrome (ACS) In Tikur Anbessa and AaBET hospitals using a structured questionnaire from January 2016 to February 2018. The data were entered, analyzed and interpreted using SPSS version 20 software.

Result: Of 142 patients with ACS, 62 (48.6%) were diagnosed as STEMI. The mean age was 57.5 ± 12.09 years. The average time from onset of ACS symptoms to presentation in the emergency department was 2.4 days (61.96 hours) ± 48.85 . In about 101 (71.1%) patients, hypertension was identified as a risk factor for development of ACS. Nearly fifteen percent (14.8 %) of ACS patients in Tikur Anbessa and AaBET hospitals were either Killip class III or IV. The in-hospital mortality was 9.8%. Predictors of inhospital mortality in Tikur Anbessa and AaBET hospitals included female sex ($P=0.016$), time from symptom onset to presentation ($P=0.04$), being Killip class III and IV ($P=0.001$), and STEMI diagnosis ($P=0.018$).

Conclusion: Patients with ACS have delayed presentation to the hospital from onset of symptoms. Patients had similar risk profiles with the developed world, but have higher mortality. Being female, delayed presentation, having STEMI, and higher Killip class was found to be independent predictors of in hospital mortality in Tikur Anbessa and AaBET Hospitals.

Key words: Acute coronary syndrome, Ethiopia, Emergency department

1. INTRODUCTION

1.1 Background

Coronary artery disease (CAD) is the leading cause of mortality and morbidity in the world and acute coronary syndromes (ACS) is the commonest causes of morbidity and mortality in patients with coronary artery disease (3). Acute coronary syndrome (ACS) is a term used to describe a range of condition (acute myocardial ischemia and/or infarction) associated with an abrupt reduction in coronary blood flow (1).

According to the World Health Organization (WHO), cardiovascular diseases (CVD) caused 17.7 million deaths, accounts for 31% of all global deaths being the leading cause of death globally. An estimated 7.4 million deaths were due to coronary heart disease (11). Coronary heart disease is the second leading cause of death in both men and women in Europe, accounting for 21% and 22% of all deaths, respectively (12). Every sixth man and every seventh woman in Europe will die from myocardial infarction (12).

Patients with acute coronary syndrome present with a variable symptoms of which chest pain is the main chief complaint. (6). some patients present with less-typical symptoms, such as nausea/vomiting, shortness of breath, fatigue, palpitations or syncope (4).

Common identified risk factors for ACS are obesity, smoking, use of cocaine, abnormal lipid profile, hypertension, diabetes mellitus, sedentary lifestyle, family history of coronary artery disease (first degree relative: male < 45 years, female < 55 years), older age, sex (male more than female), prior manifestation of CAD (previous myocardial infarction (MI), PCI (percutaneous coronary intervention), coronary artery bypass graft (CABG surgery) (2).

For long, Sub Saharan Africa has suffered from communicable diseases, but nowadays with changes in the lifestyle, the westernization of the food practices, the increasing prevalence of diabetes mellitus and hypertension, epidemiologic transition has occurred. As result sub Saharans are facing a double disease burden (13).

1.2 Statement of the problem

According to the World Health Organization, cardiovascular disease will be the leading worldwide cause of morbidity and mortality by the year 2020, and developing countries will be a major contributor to this increase (37).

For long, Africa, including Ethiopia has suffered from communicable diseases. Globalization and the progressive economic growth of the country has exposed the population to more sedentary and unhealthy lifestyle (13). As a result, Ethiopia is facing a double disease burden.

The prevalence of the risk factor for ACS in Ethiopia is progressively increasing. For eg. A population-based prevalence study conducted in 2009 in Addis Ababa, Ethiopia on hypertension, reported a 31.5% and 28.9% prevalence among males and females respectively (2). Another study done in Gonder in 2012 showed that, the overall prevalence of hypertension was 28.3%, of whom more than a third (37.0%) did not know they had hypertension (8).

In addition, a community based comparative cross-sectional study conducted in Ethiopia showed that, the prevalence of diabetes mellitus was 3.3%; while it was 2.0% for rural and (4.6%) for urban dwellers (10). Another community based comparative study done in Gondar found that the prevalence of diabetes mellitus among adults aged 35 years and above was 3.6%, while it was 5.1% for urban and 2.1% for rural dwellers. The majority (69%) of diabetic cases were newly diagnosed; with the highest proportion (82.6%) in rural residents (7).

Although there is no nationwide study regarding the prevalence of ACS, one study done in our country at Tikur Anbessa hospital showed Cardiovascular disease has increased steeply over the past thirty years. In the last one decade, admissions for acute coronary syndrome, heart failure and stroke in the medical ICU increased from 22% in 1981/82 to 58% in 2011/12 (15). According to this study ACS was the first leading cause of admission from cardiovascular cases and the third leading cause of death in medical ICU of TASH with a case fatality rate of 15.8% (15).

In Ethiopia, although there is no formal registry for ACS and little is known about clinical profile, prevalence and outcome of patients, a retrospective study was conducted at Addis Cardiac Hospital, Addis Ababa, Ethiopia (private hospital), which showed that, 83% were males. ACS was the clinical diagnosis in 161 (53.7%) of patients, of which 100 patients (33.3% of the total) had ST segment elevation myocardial infarction (STEMI) (5).

1.3 Significance of the study

The study will be first of its kind to be done in two emergency hospitals of Addis Ababa. This study was mainly focused on the clinical presentation, the average time from ACS symptom onset to presentation, possible risk factors, emergency management and outcome of patients presented to ED.

It can be used to advocate for adopting standard treatment and will help us to improve the service and to design prevention strategies of ACS in Ethiopia.

2. LITERATURE REVIEW

2.1 Burden of disease

Africa is home to more than one billion people, and is a major contributor to the global burden of CVD .(28) In 2013, an estimated 1 million deaths were attributable to CVD in sub-Saharan Africa alone, which constituted 5.5% of all global CVD-related deaths and 11.3% of all deaths in Africa. CVD-related deaths contributed to 38% of all no communicable disease-related deaths in Africa, reflecting the growing threat of both no communicable disease and CVD.(29) CHD by itself is the single most common cause of death in Europe: accounting for 1.8 million deaths in Europe each year. Over one in five women (22%) and one in five men (20%) die from the disease (17).

2.2 Socio demographic data

Elderly individuals are at higher risk of developing ACS. Consistent study reports have concluded that older patients have an increased prevalence of multiple risk factors. According to a study done in Government Medical College, Haldwani, Uttarakhand, India Mean age of presentation was 55.86 ± 13.4 years (18). A similar study done in South African Asian Indian Patients a mean age of presentation was 54.6 ± 10.9 years (19). According to study done in Qatar More than 70% patients with ACS were in the age group of 41 to 60 years of age (20). Similarly According to Ladysmith Provincial Hospital, South Africa study the mean age was 55.8 ± 12.8 years, (16) which was similar to the mean age of 58.0 ± 12.1 years reported in the ACCESS study (21).

Coronary artery disease (CAD) is the leading cause of mortality in both men and women in high-income countries, but women tend to experience CAD almost a decade later in their life. A study done in Major Center in Kerala India showed (72.9%) of the patient were males and 27.1% were females (22). And study done in Qatar showed (72.7%) were males and (27.3%) females.

Similarly According to Ladysmith Provincial Hospital, South Africa study the overall sex distribution in this study was 56% males and 44% females (16), and The ACCESS study of south Africa reported an overall 76% male and 24% female gender distribution(21).

2.3 Risk factors

Risk factors associated with ACS can be divided into modifiable and non-modifiable risk factors. The study done in Qatar showed (76.2%) of the patient had hypertension, (50.7%) had diabetes mellitus and (43.3%) were smokers (20).

In a hospital based observational study done at Universal College of Medical Science Teaching Hospital, Bhairahawa, Nepal, Hypertension was the most commonly identified risk factor for ACS occurred in 64% of patients, dyslipidemia in 62% of patients, history of cigarette smoking in 39% and DM in 19% of patients (23).

Similarly According to Ladysmith Provincial Hospital, South Africa study showed The prevalence of previous (ACS) was 27.5% ,family history 18.1% , previous heart surgery 6.3% , obesity (BMI > 30 kg/m²) 28.1% , hypercholesterolemia 28.8% , diabetes 26.3% , hypertension 47.5% , and renal failure 16.9%. Hypertension was the most frequent risk factor among the study patients (16).

In a retrospective study which done at Cardiology department of Yalgado Ouedraogo University Hospital, Burkina Faso. The following risk factor was identified hypertension in (33%) of the patients, obesity in (33%), smoking in (27%), diabetes in (27%), dyslipidemia in (20%), and family history of CHD in 7% of cases (24).

2.4 Clinical presentation

The main symptom of Acute Coronary Syndrome is chest pain although Presentations with atypical features or silent myocardial ischemia are common. According to a study done in Lumbini Medical College and Teaching Hospital in Nepal (42.5%) presented with central chest pain, (32.5%) presented with left sided chest pain, (10%) presented with acute shortness of breath. (10%) patient presented in the state of cardiogenic shock and (5%) presented with the Ventricular tachycardia (VT) as their complication (25). According to a GRACE study in which 8.4% of patients had no chest pain during admission.

The dominant presenting symptoms in these patients were shortness of breath (49.3%), diaphoresis (26.2%), and nausea or vomiting (24.3%). (26)

In study done in USA the median Time from symptom onset to Presentation in the Emergency Department, (61.6%) of women and men (53.5%) presented to the ED \geq 6 hours after symptom onset (27).

2.5 Class of ACS

The ECG continues to be the most important, cost-effective and immediately available initial test in identifying coronary occlusion and in the decision-making process for emergency reperfusion therapy as it allows categorizing ACS as STEMI or NSTEMI / UA. According to South African Asian Indian Patients [The AIR Study] majority of the patient presented with STEMI [75%], 16% had NSTEMI, and 9% unstable angina (19).

The same study done in Qatar showed (8%) Patients had STEMI, (59.8%) NSTEMI and (32.2%) had unstable angina (20). A study done Madras Medical Mission Tertiary hospital in India (33.9%) of the patient had ST segment elevation myocardial infarction (STEMI), (44.2%) had Non ST segment elevation myocardial infarction and (21.9%) unstable angina (41).

2.5 In-hospital mortality

Improvement in mortality after ACS has come from increased use of fibrinolytic therapy and PCI, as well as increased use of aspirin, ACE inhibitors, statins, and beta blockers (1). In-hospital mortality was 7.66% in Meta-analysis of 2128 patients from 20 tertiary hospitals in Heilongjiang Province in China (42).

In a study done at 32 hospitals within the Andalusian Public Health System in-hospital mortality was 9.6%, with 11.8% for women and 8.3% for men (30). The in-hospital mortality was 7% for STEMI, 4% for NSTEMI and 3% for UA patients in GRACE registry (26).

2.6 Predictors of in-hospital mortality

Several factors have been considered as possibly related to high in-hospital mortality rate for ACS. A study from ACCESS registry of south Africa determined Clinical factors associated with higher risk of death at 12 months which included age ≥ 70 years, presence of diabetes mellitus on admission, and a history of stroke/transient ischemic attack (TIA) (21).

Use of aspirin, clopidogrel, ACEI, statin, and PCI were significantly associated with in-hospital mortality in a study done in China (42). In GRACE eight risk factors accounted for 89.9% of the prognostic information which includes older ages, higher Killip class, systolic blood pressure, ST-segment deviations, and cardiac arrest during presentation, serum creatinine level, positive initial cardiac enzyme finding and heart rate (26).

3. OBJECTIVES

3.1 General objective

To assess the Clinical profile of patients with Acute Coronary Syndrome at Tikur Anbessa Specialized Hospital, Addis Ababa University and AaBET Hospital , St. Paul millennium medical college, Addis Ababa Ethiopia.

3.2 Specific objective

- ☞ To describe the socio-demographic factors of patients with ACS
- ☞ To illustrate identified risk factors and time from symptom onset to presentation.
- ☞ To demonstrate the most common clinical presentations
- ☞ To determine the initial management of patients in the emergency room
- ☞ To describe identified complications during hospital stay.
- ☞ To demonstrate the outcome of patients at hospital discharge

4. METHODOLOGY

4.1 Study Area and Period

The study was conducted at Tikur Anbessa and AaBET Hospitals which are located in Addis Ababa capital city of Ethiopia. Tikur Anbessa Specialized Hospital is one of the oldest and biggest teaching referral hospital in the country giving services for patients who come from all direction of Ethiopia. TASH is the largest tertiary hospital in Ethiopia providing services with many specialties and over 800 in-patient beds and 16 ICU beds.

There are a lot of postgraduate specialties being given in the hospital including postgraduate specialty in Emergency medicine and critical care which was started in 2010. TASH is the cardiology center that provide sub specialty training and it is one of the government hospitals that provide PCI service.

St. Paul Millennium Medical College and Hospital was established in 1968 as a hospital and in 2007 established as Medical School. It is administered under federal Ministry of Health. It has many department within, AaBET is the first fully dedicated emergency, burn and trauma center. Which started EM and critical care specialty training in July 2016. Those are the only two centers providing emergency medicine residency training in the country. Those two hospitals receive patient from all over the country

The study was conducted from January 1 – March 30, 2018 from medical chart of ACS patients presented to Tikur Anbessa and AaBET hospitals from January 2016 to February 2018.

4.2 Study design

A retrospective cross-sectional study design was conducted from Patient's Medical chart record to assess the clinical Profile of ACS in Tikur Anbessa and AaBET hospitals, A.A, Ethiopia

4.3 Source Population

The source population was all patients who presented to Tikur Anbessa and AaBET hospitals FROM January 2016 to February 2018.

4.4 Study Population

The study population consisted of patients that presented to Tikur Anbessa and AaBET hospitals ED and had a final diagnosis of ACS from January 2016 to February 2018.

4.5 Inclusion and Exclusion criteria

4.5.1 Inclusion criterion

- All patients with a final diagnosis of STEMI.
- All patients with a final diagnosis of NSTEMI.
- All patients with a final diagnosis of UA.

4.5.2 Exclusion criteria

- ACS Patients whose medical records could not be accessed.
- ACS Patients transferred to another hospital
- ACS Patients discharged against medical advice

4.6 Sample size determination

. All Patient with ACS treated from January 2016 to February 2018 was included in the study.

4.7 Methods of Data Collection

A structured questionnaire or Checklist was adapted from reviews of different standard literatures and pretest was done and adjusted accordingly. Data was collected by three interns who received training For two days on how to collect the data. Supervision was made by the primary investigator for completeness and consistency.

4.8 Variables

4.8.1 Dependent variables

- Outcome Of ACS

4.8.2 Independent variables

- Socio demographic variables (Age and Sex)
- Blood pressure,pulse rate,respiratory rate during admission
- Risk Factor for ACS
- Presenting features of ACS
- Time from symptom onset until presentation to ED
- Serum lipid levels
- Ejection fraction
- Diagnosis type
- Killip class
- Use of aspirin on admission
- Use of beta blocker on admission
- Use of anticoagulants

4.9 Data Collection

The HMIS registration book of emergency department was used to get the card numbers of ACS patients who were admitted during the study period. After getting the card numbers, patient charts were retrieved from the record and documentation office.

4.10 Data Quality Control

To assure the quality of data, the following measures were undertaken. The appropriately designed data collection instrument was used. The checklist or format was pretested and Clarity of language, of checklists was checked.

Every day the collected data was reviewed and checked for completeness and consistency of the response by the primary investigator.

4.11 Data Analysis and interpretation

Data was entered, cleaned and analyzed using Statistical Package for Social Science (SPSS version 20). Descriptive analysis was used to describe the Sociodemographic data and the pattern of each independent variables. Chi square test with P –value was used when appropriate to test the significance of changes in these variables. Logistic regression was used to determine crude and adjusted odds ratio. Bivariate Logistic regression analyses was carried out to assess the association between the dependent and independent variables and to identify candidate for multivariate analysis. Then, multivariate analysis was performed on the variables which have P-value < 0.1 to determine the independent predictors of in-hospital mortality. Statistical significance was measured by p-values < 0.05 and adjusted odds ratio (AOR) with 95% confidence interval (95% CI).

4.12 Ethical considerations

Ethical clearance was obtained from AAU, Department of Emergency Medicine Research Ethics Committee (REC) and from Aabet Hospital, Department of Emergency Medicine. Before data collection, permission was obtained from the out-patient directorate of Tikur Anbessa and Aabet Hospitals. The names of patients were replaced with codes to avoid individual identifiers.

4.13 Dissemination of the result

The study result will be presented to Addis Ababa University, Faculty of Medicine department of emergency medicine and documents will be disseminated to all responsible bodies in the study area, the hospitals where the study is conducted and MOH.

4.14 Operational definitions

- **Treatment outcome:** treatment outcome of patients with ACS is explained mainly by in-hospital mortality. It will be calculated by taking the denominator; all ACS patients participated in the study and the numerator patients who died during their hospital stay. In-hospital mortality is defined as the percentage of patients who died during their hospital stay.
- **ST-segment elevation myocardial infarction (STEMI):** is a clinical syndrome defined by characteristic symptoms of myocardial Ischemia in association with persistent ECG ST elevation and subsequent release of biomarkers of myocardial necrosis.
- **Non-ST-STEMI (NSTEMI):** patient with documented these clinical features develops evidence of myocardial necrosis, as reflected in abnormally elevated levels of biomarkers of cardiac necrosis
- **Unstable angina (UA):** a patient with documented Ischemic symptoms suggestive of an ACS and no elevation in troponin, with or without ECG indicative of ischemia.
- **Prior angina:** History of angina before the current admission. Angina “refers to evidence or knowledge of symptoms before this acute event described as chest pain or pressure, jaw pain, arm pain, or other equivalent discomfort suggestive of cardiac ischemia.
- **Previous myocardial infarction (MI):** The patient has had at least 1 documented previous MI before admission.
- **Family history of premature CAD:** Documented history of any direct blood relatives (parents, siblings, and children) who have had any of the following at age less than 55 years (for first degree male relatives) and 65 years (for first degree female relatives): angina, MI, or sudden cardiac death without obvious cause.
- **Dyslipidemia:** The patient has had at least 1 documented dyslipidemia or who have elevated lipid profile level on admission.

- **Smoking History:** Patient who were / are smokers.
- **Killip class:** Killip class of the patient at the time of hospital admission:
 - Class 1: Absence of documented Rales over the lung fields and absence of S3
 - Class 2: Documented Rales over 50% or less of the lung fields or the presence of an S3
 - Class 3: Documented Rales over more than 50% of the lung fields
 - Class 4: Documented Shock

5. RESULTS

5.1 Socio-demographic characteristics

Six hundred fifty case were seen in Tikur Anbessa and AaBET emergency room during the study period with suspected ACS, of which, 142 cases qualified the inclusion criteria and their data was analyzed in the study. The mean age was 57.5 ± 12.09 years and for male, it was 57.8 (SD ± 12.76) years and for female, it was $56.9(\pm 10.52)$ years. Out of the one hundred forty two patients, Ninety nine (69.7%) patients were male and forty three (30.3%) were female making the M: F, 2.3:1.

5.2 Clinical presentation

Over eighty percent of patients (n=116, 81.7%), experienced chest pain. The location of chest pain was on the left side in 62.9%, retrosternal in 32.75% and bilateral in 4.3%. Hundred fifteen (81%) of patients had shortness of breath and 39/142 (27.5%) patients had nausea or vomiting. Twenty six patients (18.3%) had no chest pain at presentation (Figure 1).

From a total of 26 study patients who reported no chest pain, their presenting symptoms were as follows, 24/26 (92%) patients had dyspnea, 2/26(7.6%) patients had diaphoresis, 6/26 (23%) patients had nausea or vomiting, 23/26 (88%) had easy fatigability and 11/26(42%) patient had epigastric pain as presenting symptom during admission to the emergency room.

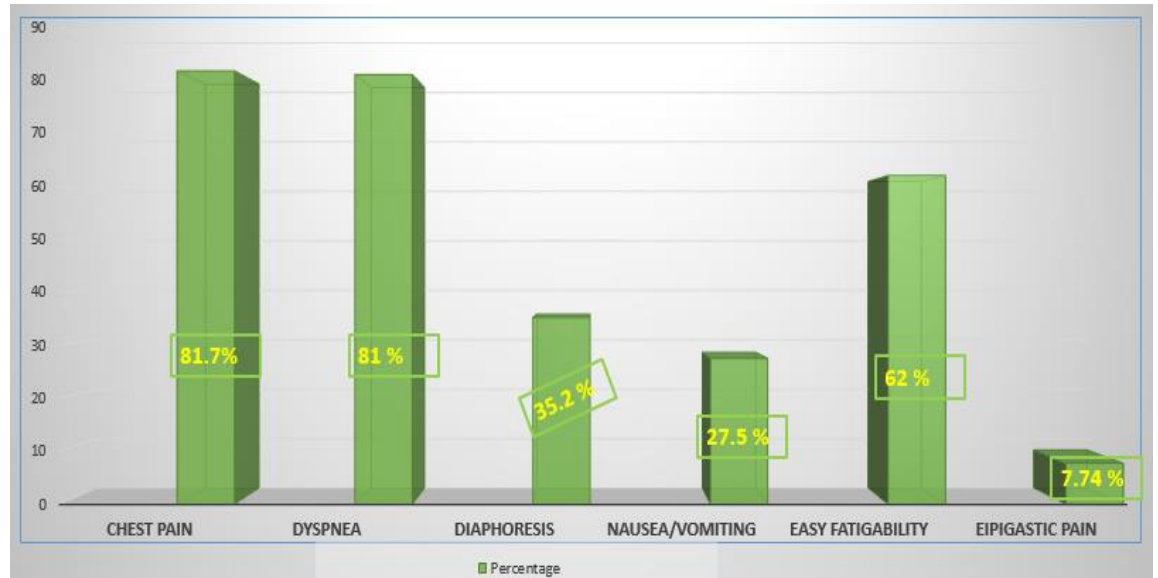


Figure 1: Frequency distribution of acute coronary syndrome symptoms of patients with ACS in Tikur Anbessa and AaBET hospitals, Addis Ababa Ethiopia, 2016-2018.

5.3 Duration of symptom from onset to presentation to the hospital

The average time from onset of ACS symptoms to presentation in the emergency department was 61.96 hours (2.4 days) with a range of 2 h to 10 days and standard deviation is 48.85. No patient arrived within the first hour of symptom onset. Twenty six patients (18.3%) arrived in between 1 hr and 12 hr period and 42 patients (29.6%) arrived in the emergency department after 3 days (72 hour) of symptom onset (Table 1).

Table 1: Duration from onset of symptoms to Emergency visit in relation to type of ACS in Tikur Anbessa and AaBET hospitals, Addis Ababa Ethiopia, 2016-2018

	STEMI	NSTEMI	UA	Total
Less than 12 Hr	10/69	6/29	10/44	26 (18.3%)
>12 -24Hr	13/69	6/29	12/44	31 (21.8%)
>24Hr-48Hr	8/69	0/29	6/44	14 (9.9%)
>48-72Hr	15/69	8/29	6/44	29 (20.4%)
>72Hr	23/69	9/29	10/44	42 (29.6%)

Keys: STEMI=ST segment elevation myocardial infarction; NSTEMI=Non-ST segment elevation myocardial infarction; UA= Unstable angina

5.4 Risk Factors

Regarding the conventional risk factors, 101/142 (71.2%) patients had a previous history of Hypertension, 51/142(35.9%) patients had DM, 47/142(33.1 %) patients had a previous history of MI, 21.8% of patients had a history of dyslipidemia and 12.7 % of patients were/are smokers (**Table 2**).

Table 2: Identified Risk factors for Acute Coronary Syndrome on ACS patients admitted to Tikur Anbessa and AaBET hospitals Addis Ababa Ethiopia, 2016-2018

Risk Factor			
	Male	Female	Total
Diabetes mellitus	34/(99)	17/(43)	51/142 (35.9%)
Hypertension	66/(99)	35/(43)	101/142 (71.1%)
Dyslipidemia	21/(99)	10/(43)	31/142(21.8%)
Smoking	18/(99)	0/(43)	18/142 (12.7%)
Previous hx of MI	34/(99)	13/(43)	47/142 (33.1%)

Keys: MI= Myocardial Infarction, TIA= Transient ischemic attack, Hx= History

5.5 Class of diagnosis

Of the 142 ACS patients who were admitted during the two years period, 62(48.6%) were Diagnosed as STEMI, 29(20.4%) as NSTEMI and the rest 44(31%) were UA patients (Fig 2).

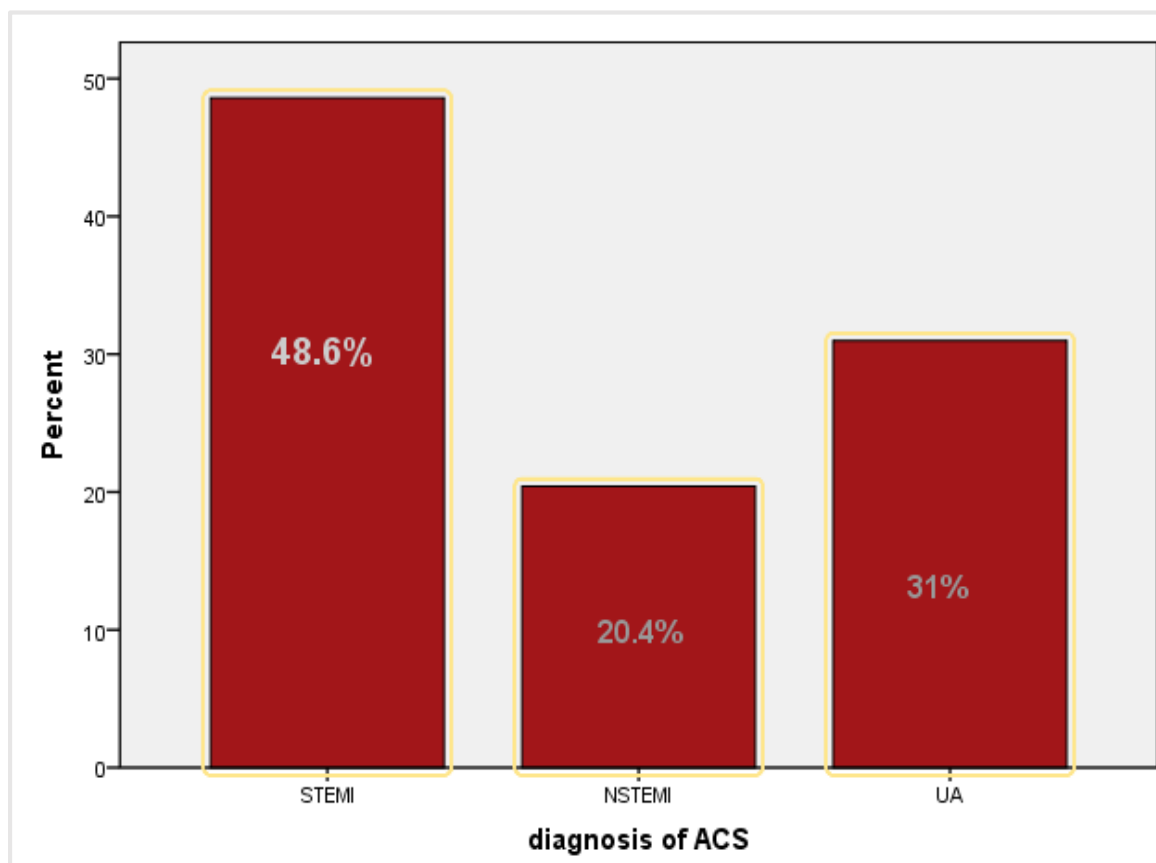


Figure 2: Class of diagnosis for Acute Coronary Syndrome patients in patients admitted with ACS Tikur Anbessa and AaBET hospitals, Addis Ababa Ethiopia, 2016-2018

Keys: STEMI=ST segment elevation myocardial infarction; NSTEMI=Non-ST segment elevation myocardial infarction; UA= Unstable angina

5.6 Initial assessment and investigations

Of the 142 ACS patients, seven (4.9%) presented with blood pressure of less than 90/60mmhg and majority of the patient 73(51.4%) had blood pressure in the range of greeter than 90/60 to 120/80 and four patient (2.8%) had highly elevated blood pressure (>180/110mmhg).(Table 5)

The mean heart rate during admission was 86(SD \pm 18.8) with a minimum 36 and a maximum of 180. The random blood sugar (RBS) was measured in only 55/142(38.7%) patients, and 22.5% had blood sugar level in the range of >70-140 mg/dl and 3/55 (2.1%) had sugar level more than 250 mg/dl.

Of the 142 patient 85.2% were on Killip class (I and II), and the rest (14.8%) were Killip class III and IV (**Table 3**). On categorizing the patients according to the acute coronary syndrome subsets, 27 patients (39.1%) with STEMI belonged to Killip class I, twenty four (34.8%) belonged to class II, eleven (15.9 %) to class III and seven (10.1%) to class IV at the time of admission to the Hospital.

Biomarkers of cardiac injury including troponins and CKMB were measured for 142(95.2%) of

Patients. CKMB and Troponins were at the normal range in (69) patient 48.6% and (45) patient 31.7% of patient respectively.

Fasting serum lipid level was measured in 65 (45.8 %) patients during their hospital stay (Table 3).

Echocardiography was done for about 67(47%) patients. From those patients who had Documented EF result, 17.9% had severe reduction in LVEF (EF < 30%). (Table 3)

Table 3: Initial assessment, class of Killip and laboratory investigation for ACS patients admitted in Tikur Anbessa and AaBET Hospitals, Addis Ababa, Ethiopia, 2016-2018.

Variables		STEMI	NSTEMI	UA	Total (Percentage)	
Blood pressure	<90/60	6	1	0	7 (4.92%)	
	≥ 90/60	41	22	30	93 (65.49%)	
	≥140/90	20	6	12	38 (26.76%)	
	≥180/110	2	0	2	4 (2.81%)	
Ejection Fraction	< 30 %	9	1	2	12 (17.9%)	
	30-40 %	13	3	4	20 (29.8%)	
	41-50 %	7	3	2	12 (17.9%)	
	51-60 %	3	7	3	13 (19.4%)	
	>60 %	3	3	4	10 (14.9%)	
Killip Class	Killip Class I	27	21	41	89 (62.7%)	
	Killip class II	24	6	2	32 (22.5%)	
	Killip Class III	11	1	1	13 (9.2%)	
	Killip Class IV	7	1	0	8 (5.6%)	
Lipid Profile	Total cholesterol	<200	22	4	18	44 (67.7%)
		≥200	7	7	7	21 (32.3%)
	LDL cholesterol	<100	22	4	17	43(66.2%)
		≥100	7	7	8	22(33.8%)
	HDL cholesterol	<40	7	7	10	24(36.9%)
		≥40	22	4	15	41(63.1%)
	Triglyceride	<150	22	4	17	43(66.1%)
		≥150	7	7	8	22(33.89)

Keys: LDL= Low density lipoprotein; HDL= High density lipoprotein

5.7 Treatment commenced during hospitalization

With regard to the medications which had been given during hospitalization, all patients had received the loading dose and maintenance dose of aspirin. About 130(91.5%) patients had received anticoagulants during their hospitalization.

From those, 91.7% of patients had used un-fractionated heparin while 8.3% of patients used enoxaparin. The use of anticoagulants is low in UA patients. At About, 83 % of patients received beta blockers during hospitalization. (**Table 4**).

Table 4: Medical treatment commenced during hospital stay for Acute Coronary Syndrome patients in Tikur Anbessa and AaBET Hospitals Addis Ababa, Ethiopia, 2016-2018

Drugs	Diagnosis			Total
	STEMI	NSTEMI	UA	Freq (%)
Aspirin	69(100%)	29(100%)	44(100%)	142/142(100%)
Clopidogrel	69(100%)	28(96.5%)	42(95.4%)	139/142 (97.8%)
Anti-coagulant	69(100%)	28(96.5%)	33(75%)	130/142 (91.5%)
Beta blocker	53(76.8%)	29(100%)	36(81.8%)	118/142 (83%)
Morphine	55(79.7%)	28(96.5%)	26(59%)	109/142 (76.6%)
Nitroglycerine	48(69.5%)	20(68.9%)	21(47.7%)	89/142 (62.7%)
ACEIs/ARBs	42(60.8%)	21(72.4%)	16(36.3%)	79/142 (55.6%)
Calcium channel blockers	0(0)	0(0)	0(0)	0/142 (0%)
Statins	68(98.5%)	29(100%)	44(100%)	141/142 (99.3%)

5.8 Treatment outcome and major in-hospital events

Twenty patients (24.6%) had developed congestive heart failure in hospital, 14 patients (9.8%), Major arrhythmia and 15 patients (10.5%) experienced re-infarction during their hospitalization. Cardiogenic shock (4.9%) was the major cause of hospital death. 1(0.7%) patient sustained stroke.

From the total of 142 patients admitted during the three years period, 14 patients (9.9%) had died in hospital where as the rest 128 (90.1%) patients discharged alive (Fig. 3).

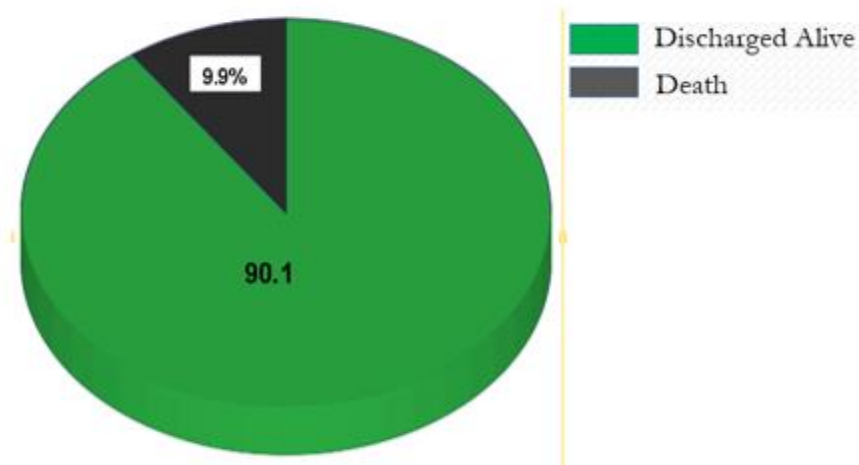


Figure 3: In-hospital mortality of Acute Coronary Syndrome patients admitted in in Tikur Anbessa and AaBET Hospitals, Addis Ababa, Ethiopia, 2016-2018

The mortality rate increased steadily with advancing age, with lowest rate in those who were less than 55 years of age (3.8%). The mortality rates in other age-groups were: 55 to 64 years – 6.8%, 65 year and above – 19.6 %.) The mortality rates in various hemodynamic subsets were as follows: Killip class me – 1.1%, class II – 9.4%, and class III – 15.4% and class IV – 100 %. High in-hospital Mortality (18.8%) was documented from patients who were diagnosed as STEMI and 3.4% for NSTEMI Patient.

5.9 Predictors of in-hospital mortality

Multivariable analysis showed that, time from symptom onset to presentation (more than forty eight hour) at ED (P=0.04), a, Killip class III and IV (P=0.001), gender being female (P=0.016) and diagnosis of STEMI (P=0.018), to have statistically significant association with in-hospital mortality (Table 5). Otherwise there was no association between in-hospital mortality and, symptoms during admission, previous history of DM, HPN, smoking and MI. In addition, medications given during admission didn't show any significant association.

According to multivariable analysis, Patients who arrived at ED after 48 hour of symptom onset were 5.76 times more likely to die as compared to patients who arrived within 24 hours of symptom onset (AOR=5.76;95% CI: 0.46-72.61).

Patients with a diagnosis of STEMI were 29.6 times more likely to face hospital death as compared to other ACS types (AOR=29.6; 95% CI: 1.76-498). Female had high mortality when compared with male (AOR=15.13(1.65-138.8)). (Table 5)

Table 5: Predictors of in-hospital mortality for Acute Coronary Syndrome patients admitted in Tikur Anbessa and AaBET hospitals, Addis Ababa Ethiopia, 2016-2018

Predictors of in-hospital mortality for ACS							
		Outcome		COR (95% CI)	P Value	AOR(95% CI)	P Value
		Yes	NO				
Age	<55	50(96.2%)	2(3.8%)	1		1	
	≥55-64	41(93.2%)	3(6.8%)	1.83(0.29-11.47)	0.519	3.08(0.18-50.88)	0.443
	≥65	37(80.4%)	9(19.6%)	6.08(1.24-29.82)	0.026	11.12(0.86-143.5)	0.065
Time from symptom onset(hr)	≤24hr	56(98.2)	1(1.8%)	1		1	
	>24-48hr	13(92.9%)	1(7.1%)	4.3(0.25-73.48)	0.313	0.8(0.009-70.51)	0.929
	>48hr	59(83.1%)	12(16.9%)	11.4(1.43-90.48)	0.02	5.76(0.46-72.61)	0.04
Diagnosis	STEMI	56(81.2%)	13(18.8%)	16.71(2.12-131.6)	.007	29.6(1.76-498)	0.018
	NSTEMI&UA	72(98.6%)	1(1.4%)	1		1	
Killip class	1&2	117(91.4%)	4(3.3%)	1		1	
	3&4	11(52.4%)	10(47.6%)	26.59(7.14-98.44)	<0.0001	28.4(4.6-174.8)	0.0001
sex	male	93(93.9%)	6(6.1%)	1		1	
	female	35(81.4%)	8(18.6%)	3.54(1.15-10.94)	0.028	15.13(1.65-138.8)	0.016

Statistically significant at P-value < 0.05

Keys: AOR= Adjusted odds ratio; COR= Crude odds ratio; STEMI=ST segment elevation myocardial infarction; NSTEMI=Non-ST segment elevation myocardial infarction; UA= Unstable angina

6. DISCUSSION

The age distribution of ACS patients in Tikur Anbessa and AaBET was 57.5 ± 12.09 years which is in line with that of a study made in Kenya (59.7 ± 3.8 years) (31), SPACE Registry 57.1 ± 13.6 years (37) and India 60.4 ± 12.1 years (32) but lower than that of Global Registry of Acute Coronary Events (The GRACE registry) (66.3 ± 10 years) which is a multinational registry of ACS (26).

In the present study chest pain was not the chief complaint in 18.3% of patients during admission. In Tikur Anbessa and AaBET, 81% of patients had shortness of breath, 27.5% of patients had nausea or vomiting and 35.2% of patients had experienced diaphoresis during admission. According to a GRACE study in which 8.4% of patients had no chest pain during admission. The dominant presenting symptoms in these patients were shortness of breath (49.3%), diaphoresis (26.2%), and nausea or vomiting (24.3%) (14).

This study shows a significant delay of patients for seeking medical care (a mean time of presentation to ED was 2.4 days). No patient in Tikur Anbessa and AaBET arrived to ED within the first hour of Symptom onset. Only 18.3% of patients arrived within 12 h of symptom onset where as 29.6% of patients arrived after 3 days of symptom onset. According to a study made in Kenya, 78% of patients arrived within 12 h of symptom onset (31). The average time delay before medical care was 14.5 h in a study done in Dacar, Senegal (33). The ENACT study: a pan-European survey of acute coronary syndromes has shown that the majority of patients (65%) presented within 12 h of the onset of pain (34). The proportion of patients presenting within 12 h was highest in Scandinavia (79%) and in Belgium (77%) and lowest in Eastern Europe (51%) (34). The significant delay in seeking medical care in this study may be because of less knowledge about signs of ACS and the benefit of visiting the nearby hospital early.

Education of patients with known coronary artery disease appears to be the only effective primary intervention to reduce denial or misinterpretation of symptoms.

Regarding the risk factors 71.2% of ACS patients in Tikur Anbessa and AaBET have previous history hypertension, 35.9% have had DM and 33.1% have previous history of MI, but according to the study done in Nepal in which 64% of ACS patients were hypertensive and 19 % were DM patients (35). The Kenyan study also reflects the same finding as hypertension and DM were the leading risk factors for development of ACS (31).

The Saudi Project for Assessment of Coronary Events (SPACE) registry reported that, history of diabetes mellitus was present in 53%, hypertension in 48%, hyperlipidemia in 31%, and 39% were current smokers (37).

High mortality in Tikur Anbessa and AaBET (71.4%) was from patients who were in Killip class III and IV. A study from the Second National Registry of MI (NRMI-2) included 190,518 patients with acute MI, of whom 19% had Killip class II or III HF on admission (40). These patients had significantly higher in-hospital mortality than those without HF (21.4 versus 7.2 %).

STEMI is the leading (48.6%) discharge diagnosis of ACS patients in Tikur Anbessa and AaBET where as 20.4% of patients were NSTEMI and 31% were UA patients. STEMI cases were relatively high in Tikur Anbessa and AaBET as compared to the ACCESS registry for South Africa in which STEMI cases were 41%, NSTEMI accounts for 32% of cases and UA accounts the rest 27% of patients (21). Patients who were in follow up at the Saudi project for assessment of coronary events (SPACE) registry also show the same trend in which 45 % were STEMI patients, 28 % NSTEMI and the rest 27 % were UA patients (37). The higher proportion of STEMI cases in TASH may be related to the delay in seeking medical care. NSTEMI and UA cases (due to partial occlusion) may progress to STEMI (due to complete occlusion).

The in-hospital mortality of ACS patients in Tikur Anbessa and AaBET was (9.9%). High mortality (18.8%) was documented from STEMI patients and 3.4% for NSTEMI Patient. The mortality rate was high in female (18.6) compared to men (6.1). Mortality during admission was 9.6% in observational study done in 32 hospitals of Spain (39). According to a prospective survey of the characteristics, treatments and outcomes of patients with ACS in Europe and the Mediterranean basin (Euro Heart Survey ACS) in-hospital mortality of STEMI was 7% and that of NSTEMI patients was 2.4% (38).

In all the previous studies in-hospital mortality was low as compared to that of Tikur Anbessa and AaBET since the studies were done in hospitals that have access for PCI and thrombolytics. It is known that these services reduce mortality from ACS significantly.

Regarding predictors of in-hospital mortality this study identified the presence of significant association between in-hospital mortality and factors such as sex, delayed time of presentation, higher Killip class and patients who were diagnosed to have STEMI. Predictors of hospital mortality in Global Registry of Acute Coronary Events (GRACE) includes age, Killip class, systolic blood pressure, ST segment deviation, cardiac arrest during presentation, serum creatinine level, positive initial cardiac enzyme finding and heart rate (26).

7. LIMITATION OF THE STUDY

Since this study is a two -centered study it may be difficult to generalize for the general population. Since retrospective method was used certain data may be missed. And patient chart was lost, hence, it was difficult to include more patients for this study.

8. CONCLUSION

This study shows that the medical management of ACS patients in Tikur Anbessa and AaBET Hospital was in line with the recommendations of international guidelines. Although only two patient in Tikur Anbessa has received PCI .Patients with ACS have delayed presentation to the hospital from onset of symptoms.

The majority of ACS patients in Tikur Anbessa and AaBET were diagnosed as STEMI. Patients had similar risk profiles with the developed world, but have higher mortality. Being female, delayed presentation, having STEMI, and higher Killip class was found to be independent predictors of inhospital mortality in Tikur Anbessa and AaBET Hospitals.

9. RECOMMENDATION

This study shows delayed presentation of ACS patients in Tikur Anbessa and AaBET Hospital. Therefore

- Focus should be given on prevention strategies and management of the risk factors like Hypertension, diabetes.
- Tikur Anbessa and AaBET Hospital should start PCI service and avail medications such as thrombolytics, to save the life of many patients and reduce complications.
- Any concerned individuals or professional associations should think of starting nationwide registries for ACS patients or generally for cardiovascular cases.
- If it is feasible it would be beneficial to open a special center for ACS patients to facilitate the management, since a little lapse of time may have an impact on the life of these patients.
- Further prospective study should be done.

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ANNEX

QUESTIONNAIRE

1. Sociodemographic and Admission Details

1.01 Occupation _____ MRN-----

1.02 Age _____

1.03 Sex Male Female

1.04 Date of Admission _____

1.05 Mode of arrival

1.05 Date of discharge/death _____

2. Initial Assessment and Investigations

2.01 Blood Pressure _____ mmHG

2.02 Heart Rate _____ B/min

2.03 Blood Sugar _____ mg/dl

2.04 Killip Class _____

2.05 Serum CK-MB measured

YES If YES peak value _____ NO

2.06 Serum Troponins measured

YES If YES peak value _____ NO

2.07 Serum Creatinine measured

YES If YES peak value _____ NO

2.08 Serum Lipid measured during admission

Total cholesterol YES _____mg/dl NO

LDL cholesterol YES _____mg/dl NO

HDL cholesterol YES _____mg/dl NO

Triglyceride YES _____mg/dl NO

2.09 Echocardiogram performed

YES NO If Yes EF----- Wall motion

Abnormality -----

3. past Medical History

3.01 Previous Myocardial Infarction YES NO

3.02 Exertional Angina Pectoris YES NO

3.03 Heart Failure YES NO

3.04 Previous Stroke or TIA YES NO

3.05 DM YES NO

3.06 Hypertension YES NO

3.07 Dyslipidemia YES NO

Unknown

3.08 Family History of Premature Coronary Heart Disease YES

NO

3.09 Obesity YES No Unknown

3.10 Smoking History

Never Smoked EX-Smoker If YES No of Years

Smoked_____

Current Smoker If YES Average No of Cigars per day_____

4. Clinical Presentation of ACS

4.01 Chest Pain

Location -----

Radiation to ----- Quality

Duration -----

Relieving factor ----- Aggravating Factor -----

4.02 Dyspnea

4.03 Sweating (Diaphoresis)

4.04 Nausea /Vomiting

4.05 Easy Fatigability

4.06 D Other_____

4.07 Time of arrival from symptom onset _____

5. Diagnosis

5.01 STEMI

If YES then max ST Elevation_____

5.02 NSTEMI

If YES then max ST Depression_____

5.03 UA

If YES then max ST Depression_____

6. Medical treatment commenced during hospitalization

6.01 Aspirin

YES NO If YES Loading Dose_____mg/d
M.Dose_____mg/day

6.02 Clopidogrel

YES NO If YES Loading
Dose_____mg/d
M.Dose_____mg/day

6.03 Glycoprotein IIb/ IIIa receptor antagonist

YES NO If YES drug name_____

6.04 Anti-coagulant

YES NO
If YES drug name_____ Loading Dose_____mg/d
M.Dose_____mg/day

6.05 Beta Blocker (PO/IV)

YES NO
If YES drug name_____ Initial Dose_____ mg/d
Max.Dose_____mg/day

6.06 Morphine

YES NO Initial Dose_____mg/d

Max.Dose_____mg/day

6.07 Nitrates (SL/IV/PO)

YES NO If YES drug name_____

Initial Dose_____mg/d Max.Dose_____mg/day

6.08 ACEIs/ARBs

YES NO If YES drug name_____

Initial Dose_____mg/d

Max.Dose_____mg/day

6.09 Ca-channel blocker

YES NO If YES drug name_____

Initial Dose_____mg/d Max.Dose_____mg/day

6.10 Statins

YES NO

If YES drug name_____

Initial Dose_____mg/d

Max.Dose_____mg/day

7. Reperfusion therapy/ revascularization

7.01 Thrombolytic therapy given YES NO

7.02 PCI performed YES NO

7.03 CABG performed YES NO

8. Major in-hospital events and hospitalization outcome

8.01 CHF

YES NO

8.02 Myocardial Infarction or re-infarction**

YES NO

8.03 Major arrhythmia YES NO

AV Block PVC Sustained Ventricular tachycardia
atrial fibrillation and flutter

8.04 Stroke YES NO

8.05 Major bleeding episode YES NO

8.06 Killip Class 1 2 3 4

8.07 Discharged alive YES NO

