OUTCOME OF PATIENTS WITH ACUTE CORONARY SYNDROME ADMITTED TO TIKUR ANBESSA SPECIALIZED HOSPITAL, ADDIS ABABA, ETHIOPIA

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Outcome of patients with Acute Coronary Syndrome admitted to Tikur Anbessa Specialized Hospital, Addis Ababa, Ethiopia

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Abstract

Outcome of patients with Acute Coronary Syndrome admitted to Tikur Anbessa Specialized Hospital, Addis Ababa, Ethiopia

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Worldwide, coronary artery disease (CAD) is the single most frequent cause of death. Over seven million people every year die from CAD, accounting for 12.8% of all deaths. The objective of this study was to assess the treatment outcome and associated factors for Acute Coronary Syndrome (ACS) patients admitted at Tikur Anbessa Specialized Hospital (TASH). A retrospective cross sectional study was conducted by chart review of patients who were discharged with a diagnosis of ACS during the period January 1, 2012 to December 31, 2014. Of 124 ACS patients who were admitted during the three years period, 90(72.6%) were diagnosed as STEMI. The mean age was 56.3 ±13.7 years. The average length of hospital stay was 9.77± 6.42 days. The average time from onset of ACS symptoms to presentation in the emergency department was 3.8 days (91.7 hours). In about 76 (61.3%) patients hypertension was the leading risk factor for development of ACS. 36.4% of ACS patients in TASH were either Killip class III or IV. Biomarkers were measured for 118(95.2%) patients. 79.2% of patients had ejection fraction (EF) of less than 40% and 29.2% had less than 30%. In-hospital medications include loading dose of aspirin (79%), anti-coagulants (77.4%), beta-blockers (88.1%), statins (85.5%), morphine (12.9%), and nitrates (35.5%). The in-hospital mortality was 27.4%. Predictors of in-hospital mortality in TASH included age (P=0.042), time from symptom onset to presentation (P=0.001), previous history of hypertension (P=0.025), being Killip class III and IV (P=0.001), and STEMI diagnosis (P=0.005). Hence, based on the results the medical management of ACS patients in TASH was in line with the recommendations of international guidelines but in-hospital mortality was very high (27.4%).

Key words: Acute Coronary Syndrome, Outcome, In-Hospital Mortality

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Contents

Acronyms

ACC/AHA	American college of cardiology/American heart association
ACEIs	Angiotensin converting enzyme inhibitors
ACS	Acute coronary syndrome
AMI	Acute myocardial infarction
ARBS	Angiotensin II receptor blockers
BP	Blood pressure
CABG	Coronary artery bypasses graft
CAD	Coronary artery disease
COX	Cyclooxygenase
CrCl	Creatinine clearance
ECG	Electrocardiogram
ED	Emergency department
ESC	European society of cardiology
GP	Glycoprotein
HF	Heart failure
LMH	Low molecular weight heparin
NSAIDS	Non-steroidal anti-inflammatory Drugs
NSTE-ACS	Non ST segment elevation acute coronary syndromes
NSTEMI	Non ST segment elevated myocardial infarction
PCI	Percutaneous coronary intervention
STE-ACS	ST-segment elevation acute coronary syndromes
STEMI	ST Segment elevated myocardial infarction
TASH	Tikur anbessa specialized hospital
tPA	Tissue plasminogen activator
UA	Unstable angina
UFH	Unfractionated heparin
WHO	World health organization

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1. INTRODUCTION

1.1 Background

Acute coronary syndrome (ACS) refers to a spectrum of conditions compatible with acute myocardial ischemia and/or infarction that are usually due to an abrupt reduction in coronary blood flow (9). ACS is most commonly caused by coronary atherosclerotic plaque and subsequent intracoronary thrombus formation, which leads to myocardial ischemia. If coronary blood flow is interrupted long enough, myocyte necrosis (infarction) can occur (5). Acute myocardial infarction (AMI) is the death of cardiac myocytes that is caused by ischemia and not by other etiologies such as inflammation or trauma. ECG and cardiac biomarkers (such as troponins) are useful for diagnosis and risk stratification and thus can guide treatment. ACS can be classified as ST-elevation myocardial infarction, non-ST elevation myocardial infarction and unstable angina (6, 7, 9).

ACS is caused primarily by atherosclerosis. Most cases of ACS occur from disruption of a previously non-severe lesion (an atherosclerotic lesion that was previously hemodynamically insignificant yet vulnerable to rupture). The vulnerable plaque is typified by a large lipid pool, numerous inflammatory cells, and a thin, fibrous cap (5). Following plaque rupture, a clot (a partially or completely occlusive thrombus) forms on top of the ruptured plaque. The thrombogenic components of the plaque are exposed to blood elements. Exposure of collagen and tissue factor induces platelet adhesion and activation which promote the release of platelet-derived vasoactive substances including adenosine diphosphate (ADP) and thromboxane A2 (TXA2). These produce vasoconstriction and potentiate platelet activation. Furthermore, during platelet activation, a change in the conformation in the glycoprotein (GP) IIb/IIIa surface receptors of platelet occurs that cross links platelets to each other through fibrinogen bridges. This is considered the final common pathway of platelet aggregation. Inclusion of platelets gives the clot a white appearance. Simultaneously, the extrinsic coagulation cascade pathway is activated as a result of exposure of blood components to the thrombogenic lipid core and disrupted endothelium, which are rich in tissue factor. This leads to the production of thrombin (factor II a), which converts fibrinogen to fibrin through enzymatic activity. Fibrin stabilizes the

clot and traps red blood cells, which gives the clot a red appearance. Therefore, the clot is composed of cross-linked platelets and fibrin strands.

STEMI is a clinical syndrome defined by characteristic symptoms of myocardial ischemia in association with persistent ST elevation and subsequent release of biomarkers of myocardial necrosis. It is caused by complete occlusion of the culprit artery in more than 80% of the cases. STEMI is diagnosed in the presence of ischemic chest pain (or equivalent) when the ECG shows new ST-segment elevation at the J-point in 2 contiguous leads with the cutoff points of ≥ 0.25 mV in men below the age of 40 years, ≥ 0.2 mV in men over the age of 40 years, or ≥ 0.15 mV in women in leads V_2–V_3 and/or ≥ 0.1 mV in other leads. STEMI also includes new or presumed-new left bundle branch block (LBBB), a finding more common in the elderly. True posterior MI should be suspected when ECG shows ST segment depression in leads V_1 throughV_4 and can be differentiated from anterior ischemia by obtaining an ECG with posterior leads (V_7 and V_8), which reveals ST segment elevation in the presence of a posterior MI (8,39,40,41,42).

Cardiac biomarkers are elevated in STEMI but are not necessary for the initial diagnosis (6, 8, 9, 10). Revascularization should be initiated immediately based on the clinical presentation and ECG finding and should not be delayed until cardiac biomarker results are available. Cardiac biomarker values are often normal during the first few hours of STEMI. Troponin (T or I) is the biomarker of choice, given its high sensitivity and specificity for myocardial necrosis. In addition to standard ancillary ACS therapy, the primary goal of treatment in STEMI, within 12 hours of symptoms onset, is rapid revascularization with either thrombolysis in the absence of contraindications or preferably, emergent percutaneous coronary intervention(PCI),when available. The earlier the revascularization, the better the outcome will be achieved. Standard ancillary ACS therapy includes oxygen, anti-platelet agents (aspirin ± clopidogrel and/or glyprotein IIb/IIIa inhibitors), nitrates, beta blockers, anticoagulants (UFH, LMH, bivalirubin, or fondaparinux), and statins (9, 39, 40, 41, 42).

UA and NSTEMI are grouped together as they are caused by incomplete occlusion of the culprit artery in 60% to 90% of cases. Elevated cardiac biomarkers are seen in NSTEMI that differentiates it from UA, which has normal cardiac biomarkers. The primary presenting symptoms is ischemic chest pain (or equivalent). The ECG may be normal but may show

ischemic changes, which includes: new horizontal or dawn sloping ST depression ≥ 0.05mV in two contagious leads and/or T-wave inversion ≥ 0.1 mV in 2 contiguous leads (10).

In addition to standard ACS therapy, primary PCI is preferred in most UA/NSTEMI patients, especially those in higher risk categories. Primary PCI is usually less urgent for UA/NSTEMI than in STEMI due to higher culprit artery patency rates and typically can be performed within 48 hours of symptoms onset. Thrombolysis is contraindicated in UA/NSTEMI due to lack of benefit and increased risk of complications. This may be due to different culprit artery patency rates as well as different pathophysiological processes between STEMI and UA/NSTEMI, including differences in thrombus composition and mechanisms of ischemia (11).

The clinical presentation of ACS is variable, but typically includes chest pain which lasts for 20 minutes or more not responding to nitroglycerin. Important clues are a history of CAD and radiation of the pain to the neck, lower jaw or left arm. The pain may not be severe. Some patients present with less-typical symptoms, such as nausea/vomiting, shortness of breath, fatigue, palpitations or syncope. These patients tend to present later, are more likely to be women, diabetic or elderly patients, and less frequently receive reperfusion therapy and other evidence-based therapies than patients with a typical chest pain presentation. Registries show that up to 30% of patients with STEMI present with atypical symptoms (6, 9).

Worldwide, coronary artery disease (CAD) is the single most frequent cause of death. Over seven million people every year die from CAD, accounting for 12.8% of all deaths (1). 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 (1). Every sixth man and every seventh woman in Europe will die from myocardial infarction (2).

In the United States, the median age at ACS presentation is 68 years with male-to female ratio of approximately 3:2. Some patients have a history of stable angina, whereas in others, ACS is the initial presentation of CAD. It is estimated that in the United States, each year, >780,000 persons will experience an ACS (3).

Ischemic heart disease (IHD) is the greatest single cause of mortality and loss of disability-adjusted life years worldwide, and a substantial portion of this burden falls on low- and middle-income countries (LMICs). Deaths from IHD and ACS occur, on average, at younger ages in

LMICs than in high-income countries, often at economically productive ages, and likewise frequently affect the poor within LMICs (4).

Studies done in Ethiopia during late 1960s and 1970s showed CVD to account for 4-13% of medical admissions to hospitals in Addis Ababa. During the period from September 1975 to August 1979, there were a total of 5667 patients admitted to the medical wards of TASH of whom 381 (6.7%) admissions were due to CVD, whereas recent studies indicated the increasing frequency of CVD in residents of Addis Ababa (45). In a report released in 2001, in an autopsy study done on bodies brought by police to the Medico-legal Department of Menilik II Memorial Hospital, after sudden death, CAD accounted for 70% of those who died due to cardiac causes (46).

A retrospective study was conducted at Addis Cardiac Hospital, Addis Ababa, Ethiopia (private hospital), with the objective of determining the pattern of CAD by coronary angiography. Diagnostic coronary angiography was done for 300 patients from May 1, 2007 to December 30, 2011.Of which, 83% were males with the age range of 29 to 87 years. The median age was 56 years with the most frequent age stratum being 50 to 59 years. 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). With catheterization, 75.7% patients had evidence of CAD, of which, 92 (40.5%) patients had multivessel disease. Among the 193 patients with significant CAD, PCI was done for 65.3% patients which resulted in TIMI III (thrombolysis in myocardial infarction flow grade III) in 116 patients (92.1%).

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 (36). In the United States, approximately 6 million patients present to the emergency department (ED) annually with chest pain and related symptoms, of whom approximately 732,000 are hospitalized for AMI (12).

Case-fatality rates from ACS can be decreased substantially by better access to high-quality acute care, including timely transportation of patients, evidence-based medical interventions and high-quality specialized health facilities such as percutaneous coronary intervention-capable centers (53).

By any measure, the ED is a critical setting for the initial management of AMI. The care that AMI patients receive during the relatively short ED stay can have a substantial effect on patient outcomes, such as in-hospital mortality. In addition, medications given in the emergency department (e.g., aspirin and beta blockers) are more likely to be maintained during hospitalization (12).

Data from the WHO MONICA (multinational monitoring trends and determinants in cardiovascular diseases) project showed that mortality rate can be decreased by about 25% by primary prevention, 29% by secondary prevention due to the reduction of risk factors, and 43% by other therapeutic improvements. The decrease in in-hospital case fatality may be linked to the increasing use of established treatment strategies like thrombolysis, aspirin and beta-blockers. Accordingly, clinical trials using the modern therapeutic strategies reported in-hospital case fatality rates as low as 2.6%. On the other hand, hospital- and population-based registries, reported higher case-fatality rates. So according to this study appropriate use of evidence based medicines will reduce mortality rate by up to 43 % (14).

There is a large practice gap between optimal and actual patterns of care for patients with acute myocardial infarction in hospitals around the world. Acute myocardial infarction is a highly treatable condition for which many advances in treatment have occurred over the past several decades. However, the uptake of many of these advances and their incorporation into routine clinical practice has often lagged behind. To reduce this gap and improve quality of care, many

developed countries are using indicators of the quality of care for patients with acute myocardial infarction. These quality indicators are intended to measure adherence to selected key clinical practice guidelines in routine clinical care and serve as a foundation for efforts to improve quality (13).

A retrospective analysis of medical-ICU admissions in TASH have showed that cardiovascular disease increased steeply over the past thirty years. The proportion of cardiovascular diseases to total admission of 1981/82, 1991/92, 2001/02 and 2011/12 accounts 21.7%, 19%, 52% and 58% respectively. ACS, heart failure and stroke cases increased progressively from 1981/82 to 2011/12 admission dates. 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 there is no formal registry for ACS hence little is known about the outcome of patients and no quality indicators were set so as to evaluate the quality of treatment of ACS regularly. Early reperfusion therapy using either PCI or fibrinolytics is very essential to decrease in hospital mortality. But in Ethiopia fibrinolytics are not available and PCI service isn't given in governmental hospitals which greatly affects the treatment outcome of patients.

Hence assessment of the outcome and management practice will help us to improve the service and to design strategies for prevention of ACS in Ethiopia.

1.3 Literature review

1.3.1 In-hospital mortality and associated factors

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. Among patients with an STEMI, approximate in-hospital or 30-day mortality rates were 13% with medical therapy alone, 6 to 7% with optimal fibrinolytic therapy, and as low as 3 to 5% with primary PCI when performed within two hours of hospital arrival (56). Among 2128 patients at 20 tertiary hospitals in Heilongjiang Province in China, 163 (7.66%) died during their hospital stay (16). In-hospital mortality is relatively higher from STEMI patients as compared to NSTEMI and UA patients. The in-hospital mortality of patients with STEACS was 7·0%, for NSTACS 2.4%, and for undetermined electrocardiogram ACS 11·8% from a prospective survey (103 hospitals, 25 countries) of 10,484 patients in Europe and the Mediterranean basin (17). In a study done at 32 hospitals within the Andalusian Public Health System over a four-year period (2000–2003) in-hospital mortality was 9.6% (4,401 cases out of 46,007), with 11.8% for women and 8.3% for men (38). The in-hospital mortality was 7% for STEMI, 4% for NSTEMI and 3% for UA patients in GRACE registry (29).

Several factors have been considered as possibly related to high in-hospital mortality rate for ACS. A retrospective study performed at a single tertiary heart centre in Northeast Thailand identified factors associated with in-hospital mortality. It includes age >60 years, left ventricular ejection fraction <40% and final TIMI flow grade 0/1 (55). 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, cardiac arrest during presentation, serum creatinine level, positive initial cardiac enzyme finding and heart rate (29). 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) (25). Use of aspirin, clopidogrel, ACEI, statin, and PCI were significantly associated with in-hospital mortality in a study done in China (16).

1.3.2 Pharmacological management of ACS

The use of evidence-based medications in the first 24 h of hospital admission and at discharge is known for reducing mortality as well as major acute coronary events.

In the absence of an absolute contraindication, anti-platelet therapy with aspirin and a platelet P2Y12 receptor blocker is indicated in all ACS patients. The use of aspirin was 71.6% in a study done in China (16), 93% in Europe and the Mediterranean basin (17), 82% in hospitals around region of Stara Zagora, Bulgaria (19), 98% in a prospective study done on 45 STEMI cases at tertiary hospital in Kenya (21) and 92.8% in a study done at Southern Italy (22).

The administration of a beta blocker following an acute MI reduced morbidity and mortality in multiple clinical trials (up to a 40% reduction in all cause mortality). The mortality benefit is in part due to a lower rate of sudden cardiac death (6). The use of beta blocker was low from the Chinese study (41.3%) (16) and better for Europe and the Mediterranean basin (77.8%)(17). It was 78% from the study done in a total of 11,731 patients from 19 developing countries in Africa, Latin America, and the Middle East (25) and 86.9% from a prospective study done at the cardiology OPD of R.G. Kar medical college in India (24).

Statin therapy should be instituted prior to hospital discharge, with some data supporting initiation at the time of diagnosis. Atorvastatin 80 mg/day, which was used in the PROVE IT-TIMI 22 and MIRACL trials is recommended (9). The compliance rates for the use of statins in prospective studies of China, Switzerland, and 19 developing countries in Africa, Latin America, and the Middle East were 80.4%, 98.6%, and 94% respectively (16, 23, 25).

Thrombin is a central mediator of clot formation through its activation of platelets, conversion of fibrinogen to fibrin, and activation of factor XIII, leading to fibrin cross-linking and clot stabilization. Anticoagulants, including heparins, direct thrombin inhibitors and fondaparinux with the activity of thrombin. Unfractionated heparin (UFH) is the most commonly utilized with in the first 24 hours of admission in studies done at GRACE (77%) (29), Europe and the Mediterranean basin (86.8%) (17) and tertiary hospital in Kenya (73%) (21).

1.3.3 Risk factors for ACS

Even though Coronary heart disease is a global health problem that affects all ethnic groups variations in the risk factor profiles for CHD, the age of onset of the disease, and mortality ratios have, however, been observed between different populations. Smoking, dyslipidemia, hypertension, diabetes and obesity are conventional risk factors. Different studies have shown variable prevalence of these risk factors (58).

In a study of 4700 patients with ACS, admitted to the coronary care unit at the R. K. Khan Hospital, Durban, South Africa over a 15 year period [May 1995 to June 2010] have shown that visceral obesity (82% of patients) was the most commonly observed risk factor, while 78% had hypercholesterolaemia and 74% had a family history of vascular disease (35).

In a hospital based observational study conducted at Universal College of Medical Science Teaching Hospital, Bhairahawa, Nepal from September 2012 to August 2013 it was found that hypertension was the most prevalent risk factor for the occurrence of ACS which occur in 64% of patients, dyslipidemia in 62% of patients, history of cigarette smoking in 39% and DM in 19% of patients (34).

A retrospective descriptive study was done from January 1st 2010 to December 31st 2012 within the Cardiology department of Yalgado Ouedraogo University Hospital, Burkina Faso. Main cardiovascular risk factors included hypertension (33%), obesity (33%), smoking (27%), diabetes (27%), dyslipidemia (20%), and family history of CHD in 7% of cases. Cardiovascular risk factors were similarly noticed among young and older patients except for hypertension which was significantly more prevalent in older patients (70.96% of cases, p=0.015) and smoking which was more prevalent among young patients compared to patients above 45 years of age (57).

2. OBJECTIVES

2.1 General objective

To assess the outcome of Acute Coronary Syndrome patients admitted to TASH

2.2 Specific objectives

- To assess the medical management of ACS patients admitted at TASH
- To determine the proportion of in-hospital mortality for ACS patients admitted to TASH
- To determine the risk factors for development of ACS in TASH
- To determine factors affecting in-hospital mortality in TASH

3. METHODOLOGY

3.1 Study area and study period

The study was conducted at TASH on patients with a discharge diagnosis of ACS during the period January 1, 2012 to December 31, 2014. Affiliated with AAU College of Health Sciences, TASH is the biggest public hospital in Addis Ababa and it is also a training center for undergraduate and post graduate medical students. TASH gives a 24 hour service for around 370,000 - 400,000 patients a year for patients coming from Addis Ababa and allover Ethiopia. The hospital has more than 800 beds (27).Currently, Internal Medicine department of TASH have 92 beds for in-patient admissions and a medical ICU. Four senior cardiologists are actively working now.

3.2 Study design

A retrospective cross-sectional study design was employed.

3.3 Population

3.3.1 Source population

All patients with acute coronary syndrome who were admitted in TASH

3.3.2 Study population

Patients who had a discharge diagnosis of acute coronary syndrome

3.4 Inclusion and exclusion criteria

Inclusion criteria

- age $\geq$ 18 years

Exclusion criteria

- Patients transferred to another hospital
- Patients discharged against medical advice

3.5 Sample size determination

All patients admitted within the study period were included

3.6 Study variables

Dependent variables

- In-hospital mortality

Independent variables

- Age
- Sex
- Time from symptom onset until presentation to ED
- Prior medical history
- Blood pressure during admission
- Killip class
- Serum lipid levels
- Ejection fraction
- Diagnosis type
- Use of aspirin on admission
- Use of beta blocker on admission
- Use of anticoagulants

3.7 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 record and documentation office. Data was collected by trained clinical pharmacists who were working in TASH using a data abstraction format from patient charts. For each case of ACS, binary data was collected as either performing or not performing each element by considering the exclusion criteria. Only patients eligible to receive the treatment were included in calculating the percent of patients taking the drugs.

3.8 Statistical analysis

The data was entered in to computer using EPI-info 3.5.4 software and the data was cleared, explored, standardized and summarized using SPSS version 20.0. Descriptive analysis was used to describe the pattern of each independent variables and logistic regression was used to determine crude and adjusted odds ratio. Bivariate analyses was carried out to assess 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).

3.9 Ethical consideration

Ethical clearance was obtained from the ethical review committee of School of Pharmacy as well as department of Internal Medicine, School of Medicine. Before data collection, permission was obtained from the out-patient directorate of TASH. The names of patients were replaced with codes to avoid individual identifiers.

3.10 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.

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.

Smoking History: confirming cigarette smoking in the past.

- Current: Smoking cigarettes within 1 month of this admission
- Recent: Stopped smoking cigarettes between 1 month and 1 year before this admission
- Former: Stopped smoking cigarettes greater than 1 year before this admission
- Never: Never smoked cigarette

Family history of premature CAD: 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

Killip class: Killip class of the patient at the time of hospital admission:

- **Class 1:** Absence of rales over the lung fields and absence of S3
- **Class 2:** Rales over 50% or less of the lung fields or the presence of an S3
- **Class 3:** Rales over more than 50% of the lung fields
- **Class 4:** Shock

Bleeding: An episode of bleeding is defined by the TIMI criteria as:

- **Major:** Overt clinical bleeding (or documented intracranial or retroperitoneal hemorrhage) associated with a drop in hemoglobin of greater than 5 g/dl (0.5 g/l) or in hematocrit of greater than 15% (absolute) Note: A patient who experiences an intracranial hemorrhage should be considered to have a major hemorrhage.
- **Minor:** Overt clinical bleeding associated with a fall in hemoglobin of 3 to less than or equal to 5 g/dl (0.5 g/l) or in hematocrit of 9% to less than or equal to 15% (absolute)
- **None**: No bleeding event that meets the major or minor definition

Percutaneous coronary intervention (PCI): A procedure that involves a cardiologist feeding a catheter with a deflated balloon via the femoral artery or radial artery to a narrowing or occlusion in the coronary vessels. At the narrowing, the balloon is inflated to open the artery, allowing blood to flow. A stent may be placed at the site of the blockage to permanently open the artery.

ST-segment elevation acute coronary syndrome/myocardial infarction/ (STEACS/MI): An acute heart attack diagnosed by a 12-lead ECG test. A heart attack occurs when an area of plaque within a coronary artery ruptures and forms a blood clot, suddenly blocking the supply of blood to a part of the heart muscle and depriving it of oxygen

Non-ST-segment elevation acute coronary syndrome (NSTEACS): A condition in which patients have acute chest pain but do not have persistent ST-segment elevation in their ECG. NSTEACS is further divided into unstable angina and non-ST elevation myocardial infarction. The ischemia is severe enough to release biomarkers of myocardial injury such as troponin I or T in case of NSTEMI but not in case of UA.

4. RESULTS

4.1 Socio-demographic characteristics and admission details

During the three years period, a total of 124 patient's charts with a diagnosis of ACS were reviewed for the study. The mean age was 56.3 (SD ±13.65) years ranging from 28 to 93 years. Ninety four (75.8%) patients were male. The mean length of hospital stay was 9.77 days (SD ± 6.42) with the minimum 1 day and the maximum 25 days. From the symptoms suggestive for ACS, 106(85.5%) patients experienced chest pain, 66(53.2%) patients had shortness of breath, and 42 (33.9%) patients had nausea or vomiting and 62 (50%) patients experienced diaphoresis during admission. The average time from onset of ACS symptoms to presentation in the emergency department was 91.7 hours (3.8 days) with a range of 2 h to 20 days. No patient arrived within the first hour of symptom onset. Twenty four patients (19.7%) arrived in between 1 h and 12 h period, 52 patients (42.6%) arrived between 12 h and 3 days period and the rest 46 patients (37.7%) arrived in the emergency department after 3 days of symptom onset. Timing of presentation of two patients was not recorded as shown in Table 1.

Table 1: Socio-demographic characteristics and admission details of Acute Coronary Syndrome patients in Tikur Anbessa Specialized Hospital, Ethiopia, 2012-2014

Variables	In-hospital mortality		Total
	Yes	No	
	Freq (%)	Freq (%)	Freq (%)
Sex			
Male	24(25.5)	70(74.5)	94(75.8)
Female	10(33.3)	20(66.7)	30(24.2)
Age			
< 55	12(23.1)	40(76.9)	52(42.0)
55-64	6(16.7)	30(83.3)	36(29.0)
≥ 65	16(44.4)	20(55.6)	36(29.0)
Symptoms			
Chest pain			
Yes	26(24.5)	80(75.5)	106(85.5)
No	8(44.4)	10(55.6)	18(14.5)
SOB			
Yes	20(30.3)	46(69.7)	66(53.2)
No	14(24.1)	44(75.9)	58(46.8)
Nausea/Vomiting			
Yes	14(33.3)	28(66.7)	42(33.9)
No	20(24.4)	62(75.6)	82(66.1)
Diaphoresis			
Yes	14(22.6)	48(77.4)	62(50.0)
No	20(32.3)	42(67.7)	62(50.0)
Time from symptom onset			
< 1 hr	0(0)	0(0)	0(0)
1 hr-12 hr	2(8.3)	22(91.7)	24(19.7)
13 hr-72 hr	10(19.2)	42(80.8)	52(42.6)
> 72 hr	20(43.5)	26(56.5)	46(37.7)
total	32(26.2)	90(73.8)	122(100)

Regarding the conventional risk factors, 76 (61.3%) patients had a previous history of hypertension, 26(21%) patients had DM, 20(16.1 %) patients had a previous history of MI, 12.9% of patients had a history of dyslipidemia, 6.5 % had prior exertional angina pectoris, 8.1% had HF previously, and 14.5 % of patients were either a current smoker or have a history of cigarette smoking previously as shown in Table 2. The average pack years for cigarette smokers was 18 pack years (SD ± 13.82) with a range of 2 up to 40 pack years.

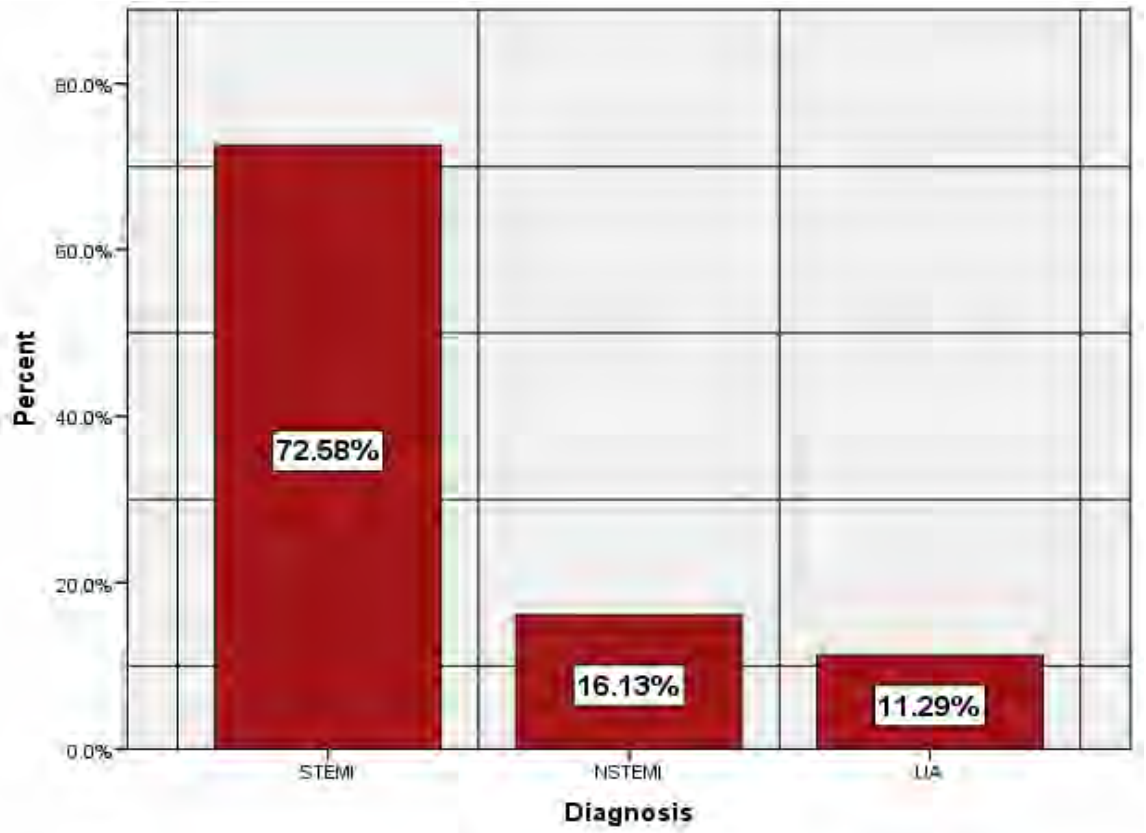
Table 2: Risk factors for Acute Coronary Syndrome patients admitted in Tikur Anbessa Specialized Hospital, Ethiopia, 2012-2014

Variables	Frequency	Percent
Hypertension		
Yes	76	61.3
No	48	38.7
Diabetes Mellitus		
Yes	26	21.0
No	98	79.0
Previous MI		
Yes	20	16.1
No	104	83.9
Smoking History		
Yes	18	14.5
No	106	85.5
Dyslipidemia		
Yes	16	12.9
No	108	87.1
Heart failure		
Yes	10	8.1
No	104	83.9
Previous angina		
Yes	8	6.5
No	116	93.5

MI=Myocardial Infarction

4.2 Class of diagnosis

Of the 124 ACS patients who were admitted during the three years period, 90(72.6%) were diagnosed as STEMI, 20(16.1%) as NSTEMI and the rest 14(11.3%) were UA patients.



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

Figure 1: Class of diagnosis for Acute Coronary Syndrome patients in Tikur Anbessa Specialized Hospital, Ethiopia, 2012-2014

4.3 Initial assessment and investigations

As shown in Table 3, the average systolic and diastolic BP during admission was 135.5(SD ± 30.33) and 84.6(SD ± 21.11), respectively. The mean heart rate during admission was 93.2(SD ± 16.6) with a minimum 59 and a maximum of 130. The random blood sugar (RBS) was measured in only 66(54.8%) patients, and the average RBS was 183.2(SD ± 90.33) with a minimum of 88 and a maximum of 441.

Table 3: Initial assessment during admission for Acute Coronary Syndrome patients admitted in Tikur Anbessa Specialized Hospital, Ethiopia, 2012-2014

Variables	Frequency	Percent
SBP(mmHg)		
<90	6	4.9
90-119	28	23.0
120-139	26	21.3
140-159	30	24.6
≥160	32	26.2
DBP(mmHg)		
< 60	8	6.6
60-79	36	29.5
80-89	24	19.7
90-99	16	13.1
≥ 100	38	31.1
Killip class		
Killip class I	22	33.3
Killip class II	20	30.3
Killip class III	16	24.3
Killip class IV	8	12.1

SBP=Systolic blood pressure; DBP=Diastolic blood pressure

The killip class of patients was documented for 66(54%) of patients. From those, 36.4% were on Killip class III and IV. High in-hospital mortality was documented from Killip class IV patients (87.5%) (Table 3).

Biomarkers of cardiac injury including troponins and CKMB were measured for 118(95.2%) of patients. Troponins and CKMB were at the normal range in 11.9% and 38.1% of patients respectively (Table 3).

Fasting serum lipid level was measured in 80 (64.5 %) patients during their hospital stay. The mean total cholesterol, LDL, HDL and triglyceride values were 182.5 ± 47.7, 118.5 ± 47.3, 40.5 ± 14.0 and 158.8 ± 84.7 respectively. High level of total cholesterol (>200 mg/dl) was documented in 26(33.3%) patients where as LDL level was more than 100 mg/dl in 44 (62.9%) patients. Low amount of high density lipoprotein was measured in 47.1% of patients. About 39.5% of patients were admitted with high amount of triglyceride level which was higher than 150 mg/dl.

Echocardiography was done for about 86(69.4%) patients. From those patients who had documented EF result, 29.2% had severe reduction in LVEF (EF < 30%), 37.5% had EF in between 30-49%, 20.8% had EF in between 50-59% and the rest 12.5% had EF of more than 60% (Table 4).

Table 4: Initial laboratory investigations for Acute Coronary Syndrome patients admitted in Tikur Anbessa Specialized Hospital, Ethiopia, 2012-2014

Variables	Frequency	Percent
Serum lipids		
Total cholesterol		
< 200	52	66.7
≥ 200	26	33.3
LDL cholesterol		
<100	26	37.1
≥ 100	44	62.9
HDL cholesterol		
<40	32	47.1
≥40	36	52.9
Triglyceride		
<150	46	60.5
≥ 150	30	39.5
Ejection fraction (%)		
< 30	14	29.2
30-49	18	37.5
50-59	10	20.8
≥ 60	6	12.5

LDL= Low density lipoprotein; HDL= High density lipoprotein

4.4 Treatment commenced during hospitalization

With regard to the medications which had been given during hospitalization, the loading dose of aspirin (162-325 mg) was given for 98(79%) patients, while all patients had received the maintenance dose of aspirin. About 96(77.4%) 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. From patients who were treated with anticoagulants, 91.7% received the anticoagulant at the ED, while the rest 8.3% of patients received the anticoagulant after they were transferred to ICU or ward. The use of anticoagulants is very low in UA patients (Table 5).

From patients who were eligible for taking beta blockers, 88.1 % of patients received beta blockers during hospitalization. From those, 94.2% received beta blockers immediately with in the first 24 hour of admission at ED and the rest 5.8% received beta blockers later in the ward. The utilization of morphine and nitroglycerine in ED was 16(12.9%) and 44(35.5%), respectively. Statins were started for about 85.5% of patients during their hospital stay. From those, 98.1% were having access for statins immediately at the ED. Atrovastatin was used in 83% of patients, simvastatin for 15.1% and lovastatin in 1.9% of patients (Table 5).

Table 5: Medical treatment commenced during hospital stay for Acute Coronary Syndrome patients in Tikur Anbessa Specialized Hospital, Ethiopia, 2012-2014

Drugs	**Diagnosis**			**Total**
	STEMI	**NSTEMI**	**UA**	
	Freq (%)	Freq (%)	Freq (%)	Freq (%)
Aspirin LD(162-325 mg)	76(84.4%)	15(75)	7(50)	98(79)
Aspirin MD	90(100)	20(100)	14(100)	124(100)
Clopidogrel LD(300 mg)	66(73.3)	10(50)	4(28.6)	80(64.5)
Clopidogrel MD(75 mg)	88(97.8)	16(80)	8(57.1)	112(90.3)
Anti-coagulant	76(84.4)	16(80)	4(28.6)	96(77.4)
Beta blocker	76(88.4)	17(89.5)	11(84.6)	104(88.1)
Morphine	14(15.6)	2(10)	0(0)	16(12.9)
Nitroglycerine	34(37.8)	6(30)	4(28.6)	44(35.5)
ACEIs/ARBs	66(73.3)	13(65)	9(64.3)	88(71)
Calcium channel blockers	6(6.7)	0(0)	2(14.3)	8(6.5)
Statins	76(84.4)	18(90)	12(85.7)	106(85.5)

LD= Loading dose; MD=Maintenance dose

From those patients who were discharged alive (N=90), only 61.1 % had a combination of drugs comprised of aspirin, clopidogrel, beta blocker, ACEI and statin on discharge (Table 6).

Table 6: Medications given on discharge for Acute Coronary Syndrome patients in Tikur Anbessa Specialized Hospital, Ethiopia, 2012-2014

Medications	Freq (%)
Aspirin	88(97.8)
Clopidogrel	70(77.8)
Beta blocker	82(91.1)
ACEIs/ARBs	70(77.8)
Statins	82(91.1)
Nitrates	8(8.9)
CCBs	2(2.2)

ACEIs= Angiotensin converting inhibitors, ARBs= Angiotensin receptor blockers

4.5 Treatment outcome and major in-hospital events

Twenty patients (16.1%) had developed congestive heart failure in hospital, 10 patients (8.1%) major arrhythmia and 6 patients (4.8%) experienced re-infarction during their hospitalization (Table 7). Cardiogonic shock (11.3%) was the major cause of hospital death. No complication was documented for UA patients at hospital.

Table 7: Major in-hospital events in Acute Coronary Syndrome patients admitted at Tikur Anbessa Specialized Hospital, Ethiopia, 2012-2014

Event	Diagnosis			total
	STEMI	NSTEMI	UA	
	Count (%)	Count (%)	Count (%)	Count (%)
CHF in hospital	18(90)	2(10)	0(0)	20(16.1)
Cardiogonic shock	14(100)	0(0)	0(0)	14(11.3)
Major arrhythmia in hospital	8(80)	2(20)	0(0)	10(8.1)
Re-infarction at hospital	6(100)	0(0)	0(0)	6(4.8)
Stroke at hospital	2(100)	0(0)	0(0)	2(1.6)
Major bleeding episode at hospital	2(100)	0(0)	0(0)	2(1.6)

STEMI=ST segment elevation myocardial infarction; NSTEMI=Non-ST segment elevation myocardial infarction; UA= Unstable angina; CHF= congestive heart failure

From the total of 124 patients admitted during the three years period, 34 patients (27.4%) had died in hospital where as the rest 90 (72.6%) patients discharged alive (Fig. 2). High in-hospital mortality (35.6%) was documented from patients who were diagnosed as STEMI.

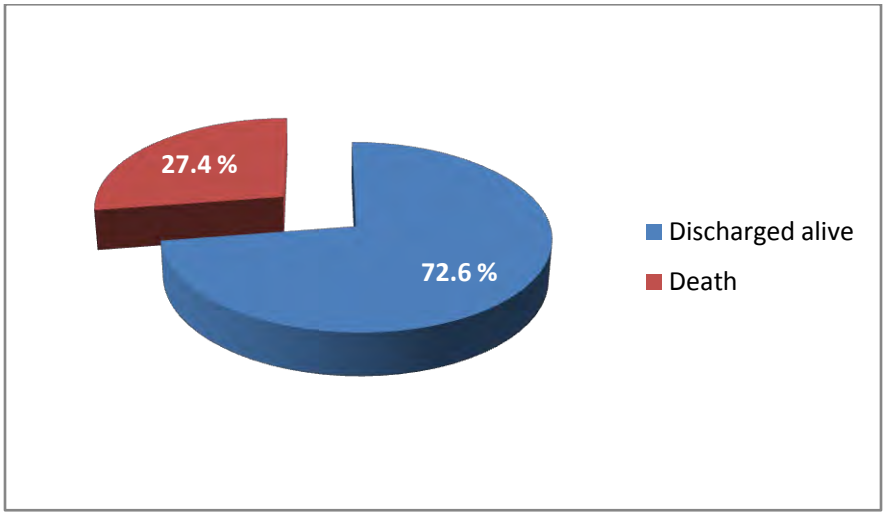


Figure 2: In-hospital mortality of Acute Coronary Syndrome patients admitted in Tikur Anbessa Specialized Hospital, Ethiopia, 2012-2014

4.6 Predictors of in-hospital mortality

Data were analyzed to determine whether there was any relationship between different variables and in-hospital mortality. Initial bivariate analysis showed that there was no relationship between in-hospital mortality and patients' sex, symptoms during admission, previous history of DM and MI. In addition, medications given during admission didn't show any significant association. However, there was a statistically significant association between in-hospital mortality and age of patients (P=0.024), time from symptom onset to presentation at ED (P=0.002), previous history of hypertension (P=0.005), Killip class (P=0.001) and class of diagnosis (P=0.004) (Table 8).

Bivariate analysis did not take into account the effect of confounding factors which may affect the relationship between these factors and in-hospital mortality. Therefore, multivariable analysis was carried out for variables which were having a P-value of < 0.1. Hence, multivariable analysis showed age ≥65 (P=0.042), time from symptom onset to presentation at ED (P=0.001), a previous history of hypertension (P=0.025), Killip class III and IV (P=0.001) and diagnosis of STEMI (P=0.005), to have statistically significant association with in-hospital mortality.

Table 8: Predictors of in-hospital mortality for Acute Coronary Syndrome patients admitted in Tikur Anbessa Specialized Hospital, Ethiopia, 2012-2014

Variables	In-hospital Mortality		COR (95% CI)	AOR(95% CI)
	Yes (%)	No (%)		
Age				
<55	12(23.1)	40(76.9)	1.00	1.00
55-64	6(16.7)	30(83.3)	0.67(0.23,1.98)	1.29(0.28,6.03)
≥65	16(44.4)	20(55.6)	2.67(1.06,6.70)*	4.72(1.06,21.08)*
Time from symptom onset(hr)				
≤ 12	2(8.3)	22(91.7)	1.00	1.00
13-72	10(19.2)	42(80.8)	2.62(0.53,13.02)	0.29(0.03,2.66)
> 72	22(45.8)	26(54.2)	9.31(1.97,44.07)*	5.52(1.05,32.22)*
Hypertension				
Yes	28(36.8)	48(63.2)	4.08(1.54,10.82)*	5.10(1.23,21.11)*
No	6(12.5)	42(87.5)	1.00	1.00
Diagnosis				
STEMI	32(35.6)	58(64.4)	8.83(1.99,39.26)*	35.28(2.88,432.27)*
NSTEMI + UA	2(5.9)	32(94.1)	1.00	1.00
Killip class				
Killip class I & II	6(14.3)	36(85.7)	1.00	1.00
Killip class III & IV	13(54.2)	11(45.8)	7.09(2.18,23.07)*	11.92(2.82,50.43)*

* Statistically significant at P-value < 0.05

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

According to multivariable analysis, patients with the age of more than 65 were 4.72 times more likely to die at hospital as compared to patients who were less than the age of 55(AOR =4.72; 95% CI: 1.06-21.08). Patients who arrived at ED after 3 days of symptom onset were 5.52 times more likely to die as compared to patients who arrived within 12 hours of symptom onset(AOR=5.52;95% CI: 1.05-32.22). Patients who have a previous history of hypertension were 5.10 times more likely to die at hospital as compared to patients who have not (AOR =5.10; 95% CI: 1.23-21.11). Patients with a diagnosis of STEMI were 35.28 times more likely to face hospital death as compared to other ACS types (AOR=35.28; 95% CI: 2.88-432.27). At last, Killip class III and IV patients were 11.92 times more likely to die at hospital as compared to Killip class I and II patients (AOR=11.92;95% CI: 2.82-50.43).

5. DISCUSSION

The age distribution of ACS patients in TASH was 56.3 ±13.65 years which is in line with that of a study made in Kenya (59.7 ± 3.8 years) (21) and India 60.1±11.2 (28) but lower in a decade than that of Global Registry of Acute Coronary Events (The GRACE registry) (66.3 ±10 years) which is a multinational registry of ACS covering 247 hospitals in 30 different countries (29).

The length of hospital stay has been considerably decreased with the improvement of therapies and implementation of evidence-based therapies in patients with ACS (6, 9).The mean length of hospital stay is very high in TASH (9.77 ± 6.42 days) as compared to a study made in Kenya, 5.3 ± 1 day (21), Brazil, 5.1 ± 8.0 days (30), US 5.56 days (31).This may be due to absence of services like PCI and thrombolytics in TASH.

In general, patients with symptoms of ACS without chest pain are less likely to be diagnosed with ACS immediately on admission, are older, have more co-morbidity, are more likely to receive suboptimal treatment and experience a higher mortality across the spectrum of ACS than those who present with chest pain (47). In the present study chest pain was not the chief complaint in 14.5% of patients during admission. High mortality was documented in TASH from ACS patients who didn't have chest pain during admission (44.4% vs. 24.5%). In TASH, 53.2% of patients had shortness of breath, 33.9% of patients had nausea or vomiting and 50% of patients had experienced diaphoresis during admission. The same finding was observed from 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%). In addition, their hospital case fatality rates were increased, with 13.0% of atypical patients were dead compared with 4.3% of typical patients (48).

Even though interventions to restore blood flow such as PCI and thrombolytics were absent in TASH, time from symptom onset until presentation in the ED have great impact on in-hospital mortality. This study shows a significant delay of patients for seeking medical care (a mean time of presentation to ED was 3.8 days). No patient in TASH arrived to ED within the first hour of symptom onset. Only 19.7% of patients arrived within 12 h of symptom onset where as 37.7% of patients arrived after 3 days of symptom onset (43.5% have died in hospital). According to a study made in Kenya, 78% of patients arrived within 12 h of symptom onset (21). The average

time delay before medical care was 14.5 h in a study done in Dacar, Senegal (32). 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 (33). The proportion of patients presenting within 12 h was highest in Scandinavia (79%) and in Belgium (77%) and lowest in Eastern Europe (51%) (33). This great delay in seeking medical care 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 patients were having previously 61.3% of ACS patients in TASH have hypertension,21% have had DM and 16.1% have previous history of MI, which is in line with that of the study done in Nepal in which 64% of ACS patients were hypertensive and 19 % were DM patients (34). The Kenyan study also reflects the same finding as hypertension and DM were the leading risk factors for development of ACS (21). The study on South African Indians with ACS showed that 82% of ACS patients have visceral obesity as the number one risk factor and family history of vascular disease (74%) and cigarette smoking (60%) the 2nd and the 3rd respectively (35). The Saudi Project for Assessment of Coronary Events (SPACE) registry reported that, history of diabetes mellitus was present in 58.1%, hypertension in 55.3%, hyperlipidemia in 41.1%, and 32.8% were current smokers (36).

Dyslipidemia is a major risk factor for CHD. The mean fasting total cholesterol, LDL, HDL and triglyceride values measured immediately during admission for ACS patients in TASH were 182.5 ± 47.7, 118.5 ± 47.3, 40.5 ± 14.0 and 158.8 ± 84.7 respectively. This was in line with the finding from The Get with the Guidelines database (231,986 hospitalizations from 541 hospitals) which was analyzed for CAD hospitalizations from 2000 to 2006 with documented lipid levels in the first 24 hours of admission. Mean lipid levels were LDL 104.9 ± 39.8, HDL 39.7 ± 13.2, and triglyceride 161 ± 128 mg/dL (52). During tissue necrosis, acute phasic changes occur that alter the lipid profile levels post acute coronary events. Modifications of serum lipids after AMI include reductions in TC, LDL and HDL, in the range of 10 - 20 %, with reciprocal increases in triglyceride (TG) approximating 20 - 30 % (50). Several mechanisms accounting for these changes include the acute phase response associated with up-regulation of LDL-receptor (R) activity and reduction in several pivotal HDL regulatory proteins. From many clinical studies it

is clear that phasic changes do occur in patients following AMI and therefore there is a recommendation for detection of hyperlipidemia in patients with AMI that the serum lipids should be assessed either within 24 hours after infarction or after 2-3 months of AMI (51).

Cardiac biomarkers complement clinical assessment and the 12-lead ECG in the diagnosis, risk stratification, triage, and management of patients with suspected ACS. Therefore, measurement of a biomarker reflecting and quantifying cardiomyocyte injury, preferably cardiac troponin (cTn) I or T, is mandatory in all patients presenting with suspected ACS(6). Biomarkers were not measured for 4.8 % of ACS patients in TASH. This may be because of financial issue or the patient may die before measurements of biomarkers have been done.

The Killip classification categorizes patients with an acute MI based upon the presence or absence of simple physical examination findings that suggest LV dysfunction. In the present study high Killip classes (Killip class III and IV) patients accounted 36.4% which is in line with the Gulf Registry of Acute Coronary Events (22%) (43). High mortality in TASH (54.2%) 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 (44). These patients had significantly higher in-hospital mortality than those without HF (21.4 versus 7.2 %). Similar findings were noted in an analysis of international data on 4830 patients with STEMI from the GRACE registry (29). Sixteen percent had Killip class II or III HF on admission; patients with HF had increased mortality in-hospital (17 versus 4 %).

The measurement of LVEF after AMI has both prognostic and therapeutic implications and is a class I clinical practice guideline recommendation by the ACC/AHA. Reduced LVEF is associated with greater mortality among patients with coronary artery disease and predicts increased risks of early all-cause mortality, as well as sudden cardiac death after AMI (49).In the present study echocardiography was done for about 69.4% patients. From those reduced EF (<50%) was documented for 66.7% of patients and 29.2% of patients have severely impaired LVEF (<30%). Among 128,845 AMI patients in ACTION Registry between January 2007 and September 2009, 93.0% had in-hospital assessment of LVEF. Among assessed patients, LVEF was abnormal (LVEF <50%) in 45.6% of patients (42.3% of NSTEMI patients and 50.5% of STEMI patients) and moderately to severely impaired (LVEF <40%) in 22.6% of patients (21.9% of NSTEMI patients and 23.7% of STEMI patients) (49).

STEMI is the leading (72.6%) discharge diagnosis of ACS patients in TASH where as 16.1% of patients were NSTEMI and 11.3% were UA patients. STEMI cases were relatively high in TASH as compared to GRACE study in which STEMI cases were 34%, NSTEMI cases were 31% and UA patients account 29% of patients (29). The ACCESS registry for South Africa reported that STEMI accounts for 41% of ACS patients, NSTEMI accounts for 32% of cases and UA accounts the rest 29% of patients (25). Patients who were in follow up at the Saudi project for assessment of coronary events (SPACE) registry also show the same trend in which 41.5% were STEMI patients, 36.4% NSTEMI and the rest 22.1% were UA patients (36). 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).

With regard to treatment commenced during hospitalization loading dose of aspirin was given only for 79% of patients. It is very low as compared to studies made in South Africa (94%), Kenya (98%), Italy (92.8%) and Global registry of acute coronary events (GRACE) (92%)(21,22,25,29). This may be due to problems on documentation. Patients may take the drug but it may not be documented on the chart. Use of beta blockers in TASH during admission was 88.1% in TASH which is higher than that of GRACE (76%), South Africa (69%) and Italy (65%) (21, 22, 25). The same is true for use of statins for ACS patients in TASH. 85.5% of patients have access for statins during hospitalization which is higher as compared to studies made in Kenya (73%), GRACE(58%), and Canada(43%)(18,21,29).The use of morphine (12.9%) and nitrates (35.5%) during arrival at ED is very low in TASH which may be because of interruption on the availability of drugs.

The in-hospital mortality of ACS patients in TASH was very high (27.4%). High mortality (35.6%) was documented from STEMI patients. Mortality during admission was 9.6% in observational study done in 32 hospitals of Spain (38). 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% (37). In GRACE study in-hospital mortality for STEMI was 7%, for NSTEMI 4% and for UA 3% (29). In India in-hospital mortality was highest (8.2%) for STEMI (28). In all the previous studies in-hospital mortality was low as compared to that of TASH 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 old age, delayed time of presentation, patients who have previous history of hypertension, 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 (29).

Discharge medications containing dual anti-platelet (Aspirin and clopidogrel), beta blocker, ACEI and statins were very helpful for reduction of complications such as re-infarction and death after discharge. In the current study only 61.1% of patients who were discharged alive received all these five drug combinations during discharge. Result from Kerala ACS registry which is the largest ACS registry in India of 25748 patients showed that 80% of discharged patients have received appropriate discharge medications (28).

6. LIMITATION OF THE STUDY

Since this study is a single-centered study it may be difficult to generalize for the general population. The HMIS registration book which was used to record patients served in the emergency department of TASH before 2012 was not available. Hence, it was difficult to include more patients for this study. Since retrospective method was used certain data may be missed.

7. CONCLUSION

The medical management of ACS patients in TASH was in line with the recommendations of international guidelines. However, No patient in TASH has received PCI or thrombolytics and the time it takes for ACS patients from onset of ACS symptoms to presentation at ED in TASH was very long. As a result, because of absence of these early revascularization methods and delay of patients in seeking medical care, in-hospital mortality in TASH was very high (27.4%). The hospital stay of ACS patients in TASH was very long. The majority of ACS patients in TASH were diagnosed as STEMI. CHF and cardiogonic shock were the major in-hospital events for these patients. Older age, time for presentation to ED, previous history of hypertension, being diagnosed as STEMI, and higher Killip class were found to be independent predictors of in-hospital mortality in TASH.

8. RECOMMENDATION

This study shows high in-hospital mortality of ACS patients in TASH. Therefore

- TASH should start PCI service and avail medications such as thrombolytics, nitroglycerine and morphine 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.
- Continuous education should be given for the whole population and specifically for patients with cardiovascular problems to avoid the risk factors for ACS and also to seek immediate medical care once patients develop angina symptoms.
- The outcome of patients after discharge should also be studied.
- At last prospective, multi-centered studies on large sample size should be carried out to have a big picture of the problem behind the management and treatment outcome of ACS patients in Ethiopia.

9. REFERENCES

1. Rayner M, Petersen S. European Cardiovascular Disease Statistics. London: *British Heart Foundation*. 2010. Available from http://www.heartstats.org
2. WHO. Fact sheet N8310.Updated on June 2011, available at http://www.who.int/mediacentre/factsheets/fs310/en/index.htm
3. Mozaffarian D, Roger VL. Heart disease and stroke statistics 2013 update: a report from the American Heart Association. *Circulation*.2013; 127: e 6-245
4. Vedanthan R, Seligman B, Fuster V. Global Perspective on Acute Coronary Syndrome; a Burden on the Young and Poor. *Circulation*.2014; 114:1959-1975
5. Pitt B, Loscalzo J, Ycas J, Raichlen JS. Lipid levels after acute coronary syndromes. *Journal of American College of Cardiology*.2008; 51:1440
6. European Society of Cardiology. ESC Guidelines for the management of acute coronary syndromes in patients presenting without persistent ST-segment elevation. *European Heart Journal*. 2016; 37:267–315
7. Stub D, Smith K, Bernard S, Nehme Z, Stephenson M, Bray JE, *et al*. Air versus oxygen in ST-segment-elevation myocardial infarction.*Circulation.*2015;131:2143–2150
8. Thygesen K, Alpert JS, White HD. Universal definition of myocardial infarction. *European Heart Journal*. 2007; 28:2525 –2538
9. AHA/ACC Guideline. AHA/ACC Guideline for the Management of Patients with Non–ST-Elevation Acute Coronary Syndromes. *Journal of the American college of cardiology.*2014; 64(24):e142-225
10. Scottish Intercollegiate Guidelines Network (SIGN). Acute coronary syndromes. Edinburgh: *SIGN*; 2013. (SIGN publication no. 93). [February 2013]. Available from URL: http://www.sign.ac.uk
11. Kontos MC, Diercks DB. Treatment and outcomes in patients with myocardial infarction treated with acute beta blocker therapy: result from the American College of Cardiology. *American Heart Journal*. 2011; 161:864-70
12. Tsai CL, Magid DJ, Sullivan AF, Gordon JA, Kaushal R, Michael P, *et al*. Quality of Care for Acute Myocardial Infarction in 58 U.S. Emergency Departments. *Academy of Emergency Medicine*. 2010; 17(9): 940–950

13. Fox KA, Goodman GS, Klein W, Brieger D, Steg PG, Dabbous O, *et al.* for the GRACE Investigators. Management of acute coronary syndromes; Variations in practice and outcome: findings from the Global Registry of Acute Coronary Events (GRACE). *European Heart Journal*. 2002; 23:1177-89
14. Kuch B, Bolte HD, Hoermann A, Meisinger C, Loewel H. What is the real hospital mortality from acute myocardial infarction? Epidemiological vs clinical view. *European Heart Journal*. 2002; 23:714–720. Available online at http://www.idealibrary.com
15. Giday A, Weldeyes E. Trends in cardiovascular disease over time: A 30-year retrospective analysis of Medical-ICU admissions in ADDIS ABABA, ETHIOPIA. *Ethiopian Medical Journal.* 2015; 53(3)
16. Wang Y, Fu R, Wang Z, Bao H, Chen Y, Yang F, *et al*. Quality and outcomes: Assessing the Quality of Care for Patients with Acute Myocardial Infarction in China. *Clinical Cardiology*. 2015;38(6):327–332
17. Mandelzweig L, Battler A, Boyko V, Bueno H, Danchin N, Filippatos G, *et al*. The second Euro Heart Survey on acute coronary syndromes: characteristics, treatment, and outcome of patients with ACS in Europe and the Mediterranean Basin in 2004. *European Heart Journal*.2006; 27: 2285–2293
18. Domes T, Szafran O, Bilous C, Olson O, Spooner R. Acute myocardial infarction quality of care in rural Alberta. *Canada Family Physician*.2006; 52:68-69
19. Ganova-Iolovska M, Kalinov K, Geraedts M. Quality of care of patients with acute myocardial infarction in Bulgaria: a cross-sectional study. *BMC Health Services Research*. 2009; 9:15
20. Hsieh DJ, Chen WK. Quality of care of patients presenting with acute coronary syndrome in emergency departments in Taiwan. *Journal of acute medicine*. 2011; 1:33-40
21. Wachira B, Andrew O, Harun A. Acute management of ST-elevation myocardial infarction in a tertiary hospital in Kenya: Are we complying with practice guidelines? *African Journal of Emergency Medicine.* 2014; 4:104-108
22. Flotta D, Rizza P, Coscarelli P, Pileggi C, Nobile GA, Pavia M, *et al*. Appraising Hospital Performance by Using the JCHAO/CMS Quality Measures in Southern Italy. *PLOS ONE.* 2012;7(11)

23. Auer R, Gencer B, Raber L. Quality of Care after Acute Coronary Syndromes in a Prospective Cohort with Reasons for Non-Prescription of Recommended Medications. *PLOS one.*2014;9(3): e93-147
24. Ghosh A, Das AK, Pramanik S. Drug utilization study in patients of acute coronary syndrome on follow-up visits at a tertiary care center in Kolkata. *Asian Journal of Pharmacy and Life Science*. 2012; 2(2):2231 – 4423
25. The ACCESS Investigators. Management of acute coronary syndromes in developing countries: Acute Coronary Events-a multinational Survey of current management Strategies. *American Heart Journal*. 2011;162(5):853-859
26. DeVon. Time to Treatment for Acute Coronary Syndromes: The Cost of Indecision. *Journal of Cardiovascular Nursing.*2010; 25(2): 106–114
27. Kaleab T. Ethiopia's main public hospital to shut its surgery rooms for renovation. 2014; Available at: http://www.zegabi.com/articles/6903
28. Kerala ACS registry. Presentation, management, and outcomes of 25748 acute coronary syndrome admissions in Kerala, India: results from the Kerala ACS Registry. *European Heart Journal*. 2013; 34:121–129
29. The GRACE Investigators. Predictors of hospital mortality in the Global Registry of Acute Coronary Events. *Arch Intern Med*; 2003;163:2345-2353
30. Laurencet ME, Girardin F, Rigamonti F, Bevand A, Meyer P, Carballo D *et al*. Early Discharge in Low-Risk Patients Hospitalized for Acute Coronary Syndromes: Feasibility, Safety and reasons for Prolonged Length of Stay. *PLOS ONE*.2016;11(8): e0161493
31. Joyce C. LaMori J. The economic impact of acute coronary syndrome on length of stay: an analysis using the Healthcare Cost and Utilization Project (HCUP) databases.2016; Pages 191-197
32. Sarr M, Ba MD, Ndiaye MB, Bodian M, Jobe M, Kane A, *et al*. Acute coronary syndrome in young Sub-Saharan Africans: *BMC Cardiovascular Disorders*.2013;13:118
33. European Network for Acute Coronary Treatment (ENACT). The ENACT study: a pan-European survey of acute coronary syndromes. *European Heart Journal*. 2000;21:1440–1449
34. Khatri P, Simkhada R. Study on conventional risk factors in acute coronary syndrome. *Journal of Universal College of Medical Sciences*. 2015;03(02):10

35. Ranjith N, Pegoraro RJ, Zaahl MG. Risk Factors Associated with Acute Coronary Syndromes in South African Asian Indian Patients [The AIR Study]. *Journal of Clinical and Experimental Cardiology*.2011;2(10):163
36. AlHabib KF, Hersi A, AlFaleh H, Kurdi M, Arafah M, Youssef M, AlNemer K, *et al*. The Saudi Project for Assessment of Coronary Events (SPACE) registry: Design and results of a phase I pilot study. *Canadian Journal of Cardiology*. 2009; 25(7): e255-e258.
37. Hasdai D, Behar S, Boyko V, Danchin N, Bassand JP, Battler A, *et al*. Cardiac biomarkers and acute coronary syndromes-The Euro Heart Survey of Acute Coronary Syndromes Experience. *European Heart Journal*. 2008;24,1189–1194
38. Medical Practice Variations Andalusian Group. Hospital mortality in acute coronary syndrome: differences related to gender and use of percutaneous coronary procedures. *BMC Health Services Research*. 2007; 7:110
39. Antithrombotic Trialists' Collaboration. Collaborative meta-analysis of randomized trials of antiplatelet therapy for prevention of death, myocardial infarction, and stroke in high risk patients. *British Medical Journal*. 2012; 324(7329):71-86.
40. Boersma E, Harrington RA, Moliterno DJ. Platelet glycoprotein IIb/IIIa inhibitors in acute coronary syndromes: a meta-analysis of all major randomized clinical trials. *Lancet*.2002; 359(9302):189-98.
41. Gracia DA, Baglin TP, Weitz JI. Parenteral anticoagulants, Antithrombotic therapy and prevention of thrombosis, 9th edition: American college of chest physicians' evidence based clinical practice guidelines. *Chest*. 2012;141: e 245-435
42. Kumar A, Cannon CP. Acute Coronary Syndromes: Diagnosis and Management. *Mayo Clin Proc*. 2013; 84(10):917-938
43. Zubaid M. Preliminary results from Gulf registry of acute coronary events (Gulf RACE). *Heart views*. 2007; 8(4): 155-158
44. Wu AH, Parsons L, Every NR. Hospital outcomes in patients presenting with congestive heart failure complicating acute myocardial infarction: a report from the Second National Registry of Myocardial Infarction (NRMI-2). *Journal of American College of Cardiology*. 2012; 40:1389.

45. Alemayehu B, Amogne M. The pattern of coronary artery diseases as diagnosed by coronary angiography and the outcome of Percutaneous Coronary Intervention (PCI) in Ethiopia. *Ethiopian journal of health development*. 2014;28(1)
46. Schneider J. Causes of sudden death in Addis Ababa, Ethiopia. *Ethiopian Medical Journal*. 2001; 39:223-239.
47. Canto JG, Shilpak MG, Rogers WJ, *et al*. Prevalence, clinical characteristics, and mortality among patients with MI presenting without chest pain. *JAMA*. 2000;282:3223-9
48. Brieger D, Goodman SG, Steg G, Budaj A, White K, Montalescot G, *et al.;* for the GRACE Investigators. Acute Coronary Syndromes without chest pain, an under-diagnosed and under-treated high-risk group, insights from the Global Registry of Acute Coronary Events.*Chest*.2004;126(2):461-469
49. Miller AL, Dib C, Li L, Chen AY, Amsterdam E, Funk M, Saucedo JF, Wang TY, *et al*. Left ventricular ejection fraction assessment among patients with acute myocardial infarction and its association with hospital quality of care and evidence-based therapy use.*Circulation*.2012; 5:662-671
50. Miller M. Lipid levels in the post-acute coronary syndrome setting. *Journal of American College of Cardiology*. 2008; 51:1446-7.
51. Nigam PK. Biochemical markers of myocardial injury. *Indian Journal of clinical biochemistry*. 2007; 22:10-7.
52. Sachdeva A, Cannon CP, Deedwania PC, LaBresh KA, Smith SC, Dai D, *et al*. Lipid levels in patients hospitalized with coronary artery disease: An analysis of 136,905 hospitalizations in Get with the Guidelines. *American Heart Journal*. 2009; 157:111-7.e2
53. OECD. "Mortality following acute myocardial infarction (AMI)", in Health at a Glance 2015: *OECD Indicators*, OECD Publishing, Paris.
54. Ahmed A, Abdulwahab A, Hesham A, Nawar W. Clinical presentation, management and outcome of acute coronary syndrome in Yemen: Data from Gulf race - 2 registry. *Heart Views*. 2013; 14:159-64.
55. Kiatchoosakun S, Wongwipaporn C, Pussadhamma B. Prognostic factors of in-hospital mortality in all comers with ST elevation myocardial infarction undergoing primary percutaneous coronary intervention. *Heart Asia.* 2016; 8:13–17

56. Cannon CP, Gibson CM, Lambrew CT. Relationship of symptom-onset-to-balloon time and door-to-balloon time with mortality in patients undergoing angioplasty for acute myocardial infarction. *JAMA*. 2000; 283:2941.
57. Millogo GR, Samadoulougou A, Kologo J, Yameogo NV, Sanou B, Seghda A, et al. Myocardial Infarction in Young Black African in Burkina Faso: Epidemiological and Therapeutic Aspects. *Journal of Cardiovascular Diseases & Diagnosis.*2015; 3:191
58. Steyn K, Sliwa K, Hawken S, Commerford P, Onen C, Damasceno A, Ounpuu S, Yusuf S, *et al.* for the INTERHEART Investigators in Africa. Risk factors associated with myocardial infarction in Africa: the INTERHEART Africa study. Circulation.2005; 112(23):3554-61
59. Dipiro JT, Talbert RL, Yee GC, Matzke GR, Wells BG, Posey LM. PHARMACOTHERAPY a pathophysiologic approach. 9th edition. United States: McGraw-Hill companies; 2014

10.ANNEX

10.1 Data abstraction format

1. Admission Details				
1.01	Patient initials	_____		
1.02	Age	_____		
1.03	Sex	□ Male		Female
1.04	Date of Admission	_____		
1.05	Date of discharge/death	_____		
1.06	Symptoms	□ Chest Pain	□ Nausea /Vomiting	
		□ Dysnea	□ Sweating	
		□ Other_____		
1.07	Time of arrival from symptom onset	_____		
2. Past Medical History				
2.01	Previous Myocardial Infarction	□ YES	□ NO	□ Unknown
2.02	Excertional Angina Pectories	□ YES	□ NO	□ Unknown
2.03	Heart Failure	□ YES	□ NO	□ Unknown
2.04	Previous Stroke or TIA	□ YES	□ NO	□ Unknown
2.05	DM	□ YES	□ NO	□ Unknown
2.06	Hypertension	□ YES	□ NO	□ Unknown
2.07	Dyslipidemia	□ YES	□ NO	□ Unknown
2.08	Family History of Premature Coronary Heart Disease	□ YES	□ No	□ Unknown
2.09	History of other major comorbidity	□ YES	□ No	□ Unknown
2.10	Smoking History	□ Never Smoked		
		□ EX-Smoker	If YES No of Years Smoked_____	
		□ Current Smoker	If YES Average No of Cigars per day____	

3. Initial Assessment and Investigations

3.01	Blood Pressure	_____mmHG	
3.02	Blood Sugar	_____mg/dl	
3.03	Heart Rate	_____beats/min	
3.04	Killip Class	_____	
3.05	Continuous ECG monitoring	□ YES □ NO	
3.06	Serum CK-MB measured	□ YES □ NO	If YES peak value_____
3.07	Serum Troponins measured	□ YES □ NO	If YES peak value_____
3.08	Serum Creatinine measured	□ YES □ NO	If YES peak value_____
3.09	Serum Lipid measured during admission		
	Total cholesterol	□ YES □ NO	If YES value_____mg/dl
	LDL cholesterol	□ YES □ NO	If YES value_____mg/dl
	HDL cholesterol	□ YES □ NO	If YES value_____mg/dl
	Triglyceride	□ YES □ NO	If YES value_____mg/dl
3.10	Echocardiogram performed	□ YES	□ NO
3.11	Stress Test Performed	□ YES	□ NO
3.12	Cardiac Catheterization performed	□ YES	□ NO

4. Diagnosis

4.01 □ STEMI — If YES then max ST elevation_____

4.02 □ NSTEMI — If YES then max ST depression_____

4.03 □ UA — If YES then max ST depression_____

5. Reperfusion therapy/ revascularization

5.01 Thrombolytic therapy given — □ YES □ NO

if yes which drug and dose
- □ Alteplase (tPA) □ Reteplase
- □ Streptokinase □ Tenecteplase
- □ Other_____
- □ Tot. Dose_____mg

Door to Needle Time _____

If NO the reason why
- □ Given before arrival □ Primary PCI
- □ Contraindication □ Not indicated
- □ Patient refused □ Unknown

5.02 PCI performed — □ YES □ NO

If yes the first procedure is
- □ Primary (Emergency)
- □ Rescue
- □ Elective

If NO the reason why
- □ Thrombolysed before arrival □ Primary thrombolysis
- □ Contraindication □ Not indicated
- □ Patient refused □ Unknown

5.03 CABG performed — □ YES □ NO

6. Medical treatment commenced during hospitalization

6.01 Aspirin — □ YES □ NO

If YES Loading Dose_____mg/d
M.Dose_____mg/day

Started in ED □ YES □ NO

If NO the main reason _____

6.02	Clopidogrel		□ YES	□ NO
		If YES	Loading Dose_____mg/d M.Dose_____mg/day	
		Started in ED	□ YES	□ NO
		If NO the major reason	_____	
6.03	Glycoprotein IIb/ IIIa receptor antagonist		□ YES	□ NO
		If YES	drug name_____ Loading Dose_____mg/d M.Dose_____mg/day	
		Started in ED	□ YES	□ NO
		If NO the major reason	_____	
6.04	Anti-coagulant		□ YES	□ NO
		If YES	drug name_____ Loading Dose_____mg/d M.Dose_____mg/day	
		Started in ED	□ YES	□ NO
		If NO the major reason	_____	
6.05	Beta Blocker(PO/IV)		□ YES	□ NO
		If YES	drug name_____ Initial Dose_____mg/d Max.Dose_____mg/day	
		Started in ED	□ YES	□ NO
		If NO the major reason	_____	
6.06	Morphine		□ YES	□ NO
		If YES	Initial Dose_____mg/d Max.Dose_____mg/day	
		Started in ED	□ YES	□ NO
		If NO the major reason	_____	

6.07	Nitrates(SL/IV/PO)		□ YES	□ NO
		If YES	drug name_____	
			Initial Dose_____mg/d	
			Max.Dose_____mg/day	
		Started in ED	□ YES	□ NO
		If NO the major reason	_____	
6.08	ACEIs/ARBs		□ YES	□ NO
		If YES	drug name_____	
			Initial Dose_____mg/d	
			Max.Dose_____mg/day	
		Started in ED	□ YES	□ NO
		If NO the major reason	_____	
6.09	Ca-channel blocker		□ YES	□ NO
		If YES	drug name_____	
			Initial Dose_____mg/d	
			Max.Dose_____mg/day	
		Started in ED	□ YES	□ NO
		If NO the major reason	_____	
6.10	Statins		□ YES	□ NO
		If YES	drug name_____	
			Initial Dose_____mg/d	
			Max.Dose_____mg/day	
		Started in ED	□ YES	□ NO
		If NO the major reason	_____	

7. Discharge Medications

7.01	Aspirin	□ YES	□ NO
7.02	Clopidogrel	□ YES	□ NO
7.03	Beta Blocker	□ YES	□ NO
7.04	ACEIs/ARBs	□ YES	□ NO
7.05	Nitrates(oral)	□ YES	□ NO
7.06	Ca^{2+}-channel blocker	□ YES	□ NO
7.07	Statins	□ YES	□ NO
7.08	Other cardiovascular Drug	□ 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
8.04	Stroke	□ YES	□ NO
8.05	Major bleeding episode	□ YES	□ NO
8.06	Discharged alive	□ YES	□ NO

**MI: in patients admitted with UAP, Re-MI: in patients admitted with MI

10.2. Specific contraindications

The specific contraindications for administered medication, clinically documented in the patient's medical record, will be defined as follows:

- **For the use of Aspirin**: intolerance, allergy, active bleeding, a history of gastrointestinal or genitourinary bleeding, ulcers, dyspepsia, a platelet count of <100,000/mm, anemia, use of other anticoagulants.
- **For β-Blockers**: allergy, hypersensitivity, bradycardia, AV-block greater than I° degree, cardiogenic shock, hypotension, chronic obstructive pulmonary disease, asthma or bronchospasm.
- **For Heparin**: active or recent bleeding, a platelet count of <100,000/mm3, ulcers or serious gastrointestinal or genitourinary bleeding, a history of known heparin-induced thrombocytopenia.
- **For lipid-lowering drugs**: allergy, hypersensitivity, hepatic or renal dysfunction, abnormal liver function test results, primary biliary cirrhosis.
- **For ACE Inhibitors**: allergy, intolerance, hypersensitivity, impaired renal function, hypotension, hyperkalemia or liver disease.