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Thesis

Atypical Presentation of Acute Coronary Syndrome in the Emergency Department of Baghdad Teaching Hospital. Prevalence, Modes of Presentation, and Risk Factors

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Received: April 28, 2019; **Published:** July 03, 2019

Abstract

Introduction: Knowledge of the characteristics of patients with atypical presentation of acute coronary syndromes may contribute to increased sensitivity in diagnosis in a given population. The purpose of this study is to quantify the prevalence of atypical presentation, to identify its prevalence, risk factors and the presenting symptoms at the emergency department of Baghdad teaching Hospital.

Patients and Methods: This is a prospective observational study in which patients with ACS (UA, Non-STEMI, and STEMI) were collected from the emergency department of Baghdad Teaching Hospital for the period between December 2011 and December 2012.

Results: From a total number of 624 patients admitted to CCU of Bagdad Teaching Hospital diagnosed with ACS, patients presented with atypical presentation of ACS were 117 constitute a percentage of 18.7%. Most common atypical presentation was dyspnea (43%) followed by altered mentation (15%) and abdominal pain (9%). Regarding risk factors for atypical presentation, the following results obtained from our patients, it had been significantly found that age older than 60 year was the more likely prevalent risk factor 66.6%, followed by female gender 59.8%, diabetes mellitus 45.2% then history of stroke 24%, $p < 0.05$.

Discussion: Study results were similar and comparable to most small cohort studies regarding symptoms, prevalence and risk factors.

Conclusion: Atypical presentation of ACS is a common presenting problem throughout the spectrum of ACS. Risk factors for ACS include: Age older than 60 yr, female gender, diabetes mellitus, prior Hx of CHF, prior Hx of stroke, COPD, CRF and rheumatoid arthritis. Missing the Dx of Atypical ACS has several serious consequences.

Keywords: *Acute Coronary Syndrome; Unstable Angina; Myocardial Infarction; Atypical Chest Pain*

Abbreviations

AHA: American Heart Association; ACS: Acute Coronary Syndrome; UA: Unstable Angina; AMI: Acute Myocardial Infarction; NSTEMI: Non-ST Elevation Myocardial Infarction; STEMI: ST-Elevation Myocardial Infarction; ADA: American Diabetes Association; CHF: Congestive Heart Failure; COPD: Chronic Obstructive Airway Disease; CRF: Chronic Renal Failure; EMS: Emergency Medical Services; CCU: Coronary Care Unit

Introduction

ACS includes the spectrum from UA, to NSTEMI and STEMI. AMI is defined as myocardial cell death and necrosis of the myocardium. The four-decade-old World Health Organization (WHO) definition for AMI has been replaced by clinical criteria developed jointly by the

European Society for Cardiology and American College of Cardiology (ACC) that focus on defining infarction as any evidence of myocardial necrosis. This definition for an acute, evolving, or recent MI requires a typical rise and fall of a cardiac biochemical marker, serum troponin, with clinical symptoms, ECG changes, or coronary artery abnormalities based on interventional evaluation [1].

AMI is further classified by findings on the ECG at presentation, as either ST elevation MI (STEMI) or non-ST elevation MI (NSTEMI). Previous descriptors such as transmural and non-transmural, as well as Q wave and non-Q wave MI fail to adequately describe the coronary event and its related pathophysiology, electrocardiographic presentation, and pathologic outcome. The differentiation between STEMI and NSTEMI has important implications in terms of management, therapeutic intervention, outcome, and prognosis for patients with AMI. In fact, the American College of Cardiology and American Heart Association have developed separate clinical guidelines for the management of patients with UA/NSTEMI and those patents with STEMI [2-4].

Clinical features

The Classic History

The term angina refers to tightening, not pain. Classic angina pectoris may not be pain at all but rather a discomfort, with a squeezing, pressure, tightness, fullness, heaviness or burning sensation. Classically, it is substernal or precordial in location and may radiate to the neck, jaw, shoulders, or arms. If the discomfort does extend down the arm, it classically involves the ulnar aspect.

Discomfort in the left chest and radiation to left-sided structures is typical, but location and radiation to both sides or to only the right side may be consistent with angina.

Radiation of the discomfort to the right arm or shoulder, or to both arms or shoulders, exceeds radiation to the left arm or shoulder in terms of likelihood of the chest pain being due to ACS, although all exceeded a positive likelihood ratio of 2 [5].

Certain chest pain characteristics decrease the likelihood of ACS namely, pain that is stabbing, pleuritic, positional, or reproducible by palpation. Conversely, chest pain that radiates to one shoulder or both shoulders or arms or is precipitated by exertion is associated with increase the likelihood of ACS. The chest pain history itself has not proven to be a powerful enough predictive tool to obviate the need for at least some diagnostic testing.

Although certain elements of the chest pain history are associated with increased or decreased likelihoods of a diagnosis of ACS or AMI, none of them alone or in combination identify a group of patients that can be safely discharged without further diagnostic testing.

Differentiating (ACS) from benign causes of chest pain is critical because of the consequences of misdiagnosis in either direction. Despite diagnostic advances, missed AMI and ACS remain problematic, with estimates ranging between 2% and 10%. Conversely, a large proportion of patients with chest pain who are admitted do not turn out to have ACS. This overtriage has enormous economic implications for the health care system.

Distinguishing whether a patient presenting with chest pain has ACS or a non- ACS problem is at best difficult. The differential diagnosis of chest pain is broad and includes many systems, such as pulmonary, musculoskeletal, gastrointestinal, dermatologic, psychiatric, and cardiovascular (including ACS and non-ACS). In addition to ACS, this differential includes other immediately life-threatening diseases such as pulmonary embolism, tension pneumothorax, and aortic dissection, necessitating rapid diagnosis and treatments that are markedly different than those for ACS [5].

The atypical history

Although a consensus exists about what represents a typical chest pain description, the equivalent definition for atypical chest pain is less clear. Heberden provided the first description of typical ischemic chest pain in 1768: a painful sensation in the breast accompanied

by a strangling sensation, anxiety, and occasional radiation of pain to the left arm. He also observed an association with exertion and relief with rest. Chest pain symptoms that do not fall into this typical category have been termed atypical.

A description of typical symptoms (crushing, retrosternal chest pain or pressure) is often lacking in ACS; this may be due to atypical features of the pain (e.g. character, location, duration, exacerbating and alleviating factors) or the presence of anginal equivalent symptoms (e.g. dyspnea, nausea, vomiting, diaphoresis, indigestion, syncope). Patients with an ultimate diagnosis of AMI or UA can have pain that is pleuritic, positional, or reproduced by palpation [6]. Some patients describe their pain as burning or indigestion, sharp, or stabbing [7].

Risk factors for atypical presentation

Age

Before age 85, chest pain is found in the majority of patients with acute MI, although dyspnea, weakness, and altered mental status are notably present. In those older than 85 years, however, atypical symptoms are more common than chest pain, with 60 to 70% of patients older than 85 presenting with an anginal equivalent complaint, especially dyspnea [8-10]. Older patients with suspected ACS were more likely to present atypically and have worse outcomes than their younger counterparts, despite having fewer major risk factors. The results highlight the importance of age as a predictor of adverse outcome [11]. Moreover, advanced age is more important predictor of atypical presentation than gender [36].

Diabetes mellitus

Patients with DM are at high risk for ACS as well as an atypical presentation such as dyspnea, nausea or vomiting, confusion, or fatigue.

The suggested mechanisms of this phenomenon are 1) autonomic neuropathy, 2) prolongation of the anginal perceptual threshold (the time from onset of 0.1 mV of ST segment depression to onset of angina during treadmill exercise).

Medically unrecognized AMI can occur in 40% of patients with diabetes mellitus compared with 25% of a nondiabetic population, and myocardial scar unaccompanied by antemortem diagnosis of MI is three times more likely in diabetics [12].

Among patients with diabetes the 1-year mortality rate was 41% versus 26% for non-diabetic patients and the 1-year reinfarction rates were 23% and 14%, respectively. Among diabetic patients the only independent risk factor for death was age. The mode of death appeared to be similar in diabetic patients as compared with non-diabetic patients [13].

Female gender

Sex difference is an important risk factor for MI without chest pain. In some series, less than 60% of women reported chest discomfort at the time of their MI, with others reporting dyspnea, indigestion, or vague symptoms such as weakness, unusual fatigue, cold sweats, sleep disturbance, anxiety, or dizziness [14,15].

Moreover, they experienced pain and other sensations in the neck area more frequently. Another feature of chest pain in women is that angina being induced by rest, sleep, mental stress instead of or addition to physical exertion [16].

Moreover, Women with ACS are more likely to have atypical symptoms such as nausea and jaw pain compared with men, but were more likely to have normal/mild angiographic coronary artery disease [16].

Associated co-morbid conditions

older adults with co-morbid chronic diseases such as stroke, chronic obstructive pulmonary disease (COPD), asthma, congestive heart failure or renal failure likely have 3.3 times more chances of having atypical symptoms compared with healthy older adults.

A significant predicting factor that helps in identifying atypical symptoms in older patients was co-morbidities that they had. This finding was consistent with a previous observational study showed that the presentation of an atypical symptom was significantly related with a prior history of heart failure or stroke [17].

Rheumatoid arthritis: Recurrent ischaemic events and death occur more often after ACS in rheumatoid arthritis. Atypical presentation is commoner in rheumatoid arthritis [18].

Clinical characteristics of anginal chest pain [19]

Character	More likely to be Angina	Less likely to be Angina
Pain type	Dull, pressure	Sharp, stabbing
Duration	Always < 15 - 20 minutes	Seconds to hours
Onset	Gradual	Rapid
Location	Substernal	Lateral chest wall, back
Reproducibility	With exertion	With inspiration
Associated symptoms	Present	Absent
Chest wall palpation	Not painful	Painful, exactly reproduce pain

Table A

Physical examination

The physical examination focuses on the cardiac, pulmonary, abdominal, and neurologic examinations, looking for signs of severe illness in patients with symptoms of ACS as well as other entities in the differential diagnosis of chest pain and the anginal equivalent syndromes.

Altered mental status, diaphoresis, and signs of CHF are all ominous findings in patients presenting with symptoms consistent with ACS. The real incidence of truly reproducible chest wall tenderness (i.e. when the patient reliably identifies to the examiner that the pain produced on palpation is identical to the pain causing the patient's presentation) in ACS is probably vanishingly small. It has been suggested that chest pain that is fully pleuritic, positional, or reproducible by palpation (the three P's) is at low risk (yet not no risk) for ACS [5].

Diagnostic investigations

ECG

The earliest ECG finding in AMI is the hyperacute T wave, which becomes tall and peaked within minutes of the interruption of blood flow. This hyperacuity may be missed on the initial ECG.

As the AMI progresses, ST segment elevation will become evident. The elevated ST segment is convex in morphology but at times, the ST segment may be concave or scooped in its elevation with AMI [14]; this morphology may progress to a convex shape or may stay the same throughout the infarction. The concave morphology, if noted in all elevated ST segments, is atypical for AMI and more commonly seen with other ST segment elevation syndromes [20,21].

Although T wave inversion is sought as a harbinger of ACS, it can also occur as an evolutionary change after MI. In MI without culprit artery reperfusion, as the ST segments return to baseline, the T waves may invert, although not particularly deeply. In hearts that have been reperfused, T wave inversion may follow ST segment elevation, in either a biphasic or deeply inverted morphology, appearing much like the T wave changes of Wellens' syndrome.

Q waves are generally representative of irreversible myocardial necrosis but are rarely the sole manifestation of AMI. Pathologic Q waves may emerge within the first hour of infarction, but most commonly develop 8 to 12 hours into the infarction. It follows that ST segment elevation with concomitant Q waves does not preclude consideration of emergent reperfusion therapy. Q waves may persist after MI as enduring markers of previous infarction on the ECG; in some cases, however, Q waves disappear with time regardless of whether the infarcted territory was reperfused [22,23].

Serum markers

Biochemical markers play a pivotal role in the diagnosis, risk stratification, and guidance of treatment. The European Society of Cardiology and ACC define the criteria for AMI diagnosis on biochemical grounds since specific markers, particularly the troponins, indicate irreversible cell damage [1].

Troponins

Because of their superior sensitivity and specificity compared with CK-MB, cardiac troponins are the best markers for myocardial cell injury. Two myocardium-specific proteins, myocardial troponin I (TnI) and troponin T (TnT), precede the release of CK-MB into the serum. The cardiac troponins are genetically distinct from troponin forms found in other muscle tissue, rendering them highly cardiac specific (although troponins can be elevated in other disease states as pulmonary embolism, sepsis and renal failure).

Troponins I and T are similar in their diagnostic and prognostic utility as well as their serum kinetics and rates of rise and fall associated with myocardial ischemia, infarction, and ACS.

The biokinetics of troponin release relate to the location of the protein within the cell. Normally, small quantities of troponins are free in the cytosol, and the majority is entwined in the muscle fiber. After injury, a biphasic rise in serum troponins corresponds to early release of the free cytoplasmic proteins, followed by a slower and greatly prolonged rise with breakdown of the actual muscle fiber. The slow destruction of the myocardial cell contractile proteins provides a sustained release of the troponins for 5 to 7 days.

Serum troponin concentrations begin to rise measurably in the serum at about the same time as CK-MB elevations become detectable, as early as 3 hours after onset, but troponin levels remain elevated for 7 days or more. The cardiac-specific troponins, determined serially, are highly sensitive for the early detection of myocardial injury. A positive test result is associated with significant risk, and serial negative results predict low risk [24].

Creatinine phosphokinase

Creatinine phosphokinase (CK) is found in large quantities not only in cardiac muscle but also in skeletal muscle, brain, kidney, lung, and the gastrointestinal tract. Myocardial cells are by far the most abundant sources of CK-MB; thus, the appearance of CK-MB in the serum is highly suggestive of MI [25].

The CK-MB fraction remains the best alternative to the troponins as a cardiac marker in the setting of AMI, CK-MB is released and is detectable in the serum as early as 3 hours after onset of the necrosis. CK-MB characteristically peaks at 20 to 24 hours and becomes normal within 2 to 3 days after injury.

Elevated CK-MB values identify a patient at considerable risk for a poor outcome but do not correlate well with infarct size. Unfortunately, skeletal muscle does contain small amounts of CK-MB, particularly the pelvic musculature. Abnormal CK-MB elevations may be seen in trauma, muscular dystrophies, myositis, rhabdomyolysis, and after extremely vigorous exercise [26].

Myoglobin

Myoglobin, a small protein (17,000 daltons) found in muscle tissue, is rapidly released into the circulation after cellular injury. In cases of myocardial injury, myoglobin rises in the initial 1 to 2 hours, peaks at 5 to 7 hours, and returns to baseline by 24 hours.

Because of its rapid rise, myoglobin is attractive as an early indicator of myocardial injury. Myocardial myoglobin, however, is not currently distinguishable immunologically from skeletal muscle myoglobin. Thus, myoglobin is elevated in any clinical situation involving the skeletal muscle, such as trauma, exercise, and significant systemic illness. In addition, myoglobin increases are seen in patients with renal failure because of reduced clearance [27].

Treatment of patients with ACS

The goals of treatment are to preserve patency of the coronary artery, augment blood flow through stenotic lesions, and reduce myocardial oxygen demand.

STEMI

Patients with STEMI usually have complete occlusion of a coronary artery. The primary goal of initial treatment is early reperfusion therapy through administration of fibrinolytics (pharmacological reperfusion) or PPCI (mechanical reperfusion). Providers should rapidly identify patients with STEMI (ECG should be performed within 10 min. of arrival) and quickly screen them for indications and contraindications to fibrinolytic therapy and PCI. Patients who are ineligible for fibrinolytic therapy should be considered for transfer to a PCI facility regardless of delay [28].

Within a STEMI system of care, the first physician who encounters a patient with STEMI determines the need and strategy (fibrinolytic or PPCI) for reperfusion therapy. Routine consultation with a cardiologist or another physician is not recommended except in equivocal or uncertain cases as consultation delays therapy and is associated with increased hospital mortality rates [28].

The goal for patients with STEMI should be to achieve a door-to-drug time of within 30 minutes and a door-to-balloon time of within 90 minutes [29,30] the earlier the better.

In patients with STEMI who are to be treated with primary PCI, delays in administering the procedure are associated with higher mortality in these patients, according to a study by Rathore., *et al* [31].

UA/NSTEMI

Unstable angina (UA) and NSTEMI are difficult to distinguish initially. These patients usually have a partially or intermittently occluding thrombus. Both may present with similar symptoms and ECG. Clinical features can correlate with the dynamic nature of clot formation and degradation (e.g. waxing and waning clinical symptoms) [28].

The ECG will demonstrate a range of findings short of diagnostic ST-segment deviation; these ECG presentations include normal, minimal nonspecific ST- segment/T-wave changes, and significant ST-segment depression and T-wave inversions [28].

An elevated biomarker separates NSTEMI from UA and has incremental value in addition to the ECG. Elevation of cardiac troponin indicates increased risk for major adverse cardiac events and benefit from an invasive strategy. Cardiac troponins indicate myocardial necrosis, although numerous conditions other than ACS may cause elevated biomarkers as myocarditis, heart failure, and pulmonary embolism) [28].

Management strategies for UA/NSTEMI include antiplatelet, antithrombin, and antianginal therapy and are based on risk stratification. Fibrinolysis is contraindicated in this heterogenous group of patients and may be harmful; an invasive strategy is indicated in patients with positive biomarkers or unstable clinical features [28].

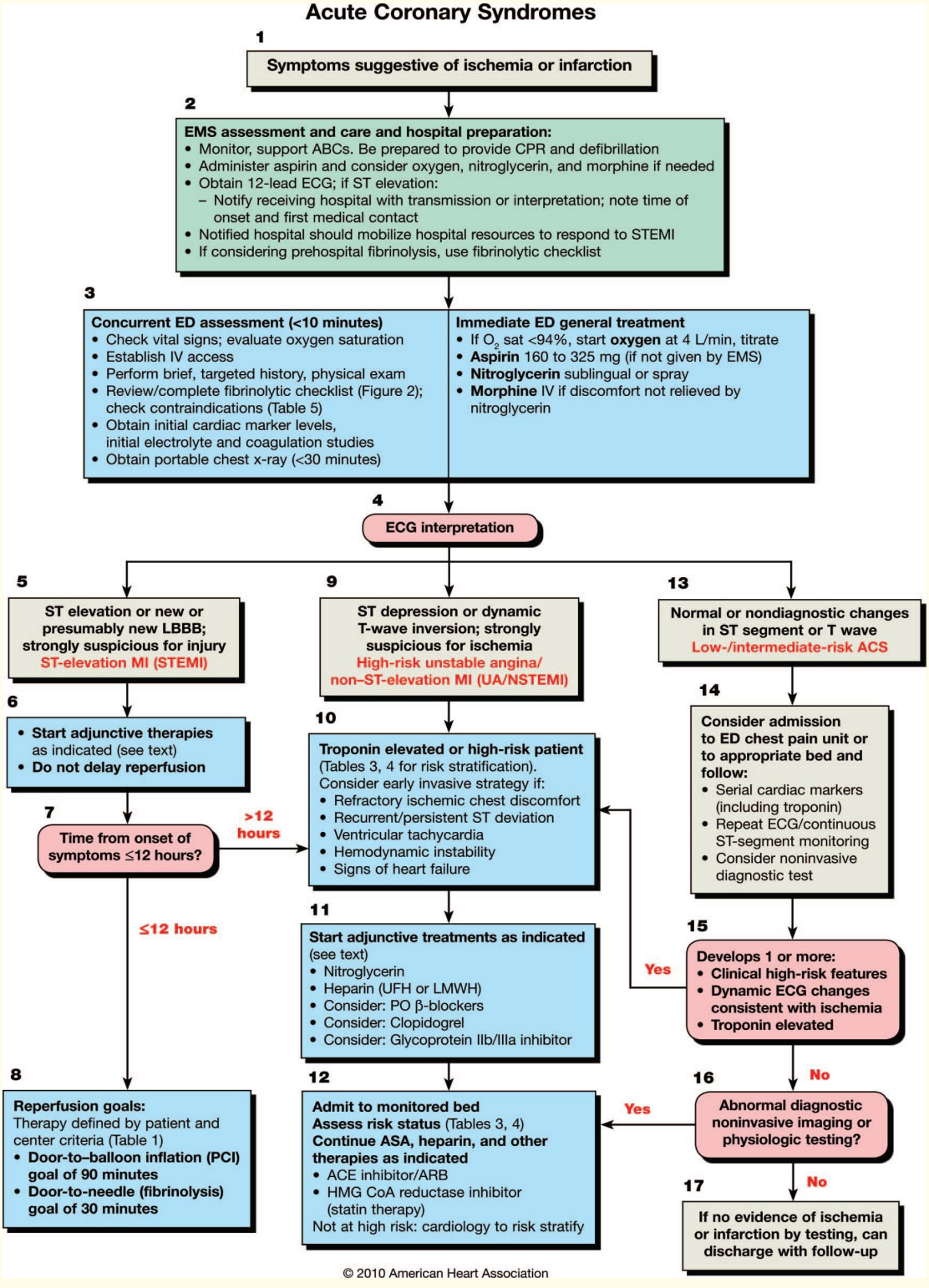
Acute Coronary Syndromes
1
Symptoms suggestive of ischemia or infarction
2
EMS assessment and care and hospital preparation:
• Monitor, support ABCs. Be prepared to provide CPR and defibrillation
• Administer aspirin and consider oxygen, nitroglycerin, and morphine if needed
• Obtain 12-lead ECG; if ST elevation:
– Notify receiving hospital with transmission or interpretation; note time of onset and first medical contact
• Notified hospital should mobilize hospital resources to respond to STEMI
• If considering prehospital fibrinolysis, use fibrinolytic checklist
3
Concurrent ED assessment (<10 minutes)
• Check vital signs; evaluate oxygen saturation
• Establish IV access
• Perform brief, targeted history, physical exam
• Review/complete fibrinolytic checklist (Figure 2); check contraindications (Table 5)
• Obtain initial cardiac marker levels, initial electrolyte and coagulation studies
• Obtain portable chest x-ray (<30 minutes)
Immediate ED general treatment
• If O_2 sat <94%, start oxygen at 4 L/min, titrate
• Aspirin 160 to 325 mg (if not given by EMS)
• Nitroglycerin sublingual or spray
• Morphine IV if discomfort not relieved by nitroglycerin
4
ECG interpretation
5
ST elevation or new or presumably new LBBB; strongly suspicious for injury
ST-elevation MI (STEMI)
6
• Start adjunctive therapies as indicated (see text)
• Do not delay reperfusion
7
Time from onset of symptoms ≤12 hours?
>12 hours
≤12 hours
8
Reperfusion goals:
Therapy defined by patient and center criteria (Table 1)
• Door-to–balloon inflation (PCI) goal of 90 minutes
• Door-to-needle (fibrinolysis) goal of 30 minutes
9
ST depression or dynamic T-wave inversion; strongly suspicious for ischemia
High-risk unstable angina/ non–ST-elevation MI (UA/NSTEMI)
10
Troponin elevated or high-risk patient
(Tables 3, 4 for risk stratification).
Consider early invasive strategy if:
• Refractory ischemic chest discomfort
• Recurrent/persistent ST deviation
• Ventricular tachycardia
• Hemodynamic instability
• Signs of heart failure
11
Start adjunctive treatments as indicated
(see text)
• Nitroglycerin
• Heparin (UFH or LMWH)
• Consider: PO β-blockers
• Consider: Clopidogrel
• Consider: Glycoprotein IIb/IIIa inhibitor
12
Admit to monitored bed
Assess risk status (Tables 3, 4)
Continue ASA, heparin, and other therapies as indicated
• ACE inhibitor/ARB
• HMG CoA reductase inhibitor (statin therapy)
Not at high risk: cardiology to risk stratify
13
Normal or nondiagnostic changes in ST segment or T wave
Low-/intermediate-risk ACS
14
Consider admission to ED chest pain unit or to appropriate bed and follow:
• Serial cardiac markers (including troponin)
• Repeat ECG/continuous ST-segment monitoring
• Consider noninvasive diagnostic test
15
Develops 1 or more:
• Clinical high-risk features
• Dynamic ECG changes consistent with ischemia
• Troponin elevated
Yes
16
Abnormal diagnostic noninvasive imaging or physiologic testing?
Yes
No
17
If no evidence of ischemia or infarction by testing, can discharge with follow-up
No
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Figure 1

The process of risk stratification

Diagnosis of ACS and risk stratification become an integral process in patients presenting with possible ACS and an initially non-diagnostic evaluation. This nondiagnostic evaluation includes a normal or nondiagnostic 12-lead ECG and normal serum cardiac biomarker concentrations.

A major goal of the risk stratification process is to identify those patients who do not appear to have high-risk features on initial assessment but are found, through the course of the diagnostic process, to have ACS and clinically significant CAD. This strategy allows physicians to target patients who would benefit from guidelines-based ACS therapies while avoiding unnecessary procedural and pharmacological risks (e.g. anticoagulation therapy and invasive cardiac catheterization) in patients with low risk for major adverse cardiac events [28].

TIMI Risk Score

The TIMI risk score comprises 7 independent prognostic variables. These variables were significantly associated with the occurrence within 14 days of at least one of the primary end points: (death, new or recurrent MI, or need for urgent revascularization). It is useful to note that traditional cardiac risk factors are only weakly associated with major adverse cardiac events. Aspirin use was found to be one of the most powerful predictors. It is possible that aspirin use identified a subgroup of patients at higher risk or on active but failed therapy for CAD.

The TIMI risk score was validated with that 3 groups of patients (STEMI, NSTEMI and UA) and 4 clinical trials showed a significant interaction between the TIMI risk score and outcome [28].

TIMI score here was assigned for patients with UA

Predictor Variable	Point Value of Variable	Definition
Age ≥65 years	1	
≥3 risk factors for CAD	1	Risk factors • Family history of CAD • Hypertension • Hypercholesterolemia • Diabetes • Current smoker
Aspirin use in last 7 days	1	
Recent, severe symptoms of angina	1	≥2 anginal events in last 24 hours
Elevated cardiac markers	1	CK-MB or cardiac-specific troponin level
ST deviation ≥0.5 mm	1	ST depression >0.5 mm is significant; transient ST elevation ≥0.5 mm for <20 minutes is treated as ST-segment depression and is high risk; ST elevation ≥1 mm for more than 20 minutes places these patients in the STEMI treatment category
Prior coronary artery stenosis ≥50%	1	Risk predictor remains valid even if this information is unknown

Calculated TIMI Risk Score	Risk of ≥1 Primary End Point* in ≤14 Days	Risk Status
0 or 1	5%	Low
2	8%	Low
3	13%	Intermediate
4	20%	Intermediate
5	26%	High

*Primary end points: death, new or recurrent MI, or need for urgent revascularization.

Figure 2: *TIMI risk score, Adapted from AHA guidelines 2010.*

Aim of the Study

This study aims to estimate the rate, evaluate the modes and identify factors associated with atypical presentation of acute coronary syndromes in the emergency department of Baghdad Teaching Hospital in order to have a high index of suspicion, earlier detection and more appropriate medical treatments of the patients with ACS within the first 24 hr to avoid grave consequences of early discharge of such patients from ER.

Patients and Methods

This is a cross sectional observational study in which patients with ACS (UA, Non-STEMI, and STEMI) were enrolled from the emergency department of Baghdad Teaching Hospital for the period between December 2011 and December 2012.

Definitions: The following definitions were used during the study:

1. **Unstable angina:** Angina occurring with minimal exertion or at rest, new- onset angina or a worsening change in a previously stable angina in terms of frequency or duration of attack, resistance to previously effective Rx or provocation with decreasing level of stress [32].
   - **a- Rest angina:** Angina occurs at rest, lasting>20 min., occurring within 1 week of presentation
   - **b- New-onset angina:** Angina with onset within the last 2 months
   - **c- Worsening (progressive) angina:** When a previously known angina becomes more frequent, longer in duration, or increased by one class in the last 2 months.
2. **Myocardial Infarction:** Is myocardial cell death and necrosis of the myocardium.
   - a- Acute, evolving or recent MI [33].

     Typical rise and gradual full(troponin) or more rapid rise and fall (CK-MB) of biochemical markers of myocardial necrosis with at least one of the following:
     - Ischemic symptoms
     - Pathological Q wave
     - Ischemic ECG changes (T wave changes or ST elevation or depression).
   - b- Established MI: Any of the following criteria [33]

New pathological Q wave (biochemical markers of myocardial necrosis may have normalized)

3. **Cardiogenic shock:** Defined as hypotension with end-organ hypoperfusion resulting from decreased cardiac output that is unresponsive to restoration of adequate preload [34].
4. **Diabetes Mellitus:** Either known diabetic on treatment OR RBS > 200 mg/dl (excluding stress hyperglycemia) or fasting RBS > 126 mg/dl.
5. Hypertension [35]

JNC-7 Classification of Hypertension			
Class	**Systolic BP (mm Hg)**		**Diastolic BP (mm Hg)**
Normal	< 120	and	< 80
Prehypertension	120 - 139	or	80 - 89
Stage 1	140 - 159	or	90 - 99
Stage 2	160	or	100

Table B

6. **Renal failure:** A: Either a known case of CRF on renal replacement therapy (Hemodialysis or conservative therapy) OR B: Increase in BUN and Creatinine twice the upper normal range.

Inclusion Criteria

The patients with the following characteristics were included in the study:

1. Adult patient (male or female), No age limit and
2. Atypical presentation was defined as absence of typical chest pain, includes:
   - Dyspnea, nausea and vomiting, disturbed level of consciousness or altered mental status, palpitation, abdominal pain (apart from epigastric)
   - Chest pain of atypical description (lateralized, stabbing, pleuritic, positional, or reproduced by palpation, pain lasting seconds or days).
3. ECG inclusion Criteria [28]
   A. ST-segment elevation or presumed new LBBB is characterized by ST segment elevation in 2 or more contiguous leads and is classified as ST- segment elevation MI (STEMI). Threshold values for ST-segment elevation consistent with STEMI are J-point elevation 0.2 mV (2 mm) in leads V2 and V3 and 0.1 mV (1 mm) in all other leads (men 40 years old); J-point elevation 0.15 mV (1.5 mm) in leads V2 and V3 and 0.1 mV (1 mm) in all other leads (women).
   B. Ischemic ST-segment depression 0.5 mm (0.05 mV) or dynamic T-wave inversion with pain or discomfort is classified as UA/NSTEMI. Nonpersistent or transient ST-segment elevation 0.5 mm for 20 minutes is also included in this category. Threshold values for ST-segment depression consistent with ischemia are J-point depression 0.05 mV (-.5 mm) in leads V2 and V3 and -0.1 mV (-1 mm) in all other leads (men and women).
   C. The nondiagnostic ECG with either normal or minimally abnormal (i.e. nonspecific ST-segment or T-wave).

ECG device: GE-MAC500.

ECG interpretation: Emergency medicine 3rd year resident in conjunction with internal medicine 4th year resident.

Troponin kit used: ACON LAB-USA.

Management in emergency department

As soon as the suspicion of ACS was made from the history (atypical chief complaint and its duration, risk factors as hypertension, diabetes mellitus, family history of ischemic heart disease, smoking and hyperlipidemia), physical examination (SPO_2, vital signs, heart and lung auscultation), the patient was immediately admitted to ER chest pain observation unit, high flow oxygen given by face mask and ECG done within 10 min. of arrival to detect changes associated with ACS.

Patients was managed according to Acute coronary syndrome algorithm set by American Heart Association (see p.15).

Patients received the following in our medical emergency department:

1. Aspirin 300 mg chewable.
2. Nitroglycerin 400 microgm SL (repeated on need up to 3 times or hypotension developed).
3. Unfractionated heparin 60 u/kg (max. 4000u) followed by IV Infusion of 12 u/kg/hr (max.1000 u/h).
4. Analgesics: Morphine 5mg IV or Pethidine 50 mg IV (with antiemetic).

Next, troponin kit was used to show positive or negative results.

Patients disposition decision was made by 4th year emergency medicine resident in conjunction with 4th year internal medicine resident, and/or Coronary Care Unit 2nd year internal medicine resident.

Disposition decision was as following:

STEMI

1. Symptoms < 90 minutes (contact-to-balloon or door-to-balloon): primary PCI (admitted to Iraqi centre for heart disease) or if no facilities available, admission to CCU of Baghdad teaching hospital) for fibrinolysis.
2. Symptoms > 90 minutes up to 12 hr: Fibrinolytics (admitted to CCU of Baghdad teaching hospital)
3. Symptoms > 12hr: Admitted to CCU of Baghdad teaching hospital to be referred to Iraqi centre of heart diseases for PCI later.

Non-STEMI/UA

Patients were admitted to CCU of Baghdad teaching hospital for antiplatelet, antithrombin, and antianginal therapy.

Fibrinolysis is contraindicated in this heterogenous group of patients and may be harmful; an invasive strategy is indicated in patients with positive biomarkers or unstable clinical features.

Statistical analysis

Data were translated into a computerized database structure. The database was examined for errors using range and logical data cleaning methods.

Statistical analyses were done using SPSS (Statistical Package for Social Sciences) version 18 computer software.

Statistical significance of difference in frequencies (percentages) was assessed using chi square test.

Data and results were presented in multiple tables and figures. Level of significance ≤ 0.05 was assumed.

Results

From a total number of 624 patients admitted to CCU of Bagdad Teaching Hospital diagnosed with ACS, patients presenting with atypical presentation of ACS were 117 constituting a percentage of 18.7%.

ACS	N (total)	ACS-Atypical	n	Percentage %	ACS-Typical	n	Percentage %
STEMI	280	STEMI	68	24.2%	STEMI	212	75.8%
NSTEMI/UA	344	NSTEMI/ UA	49	14.2%	NSTEMI/ UA	295	85.8%
Total	624		117	18.7%		507	81.3
Chi square = 6.42; P. value = 0.011 sig							

Table 1: P*ercentage of atypical presentation of ACS in relation to total no. of patients admitted.*

Age (years)	Patients with atypical presentation (no.)	Percentage (%)	Patients with typical presentation (no.)	Percentage (%)
≤ 39	8	6.8 %	0	0%
40 - 49	8	6.8 %	10	2%
50 - 59	23	19.6 %	165	32.5%
60 - 69	39	33.3 %	210	41.4%
70 - 79	28	23.9 %	105	20.7%
≥ 80	11	9.4 %	17	3.4%
Total	117	100%	507	100%
Chi square= 13.42; P. value= 0.001 Sig.				

Table 2: *Age of presentation of patients with symptoms of ACS.*

Age (years)	Male patients with atypical presentation		Female patients with atypical presentation		Male patients with typical presentation		Female patients with typical presentation	
	No.	(%)*	No.	(%)*	No.	(%)*	No.	(%)*
<=39	8	(6.8%)	0	(0%)	0	(0%)	0	(0%)
40 - 49	7	(5.9%)	1	(0.9%)	5	(0.9%)	5	(0.9%)
50 - 59	10	(8.6%)	13	(11%)	110	(21.6%)	55	(10.8%)
60 - 69	12	(10.3%)	27	(23%)	140	(27.6%)	70	(13.8%)
70 - 79	8	(6.9%)	20	(17%)	87	(17%)	18	(3.5%)
>= 80	2	(1.7%)		(7.7%)	15	(3%)	2	(0.4%)
Total	47	(40.2%)	70	(59.8%)	357 (70.4%)		150	(29.6%)
Chi Square = 17.2; P. value = 0.004 Sig.								

Table 3: *Gender differences in patients with symptoms of ACS.*

**Percentage from total no. of patients with atypical presentation (n.117).*

Regarding atypical symptoms the following symptoms were recorded in our patients sample.

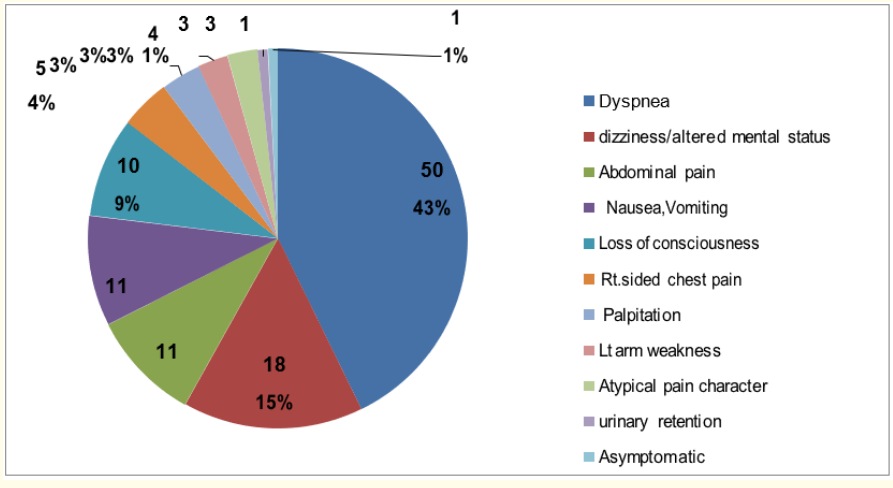

Figure 3: *Atypical presentation of studied group.*

Regarding risk factors for atypical presentation, the following results obtained from our patients, it has been significantly found that age older than 60 year was the more likely prevalent risk factor 66.6%, followed by female gender 59.8%, diabetes mellitus 45.2% then history of stroke 24%, $p < 0.05$.

Risk Factor	Patients (n)	Percentage (%)*
Age older than 60yr	78	66.6%
Female Gender	70	59.8%
Diabetes Mellitus	53	45.2%
Prior Hx of CHF	28	24%
Prior Hx of Stroke	19	16.2%
Chronic Obstructive Airway Disease	12	10.2%
Chronic Renal Failure	6	5%

***Table 4**: Risk factors for atypical presentation.*

**Out of 117 patients with atypical symptoms.*

Discussion

Over a 12-months period, 624 patients were diagnosed with ACS and admitted to CCU of Baghdad Teaching Hospital. Of these 624 patients, 117 patients presented with symptoms other than chest pain (i.e. Atypical presentation), these constitutes 18.7%.

The results of our study were comparable to a study done by Meshack et al which showed that "atypical presentation constitutes 16.8%" [36].

A comparable multicenter, multinational observation study done in Arabian Gulf medical centers over a period of 6 months showed that "atypical presentation in ACS constitutes 21%" [37].

The GRACE study which involved 95 hospitals in 14 countries reported that" 23.8% of patients with ACS present to the hospital without chest pain".

Other similar studies showed variable results regarding the prevalence of atypical symptoms.

In a review article done by John G. Cango., *et al.* "the incidence of atypical symptoms in small cohorts ranged from as low as 3% to as high as 50% with a cumulative percentage of 25%, whereas in large cohorts, atypical presentation constitutes about 33%" [36].

The discrepancy in results of these studies in comparison to ours may be related to better education programs regarding awareness of atypical symptoms targeting general population, EMS personnel, nursing staff, and physicians thus increasing the index of suspicion for atypical symptoms especially in high risk group mentioned.

In our study, STEMI was the most common form of ACS that presented atypically. The results were similar to an article published in Australian medical journal stated that" STEMI patients had higher incidence of atypical presentation" [38].

Another study done by Seon Young Ywang., *et al.* also showed that STEMI was the most common form of ACS that presented atypically with prevalence of 43.3% followed by UA (35.6%) and NSTEMI (21.1%) [17].

Among patients with STEMI, atypical presentation was seen in 24.2%.

These results are similar to those obtained in a small cohort done by Then., *et al.* which also showed that atypical presentation of patients with AMI constitute 24.2% (table above) [36].

In 2 separate studies from the population-based Worcester Heart Attack Study, the overall MI prevalence without chest pain was 20% and 33% [39].

Other study done by Canto JG., *et al.* showed that atypical presentation in STEMI constitute 33% [40]. The discrepancy in results of this study with ours may be attributed to the fact that: this study is a large cohort recruited more than 400 000 patients in more than 1600 hospital and data were collected over 4 years duration

Several cohort studies investigated the prevalence of unrecognized or silent AMI and showed that more than one-quarter of patients with MI in the cohort studies reviewed had silent or unrecognized MI [36].

In our study, the commonest age group for atypical presentation was from 60 to 69 years which constitutes 33.3% from total patients with atypical presentation. Moreover, patients older than 60 years represent 66.6% of patients with atypical presentation

This finding was supported by several studies.

"Patients with AMI without chest pain are 7 years older than those with chest pain (74.2 vs 66.9 years)" Canto JG., *et al* [40].

"Females and patients older than 75 years are more likely to present without chest pain" Brieger D, Eagle KA, Goodman SG., *et al*. GRACE Investigators [41]

"Patients with atypical presentation are older and more likely to be female" Seon Young Ywang., *et al* [17].

"Old age is a factor affecting atypical presentation" Han JH., *et al* [42].

"Older patients are less likely to present with chest pain and more likely to present with dyspnea or collapse" Roy L Soiza., *et al*

In our study, female patients were more commonly presented with atypical symptoms than male patients and were older at time of presentation. Out of these 117 patients with atypical symptoms, 70 cases were females and 47 cases were male with F:M Ratio of 1.5:1.

Among patients with atypical presentation, females constitute about 60%.

Our results were similar to other studies.

"Women are older than men and more likely to have atypical presentation" S. Dey., *et al* [43].

"Patients from atypical ACS in comparison to typical ACS group were more often women (49 vs. 39%)" Zdzienicka J., *et al* [44].

"Of all patients diagnosed as having MI (33%) did not have chest pain on presentation. Those with atypical symptoms were 7 years older than those with chest pain, with a higher proportion of women (49.0% vs 38.0%)" Canto JG., *et al* [40].

"Women are less likely to report chest pain compared to man and they are decade older" John G Canto., *et al* [36].

"Women and patients older than 75 years are more likely to present without chest pain" GRACE study [41].

"Women are more likely to present without chest pain as initial AMI presentation" Vaccarino V., *et al* [45].

"Women presented with ACS are older, have atypical symptoms" Ayman El- Menyar., et al [37].

In our study sample, the most common atypical presentation was Dyspnea (43%) followed by disturbed level of consciousness (15%) and then Abdominal pain (9%).

The fact that dyspnea is the most common atypical presentation was supported by the following studies.

A study done by Brieger D., *et al.* also showed that dyspnea was the most dominant symptom in patients with atypical presentation [41].

Similar results to our study were shown by another descriptive cross sectional study done in National Hospital of Sri Lanka includes 130 patients diagnosed with ACS. In those with Atypical presentation, the dominant presenting symptoms were shortness of breath (44%), dizziness (16%) and Epigastric pain (11%) [38].

A study done by Seon Young Hwang., *et al.* showed that dyspnea was the most common atypical presentation (33%) followed by abdominal pain (18%) and indigestion (17%) [17].

The GRACE study stated that "Dominant symptoms in patients with ACS without chest pain were dyspnea (49.3%) and diaphoresis (26.2%)" [41].

In our study, the most common risk factors for atypical presentation were age older than 60yr (most common) followed by female gender, diabetes, prior Hx of CHF, prior Hx of Stroke, Chronic Obstructive Airway Disease, and Chronic Renal Failure.

Regarding co-morbidities associated with atypical presentation, Diabetes was the most common (45.2%) followed by Hx of CHF (24%), Hx of stroke (16.2%), COPD (10.2%) and renal failure (5%).

Our results are supported by several studies.

"Atypical presentation of AMI is higher in Diabetics (32.6% vs.25.4%) and in patients with prior Heart Failure (26.4% vs.12.3%)" Canto JG., et al [40].

"Patients with atypical symptoms are more likely to have diabetes" John G Canto., *et al* [36].

In NRMI-2 registry, variables such as old age, gender, race, and co- morbidities (diabetes, stroke, heart failure) were considered as a risk factor for atypical symptom [46].

"In terms of the risk factors that patients had, the patients presenting with atypical symptoms were more likely to have a history of diabetes and greater prevalence of co-morbid conditions (stroke, COPD, Renal failure, CHF) but they were less likely to have hyperlipidemia compared to the patients with typical symptoms ($P < 0.001$)" Seon Young Hwang., et al [17].

"Younger adults with diabetes have 2.5 times more chances of experiencing atypical symptoms compared with the younger adults without diabetes" Seon Young Hwang., *et al* [17].

"patients with atypical symptoms were more likely to have diabetes compared with patients having typical symptoms" Brieger D., *et al.* [41], Milner K., *et al.* [47], Then KL., *et al* [48].

"diabetes is an independent predictor of atypical presentation in women with AMI" [49].

"Older adults with co-morbid chronic diseases such as stroke, chronic obstructive pulmonary disease (COPD), asthma, congestive heart failure or renal failure likely have 3.3 times more chances of having atypical symptoms compared with healthy older adults" Seon Young Hwang., *et al* [17].

"The AMI patients without chest pain were more likely to have a prior history of congestive heart failure than patients with chest pain" Canto JG., *et al* [40].

"A significant predicting factor that helps in identifying atypical symptoms in older patients was co-morbidities that they had. This finding was consistent with a previous observational study that the presentation of an atypical symptom was significantly related with a prior history of heart failure or stroke" Canto JG., *et al* [40].

"Age, heart rate (HR), diabetes mellitus (DM), renal failure and Killip class>1 were significant predictors of atypical presentation" Ayman El-Menyar et al [37].

During the course of our study, we would like to mention a case report seen during study. A case of urinary retention received in triage and sent to the surgical emergencies to relieve retention. The patient looked terribly ill, severely dyspneac, sweaty with hemodynamic instability. ECG done immediately and showed Ant. STEMI and was eventually diagnosed as a case of cardiogenic shock due to STEMI.

Conclusion

In context of our study, the following points should be kept in mind:

1. Atypical presentation of ACS is a common presenting problem throughout the spectrum of ACS.
2. Risk factors for ACS include: Age older than 60 yr, female gender, diabetes mellitus, prior Hx of CHF, prior Hx of stroke, COPD, CRF.

Recommendations

1. ACS without chest pain is a critical entity in the spectrum of ACS, and represent a serious health care problem and should be investigated and looked for aggressively by physician who should have a high index of suspicion and low threshold for performing ECG in any patient with risk factor for atypical presentation(old age, female gender, D.M, COPD, CRF, prior Hx of stroke or CHF).
2. Medical and surgical emergency departments should be unified in a single unit (not Separated) as many patients presented with mixed complaints (medical and surgical) that should be addressed together.

Also, unifying medical and surgical units will avoid unnecessary shifting of the patients among various specialties which is contraindicated in unstable patients.

3. Emphasis on Continuous Medical Education (CME) programs regarding awareness of atypical symptoms targeting general population (via TV commercials, internet, and social networks), EMS personnel, nursing staff, and physicians thus increasing the index of suspicion for atypical symptoms especially in high risk group mentioned.

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Volume 3 Issue 7 July 2019
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