



Clinical and Pharmacological Analysis of Patients With Acute Coronary Syndrome Under 45 Years of Age: A Prospective Cohort Study

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Abstract

Background/Aim: Acute coronary syndrome (ACS) in young people is a problem of growing concern. There is an increasing need to evaluate this disease and predict its sequelae for better prevention and management. Aim of this study was to analyse clinical and pharmacological aspects of ACS hospitalised patients for a better evaluation and prediction.

Methods: The study included questionnaire based data taken from 225 patients (207 males, 18 females) admitted to Ibn Al-Nafees tertiary cardiac centre. Socio-economic, clinical and pharmacological data were obtained from all patients with follow up from time of admission to discharge.

Results: Male to female ratio was 11.5:1, anterior infarction was the predominant site (54.6 %), mortality rate was 1.3 %. Ejection fraction (LVEF) was below 45 % in 66.7 % of the patients, majority (70.7 %) with ischaemic hypokinesia. Smoking was the most common risk factor (77.3 %). Heart failure (HF) was the most common complication (57.3 %). There were significant relationship between HF occurrence and number of risk factors, LVEF, anterior site of ACS and number of echo findings. There were non-significant increase in relative risk of HF with each risk factor, positive troponin and pre-admission pain duration. Prediction tests showed an ascending positive slope of HF risk with number of risk factors, duration of admission and age.

Conclusion: There was a high rate of HF occurrence in this study which is mostly attributed to major wall damage due to blockage of the main coronary artery. Analysis demonstrated a good survival rate but high rate of HF occurrence urges for more consideration of guideline-directed management.

Key words: Acute coronary syndrome; Myocardial infarction; Heart failure; Ticagrelor; Clopidogrel; Antiplatelets.

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Introduction

Acute coronary syndrome (ACS) is a subset of coronary heart disease which includes myocardial symptomatic clinical changes with or without electrocardiogram (ECG) changes and cardiac troponin¹ - unstable angina, non-ST-segment elevation myocardial infarction (NSTEMI)

and ST-segment elevation myocardial infarction (STEMI).² ACS is responsible for a significant number of inpatient admissions worldwide, with 175,000 inpatient admissions in the United Kingdom in 2012.³ ACS is more common in males than females, with a male to female ratio of 2.19:1.⁴

ACS is caused by the rupture of an atherosclerotic plaque in the coronary artery, leading to the formation of a blood clot that obstructs blood flow to the heart muscle. Many factors can precipitate ACS, including physical or emotional stress, drug use and spontaneous implantable cardioverter defibrillator shocks.⁵ Treatment for ACS includes medications such as a bullous dose of acetylsalicylic acid (300 mg), heparin, antiplatelet therapy (clopidogrel or ticagrelor) and nitroglycerin, as well as invasive procedures such as percutaneous coronary intervention (PCI) and coronary artery bypass grafting (CABG).⁶

Coronary artery disease (CAD) is a major cause of morbidity and mortality worldwide due to obstructive atherosclerotic coronary changes. There are two main forms of CAD: chronic stable ischaemic heart disease where coronary arteries slowly and progressively narrow over the years. The other type is ACS. STEMI involves complete occlusion of coronary artery due to atherosclerotic plaque, characterised by ST-segment elevation and raised cardiac biomarkers.⁷ The commonly predicted risk factors of CAD are hyperlipidaemia, hypertension, smoking, diabetes, obesity, age factor including females above 55 years and males above 45 years and positive family history.⁸

The common symptoms of CAD include chest discomfort or anginal pain, shortness of breath or dyspnoea, dizziness or lightheaded, palpitations, nausea, stomach discomfort or vomiting and sometimes weakness. Females may demonstrate atypical symptoms. Over the years, CAD can viliate the heart and lead to complications like arrhythmias most likely atrial fibrillation, cardiac arrest, cardiogenic shock and heart failure (HF).⁹

Treatment and prevention for CAD embraces lifestyle changes, risk factor prevention and medications. The minimally invasive coronary revascularisation procedure like PCI or coronary angioplasty helps to improve blood flow to the heart. CABG is another surgical method to create a new path for the blood to flow around blockages. Medications include nitrates, beta blockers, angiotensin-converting-enzyme (ACE) inhibitors, angiotensin II receptor blockers (ARBs), statins and antiplatelet agents. High and moderate risk patients typically undergo surgery within 24-48 h. To evade high morbidity and mortality related with ACS, it must be quickly and appropriately diagnosed and managed.^{10,11}

The age of onset of ACS varies widely, with patients ranging from 18 to 69 years old, with a median age of 28 years.⁴ It is well known that ACS risk increases with age. Therefore, it occurs more often in older than younger age groups. Although atherosclerotic changes appear early in arteries but serious symptoms of disease usually needs many years to be clinically prominent.¹² The cut off age of 45 years old had been suggested by most researchers to define ACS in young patients.¹³

There are increasing indicators of concern regarding the rates of ACS among young people but data still deficient about disease management outcomes which urge to more study of this subject.¹⁴ About 6-10 % of cardiac infarctions in United States occurs in patients below 45 years old.¹⁵ Regarding Iraqi data a study conducted in Duhok City revealed that in 36 out of 380 (9.47 %) ACS patients were less than 45 years age¹⁶ while another study conducted in Sulaimaniyah showed that patients below 45 years old were 21.6 %.¹⁷

The main objective of this study was to analyse different clinical and pharmacological aspects related to ACS in hospitalised patients under 45 years of age and their effects in cure and prediction of complication occurrence.

Methods

This was a prospective observational cohort study conducted in the Critical Care Unit of Ibn Al-Nafees Cardiac Care Tertiary Centre, Al-Rusafa Health Directorate, Baghdad-Iraq. Study included 225 patients (207 males, 18 females) admitted for a period of 18 months from January 2020 to June 2021. Data collection was done through a detailed well-organised questionnaire forms. Data were obtained directly from the patients and some missed data were obtained from the clinical records. Inclusion criteria included: patients lower than 45 years age from both sexes, presented with typical chest pain and approved to be ACS, treated within the adopted regime by giving an urgent loading dose of antiplatelet (ticagrelor 180 mg or clopidogrel 300 mg) in addition to acetylsalicylic acid 300 mg and other needed medications, then being admitted urgently for PCI and later followed-up until their discharge.

Prescriptions of all patients of either sex diag-

nosed with ACS from the time the patient was admitted were collected and documented in a soft and hard copy of case record form (CRF) including the patient’s particulars and drug details. The prescriptions were analytically scrutinised using the WHO core prescribing indicators. Pregnant females and patients with other interrelated cardiac disease like arrhythmias, endocarditis and rheumatic heart disease and other non-complying with inclusion criteria were excluded. All patients were diligently followed from the time of admission till discharge. The past medical history of the patient was also reviewed.

Socio-economic class was classified into low, intermediate and high according to a specific questions including residence, occupation, income and other related information. Other data collected directly from the patients, their relatives and CRF.

Data analysis was done by Statistical Package for Social Science (SPSS) version 24. Analysis and interpretation of data was implemented by using descriptive statistics to obtain frequencies and proportions. Inferential statistics were conducted to obtain odds ratio, relative risk, Chi-square test and logistic regression wherever needed. Figures and tables were used for interpretation and displaying of data. At 95 % confidence interval (CI), $p < 0.05$ was considered statistically significant in all tests.

Results

In this study, socio-demographic data of the patients which are listed in Table 1 had shown that majority of the patients (70.7 %) were between 36-45 years. Majority of the patients were male (92 %) with male to female ratio 11.5:1, married (80.9 %) and from low socio-economic class (88.0 %). Most of them were employed (53.4 %) and college graduated (54.2 %).

Regarding clinical findings, it was found that majority of the infarction sites were anterior (54.6 %). Left ventricular ejection fraction (LVEF) was above 55 % in (37.3 %) of the patients. Echo findings revealed that ischaemic hypokinesia (70.7 %) and left ventricular (LV) systolic dysfunction (61.3%) were the most presenting features. Coronary angiography demonstrated that

Table 1: Socio-demographic characteristics of the patients with the acute coronary syndrome

Socio-demographic variables	N	%
Age		
≤ 25	4	1.8
26-35	62	27.5
36-45	159	70.7
Sex		
Male	207	92.0
Female	18	8.0
Marital status		
Married	180	80.0
Single	40	17.8
Divorced	5	2.2
Socio-economic class		
Low	198	88.0
Intermediate	18	8.0
High	9	4.0
Employment		
Employed	120	53.4
Unemployed	105	46.6
Education		
Illiterate	24	10.9
Primary school	38	16.8
Elementary school	35	15.5
College	122	54.2
High degree	6	2.6

N: number of patients; %: percentage of total number of patients;

left anterior descending artery (61.8 %) was the most frequently blocked artery. Nausea and vomiting (49.8 %) was the most frequent presenting symptom after chest pain which was excluded because it occurred in all patients and adopted as a major inclusion criterion. Smoking (77.3 %) was the most frequent risk factor. Troponin test was negative in (58.7 %) of the patients. HF was the most common complication in more than half of the patients (57.3 %). Majority of the patients (91.1 %) presented to the hospital within 1 day of symptom appearance and about half (50.6 %) were discharged after 4 days of hospital admission. Details are listed in Table 2.

Table 3 demonstrates the relationship between the major complication (HF) and different clinical features of the patients. The link between HF occurrence and risk factors number was highly significant ($p < 0.00001$). The same result was obtained in relation to type of ACS, LVEF, echo findings and duration of hospital admission.

Variables included were only those which were related to HF (213 out of 225 patients). Chi-square test was done, p-value was significant (< 0.05).

There was no significant relationship between age ($p = 0.153$), sex ($p = 0.292$) and employment ($p = 0.880$) of the patients with occurrence of HF (Table 4). On the other hand, there was a highly significant relationship between marital status and HF ($p < 0.00001$).

Table 2: Clinical findings of patients with acute coronary syndrome under 45 years of age

Variable	N	%
Type of ACS (infarction site)		
Anterior	123	54.6
Inferior	63	28.0
Posterior	0	0.0
Lateral	6	2.7
Stable angina	3	1.3
Unstable angina	30	13.3
Left ventricular ejection fraction (LVEF)		
> 55 %	84	37.3
45-55 %	69	30.7
35-44 %	60	26.7
< 35 %	12	5.3
Echo findings*		
Normal	21	9.3
LVDD	42	18.7
LVSD	138	61.3
Hypokinesia (ischemia)		
RVD	15	6.7
MR	22	9.7
TR	4	1.7
AR	5	2.2
HHD	17	7.5
LV thrombosis	3	1.3
MVP	3	1.3
LVH	18	8.0
Findings of coronary angiography*		
LMB	9	4.0
LAD	139	61.8
CX	48	21.3
RCA	74	33.3
OM	3	1.3
Diagonal	0	0.0
Ramus	7	3.1
None	54	24.0
Clinical symptoms (other than chest pain)		
Epigastric pain	22	9.8
Dyspnoea	42	18.6
Nausea and vomiting	112	49.8
Diaphoresis	6	2.7
None	43	19.1
Risk factors*		
Diabetes mellitus	60	26.7
Smoking	17	7.7
Hypertension	75	33.3
Dyslipidaemia	12	5.3
Stress	129	57.3
Family history	36	16.0
COVID-19	18	8.0
None	3	1.3

Troponin			
Positive	97	1.3	
Negative	128	58.7	
Complications			
None	84	37.4	
Arrhythmia	9	4.0	
HF	129	57.3	
Death	3	1.3	
Time of admission after pain			
Within 1 day	205	91.1	
2 days	18	8.0	
More than 2 days	2	0.9	
Duration of admission (days)			
2	18	8	
3	54	24	
4	114	50.6	
5	24	10.7	
6	15	6.7	

*more than one feature could be presented in the patient. ACS: acute coronary syndrome; LVD: left ventricular diastolic dysfunction; LVSD: left ventricular systolic dysfunction; RVD: right ventricular dysfunction; MR: Mitral regurgitation; TR: tricuspid regurgitation; AR: aortic regurgitation; HHD: hypertensive heart disease; LV: left ventricle; MVP: mitral valve prolapse; LVH: left ventricular hypertrophy; LMB: left marginal branch; LAD: left anterior descending; CX: circumflex; RCA: right coronary artery; OM: obtus marginal; HF: heart failure; N: number of patients; %: percentage of total number of patients;

Table 3: Heart failure (HF) probability in relation to different clinical variables

Variables	HF-Yes	HF-No	Total	p-value
Number of risk factors				
1	3	24	27	0.00001*
2	63	30	93	
3 and more	51	27	78	
None	12	3	15	
Site of ACS				
Anterior	84	24	108	0.000012*
Inferior	33	30	63	
Lateral	3	6	9	
Stable/ unstable angina	9	24	33	
LVEF				
> 55 %	3	78	81	< 0.00001*
45-55 %	66	3	69	
< 44 %	60	3	63	
Echo findings				
1	9	33	42	< 0.00001*
2	84	24	108	
3 and more	34	6	40	
None	2	21	23	
Duration of admission (days)				
2	2	16	1	< 0.00001*
3	18	36	54	
4	84	22	109	
5	16	5	21	
6	9	5	15	
Total	129	84	213	

Variables included are only those which were related to heart failure (213 out of 225 patients). ACS acute coronary syndrome; LVEF: left ventricular ejection fraction;

*Chi-square test was done, p-value was significant (< 0.05).

Table 4: Heart failure (HF) patient complication probability according to socio-demographic variables

Socio-demographic variables	HF-Yes	HF-No	Total	p-value
Age / years				
22-33	18	18	36	0.1530
34-45	111	66	177	
Sex				
Male	120	81	201	0.2920
Female	9	3	12	
Marital status				
Married	119	56	175	0.0001*
Single / divorced	10	28	38	
Employment				
Employed	72	46	118	0.8800
Unemployed	57	38	95	
Total	129	84	213	

*Chi-square test was done, p-value was significant (< 0.05);

Table 5: Relative risk and odd ratio of heart failure (HF) according to risk factors, troponin value, pre-admission pain time and antiplatelet drug administered

Socio-demographic variables	Total	HF-Yes	HF-No	RR	95 % CI	p-value	OR
Smoking							
Yes	177	108	69	1.22	0.898 - 1.658	0.200	1.57
No	48	24	24				
Dyslipidaemia							
Yes	12	6	6	0.87	0.486 - 1.542	0.620	0.73
No	213	123	90				
Hypertension							
Yes	75	48	27	1.18	0.946 - 1.484	0.130	1.51
No	150	81	69				
Diabetes mellitus							
Yes	60	39	21	1.19	0.945 - 1.503	0.140	1.55
No	165	90	75				
Troponin							
Positive	97	60	37	1.15	0.917 - 1.435	0.230	1.39
Negative	128	69	59				
Pre-admission pain duration							
Within 1 day	205	120	85	1.30	0.791 - 2.141	0.300	1.73
More than 1 day	20	9	11				
Antiplatelet drug on admission							
Ticagrelor	72	47	25	1.15	0.923 - 1.427	0.210	1.43
Ticagrelor + ASA	153	87	66				

HF: heart failure; RR: relative risk; CI: confidence interval; OR: odd ratio; ASA: acetylsalicylic acid;

Relative risk and odds ratio of HF according to different variables are listed in Table 5 which revealed no significant association between presence of all these variables and occurrence of HF although some numbers suggested an increased risk and odds ratio but still not significant.

Binary logistic regression was employed to determine predictors of HF as a complication of ACS in the following factors: age, duration of hospital admission and number of risk factors of the patients, as demonstrated in Figures 1, 2 and 3, respectively. There was a positive association between these factors and number of patients with HF.

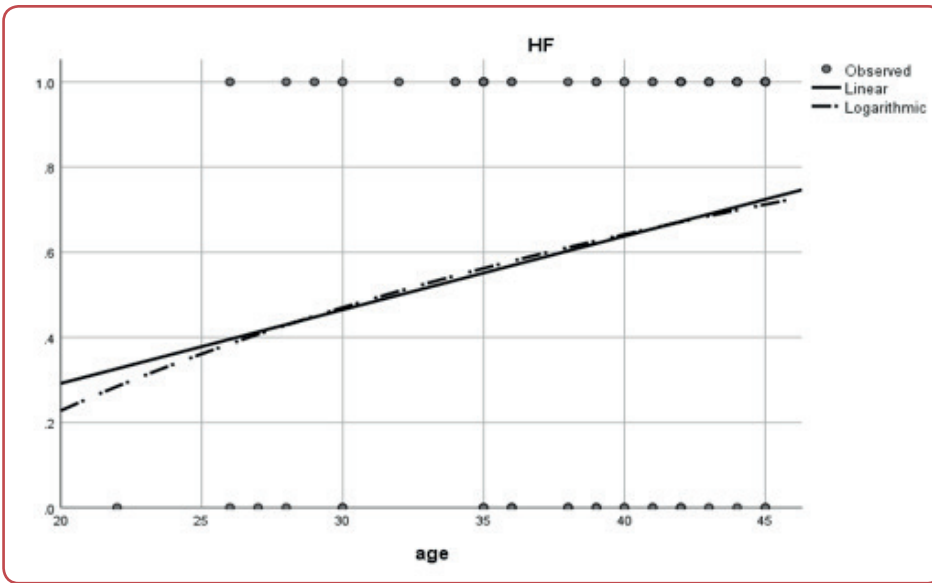


Figure 1: Logistic regression between dependent factor (heart failure) and independent factor (age)

p-value: linear 0.089, logistic 0.094;

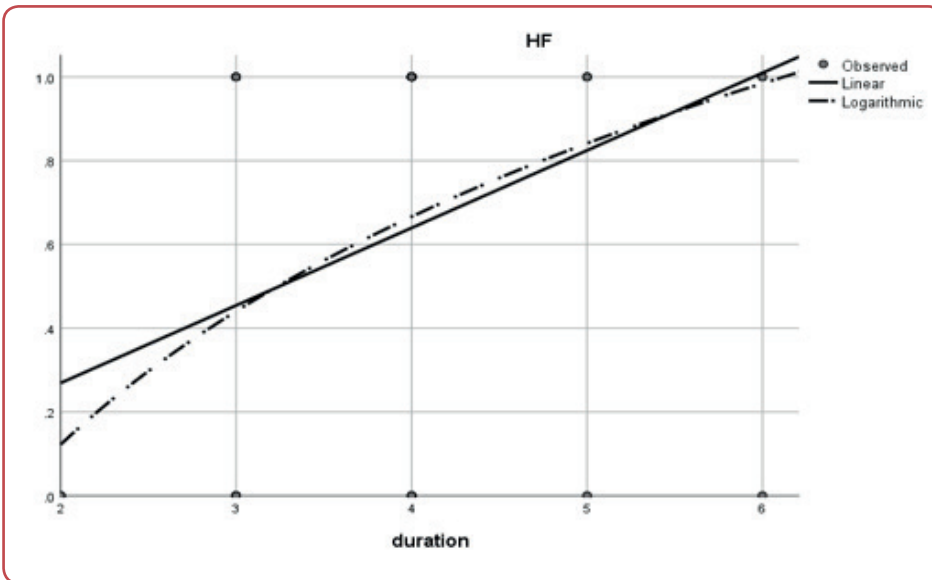


Figure 2: Logistic regression between dependent factor (heart failure) and independent factor (duration of hospital admission)

p-value: linear 0.002, logistic 0.000;

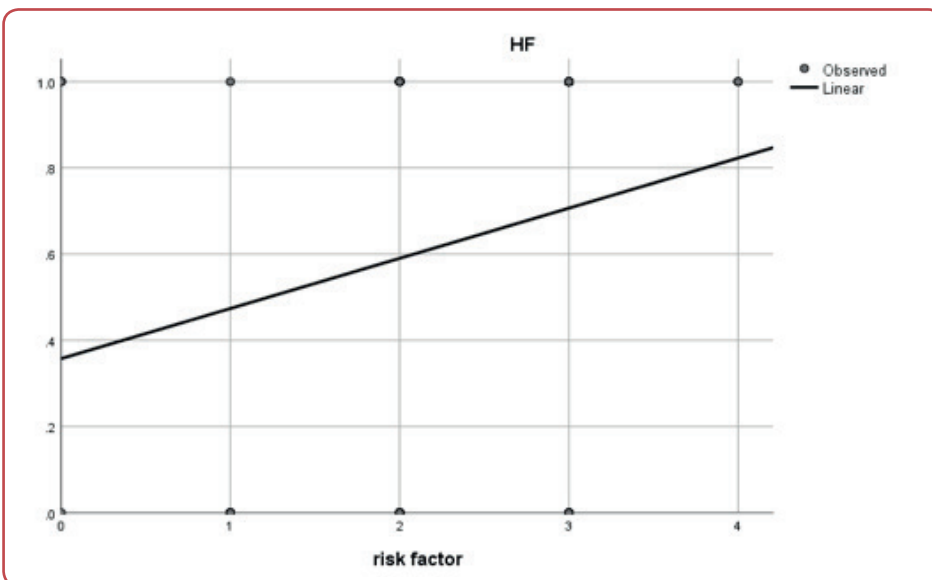


Figure 3: : Logistic regression between dependent factor (heart failure) and independent factor (number of risk factors)

p-value: linear 0.065, logistic 0.017

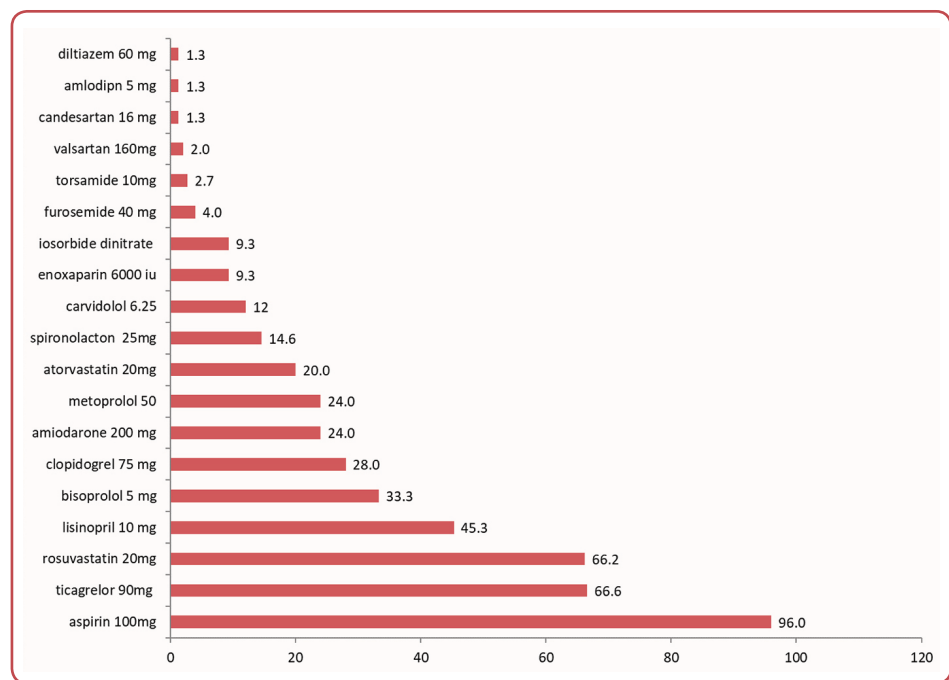


Figure 4: Percentage ranking of discharge medications prescribed to the patients

The prescribed medications on discharge were antiplatelet drugs, 66.6 % of the patients received ticagrelor 90 mg while 28.0 % of them received clopidogrel 75 mg and 96.0 % received acetylsalicylic acid 100 mg. Bisoprolol 5 mg was the most prescribed beta blocker agent (33.3 %). Among statins rosuvastatin was the most prescribed drug (66.2 %) followed by atorvastatin 40 mg (20.0 %). Between ACEI and ARBS lisinopril 5 mg was the most prescribed (45.3 %) (Figure 4).

Discussion

This study analysed 225 patients of ACS during a period of 18 months in the cardiac care unit of Ibn Al-Nafees Tertiary Care Hospital in Baghdad. All of them were under 45 years of age but 70.7 % were in the age group 36-45 years (mean age was 38.17 ± 6.32 years) this results seems to be near to the mean age calculated by another comparable study conducted in Malaysia on 282 patients which was (39.2 ± 5.1 years),¹⁸ majority of them were males (92 %). These data complied with most other studies as ACS is more common in older age group and in male population due to physiological mechanisms and presence of risk factors.^{17, 19} Regarding male to female ratio (11.5:1) in this study, this can be explained by far less exposure of females in sampled community to risk factors like smoking, stress and alcohol

than males. In addition, oestrogen tends to confer young females a protective effect against coronary atherosclerosis.²⁰

Most of the patients (53.4 %) were employed linking work related stress factors to ACS. Married patients were in majority (80.2 %) which goes against many studies which have shown that unmarried people are more likely to develop coronary artery disease²¹ but this can be explained by link of low socio-economic status of the majority of the patients (88.0 %) and psychological stress as the second important risk factor (57.3 %) which imposes familial responsibilities as an additional psychological burden on the patients below 45 years of age. Regarding risk factors, smoking (77.3 %) and stress (57.3 %) were the most common risk factors in patients which is correlated with the study of Wang et al.²² Zupancic study concluded that psychological stress is associated with ACS especially in patients with previously silent disease.²³

Many studies suggested hypertension as the first risk factor in ACS patients^{24, 25} but the probable reason for these factors retreat in this study is the young age of the patients sample since hypertension tends to occur in older age which is associated with structural changes in arteries.²⁶ Family history of ACS was found in 16 % of the patients in this study which was lower than that of another Iraqi study in a comparable sample which found that it was 24 %.²⁷

Echo findings demonstrated that ischaemic heart disease patients were maximum 61.3 % and LV systolic dysfunction was more than LV diastolic dysfunction. Echo finding can help in early detection and diagnosis of ACS and guide in proper management thereby decreasing mortality. These finding can be used as independent predictors and can help in identifying high risk-patients, patients who need medical therapy or surgical intervention and follow them to improve their outcome. High percentage of LV ischaemic damage occurred mostly due to high percentage of blockage in left anterior descending artery (the largest coronary artery) (61.8 %) which lead to systolic and diastolic dysfunction and that explains the high proportion of HF complication (57.3 %) of patients in the current study which was higher than the Malaysian study (35.4 %). Incidence of HF among patients hospitalised for an acute MI varies among studies, starting from 14-36 %.²⁸ In spite of the lower mortality rate in this study than the global rate, HF occurrence was much higher.

As for complications, 37.4 % of the patients escaped with no complications but most of the patients (57.3 %) developed HF. Mortality rate was 1.3 % which is lower than the global rate of mortality that was estimated by 7 %.²⁹ This is mostly due to rapid coronary intervention and young age of the patients. Arrhythmia occurred in 4 % of the patients which was lower in comparison to the Malaysian study (18.4 %).

For HF as a major complication in this study, relations with different parameters were assessed to predict the future probability of occurrence. Regarding the relation between HF occurrence with number of risk factors per each patient there was an extremely significant difference among groups since its occurrence was higher in patients with 2 and more risk groups in comparison to none and single risk groups which imposes a strong relationship between number of risk factors and HF as a complication of ACS. This finding suggests clearly that ACS in young people is mostly an outcome of more than one independent risk factor synergism.

The type of ACS was significantly associated with HF occurrence ($p < 0.000012$) as 84/108 (about 87 %) of patients with anterior type ended with HF. Anterior wall infarction is associated with a higher risk of adverse remodelling and HF.³⁰ The higher risk of HF associated with anterior MI is caused by the greater magnitude of irreversible

LV damage, as compared with other MI locations.³¹ On the other hand LVEF was extremely significant in association between HF and reduced ejection fraction results, this suggest higher area of LV wall damage due to blockage of main anterior coronary artery. Also, there were extremely significant association between 2 and more echo findings and HF occurrence which can be explained by the previously mentioned causes. In addition and for the same reasons patients who developed HF had significantly higher duration of hospital stay.

Relative risk and odds ratio of developing HF were higher but with non-significant manner in all factors except dyslipidaemia which was associated with lower risk, this seems to be due to the low effect of dyslipidaemia as an independent risk factor of ACS in young population. Regarding troponin, pre-admission pain duration and antiplatelet drug(s) on admission there was a non-significant increase of relative risk and odd ratio predicting a non-significant increase in HF occurrence in presence of these factors.

HF risk prediction was assessed with logistic regression test in regard to the following independent factors (age, duration of hospital admission and number of risk factors). The results have shown that there is a positive correlations between increased number of HF patients and increase of each of these independent factors consolidating the previous results of relation between HF occurrence and these factors in the form that it can be expected HF more often as a complication of ACS in the presence of these factors. Improving prediction of ACS patients at risk of HF development is needed since timely initiation of guideline-directed HF therapy can reduce the risk of further LV remodelling, morbidity and mortality.³¹⁻³³

In light of the above results the discharge treatment strategy should concentrate on the prevention of post MI complication development especially HF alongside with inhibition of further atherosclerotic process development. It is recommended to consider an urgent interventional management for the ischaemic patients with anterior ischemia and those who have more than 2 risk factors prior to MI development.

In the current study, beta blocker drugs (metoprolol, bisoprolol and carvedilol) were prescribed for 69.3 % of the discharged patients which

seems to be covering all patients with HF but not all the guidelines directed indications which imposes an urgent revision of beta blockers prescription policy in this centre. Beta blockers are one of the fundamental guideline-recommended therapies that must be considered as a first line therapy in patients with ventricular tachycardia or fibrillation in the acute and sub-acute phase of an ACS since it plays a crucial role in inhibition of matrix metalloproteinases (MMPs) responsible for tissue remodelling.³⁴

P2Y12 inhibitors anti-platelets (ticagrelor and clopidogrel) were prescribed for 94.6 % of the discharged patients while acetylsalicylic acid was prescribed for 96 % of them. All patients should be put under antiplatelet therapy of both a P2Y12 inhibitor drug and acetylsalicylic acid unless one of them or both were contraindicated. Dual antiplatelet therapy of both P2Y12 inhibitor and acetylsalicylic acid, is the standard therapeutic strategy in patients with ACS who underwent to PCI according to the current guidelines in order to optimise antiplatelet effects.³⁵ Most of the patients were prescribed ticagrelor (66.6 %) in comparison to those prescribed clopidogrel (28 %) and this goes with results of the studies which gives superiority to ticagrelor on clopidogrel.^{36,37}

Statins (HMG-CoA reductase inhibitors) specifically atorvastatin and rosuvastatin were prescribed in 86.6 % of the patients. Current European and American guidelines recommend the administration of high-potency statins as early as possible in ACS.³⁸ Antihypertensive drugs especially ACEI and ARBs were prescribed for less than half of the patients and the most common agent used was lisinopril (45.3 %). The rationale for such percentage is that most of the patients (66.7 %) had no history of hypertension. But this pattern is not going with rationale with regard to the majority of the patients who developed HF.

Beyond beta blockers and ACEIs, there were no prominent guideline-directed prescription with regard to HF especially HF with reduced ejection fraction (HFrEF) in which ejection fraction is less than 40 %.³⁹ About 13 % of the patients in the current study ended with HFrEF and this need to be treated according to current guidelines which include in addition to beta blockers and ACEIs, mineralocorticoid receptor antagonists (eplerenone and spironolactone), sodium-glucose co-transporter-2 (SGLT2) inhibitors (dapagliflozin and empagliflozin), angiotensin receptor-neprilysin

inhibitors (ARNIs) (sacubitril).¹⁹ All these agents were minimally or not prescribed. More consideration should be paid to the goal of management of ACS complications especially HF and HFrEF alongside with the goal of ACS recurrence inhibition.

The present research highlights the importance of rational drug prescribing in ACS patients. Early detection, avoiding risk factors, patient awareness and education especially if family history is present, multidisciplinary approach for treating such patients can improve the prognosis in long term and improve survival rate. Drug therapy prescribing should be in accordance with guidelines in order to further reduce the complications, decrease the economic burden on the patient and incidence of drug interactions and adverse reactions.

Conclusion

There was a high rate of HF occurrence in this study which is mostly attributed to major wall damage due to blockage of the main coronary artery. Analysis demonstrated a good survival rate which suggests a good submission to therapeutic guidelines but high rate of HF occurrence urges for more consideration of guideline-directed management.

Ethics

The study was approved by the Al-Kindy College of Medicine Scientific Unit Ethics Committee, decision No KCM-N521-23, dated 22 June 2023. All participants gave a written and oral consent for use of their anonymised medical data in this study.

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Conflicts of interest

The authors declare that there is no conflict of interest.

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Data access

The data that support the findings of this study are available from the corresponding author upon reasonable individual request.

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References

1. Byrne RA, Rossello X, Coughlan JJ, Barbato E, Berry C, Chieffo A, et al; ESC Scientific Document Group. 2023 ESC Guidelines for the management of acute coronary syndromes. *Eur Heart J.* 2023 Oct 12;44(38):3720-826. doi: 10.1093/eurheartj/ehad191.
2. Thygesen K, Alpert JS, Jaffe AS, Simoons ML, Chaitman BR, White HD, et al; Writing Group on the Joint ESC/ACCF/AHA/WHF Task Force for the Universal Definition of Myocardial Infarction; ESC Committee for Practice Guidelines (CPG). Third universal definition of myocardial infarction. *Eur Heart J.* 2012 Oct;33(20):2551-67. doi: 10.1093/eurheartj/ehs184.
3. Tan YC, Sinclair H, Ghoorah K, Teoh X, Mehran R, Kuna-dian V. Gender differences in outcomes in patients with acute coronary syndrome in the current era: A review. *Eur Heart J Acute Cardiovasc Care.* 2016 Nov;5(7):51-60. doi: 10.1177/2048872615610886.
4. Naji AA, Abbas AA, Hashem RB. Evaluation of serum RANKL level in acute coronary syndrome. *Al-Kindy Coll Med J.* 2014;10(2):45-8.
5. Freedman JE, Loscalzo J. Platelet-monocyte aggregates: bridging thrombosis and inflammation. *Circulation.* 2002 May 7;105(18):2130-2. doi: 10.1161/01.cir.0000017140.26466.f5.
6. Gilutz H, Shindel S, Shoham-Vardi I. Adherence to NSTEMI guidelines in the emergency department: regression to reality. *Crit Pathw Cardiol.* 2019 Mar;18(1):40-6. doi: 10.1097/HPC.000000000000165.
7. Singh A, Museedi AS, Grossman SA. Acute coronary syndrome. 2023 Jul 10. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2024 Jan-. PMID: 29083796. Available at: <https://pubmed.ncbi.nlm.nih.gov/29083796/>.
8. Karthikeyan T, Raja M, Radha D, Gaur T A, Geetha J, Sakthivadivel V. Risk factors and inflammatory markers in acute coronary syndrome-ST elevation myocardial infarction (STEMI). *Horm Mol Biol Clin Investig.* 2023 Mar 20;44(2):115-20. doi: 10.1515/hm-bci-2021-0106.
9. Dauriz M, Morici N, Gonzini L, Lucci D, Di Chiara A, Boccanelli A, et al. Fifteen-year trends of cardiogenic shock and mortality in patients with diabetes and acute coronary syndromes. *Am J Med.* 2020 Mar;133(3):331-9.e2. doi: 10.1016/j.amjmed.2019.07.044.
10. Guedeney P, Collet JP. Diagnosis and management of acute coronary syndrome: what is new and why? Insight From the 2020 European Society of Cardiology Guidelines. *J Clin Med.* 2020 Oct 28;9(11):3474. doi: 10.3390/jcm9113474.
11. Poudel N, Alurkar VM, Jha GS, Kafle R, Sapkota S, Lam-sal L. Profile of acute coronary syndrome in young people: a hospital based observational study in western Nepal. *BJHS.* 2018;3(1):361-5. doi: 10.3126/bjhs.v3i1.19759.
12. Choudhury L, Marsh JD. Myocardial infarction in young patients. *Am J Med.* 1999;107(3):254-61. doi: 10.1016/S0002-9343(99)00218-1.
13. Avezum A, Makdisse M, Spencer F, Gore JM, Fox K, Montalescot G, et al. Impact of age on management and outcome of acute coronary syndrome: observations from the Global Registry of Acute Coronary Events (GRACE). *Am Heart J.* 2005 Jan;149(1):67-73. doi: 10.1016/j.ahj.2004.06.003.

14. Dakhil Z. 67 young patients with non-ST elevation acute coronary syndromes: baseline characteristics, in-hospital management and outcomes. *Heart.* 2021;107:A55-A56. doi: 10.1136/heartjnl-2021-BCS.67.
15. Chouhan L, Hajar HA, Pompisello JC. Comparison of thrombolytic therapy for acute myocardial infarction in patients aged <35 and >55 years. *Am J Cardiol.* 1993;71:157-9. doi: 10.1016/0002-9149(93)90731-q.
16. Mohammad AM, Abdulhaleem BH, Habeeb QS. First 24 h' outcomes of acute coronary syndrome in Iraq. *Med J Babylon.* 2020;17:154-8. doi: 10.4103/MJBL.MJBL_15_20.
17. Jalal Khaznadar AA, Salh RW. Impact of age on risk factors and clinical manifestations of acute coronary syndrome: observations from the coronary care unit of Sulaimani, Iraq. *Hosp Pract Res.* 2020;5(1):28-34. doi: 10.34172/hpr.2020.06.
18. Che-Muzaini CM, Norsa'adah B. Complications of acute coronary syndrome in young patients. *Iran J Public Health.* 2017 Jan;46(1):139-40. PMID: 28451542.
19. Swaroop G. Post-myocardial infarction heart failure: a review on management of drug therapies. *Cureus.* 2022 Jun 8;14(6):e25745. doi: 10.7759/cureus.25745.
20. Mendelsohn ME, Karas RH. The protective effects of estrogen on the cardiovascular system. *N Engl J Med.* 1999 Jun 10;340(23):1801-11. doi: 10.1056/NEJM199906103402306.
21. Wong CW, Kwok CS, Narain A, Gulati M, Mihalidou AS, Wu P, et al. Marital status and risk of cardiovascular diseases: a systematic review and meta-analysis. *Heart.* 2018 Dec;104(23):1937-48. doi: 10.1136/heartjnl-2018-313005.
22. Wang W, Zhao D, Sun JY, Wang WH, Cheng J, Liu J, et al. [Risk factors comparison in Chinese patients developing acute coronary syndrome, ischemic or hemorrhagic stroke: a multi-provincial cohort study]. *Zhonghua Xin Xue Guan Bing Za Zhi.* 2006 Dec;34(12):1133-7. Chinese. PMID: 17274911.
23. Zupancic ML. Acute psychological stress as a precipitant of acute coronary syndromes in patients with undiagnosed ischemic heart disease: a case report and literature review. *Prim Care Companion J Clin Psychiatry.* 2009;11(1):21-4. doi: 10.4088/pcc.08r00623.
24. Desta DM, Nedi T, Hailu A, Atey TM, Tsadik AG, Asgedom SW, et al. Treatment outcome of acute coronary syndrome patients admitted to Ayder Comprehensive Specialized Hospital, Mekelle, Ethiopia; A retrospective cross-sectional study. *PLoS One.* 2020 Feb 13;15(2):e0228953. doi: 10.1371/journal.pone.0228953.
25. Mohanan PP, Mathew R, Harikrishnan S, Krishnan MN, Zachariah G, Joseph J, et al. Presentation, management and outcomes of 25 748 acute coronary syndrome admissions in Kerala, India: results from the Kerala ACS Registry. *Eur Heart J.* 2013 Jan;34(2):121-9. doi: 10.1093/eurheartj/ehs219.
26. Pinto E. Blood pressure and ageing. *Postgrad Med J.* 2007 Feb;83(976):109-14. doi: 10.1136/pgmj.2006.048371.
27. Mirza AJ, Taha AY, Khdir BR. Risk factors for acute coronary syndrome in patients below the age of 40 years. *Egypt Heart J.* 2018 Dec;70(4):233-5. doi: 10.1016/j.ehj.2018.05.005.
28. Fox KA, Eagle KA, Gore JM, Steg PG, Anderson FA; GRACE and GRACE2 Investigators. The Global Registry of Acute Coronary Events, 1999 to 2009--GRACE. *Heart.* 2010 Jul;96(14):1095-101. doi: 10.1136/hrt.2009.190827.
29. Ahmad WAW, Zambahari R, Ismail O, Sinnadurai J, Rosman A, Piaw CS, et al. Malaysian National Cardiovascular Disease Database (NCVD)--Acute Coronary Syndrome (ACS) registry: How are we different? *CVD Prev Control* 2011;6(3):81- 9. doi: 10.1016/j.cvdpc.2011.04.004.
30. Gaudron P, Eilles C, Kugler I, Ertl G. Progressive left ventricular dysfunction and remodeling after myocardial infarction. Potential mechanisms and early predictors. *Circulation.* 1993 Mar;87(3):755-63. doi: 10.1161/01.cir.87.3.755.
31. Jenča D, Melenovský V, Stehlik J, Staněk V, Kettner J, Kautzner J, et al. Heart failure after myocardial infarction: incidence and predictors. *ESC Heart Fail.* 2021 Feb;8(1):222-37. doi: 10.1002/ehf2.13144.
32. Ponikowski P, Anker SD, AlHabib KF, Cowie MR, Force TL, Hu S, et al. Heart failure: preventing disease and death worldwide. *ESC Heart Fail.* 2014 Sep;1(1):4-25. doi: 10.1002/ehf2.12005.
33. Lewis EF, Velazquez EJ, Solomon SD, Hellkamp AS, McMurray JJ, Mathias J, et al. Predictors of the first heart failure hospitalization in patients who are stable survivors of myocardial infarction complicated by pulmonary congestion and/or left ventricular dysfunction: a VALIANT study. *Eur Heart J.* 2008 Mar;29(6):748-56. doi: 10.1093/eurheartj/ehn062.
34. DeLeon-Pennell KY, Meschiari CA, Jung M, Lindsey ML. Matrix metalloproteinases in myocardial infarction and heart failure. *Prog Mol Biol Transl Sci.* 2017;147:75-100. doi: 10.1016/bs.pmbts.2017.02.001.
35. Gagnano F, Capolongo A, Terracciano F, Gargiulo G, De Sio V, Cesaro A, et al. Escalation and de-escalation of antiplatelet therapy after acute coronary syndrome or PCI: available evidence and implications for practice. *J Clin Med.* 2022 Oct 23;11(21):6246. doi: 10.3390/jcm11216246.
36. Wallentin L, Becker RC, Budaj A, Cannon CP, Emanuelsson H, Held C, et al; PLATO Investigators; Freij A, Thorsén M. Ticagrelor versus clopidogrel in patients with acute coronary syndromes. *N Engl J Med.* 2009 Sep 10;361(11):1045-57. doi: 10.1056/NEJMoa0904327.
37. Wiviott SD, Braunwald E, McCabe CH, Montalescot G, Ruzyllo W, Gottlieb S, et al; TRITON-TIMI 38 Investigators. Prasugrel versus clopidogrel in patients with acute coronary syndromes. *N Engl J Med.* 2007 Nov 15;357(20):2001-15. doi: 10.1056/NEJMoa0706482.
38. Ibanez B, James S, Agewall S, Antunes MJ, Bucchiarelli-Ducci C, Bueno H, et al; ESC Scientific Document Group. 2017 ESC Guidelines for the management of acute myocardial infarction in patients presenting with ST-segment elevation: The Task Force for the management of acute myocardial infarction in patients presenting with ST-segment elevation of the European Society of Cardiology (ESC). *Eur Heart J.* 2018 Jan 7;39(2):119-77. doi: 10.1093/eurheartj/ehx393.
39. Bloom MW, Greenberg B, Jaarsma T, Januzzi JL, Lam CSP, Maggioni AP, et al. Heart failure with reduced ejection fraction. *Nat Rev Dis Primers.* 2017 Aug 24;3:17058. doi: 10.1038/nrdp.2017.58.