Nassr OA, Forsyth P, Johnson CF. Evaluation of discharge prescriptions for secondary prevention in patients with acute coronary syndromes in Iraq. Pharmacy Practice 2019 Jan-Mar;17(1):1372.

https://doi.org/10.18549/PharmPract.2019.1.1372

# **Original Research**

# Evaluation of discharge prescriptions for secondary prevention in patients with acute coronary syndromes in Iraq

Ola A. NASSR<sup>10</sup>, Paul FORSYTH<sup>10</sup>, Chris F. JOHNSON<sup>10</sup> Received (first version): 14-Sep-2018 Accepted: 27-Jan-2019 Published online: 11-Mar-2019

# Abstract

Background: Optimal prescribing of secondary prevention medications after acute coronary syndrome (ACS) events has been shown to reduce morbidity and mortality. However, it is unknown whether these medications are optimally prescribed at discharge from acute care in Iraq.

Objective: To evaluate whether patients with ACS received optimal secondary prevention medications: antiplatelets, statins, angiotensin-converting enzyme inhibitors/angiotensin II receptor blockers (ACEI/ARBs), and beta-blockers at discharge from a cardiology unit, and to assess whether statins, ACEI/ARBs and beta-blockers were prescribed at target doses based on the American Heart Association/American College of Cardiology (AHA/ACC) guidelines.

Methods: Observational retrospective cross-sectional study of patients with ACS admitted to a hospital in Baghdad and survived to discharge between May 2016 and January 2017. Patient-level data and secondary prevention medications at discharge were extracted from routine medical records. Optimal dosing was defined as ≥75%, moderate dosing as 50–74%, and low dosing as <50% of the target dose.

Results: 45.6% (200/439) of eligible patients were included in the study who were aged 25 to 90 years (mean 57.8 years) with 78.0% (156/200) being male. Of those included, 84.5% had a myocardial infarction and 15.5% unstable angina, and the length of hospital stay ranged from 1 to 29 days (median 4 days). In total, 53.5% of patients were prescribed all five secondary prevention medications at discharge, and after accounting for contraindications, 60.0% were treated according to AHA/ACC guidelines. The prescription rate of dual antiplatelet therapy, statins, ACEI/ARBs and beta-blockers was 92.5%, 94.5%, 69.5% and 87.0% respectively. Hypertension, diabetes mellitus and the prescription of oral nitrates were associated with the prescription of optimal secondary prevention therapy. Although 80.9% of patients were prescribed target doses of antiplatelets and statins, only 12.2% and 9.2% were prescribed target doses of ACEI/ARBs, and beta-blockers respectively.

Conclusions: Approximately one in two patients received the recommended secondary prevention therapy. However, only a minority of patients were prescribed optimal doses of ACEI/ARBs and beta-blockers, in line with guidance. Quality improvement strategies should be implemented, which may include greater involvement of pharmacists within the cardiology multidisciplinary team.

#### Keywords

Acute Coronary Syndrome; Professional Practice; Guideline Adherence; Drug Utilization; Angiotensin-Converting Enzyme Inhibitors; Angiotensin Receptor Antagonists; Clinical Audit; Iraq

# INTRODUCTION

Cardiovascular disease is the leading cause of morbidity and mortality globally.<sup>1</sup> In Iraq, cardiovascular disease is the primary cause of hospitalisations and accounts for 33% of total deaths.<sup>2,3</sup> Acute coronary syndrome (ACS) is an umbrella term referring to any group of clinical signs and symptoms consistent with acute myocardial ischemia.<sup>4</sup> ACS includes unstable angina, non-ST-segment elevation myocardial infarction (NSTEMI), and ST-segment elevation myocardial infarction (STEMI), all of which are lifethreatening events and major causes of hospitalisations, rising healthcare costs, morbidity, and mortality. 5,6

In the acute phase of ACS, aggressive management is

required to improve prognosis.<sup>7</sup> Patients surviving ACS are at a high-risk of subsequent cardiovascular events and death:<sup>7-9</sup> one in four men and one in five women will die within 12 months of an ACS event.<sup>7</sup> Fortunately, a better understanding of the pathophysiological mechanisms involved in ACS has allowed the development of invasive interventions such as percutaneous coronary intervention and coronary artery bypass grafting and non-invasive secondary prevention medications, including dual antiplatelet therapy, angiotensin-converting enzvme inhibitors/angiotensin II receptor blockers (ACE/ARBs), beta-blockers, and statins.<sup>5,9,10</sup>

Regular use and optimal dosing with secondary prevention medications improve quality of life and survival; reducing cardiovascular events and mortality by up to 80%.<sup>11,12</sup> Therefore, the American Heart Association/American College of Cardiology (AHA/ACC) guidelines, which are used as national guidance in Iraq, recommend prescribing secondary prevention medications before discharge to all patients without contraindications.<sup>13,14</sup>

Unfortunately, the literature indicates that secondary prevention medications are inconsistently prescribed, commonly at suboptimal doses, and poorly adhered to by



Ola Ali NASSR. MSc, BSc (Hons). Assistant Lecturer. Department of clinical pharmacy, College of Pharmacy, Mustansiriya University. Baghdad, (Iraq). ola.nassr@uomustansiriyah.edu.iq

Paul FORSYTH. MSc (Primary Care), MPharm, IP. Lead Pharmacist for Clinical Cardiology (Primary Care). NHS Greater Glasgow and Clyde, West Glasgow Ambulatory Care Hospital. Glasgow, Scotland

<sup>(</sup>United Kingdom). paul.forsyth@nhs.net Chris F. JOHNSON. MRes, MSc, BSc (Hons), IP. Specialist Mental Health and Prescribing Support Pharmacist Primary Care, Pharmacy and Prescribing Support Unit, NHS Greater Glasgow and Clyde, West Glasgow Ambulatory Care Hospital. Glasgow, Scotland (United Kingdom). c.johnson2@nhs.net

Nassr OA, Forsyth P, Johnson CF. Evaluation of discharge prescriptions for secondary prevention in patients with acute coronary syndromes in Iraq. Pharmacy Practice 2019 Jan-Mar;17(1):1372.

patients.<sup>4,10,11,15,16</sup> Statins can be initiated at optimal doses, while ACE/ARBs and beta-blockers need to be titrated to the optimal dose.<sup>11</sup> Although optimising doses before discharge is recommended, some patients may have contraindications or be unable to tolerate dose titration due to common factors such as hypotension, bradycardia, or worsening renal function.<sup>11,13,17</sup> However, by ensuring patients are prescribed optimal secondary prevention medications at discharge, physicians can increase the likelihood of adherence to these medicines post-discharge and optimise long-term outcomes.<sup>9,11</sup>

Studies evaluating current practices in Iraq against AHA/ACC guidelines are sparse. Therefore, this study's objectives were (1) to evaluate whether ACS patients receive optimal secondary prevention medications, consisting of dual antiplatelet therapy, statins, ACE/ARBs and beta-blockers at discharge from a cardiology unit at a government teaching hospital in Baghdad, as per AHA/ACC guidelines and (2) to assess whether statins, ACEI/ARBs and beta-blockers were prescribed at optimal doses to these patients.<sup>13,14</sup>

#### METHODS

#### Ethics approval

This study received ethical approval from the College of Pharmacy at the University of Mustansiriyah. In addition, the hospital gave approval for patient-level data to be collected from medical records. All patient-level data were anonymised prior to analysis to ensure patient confidentiality.

#### Study design and setting

This study used an observational retrospective crosssectional design, applied to routinely collected patient-level data. The study was conducted within a major teaching hospital in Baghdad, Iraq's largest city, which provides free state-funded health care and delivers ACS care to approximately 700 patients per year.

#### Participant identification and data collection

Patients were eligible for this study if they were admitted to the study site and survived an ACS event from May 2016 to January 2017. For the purposes of the study an ACS event was defined as incident STEMI, NSTEMI, or unstable angina recorded in the medical notes of an admitted patient, plus clinical signs/symptoms of chest pain associated with electrocardiography changes and/or troponin level elevation. Patients were excluded from the study if they left against medical advice, died or were transferred to another hospital. If patients were admitted twice during the study, only their first admission was included. Given the descriptive nature of the study, resource constrains and the incidence rate of ACS within the site, a sample size of 200 patients was deemed appropriate. These patients were identified via convenience sampling by hospital administrative staff who screened medical records for incident ACS until 200 patients were included. The sampling methodology was not random and did not include consecutive patients.

Following identification, retrospective patient-level data were collected from written medical records, from October 2016 to February 2017, by one experienced clinical

Characteristics	All patients n=200 (%)	Five medications received n=107 (53%)	Five medications not received n=93 (46%)	Univariate p-value
Mean age, years (range)	57.8 (25-90)	58.1 (25-90)	57.4 (28-85)	0.677
Gender				0.866
Male	156 (78.0)	84 (78.5)	72 (77.4)	
Female	44 (22.0)	23 (21.5)	21 (22.6)	
Type of ACS				0.509
STEM	134 (67.0)	68 (63.5)	66 (70.9)	
NSTEMI	35 (17.5)	20 (18.7)	15 (16.1)	
Unstable angina	31 (15.5)	19 (17.8)	12 (12.9)	
Past medical history				
Hypertension	117 (58.5)	70 (65.4)	47 (50.5)	0.044
Diabetes mellitus	77 (38.5)	32 (29.9)	45 (48.4)	0.009
Ischemic heart disease	63 (31.5)	38 (35.5)	25 (26.9)	0.223
Heart failure or LVSD	12 (6.0)	8 (7.5)	4 (4.3)	0.388
Cerebrovascular accident	10 (5.0)	5 (4.7)	5 (5.4)	1
Peptic ulcer	6 (3.0)	2 (1.9)	4 (4.3)	0.420
Number of Co-morbidities				0.542
0	37 (18.5)	17 (15.9)	20 (21.5)	
1	70 (35.0)	40 (37.4)	30 (32.3)	
≥2	93 (46.5)	50 (46.7)	43 (46.2)	
Other Medications				
Diuretics	40 (20.0)	22 (20.6)	18 (19.4)	0.861
Nitrates	32 (16.0)	24 (22.4)	8 (8.6)	0.011
Calcium channel blockers	11 (5.5)	5 (4.7)	6 (6.5)	0.758
Vitals at Discharge				
Mean SBP, mmHg (range)	123.8 (85-180)	125.8 (92-180)	121.5 (85-180)	0.114
Mean DBP, mmHg (range	73.3 (50-104)	74.9 (50-104)	71.6 (50-90)	0.036
Mean HR, bpm (range)	78.3 (46-120)	78.2 (46-120)	78.4 (46-110)	0.906
Mean length of hospital stay, days (range)	4.3 (1-29)	4.1 (1-19)	4.6 (1-29)	0.380



Nassr OA, Forsyth P, Johnson CF. Evaluation of discharge prescriptions for secondary prevention in patients with acute coronary syndromes in Iraq. Pharmacy Practice 2019 Jan-Mar;17(1):1372.

https://doi.org/10.18549/PharmPract.2019.1.1372

Prescribed medications		Target Dosing Range			
	On Therapy n (%)	Appropriate secondary prevention therapy <sup>a</sup> n (%)	Low n (% <sup>b</sup> )	Medium n (% <sup>b</sup> )	High n (% ⁵)
Clopidogrel	196 (98.0)	196 (98.0)	N/A	N/A	196 (100)
Aspirin	187 (93.5)	190 (95.0)	N/A	N/A	187 (100)
Dual antiplatelet therapy	185 (92.5)	188 (94.0)	N/A	N/A	185 (100)
Statin	189 (94.5)	189 (94.5)	N/A	36 (19.1)	153 (80.9)
Beta-blockers	174 (87.0)	182 (91.0)	76 (43.7)	82 (47.1)	16 (9.2)
ACE/ARBs	139 (69.5)	147 (73.5)	98 (70.5)	24 (17.3)	17 (12.2)
All five medications	107 (53.5)	120 (60.0)	NA	N/A	2 (1.9 )

pharmacist using a standardised data collection form. Data included: age, gender, primary diagnosis, past medical history, blood pressure at discharge, heart rate at discharge, and prescribed drugs and doses on the day of discharge. The hospital inpatient prescription on the day of discharge was used to confirm the discharge medication, as the formal discharge prescription is not permanently stored in the patient's records, but given to the patient at discharge.

#### **Measurement of outcomes**

The primary endpoint was the number of patients prescribed appropriate secondary prevention medications at discharge. For the purpose of the study, appropriate secondary prevention medications were defined as being prescribed dual antiplatelet therapy, statin, ACEI/ARB and beta-blocker at discharge in accordance with AHA/ACC guidance. When patients had a clinical contraindication, in accordance with AHA/ACC guidance, precluding the use of one or more medications this was also counted as appropriate secondary prevention therapy.<sup>13,14</sup>

Secondary endpoints were the number of patients receiving optimal doses of ACEI/ARBs, beta-blockers, and high-intensity statins at discharge.<sup>13,14</sup> The following daily target doses were used: beta-blockers (metoprolol 200 mg; atenolol 100 mg; carvedilol 50 mg; and bisoprolol 10 mg) ACEI/ARBs (captopril 150 mg; enalapril 20 mg; lisinopril 10 mg; ramipril 10 mg; valsartan 320 mg; losartan 150 mg; and candesartan 32 mg) and high-intensity statins (atorvastatin 80 mg or rosuvastatin 20 mg or 40 mg).<sup>15,16,18</sup> A dose intensity ranking was then used to define optimal doses as low (<50% of target dose), medium (50–74%) and high ( $\geq$ 75%).<sup>11</sup> Systolic blood pressure and heart rate were evaluated for patients to determine whether low systolic blood pressure prevented dose optimization in low dose users of ACEI/ARBs and beta-blockers.

#### Statistical analysis

Descriptive statistics were used to describe patient demographics, the proportion and percentage of patients receiving secondary prevention medications, and target doses at discharge. Pearson's chi-squared test, Fisher's exact test (categorical variables) and the independent t-test (continuous variables) were used as appropriate, depending on the data, to test for associations between demographic characteristics and the use of medications at discharge. Based on the results of the above tests, variables with statistical significance associated with receiving all five medications at discharge were also subjected to binary logistic regression in order to determine independent predictors associated with receiving all five medications at discharge. Data were analysed using SPSS version 26.0 (INM Corp, Chicago, IL) and two-tailed p- values less than 0.05 were used to indicate statistical significance.

# RESULTS

#### Prescription of secondary prevention medications

During the study period, 522 patients were admitted with ACS. Of these, 439 (84.1%) were eligible for the study, and 45.6% (200/439) were included. Of the 83 (15.9 %) ineligible patients, 39 left against medical advice, 31 died, and 13 transferred to another hospital.

Included patients varied in age from 25 to 90 years old (mean 57.8) and 78.0% (n=156) were male, with 84.5% (n=169) having a primary diagnosis of myocardial infarction and 15.5% (n=31) having unstable angina. Baseline cardiac risk factors included; 58.5% (n=117) hypertension; 38.5% (n=77) diabetes and 31.5% (n=63) with a previous history of ischemic heart disease. The median duration of hospital stay was 4 days, (range 1 to 29 days); see Table 1.

In total, 53.5% (n=107) of patients were prescribed all five medications, see Table 2. Thirteen additional patients had contraindications for one or more secondary prevention medications. Therefore, when valid contraindications were accounted for, 60.0% (n=120) of patients were assessed against guidelines to be prescribed appropriate secondary prevention therapy. Most commonly prescribed medications were: clopidogrel 98.0% (n=196), statins 94.5% (n=189) (52.4% atorvastatin, 47.6% rosuvastatin), aspirin 93.5% (n=187), dual antiplatelet therapy 92.5% (n=185) (aspirin and clopidogrel in all cases), beta-blockers 87.0% (n=174) (78.2% metoprolol, 14.4% carvedilol, 5.7% bisoprolol and 1.7% atenolol) and ACEI/ARBs 69.5% (n=139) (82.7% captopril, 5.0% enalapril, 2.2% lisinopril, 0.7% ramipril, 5.8 % candesartan, 2.2% valsartan and 1.4% losartan). No patients were co-prescribed ACEI and ARB. There was statistically significant association between the use of all five medications and mean diastolic blood pressure. In addition, there was a significant association between ACE/ARBs prescribing and hypertension, diabetes mellitus and being discharged on oral nitrate, see Table 3.

Binary logistic regression indicated that comorbidities such as hypertension (odd ratio=2.05, 95%Cl 1.11 to 3.79; p=0.022) and diabetes mellitus (odd ratio=0.42, 95%Cl 0.23 to 0.78; p=0.006) as well as oral nitrate prescription (odd ratio=2.95 95%Cl 1.22 to 7.12; p=0.016) were associated with receiving all five medications at discharge.



Nassr OA, Forsyth P, Johnson CF. Evaluation of discharge prescriptions for secondary prevention in patients with acute coronary syndromes in Iraq. Pharmacy Practice 2019 Jan-Mar;17(1):1372.

Table 3. Univariate statistical significance of receiving secondary prevention therapy by clinical characteristics								
Clinical characteristics	Aspirin	Clopidogrel	Statins	Beta-blockers	ACEI/ARBs			
Hypertension	0.725	1	0.531	0.736	0.017			
Diabetes mellitus	0.554	1	0.341	0.196	0.040			
Receiving oral nitrate	0.697	1	0.218	1	0.016			

#### Dosing of secondary prevention medications

Regarding optimal dosing, all patients prescribed antiplatelets received optimal doses: aspirin 100 mg and/or clopidogrel 75 mg daily. Of the 94.5% of patients (n=189) who received a statin, 80.9% (n=153) were prescribed a high-intensity statin. Of the 69.5% of patients (n=139) that received ACEI/ARBs, 12.2% (n=17) were prescribed a dose in the high target range. Of the 87.0% of patients (n=174) that received a beta-blocker, 9.2% (n=16) were prescribed a dose in the high target range. (Table 2). Of the 53.5% of patients (n=107) prescribed all five medication classes, only 1.9% patients (n=2) were prescribed all five medication classes within the high target dose range.

The number of patients who remained on low or moderate dose of beta-blockers (n=158) and were affected by marginal hemodynamics was low; 4.4% (7/158) had a heart rate >60 beats per minutes (bpm) and were therefore not candidates for titration to target dose whereas 83.5% (132/158) had a heart rate of  $\geq$ 70 bpm. Only 20.9% (33/158) had a systolic blood pressure reading >110 mmHg, 24.1% (38/158) had blood pressure level between 110-119 mmHg and 55.1% (87/158) had blood pressure  $\geq$ 120mmHg.

Of the patients who remained on low or moderate doses of ACEI/ARBs (n=122), only 17.2% (21/122) had blood pressure >110 mmHg and were not considered for dose uptitration whereas 18.9% (23/122) had blood pressure reading between 110-119 mmHg with the majority 63.9% (78/122) had blood pressure over 120 mmHg.

# DISCUSSION

This observational study is the first study to deliver a detailed assessment of prescribing, including optimal dosing, of secondary prevention medications at hospital discharge in Iraq. Just over half (53.5%) of patients admitted with ACS were prescribed all five secondary prevention medications at discharge, as advised in AHA/ACC guidelines and the guideline adherence rate was 60% after accounting for valid contraindications.<sup>13,14</sup> The highest adherence was for clopidogrel and the lowest for ACEI/ARBs. While an overwhelming majority of patients were prescribed target antiplatelet and high-intensity statin doses, only a minority were prescribed optimal ACEI/ARB and beta-blocker doses (12.2% and 9.2%, respectively).

This study's main finding that 60% of patients were treated according to the ACC/AHA guidelines when accounting for contraindications is comparable with previous studies from Western countries which found 69.1% adherence to guidance.<sup>8</sup> and from within the Middle East, which showed 62.9% adherence.<sup>5</sup> The prescribing of individual medications within this study is also broadly similar to or higher than studies from Western countries.<sup>8,9,19</sup> Hypertension, diabetes mellitus and being on oral nitrates were associated with receiving all five medications at discharge as observed in previous studies.<sup>8,20</sup> Although

these findings show that Iraqi care is in line with current international benchmarks, physicians can still improve the prescribing of these cost-effective medications and thereby reduce further avoidable morbidity and mortality.<sup>8,10</sup>

Early initiation of intensive statin therapy following ACS contributes to improved long-term survival.<sup>21</sup> This study showed a high rate of prescribing statins, i.e., 94.5% of patients, with 80.9% of those receiving a high-intensity statin. However, almost half of the patients received rosuvastatin, for which a-priori mortality and morbidity evidence to support its use in secondary prevention is currently inadequate compared to atorvastatin.<sup>13,17,21,22</sup> In addition, only 63.6% of patients prescribed atorvastatin received a dose of 80 mg while 100% of those prescribed rosuvastatin received a dose  $\geq$ 20 mg. A preference for prescribing rosuvastatin is not in line with Western practice, where almost all patients receive atorvastatin rather than rosuvastatin in this study are unclear.

The ACC/AHA Guidelines indicate that all eligible patients should receive ACE/ARBs before discharge unless contraindicated.<sup>13,14</sup> However, as with previous Dutch and Malaysian studies, ACE/ARBs were the least prescribed medications, and more likely to be missed, with only 69.5% of patients receiving them, and only 4.0% of patients having a valid contraindication.<sup>8,24</sup> In certain patient groups, such as those with heart failure, hypertension, or diabetes, these medications have a strong evidence base (class A, level of evidence A) and are vitally important in reducing morbidity and mortality, and are commonly used as a quality performance measure.<sup>13,14</sup> In this study, there were univariate associations between ACEI/ARB prescribing and target dosing and a history of diabetes or hypertension (see Table 3). A past medical history of heart failure could not be tested due to the small numbers involved. The primary reason for favoring captopril during admission is not entirely clear but may include the fact that it is short acting and avoids a longer period of hypotension caused by longer acting ACEI/ARBs. Within the institution, captopril is also favored due to its generic nature, consistent supply from wholesalers and low acquisition cost which eases economic burden on the patient and hospital.

The percentage of patients prescribed ACEI/ARBs (12.2%) and beta-blockers (9.2%) in the high target range was lower than previous studies where 1 in 3 patients received optimal doses.<sup>11</sup> However, our findings are consistent with a French study and better than a Danish study which reported that 33.0% of ACE/ARBs and 8.0% of beta-blocker users respectively received  $\geq$ 50.0% of the target doses (moderate to high dose range).<sup>15,16</sup> Previous literature demonstrates that optimal ACEI dosing is achievable with upward titration over 3 days for patients admitted with ACS. However, these patients were not receiving beta-blocker titration at the same time, and so this reflects the challenges of routine clinical practice compared to single drug-disease trial models.<sup>25</sup>



Possible explanations for suboptimal dosing are unknown but may include a lack of physician knowledge regarding target dosing, marginal clinical parameters such as hypotension, worsening renal function, and/or that prescribers do not consider dose optimisation a priority during a short hospital stay (median hospital stay in this study was 4 days).<sup>11</sup> However, only 4.4% of low and moderate dose beta-blocker users had a heart rate of less than 60 bpm and only 17.2% (21/122) and 20.9% (33/158) of ACEI/ARB and beta-blocker users respectively had a blood pressure reading of less than 110 mmHg and were therefore not able to titrate to the target dose. This is in line with a US study which reported that only 19.0% of eligible patients were discharged on goal doses of betablockers and that 34.0% and 45.0% of those prescribed low and moderate doses of ACEI/ARBs respectively at discharge had a blood pressure ≥120 mmHg.<sup>11</sup> Thus, it is unlikely that marginal hemodynamic results prevented dose optimization during admission. In such cases, given the nature of the Iraqi healthcare system and with the benefit of secondary prevention medications being dose-related, every effort should be made to optimise doses during the inpatient stay or the importance of post-discharge titrations to optimal doses should be explained to the patient.

## Strengths

This is the first study to evaluate the in-depth prescribing of secondary prevention medications, including dose, after ACS in Iraq. The cohort represents nearly half of the eligible patients admitted during the study period and hence should be representative of hospital admissions. The data were collected by one experienced clinical pharmacist, thus limiting inter-researcher variation. Utilizing routine medical records overcomes coding issues associated with electronic databases and thus, represents a more accurate method for data collection.<sup>9,20</sup> Moreover, measuring guideline adherence for prescribing optimal doses of secondary prevention medications overcomes the limitation of previous studies.<sup>8,20</sup>

#### Limitations

As a retrospective study using routinely collected patientlevel data, the study was limited by data accuracy due to record-keeping errors, such undocumented as contraindications or medication intolerance. However, the clinical pharmacist who collected the data was aware of such potential issues and took time to identify contraindications and drug allergies during data collection. The sampling methodology was not random and did not include consecutive patients, which may introduce bias; however, the final cohort constituted 45.6% of eligible patients during the study period. The presence of full echocardiogram and angiography results, incorporating post-infarct left ventricular function and the presence and burden of residual coronary heart disease, was also unavailable. These results may have influenced physician decisions around ACE/ARB and beta-blocker prescribing. As this study was conducted in a single hospital, it may not reflect wider Iraqi practice. Finally, given the crosssectional nature of the study data on post-discharge mortality rates, new hospitalizations and disease recurrence were not available and would require further research.

#### Policy, practice and research implications

This study concentrated on the short-term prescription of secondary prevention medications during the discharge phase of ACS hospital care. To date, there is no published literature on the post-discharge phase of Iraqi ACS care. Standard Iraqi post-discharge care, usually involves a patient visiting a cardiologist either in a state-funded or in a private primary care facility. In such settings, the prescriber is expected to optimise ACEI/ARB and beta-blocker doses to achieve the target dose based on the patient's tolerance and hemodynamics. The cost of medication and certain aspects of healthcare is however a potential barrier to the long-term persistence with therapy. In addition, the quality of care in the public sector is suboptimal due to the heavy workload experienced by physicians.<sup>26</sup> Thus, every attempt should be made to titrate the doses during hospital admission, whenever possible. 13,17

The exact individual reasons for 40.0% of patients not being treated according to guidelines are unknown. The regression analysis showed that patients with hypertension or those using oral nitrates were more likely to be treated in accordance with guidelines. Both of these cohorts represent 'higher' risk cohorts and that may have influenced clinician behaviour. It is uncertain why diabetic patients, another high risk cohort, were less likely to be treated in accordance with guidelines.

Quality improvement strategies such as continued education, integrated care, and pre-discharge checklists have been shown to enhance compliance with evidencebased guidelines.<sup>8,27,28</sup> Addressing the issue of suboptimal ACEI/ARB and beta-blocker prescribing, which is also common in Europe, North America, and the Middle East, seems key.<sup>5,11,15,16</sup> In other countries, pharmacists working in primary and secondary care have been shown to be effective in improving the prescribing rates and dosing of secondary prevention cardiac medications.<sup>29,30</sup> In Iraq, clinical pharmacists are not usually involved in the coronary care unit, as their role is limited to dispensing medications.<sup>31</sup> Thus, the incorporation of pharmacists into the multidisciplinary team to improve the prescribing and dosing of secondary prevention medications may improve the quality of care for these patients.<sup>29,30</sup> In addition, pharmacists can educate patients and caregivers as per the guidelines recommendations about drug therapy, discussing indications, possible side effects, drug-drug or food-drug interactions, and monitoring.<sup>13,14,33</sup>

Iraq has a workforce of over 11,000 practicing pharmacists, most of whom work in state-funded primary and secondary care or privately owned community pharmacies, where services centre on traditional dispensing and distribution of medicines.<sup>31</sup> The opportunities for Iraqi pharmacists to assume clinical roles have grown over the last 20 years.<sup>31</sup> Specialisation, involving post-graduate qualifications and board certification, is becoming commonplace.<sup>31</sup> A future opportunity, therefore, exists to develop extended roles in specialities such as cardiology, as seen in the US and the UK.<sup>32,33</sup> Government funding models and legislation changes many ultimately be required to facilitate this.<sup>31</sup>



Future studies in Iraq should assess barriers and variations to optimal prescribing of ACEI/ARBs and beta-blockers in clinical practice using quantitative and qualitative methods. These studies should also consider assessing and evaluating clinical pharmacist interventions in optimising patient care to support future professional and service developments.

#### CONCLUSIONS

Approximately one in two patients received the recommended secondary prevention medicines. However, only a few patients were prescribed target doses of ACEI/ARBs and/or beta-blockers. Quality improvement strategies and further research should be implemented to optimise prescribing. This may include greater involvement of pharmacists within the cardiology multidisciplinary team.

#### ACKNOWLEDGEMENTS

The authors would like to thank Mustansiriya University (www.uomustansiriyah.edu.iq) Baghdad, Iraq for its support in the present work. Thanks are also extended to the hospital medical and non-medical staff for assisting with the study.

#### CONFLICT OF INTEREST

None.

# FUNDING

No funding was obtained for this study.

#### References

- Isma'eel H, Mohanna Z, Hamadeh G, Alam E, Badr K, Alam S, Rebeiz A. The public cost of 3 statins for primary prevention of cardiovascular events in 7 Middle East countries: not all of them can afford it. Int J Cardiol. 2012;155(2):316-318. doi: <u>10.1016/j.ijcard.2011.12.011</u>
- Government of Iraq, Ministry of Health in collaboration with World Health Organization. Chronic non-communicable diseases risk factors survey in Iraq. Available at: <u>http://www.who.int/chp/steps/IraqSTEPSReport2006.pdf</u> (accessed May 23, 2018).
- World Health Organization. Noncommunicable diseases (NCD) country profiles, Iraq. Available at: <u>http://www.who.int/nmh/countries/irg\_en.pdf</u> (accessed June 26, 2018).
- Choi E, Byeon H, Yang Y. Optimal medical therapy for secondary prevention after an acute coronary syndrome: 18-month follow-up results at a tertiary teaching hospital in South Korea. Ther Clin Risk Manag. 2016;12:167-175. doi: <u>10.2147/TCRM.S99869</u>
- Sheikh-Taha M, Hijazi Z. Evaluation of proper prescribing of cardiac medications at hospital discharge for patients with acute coronary syndromes (ACS) in two Lebanese hospitals. Springerplus. 2014;3:159. doi: <u>10.1186/2193-1801-3-159</u>
- Jan S, Lee SW, Sawhney JP, Ong TK, Chin CT, Kim HS, Krittayaphong R, Nhan VT, Itoh Y, Huo Y. Catastrophic health expenditure on acute coronary events in Asia: a prospective study. Bull World Health Organ. 2016;94(3):193-200. doi: <u>10.2471/BLT.15.158303</u>
- Roger VL, et al. Heart disease and stroke statistics--2012 update: a report from the American Heart Association. Circulation. 2012;125(1):e2-e220. doi: <u>10.1161/CIR.0b013e31823ac046</u>
- Tra J, van der Wulp I, Appelman Y, de Bruijne MC, Wagner C. Adherence to guidelines for the prescription of secondary prevention medication at hospital discharge after acute coronary syndrome: a multicentre study. Neth Heart J. 2015;23(4):214-221. doi: <u>10.1007/s12471-015-0664-y</u>
- 9. Halvorsen S, Jortveit J, Hasvold P, Thuresson M, Oie E. Initiation of and long-term adherence to secondary preventive drugs after acute myocardial infarction. BMC Cardiovasc Disord. 2016;16:115. doi: <u>10.1186/s12872-016-0283-6</u>
- Becerra V, Gracia A, Desai K, Abogunrin S, Brand S, Chapman R, García Alonso F, Fuster V, Sanz G. Cost-effectiveness and public health benefit of secondary cardiovascular disease prevention from improved adherence using a polypill in the UK. BMJ Open. 2015;5(5):e007111. doi: <u>10.1136/bmjopen-2014-007111</u>
- Arnold SV, Spertus JA, Masoudi FA, Daugherty SL, Maddox TM, Li Y, Dodson JA, Chan PS. Beyond medication prescription as performance measures: optimal secondary prevention medication dosing after acute myocardial infarction. J Am Coll Cardiol. 2013;62(19):1791-1801. doi: <u>10.1016/j.jacc.2013.04.102</u>
- 12. Wald NJ, Law MR. A strategy to reduce cardiovascular disease by more than 80%. BMJ. 2003;326(7404):1419. doi: 10.1136/bmj.326.7404.1419
- 13. O'Gara PT, Kushner FG, Ascheim DD, Casey DE Jr, Chung MK, de Lemos JA, Ettinger SM, Fang JC, Fesmire FM, Franklin BA, Granger CB, Krumholz HM, Linderbaum JA, Morrow DA, Newby LK, Ornato JP, Ou N, Radford MJ, Tamis-Holland JE, Tommaso CL, Tracy CM, Woo YJ, Zhao DX. 2013 ACCF/AHA guideline for the management of ST-elevation myocardial infarction: a report of the American College of Cardiology Foundation/American Heart Association Task Force on Practice Guidelines. J Am Coll Cardiol. 2013;61(4):e78-e140. doi: 10.1016/j.jacc.2012.11.019
- 14. Amsterdam EA, Wenger NK, Brindis RG, Casey DE Jr, Ganiats TG, Holmes DR Jr, Jaffe AS, Jneid H, Kelly RF, Kontos MC, Levine GN, Liebson PR, Mukherjee D, Peterson ED, Sabatine MS, Smalling RW, Zieman SJ; ACC/AHA Task Force Members; Society for Cardiovascular Angiography and Interventions and the Society of Thoracic Surgeons. 2014 AHA/ACC guideline for the management of patients with non-ST-elevation acute coronary syndromes: executive summary: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines. Circulation. 2014;130(25):2354-2394. doi: 10.1161/CIR.000000000000133
- Pedersen SB, Nielsen JC, Botker HE, Goldberger JJ. Beta-blocker therapy early after myocardial infarction: a comparison between medication at hospital discharge and subsequent pharmacy-dispensed medication. Drugs Real World Outcomes. 2016;3(3):279-288. doi: <u>10.1007/s40801-016-0079-0</u>



- Grall S, Biere L, Le Nezet M, Bouvier JM, Lucas-Chauvelon P, Richard C, Abi-Khalil W, Delepine S, Prunier F, Furber A. Relationship between beta-blocker and angiotensin-converting enzyme inhibitor dose and clinical outcome following acute myocardial infarction. Circ J. 2015;79(3):632-640. doi: <u>10.1253/circj.CJ-14-0633</u>
- National Institute for Health and Care Excellence, NICE guidelines [CG172]. Myocardial infarction: cardiac rehabilitation and prevention of further cardiovascular disease. Available at: <u>https://www.nice.org.uk/guidance/CG172/chapter/1-Recommendations#drug-therapy-2</u> (accessed May 3, 2018).
- Smith MB, Lee NJ, Haney E, Carson S. Drug Class Review: HMG-CoA Reductase Inhibitors (Statins) and Fixed-dose Combination Products Containing a Statin: Final Report Update 5. Available at: <u>http://www.ncbi.nlm.nih.gov/books/NBK47273/pdf/Bookshelf\_NBK47273.pdf</u> (accessed Jul 3, 2018).
- Chung SC, Gedeborg R, Nicholas O, James S, Jeppsson A, Wolfe C, Heuschmann P, Wallentin L, Deanfield J, Timmis A, Jernberg T, Hemingway H. Acute myocardial infarction: a comparison of short-term survival in national outcome registries in Sweden and the UK. Lancet. 2014;383(9925):1305-1312. doi: <u>10.1016/S0140-6736(13)62070-X</u>
- Al-Zakwani I, Sulaiman K, Za'abi M, Panduranga P, Al-Habib K, Asaad N, Al Motarreb A, Hersi A, Al Faleh H, Al Saif S, Almahmeed W, Amin H, Alsheikh-Ali A, Al Lawati J, Al Suwaidi J. Impact of evidence-based cardiac medications on short and long-term mortality in 7,567 acute coronary syndrome patients in the Gulf RACE-II registry. Int J Clin Pharmacol Ther. 2012;50(6):418-425. doi: 10.5414/CP201667
- Cannon CP, Braunwald E, McCabe CH, Rader DJ, Rouleau JL, Belder R, Joyal SV, Hill KA, Pfeffer MA, Skene AM; Pravastatin or Atorvastatin Evaluation and Infection Therapy-Thrombolysis in Myocardial Infarction 22 Investigators. Intensive versus moderate lipid lowering with statins after acute coronary syndromes. N Engl J Med. 2004;350(15):1495-1504. doi: <u>10.1056/NEJMoa040583</u>
- 22. Schwartz GG, Olsson AG, Ezekowitz MD, Ganz P, Oliver MF, Waters D, Zeiher A, Chaitman BR, Leslie S, Stern T; Myocardial Ischemia Reduction with Aggressive Cholesterol Lowering (MIRACL) Study Investigators. Effects of atorvastatin on early recurrent ischemic events in acute coronary syndromes: the MIRACL study: a randomized controlled trial. JAMA. 2001;285(13):1711-1718. doi: 10.1001/jama.285.13.1711
- Turner RM, Yin P, Hanson A, FitzGerald R, Morris AP, Stables RH, Jorgensen AL, Pirmohamed M. Investigating the prevalence, predictors, and prognosis of suboptimal statin use early after a non-ST elevation acute coronary syndrome. J Clin Lipidol. 2017;11(1):204-214. doi: <u>10.1016/j.jacl.2016.12.007</u>
- Kassab YW, Hassan Y, Aziz NA, Akram H, Ismail O. Use of evidence-based therapy for the secondary prevention of acute coronary syndromes in Malaysian practice. J Eval Clin Pract. 2013;19(4):658-663. doi: <u>10.1111/j.1365-</u> <u>2753.2012.01894.x</u>
- Pfeffer MA, Greaves SC, Arnold JM, Glynn RJ, LaMotte FS, Lee RT, Menapace FJ Jr, Rapaport E, Ridker PM, Rouleau JL, Solomon SD, Hennekens CH. Early versus delayed angiotensin-converting enzyme inhibition therapy in acute myocardial infarction. The healing and early afterload reducing therapy trial. Circulation. 1997;95(12):2643-2651.
- Al Hilfi TK, Lafta R, Burnham G. Health services in Iraq. Lancet. 2013;381(9870):939-948. doi: <u>10.1016/S0140-6736(13)60320-7</u>
- Peterson GM, Thompson A, Pulver LK, Robertson MB, Brieger D, Wai A, Tett SE; DMACS Project Group. Management of acute coronary syndromes at hospital discharge: do targeted educational interventions improve practice quality?. J Healthc Qual. 2012;34(1):26-34. doi: 10.1111/j.1945-1474.2011.00137.x
- Wilkins B, Hullikunte S, Simmonds M, Sasse A, Larsen PD, Harding SA. Improving the prescribing gap for guideline recommended medications post myocardial infarction. Heart Lung Circ. 2019;28(2):257-262. doi: 10.1016/j.hlc.2017.10.025
- Hassan Y, Kassab Y, Abd Aziz N, Akram H, Ismail O. The impact of pharmacist-initiated interventions in improving acute coronary syndrome secondary prevention pharmacotherapy prescribing upon discharge. J Clin Pharm Ther. 2013;38(2):97-100. doi: <u>10.1111/jcpt.12027</u>
- 30. Lowrie R, Mair FS, Greenlaw N, Forsyth P, Jhund PS, McConnachie A, Rae B, McMurray JJ; Heart Failure Optimal Outcomes from Pharmacy Study (HOOPS) Investigators. Pharmacist intervention in primary care to improve outcomes in patients with left ventricular systolic dysfunction. Eur Heart J. 2012;33(3):314-324. doi: <u>10.1093/eurhearti/ehr433</u>
- Al-Jumaili AA, Hussain SA, Sorofman B. Pharmacy in Iraq: history, current status, and future directions. Am J Health Syst Pharm. 2013;70(4):368-372. doi: <u>10.2146/ajhp120415</u>
- 32. Milfred-LaForest SK, Chow SL, DiDomenico RJ, Dracup K, Ensor CR, Gattis-Stough W, Heywood JT, Lindenfeld J, Page RL 2nd, Patterson JH, Vardeny O, Massie BM. Clinical pharmacy services in heart failure: an opinion paper from the Heart Failure Society of America and American College of Clinical Pharmacy Cardiology Practice and Research Network. Pharmacotherapy. 2013;33(5):529-548. doi: 10.1002/phar.1295
- 33. Forsyth P, Warren A, Thomson C, Bateman J, Greenwood E, Williams H, Khatib R, Hadland R, McGlynn S, Khan N, Duggan C, Beezer J; United Kingdom Clinical Pharmacy Association Heart Failure Group and the Royal Pharmaceutical Society. A competency framework for clinical pharmacists and heart failure. Int J Pharm Pract. 2018 [Epub ahead of print]. doi: 10.1111/jipp.12465