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Glycemic Control of Diabetes Mellitus (DM) in Acute Coronary Syndrome (ACS) Patient

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Introduction: Diabetes mellitus (DM) is a predictor of recurrent ischaemic events in patients with the acute coronary syndrome (ACS) whilst cardiovascular disease remains the leading cause of mortality among patients with diabetes. This study aims to determine the prevalence of DM, glycemic control and predictors of poor glycemic control patients diagnosed with ACS in our population. Methods**:** This is a single centre, cross-sectional study of ACS patients admitted to cardiology wards, Hospital Serdang. A chi-square test was used to test the association between the prescribing pattern of antihyperglycemic agents and the glycemic control of DM patients. Logistic regression analysis was performed to determine the predictors of poorly glycemic controlled among DM patients with ACS. Results: A total of 486 patients were included (male 73.4%; mean age 57.3(12.5) years). The prevalence of DM among ACS patients was 207 (42.6%). Of these, 88 (42.1%) had poorly-controlled DM with the HbA1c > 8% and 81 (47.9%) had well control the HbA1c≤8%. Significant association was found between antihyperglycemic agents, i.e. insulin (p<0.034), metformin (p<0.038) and sulphonylurea (p<0.022). In poor control group, insulin is the most prescribed antihyperglycemic agents, 35 (37.2%) compared to well control, metformin is the highest proportion, 25 (34.7%). In multivariate analysis, only age was independently predictive of poorly controlled among DM patients with ACS (adjusted OR 0.94; 95% CI 0.90-0.97; p<0.001). Conclusion**:** This study found, the prevalence of DM was high among ACS patient, with half of them demonstrate poor glycemic control. This study found that increasing age was associated with a lower risk of poor glycemic control among DM patients with recent ACS.

Keywords: diabetes mellitus; acute coronary syndrome; glycemic control; prescribing pattern

I. INTRODUCTION

Diabetes mellitus (DM) is a metabolic disorder characterised by chronic hyperglycaemia with multiple aetiologies (Asmat *et. al.,* 2016; Diabetes, 2013; Tsalamandris *et al.,* 2019). DM can lead to multiple acute and chronic complications (Asmat *et al.,* 2016). Acute complications include hypoglycaemia, hyperglycaemic states and microbial infections (Diabetes, 2013). On the other hand, chronic complications comprise of microvascular complications such as retinopathy, nephropathy, and neuropathy, as well as macrovascular complications such as cerebrovascular, peripheral vascular diseases and cardiovascular complications (Asmat *et. al.,* 2016; Kamaruddin *et al.,* 2015).

DM is a prime risk factor for cardiovascular diseases (Dokken, 2008). In a study by Zhou *et al.* (2018) in China, a prevalence of 37.6% (n=23,880) for diabetes or possible diabetes was reported in patients with a definitive diagnosis of ACS. The authors also demonstrated considerable excess risks for early mortality and major adverse cardiovascular events among the DM population (Zhou *et al.,* 2018). Locally, a prospective observational study by Lu *et al.* (2014) revealed a combined prevalence of 50.7% for diabetes among 13,591

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patients with ACS from 2006 to 2010 in Malaysia (Lu *et al.,* 2014).

One of the major tool for assessing glycaemic control is haemoglobin A1C (HbA1c), as it reflects average glycaemia control over the previous 2-3 months and has a strong predictive value for diabetes complications (Inzucchi *et. al.,* 2012; Sherwani *et al.,* 2016) and is used as a guide in determining the choice of pharmacological agents in managing DM (Kamaruddin *et al.,* 2015). This study aims to determine the prevalence of DM and their glycemic control among patients diagnosed with ACS in our population. Beside the predictors of poorly glycemic control, the prescribing pattern of antihyperglycemic agents between well and poor glycemic control group were also studied.

II. MATERIALS AND METHOD

A. Study Design

A retrospective observational study was conducted in Hospital Serdang, a tertiary hospital in Kajang, Selangor. Ethical approval for this study was obtained from the Medical Research and Ethics Committee (MREC), Ministry of Health Malaysia (NMRR-19-2676-49351).

B. Study Setting and Study Population

The present study utilised study subjects consisting of patients diagnosed with ACS who were admitted to Hospital Serdang from 1st January 2016 to 31st December 2016. The sampling method used for this study was universal sampling. Patients with ACS were screened based on International Classification of Diseases-Tenth revisions (ICD-10) codes data in the electronic hospital information system (eHIS). ACS was defined by ICD-10 codes (I20, I21 or I22). Data collection form was used for medical clerking. Patient came in with elective admission for a coronary angiogram or with missing data on HbA1c, fasting blood glucose (FBG) readings were excluded.

All data on baseline characteristic, diagnosis of DM, co-morbidities and glycemic control were collected through a comprehensive review of medical records in eHIS. Patient's medications history was acquired from in patient's drug profile in eHIS. In order to protect the privacy of patients' information, each patient was allocated a patient identifier number which matched the registration number documented in the data collection form.

The glycemic control of the patients was defined based on glycemic markers of patients (HbA1c and/or FBG). Patients with HbA1c 8% and less were classified as well control whereas, patients with HbA1c of more than 8% were categorised as poor control (Kamaruddin *et al.,* 2015). All laboratory parameters including the recent HbA1c level were extracted from the medical laboratory chart in eHIS.

C. Statistical Analysis

Baseline characteristics were summarised using frequencies and percentage for categorical variables and mean [standard deviation (SD)] for continuous variables. The characteristics between DM vs non-DM; and well control vs poor control were compared using chi-square test.

To examine the predictors of poor glycemic control diabetic patients with ACS, we performed the logistic regression analysis to calculate the odds ratios (OR) and 95% confidence intervals (CI). In univariate analysis, only the variable age was found to be significant ($p<0.001$). The model was then repeated and adjusted to body mass index (Knowler *et al.,* 2002), smoking status (Odeberg *et al.,* 2014) and chronic kidney disease (Lin *et al.,* 2017) by using multivariate analysis.

A chi-square test was performed to test the association of the prescribing pattern of antihyperglycemic agents and the glycemic control of DM patients. Yates correction was employed when the expected cell frequencies are below ten. Statistical analyses were performed using IBM SPSS Statistics for Windows, version 20. A p-value of less than 0.05 was considered significant.

III. RESULT AND DISCUSSION

A. Prevalence of DM in ACS

From 506 patients with ACS patients, 486 patients were included (Figure 1). Of these, 394 (73.4%) were male with mean age of 57.3 (12.5) years). Data on the diagnosis of DM were retrieved based on medical records in eHIS. Of 486 patients, the prevalence of DM among ACS patients was 207 (42.6%). Thirty-eight patients were subsequently excluded from further analysis due to missing data on HbA1c or FBG. Of 169 patients, 88 (52.1%) had poor control with the HbA1c >8% and 81 (47.9%) had well control with the HbA1c ≤8%. Baseline characteristics between DM vs non-DM and well-control vs poor-control are shown in Table 1.

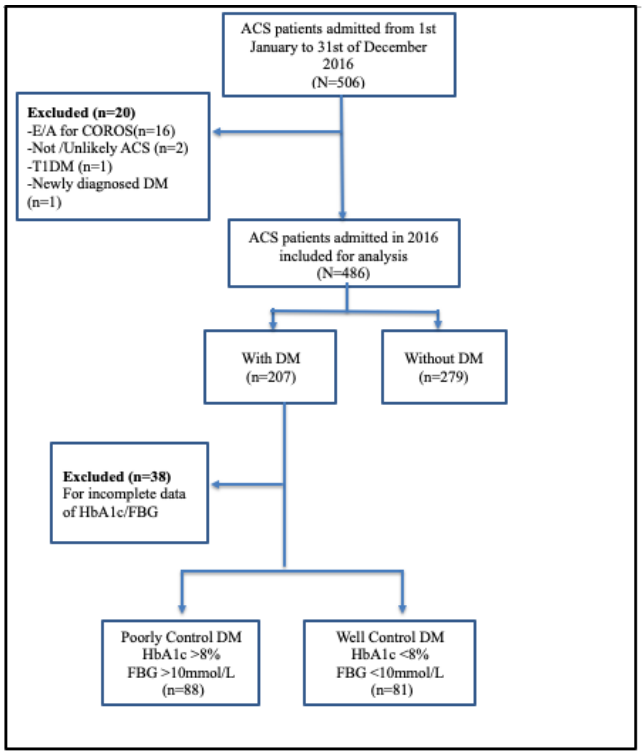

Figure 1. Selection process of eligible Diabetes Mellitus (DM) in Acute Coronary Syndrome (ACS) patient

Table 1. Baseline Characteristics

Characteristic	All patient n = 486	DM n = 207	Non DM n=279	*p-value*	Well Control n=81	Poor Control n=88	*p-value*
Age, years (Mean ± SD)	59.40 ± 12.50	59.62 ± 11.53	55.62 ± 12.91	<0.001	63.11 ± 11.63	56.58 ± 10.47	p<0.001
BMI, kg/m2 (Mean ± SD)	24.20± 4.80	26.98 ± 4.69	29.26 ± 5.01	0.891	27.03 ± 4.82	27.13 ± 4.65	p<0.001
HbA1c (Mean ± SD)	-	8.86±2.42	-	-	6.91±1.21	10.23±2.08	1.000
FBS (Mean ± SD)	-	11.76±7.54	-	-	6.66 ±4.38	8.44±8.61	0.182
Gender				<0.001			0.618
- Male	394 (81.1)	152 (73.4)	242 (86.7)		58 (71.6)	66 (75.0)	
- Female	92 (18.9)	55 (26.6)	37 (13.3)		23 (28.4)	22 (25.0)	
Ethnic group				0.014			0.062
- Malay	228 (46.9)	101 (48.8)	130 (46.6)		36 (44.4)	44 (50.0)	
- Chinese	103 (21.2)	40 (19.3)	59 (21.1)		21 (25.9)	13 (14.8)	
- Indian	128 (26.3)	61 (29.5)	67 (24.0)		21 (25.9)	31 (35.2)	
- Others	27 (5.6)	5 (2.4)	23 (8.2)		3 (3.7)	0 (0)	
Smoking status				<0.001			0.350
-Non-smoker	204 (42.0)	108 (61.0)	96 (37.6)		43(53.1)	55 (62.5)	
-Active smoker	167 (34.4)	40 (22.6)	127 (49.8)		17 (21.0)	18 (20.5)	
-Former smoker	60 (12.3)	28 (15.8)	32 (12.5)		15 (18.5)	10 (11.4)	
-Unknown status	55 (11.3)	31 (15.0)	24 (8.6)		6 (7.4)	5 (5.7)	
Co-morbidities							
-Hypertension	292 (41.4)	159(41.6)	133 (41.0)	<0.001	63(39.6)	62 (41.9)	0.278
-Dyslipidaemia	112 (15.9)	54 (14.1)	58 (17.9)	0.217	21 (13.2)	24 (16.2)	0.843
-CKD	50 (7.1)	37 (9.7)	13 (4.0)	<0.001	19 (11.9)	13 (8.8)	0.150
-COPD/ Asthma	34 (4.8)	22 (5.8)	12 (3.7)	0.02	10 (6.3)	9 (6.1)	0.295
-Stroke/ TIA	20 (2.8)	14 (3.7)	6 (1.9)	0.031	6 (3.8)	5 (3.4)	0.65
-Atrial fibrillation	10 (1.4)	2 (0.5)	8 (2.5)	0.227	1 (0.6)	1 (0.7)	1.000
-Heart failure	3 (0.4)	2 (0.5)	1 (0.3)	0.580	0 (0.0)	1 (0.7)	1.000
-IHD	185 (26.2)	92 (24.1)	93 (28.7)	0.018	39 (24.5)	33 (22.3)	0.162

All values are reported as no (%) unless otherwise noted.
BMI: body mass index; **HbA1c**: Hemoglobin A1c; **FBS**: Fasting Blood Sugar; **CKD**: chronic kidney disease; **COPD**: chronic obstructive pulmonary disease; **DM**: diabetes mellitus; **DVT**: deep vein thrombosis; **IHD**: ischemic heart disease; **SD**: standard deviation; **TIA**: transient ischemic attack.

B. Prescribing Pattern of Antihyperglycemic Agents in ACS Patient

Figure 2 shows prescribing pattern of antihyperglycemic agents in ACS patient between well and poor control. Our study found a significant association between antihyperglycemic agents in prescribing pattern between well and poor control, i.e. insulin (p<0.034), metformin (p<0.038), sulphonylurea (p<0.022) and others (p<0.008). In poor control group, insulin was the most prescribed antihyperglycemic agents 35 (37.2%), whereas, in well control group, metformin was the most prescribed of antihyperglycemic agents 25 (34.7%).

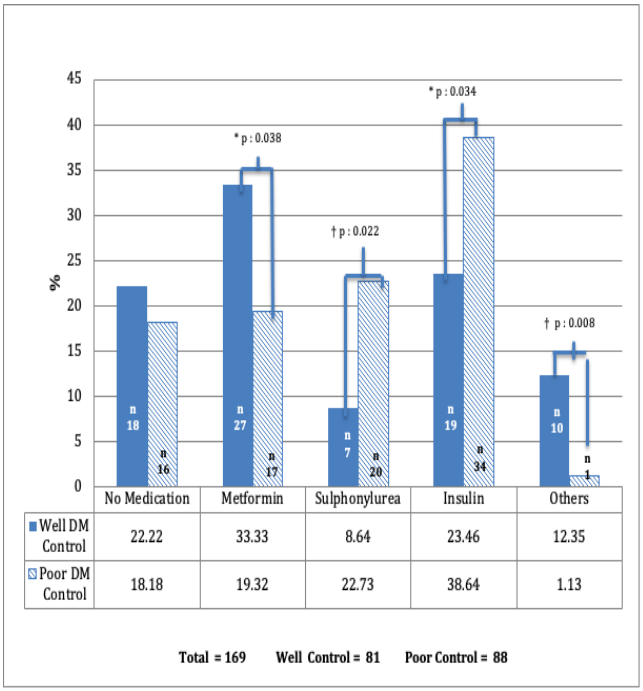

Figure 2. Prescribing pattern of antihyperglycemic agents in ACS patient between well and poor DM control

C. Predictors of Poor Glycemic Control Diabetic Patients with ACS

The univariable and multivariable analysis of possible predictors of risk of poor glycemic control diabetic patients with ACS is presented in Table 2. In multivariate analysis, only age was independently predictive among DM patients with ACS (adjusted OR 0.94; 95% CI 0.90-0.97; p<0.001).

Table 2. Unadjusted and adjusted characteristic of poorly glycemic controlled DM in ACS

Characteristic	Unadjusted OR (95% CI)	*p-value*	Adjusted OR (95% CI)	*p-value*
Age, years (Mean ± SD)	0.95 (0.92-0.98)	<0.001	0.94(0.90-0.97)	<0.001
BMI, kg/m2 (Mean ± SD)	1.00 (0.94-1.08)	0.891	0.98(0.94-1.08)	0.472
Gender				
- Male (ref)	.	.		
- Female	1.19 (0.60-2.36)	0.618		
Ethnic group				
- Malay (ref)	.	.		
- Chinese	0.51 (0.22-1.15)	0.104		
- Indian	1.21 (0.60 -2.45)	0.601		
Smoking status			0.76(0.94-1.17)	0.218
- Non-smoker (ref)	.	.		
- Active smoker	0.52(0.21-1.27)	0.153		
- Former smoker	0.83 (0.38-1.79)	0.632		
Co-morbidities				
- Hypertension	0.68 (0.34-1.37)	0.280		
- Dyslipidaemia	1.07(0.54-2.12)	0.843		
- CKD	0.57(0.26-1.24)	0.153	0.57(0.23-1.40)	0.221
- COPD/ Asthma	0.60(0.26-1.38)	0.230		
- Stroke/ TIA	0.75 (0.22-2.57)	0.651		
- Atrial fibrillation	0.92 (0.06-14.95)	0.953		
- IHD	0.65 (0.35-1.19)	0.163		

IV. DISCUSSION

In our study population, 43% of ACS patients were diabetic and majority of them were male. A total of 42% of the study subject appeared to have poor controlled DM in ACS. Only age was reported to significantly predict the poor glycemic control among diabetic patients with ACS. Our study demonstrates that insulin was the most antihyperglycemic agents used in the poor control group. At the same time, metformin was the most prescribed antihyperglycemic agents among the well control glycemic group.

A. Prevalence of DM in ACS

The prevalence of diabetic patients among ACS patients in the present study was 43%, which is consistent with a study conducted in Sri Lanka (Indrakumar *et al.,* 2009). The Malaysian National Cardiovascular Disease Database-Acute Coronary Syndrome (NCVD-ACS) registry by Lu *et al.* (2014) reported a prevalence of 50.7% for diabetes among 13,591 patients with STEMI. Conversely, our prevalence differed from the conclusions of the Prevention of Recurrences of Myocardial Infarction and Stroke (WHO-PREMISE), where they found a prevalence of DM (31.5%) among patients who exhibits coronary heart disease and cerebrovascular disease (Mendis *et al.,* 2005). Owing to the single-centre setting of our study and may not accurately reflect the actual prevalence of DM in the general ACS population.

We categorised patients into well and poor control group in DM patients with ACS. In patients with ACS, the present study found 42.1% patients had poorly-controlled DM. Previous studies demonstrated between 24% to 30% of DM patients experienced hyperglycemia with recent ACS (Sewdarsen1 *et. al.,* 1989; Lynch *et al.,* 1994). Poor glycemic control reflects the inadequacy of insulin which the effect may be amplified in acute stress such as ACS (Allison *et al.,* 1998). Stress hyperglycemia is a marker suggestive of poor prognosis of the extensive cardiac damage in acute myocardial infarction (Tansey *et al.,* 1986). Poor dietary adherence and sedentary lifestyle among our populations reported by Hussein *et al. (*2015) may have contributed to the high prevalence of poorly controlled DM in recent ACS.

B. Prescribing Pattern of Antihyperglycemic Agents in ACS Patient

Among diabetics patients with ACS, we found that metformin was the most prescribed antihyperglycemic agents among the well control group. From the literature, metformin was associated with lower mortality in DM patients with ACS (Jong *et al.,* 2019) and proved to reduce cardiovascular risk in these population (Turner, 1998). Thus, metformin is recommended as the first line of antihyperglycemic agent in most of the guidelines (Kamaruddin *et. al.,* 2015; Turner, 1998). On the other hand, insulin was reported to be the most utilised antihyperglycemic agents among the poor glycemic control group. In patients with poor glycemic control with recent ACS, insulin initiation would be the preferred choice of therapy (Roffi *et. al.,* 2016; Vergès *et al.,* 2012).

C. Predictors of Poor Glycemic Control Diabetic Patients with ACS

Only age played an independent role in predicting glycemic control among DM patients with recent ACS in our population. Previous studies also reported that better glycemic control can be achieved among older age group (Barrot-De La Puente *et. al.,* 2015; Benoit *et. al.,* 2005; Shamshirgaran *et al.,* 2017). A study by Barrot-de la Puente *et al.* (2015) demonstrated that a better glycemic control among elderly independent of disease duration, body mass index (BMI) and presence of cardiovascular disease. The possible reasons for it might be due to increased awareness among elderly in blood glucose management, which recommends the need for the young population to pay more attention to better monitoring of glycemic control.

Our study has its limitations as a retrospective study design. Our study populations were predominantly male patient and single centre, which might affect the generalisability of the results. Some laboratory parameters were not accessible for determining glycemic control of study populations.

The main strength of our study is local population-based study design on DM patients with recent ACS which allow a better understanding of our local practice. Our study had full information on DM prevalence, glycemic control and prescribing pattern in patients with recent ACS. Also, we assessed the predictors of poor glycemic control diabetic patients with ACS, which is not assessed in previous studies (Lynch *et. al.,* 1994; Lu *et al.,* 2014).

V. CONCLUSION

The prevalence of DM was high among ACS patient, with half of them demonstrate poor glycemic control. This study found that increasing age was associated with a lower risk of poor glycemic control among DM patients with recent ACS.

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