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Chronic Hyperglycemia as a Predictor of Acute Kidney Injury Requiring Continuous Renal Replacement Therapy (CRRT) in Patients Undergoing Coronary Artery Bypass Graft (CABG) Surgery

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Abstract **Original Research Article**

Background*:** Chronic Hyperglycaemia with HBA1C is an indicator affecting postoperative care after CABG. AKI is one of the frequent postoperative complications after CABG, impacting short- and long-term outcomes. This research project will investigate the association between chronic hyperglycemia and post operative incidence of AKI requiring CRRT in CABG patients. ***Methods: A retrospective study was conducted from 1st January 2016 to 31st December 2019 who underwent isolated CABG in Institut Jantung Negara, Malaysia. Patients were divided into two groups; patients who have HbA1c ≤6 and patients who have HbA1c >6. Primary outcome measured were the incidence of AKI that leads to CRRT. Secondary outcome measured were, mortality, chest reopen, length of ICU stay and total hospital stay. ***Results***: Total of 2019 patients were included. Baseline characteristic were measured. BMI, hypertension and high cholesterol were significantly higher in the HbA1c > 6. The rest of the baseline characteristic including age, smoking status and COPD status showed no significant differences in both groups. 17 patients (1.5% p<0.05) develop AKI which requires CRRT in the HbA1c>6 group, compare to 3 patient (0.3% p<0.05) in the HbA1c ≤6 group. There were no significant differences in mortality and chest reopen rates. However, ICU length of stay is longer in the HbA1c>6 group at 2.3 ±3.1 days p<0.05, compare to HbA1c ≤6 at 2.1±3 days p<0.05. Total length of post-op hospital stay was also higher in the HbA1c>6 group at 8.3 ± 6.6 days p<0.05, compare to HbA1c ≤6 at 7.6 ± 4.5 days p<0.05. ***Conclusion***: This study suggests chronic hyperglycaemia defined on a single measurement of HbA1c >6 was associated with higher incidence of AKI requiring CRRT. Length of ICU and post-op hospital stay were higher in the HbA1c >6 group. This finding might implicate the importance of sugar control preoperatively, especially in diabetes patients.

Keywords: Hyperglycemia, Diabetes Mellitus, CABG, AKI, CRRT.

BACKGROUND

Chronic Hyperglycaemia with HBA1C is an indicator affecting postoperative care after Coronary Artery Bypass Graft Surgery. Acute kidney injury is one of the frequent postoperative complications after CABG impacting short- and long-term outcomes.

AIM

This research project will investigate between the association between chronic hyperglycemia and post operative incidence of AKI requiring CRRT in CABG patients.

METHODS

A retrospective study was conducted over four years period from 1st January 2016 to 31st December 2019 who underwent isolated CABG in Institut Jantung Negara. Patients were divided into two groups; patients who have HbA1c ≤6 and patients who have HbA1c >6. Primary outcome measured were the incidence of acute kidney injury that leads to CRRT. Secondary outcome measured were mortality, chest reopen, length of ICU stay and total hospital stay.

RESULTS

Total of 2019 patients were included in the study. Baseline characteristic were measured. Mean age of the population was 59.9 ± 8.5 years old. Majority of

the enrolled patients were male at 84.3%. More than half of the patient in the HbA1c > 6 group are Malay at 58.7%. BMI, hypertension and high cholesterol were significantly higher in the HbA1c > 6. The rest of the baseline characteristic including age, smoking status and COPD status showed no significant differences in both groups. 17 patients (1.5% p<0.05) develop AKI which requires CRRT in the HbA1c>6 group, as oppose to 3 patient (0.3% p<0.05) in the HbA1c ≤6 group. There were no significant differences in mortality and chest reopen rates. However, ICU length of stay is longer in the HbA1c>6 group at 2.3 ±3.1 days p<0.05, compare to HbA1c ≤6 at 2.1±3 days p<0.05. Total length of post-op hospital stay was also higher in the HbA1c>6 group at 8.3 ± 6.6 days p<0.05, compare to HbA1c ≤6 at 7.6 ± 4.5 days p<0.05.

CONCLUSION

This study suggests chronic hyperglycaemia defined on a single measurement of HbA1c >6 was associated with higher incidence of AKI requiring CRRT. Length of both ICU and post-op hospital stay were higher in the HbA1c >6 group. This finding might implicate the importance of sugar control preoperatively, especially in diabetes patients.

INTRODUCTION

Chronic Hyperglycaemia with HBA1C is an indicator to predict postoperative mortality and morbidity after Coronary Artery Bypass Graft Surgery [9].

One of the most common complications of cardiac surgery is acute kidney injury (AKI) which can occur in 5-30% of the cases [9]. Studies reported that between 1-6% of cases will require renal replacement therapy [10, 11]. The development of AKI may also affect the short- and long-term outcomes in patients who underwent cardiac surgeries.

Most patients who need to undergo cardiac surgery will be required to go through pre-operative assessments, including a blood test. One of the blood tests is HbA1c where it measures the average blood glucose concentration in the preceding 2-3 months regardless whether the diagnosis of diabetes mellitus has ever been established.

There are multiple factors which may increase the likelihood of AKI. This includes long cross time, long bypass time, the presence of chronic kidney disease. This research project will investigate whether is there any association between chronic hyperglycemia and post-operative incidence of AKI needing renal replacement therapy in CABG patients.

Methods

This is a retrospective study in a single centre. Data were obtained from Cardiothoracic Clinical Database. Measured study patients baseline characteristics included age, gender, ethnicity (Malay, Chinese, Indian, others), Body Mass Index (BMI), hypertension, hypercholestrolaemia and COPD. Included patients were those who underwent isolated CABG in Institut Jantung Negara, Kuala Lumpur, Malaysia from 1st January 2016 to 31st December 2019. Inclusion criteria comprised of adult patients (>18 years old), elective CABG and normal LV function (EF >50%). Exclusion criteria for the study were patients who have CKD and off-pump CABG. Patients were divided into two groups; patients with HbA1c ≤6 against patients with HbA1C>6. Primary outcomes measured were the incidence of acute kidney injury that leads to CRRT. Secondary outcomes measured included mortality rates, chest reopen rates, length of ICU stay and total hospital stay. Data analysis was carried out with IBM SPSS Statistics 24.

RESULTS

A total of 6018 isolated CABG cases were conducted between 1st January 2016 to 31st December 2019. Inclusion and exclusion criterias were applied, and a total of 2019 patients were included in the study. The HbA1c ≤6 group has 868 patients and the HbA1C>6 has 1151 patients. Table 1 showed the baseline characteristics in both groups. Majority of the enrolled patients were male at 84.3%. The mean age of the whole study population is 59.9 ± 8.5 years. More than half of the patients in the HbA1c > 6 group were Malay at 58.7%. In the HbA1C > 6 group, Indians has the lowest rates of AKI development post-operatively at 16.9%. BMI in the HbA1c > 6 group was higher at 27.5 ± 4.3, compared to 26.4 ± 4.1 of the HbA1c ≤6.

Diabetes Mellitus in the HbA1c > 6 group is higher at 81.8%, compared to 16.3% (p<0.05) of the HbA1c ≤6. Hypertension and hypercholesterolaemia was also significantly higher at 86.8% and 86.2% (p<0.05), compare to the HbA1c ≤6 group at 73.7% and 77.1% (p<0.05) respectively.

There were no significant difference in terms of smoking history between the HbA1c > 6 group and the HbA1c ≤6 group at 46.6% and 50.4% (p = 0.091) respectively. The proportion of COPD was also similar between the HbA1c > 6 group and the HbA1c ≤ 6, where the proportion is 3% and 2.3% (p=0.373) respectively.

Table-1

Variables		HbA1c <= 6 (n = 868)		HbA1c > 6 (n = 1151)		p-value
Pre-operative						
Age, mean ± SD		59.6 ± 9.1		60.0 ± 8.1		0.590
Male, n (%)		777	89.5%	925	80.4%	<0.001
Race, n (%)						
	Malay	438	50.5%	676	58.7%	<0.001
	Chinese	253	29.1%	197	17.1%	
	Indian	86	9.9%	194	16.9%	
	Others	91	10.5%	84	7.3%	
BMI, mean ± SD		26.4 ± 4.1		27.5 ± 4.3		<0.001
Dibetes Mellitus, n (%)		141	16.3%	942	81.8%	<0.001
Hypertension, n (%)		639	73.7%	997	86.8%	<0.001
Hypercholesterolemia, n (%)		665	77.1%	983	86.2%	<0.001
Smoker, n (%)		429	50.4%	522	46.6%	0.091
COPD, n (%)		20	2.3%	34	3.0%	0.373

Table 2 shows the primary outcomes measured. In this study, 20 patients developed post-operative AKI which required CRRT (1%, p<0.05). The incidence is higher in the HbA1c > 6 group at 1.5% (p<0.05) when compared to 0.3% in the HbA1c ≤6 group.

Table-2

Variables	HbA1c <= 6 (n = 868)		HbA1c > 6 (n = 1151)		p-value
Post-operative					
CRRT, n (%)	3	0.3%	17	1.5%	0.011

Table 3 is reporting the study's secondary outcomes. There is no statistically significant difference in mortality rates between the HbA1c > 6 group and the HbA1c ≤6 at 1.4% (p=0.134) and 0.7% (p=0.134) respectively. The study's mortality rate is 1.1% (n=22), whereas chest re-open rate is 3.3% (n=67). There was no statistical difference in the above findings between the two groups.

Table-3

Variables	HbA1c <= 6 (n = 868)		HbA1c > 6 (n = 1151)		p-value
Post-operative					
Mortality, n (%)	6	0.7%	16	1.4%	0.134
Chest reopens n (%)	30	3.5%	37	3.2%	0.764

However on the other hand, the ICU length of stay was longer for the HbA1c > 6 group at 2.3 ± 3.1 days compare to the HbA1c ≤6 group at 2.1 ± 3.0 days (p<0.05) as shown in table 4. Total length of hospital stay was also longer for the HbA1c > 6 group at 8.3 ± 6.6 days when compared to HbA1c ≤6 group at 7.6 ± 4.5 days and this difference is statistically significant with p <0.05.

Table-4

Variables	HbA1c <= 6 (n = 868)	HbA1c > 6 (n = 1151)	p-value
Post-operative			
ICU LOS stay, mean ± SD	2.1 ± 3.0	2.3 ± 3.1	0.016
Post op stay, mean ± SD	7.6 ± 4.5	8.3 ± 6.6	<0.001

DISCUSSION

It is well known that HbA1c is an important tool to predict in-hospital mortality and morbidity post-operatively [6]. Morbidity may include the development of AKI as well as the length of hospital stay. In patients with diabetes mellitus, it is an important risk factor for atherosclerosis [4]. Particularly in the kidney, there is

an increase in thickness of the basement membrane, accumulation of extracellular matrix of basement, tubular and glomerular fibrosis and sclerosis [4]. Subsequently, local vascular and glomerular dysfunction may increase the likelihood of patients developing AKI [4]. Hemodynamics is a vital pathophysiology of AKI in cardiac surgery [4] and this includes the use of CPB and low cardiac output state.

Particularly, in patients who are undergoing major surgery, HbA1c is a very good marker for to assess the long-term and the glycaemic state of the patient weeks prior to the surgery. HbA1c is also a good indicator for insulin resistance [1]. Additionally, HbA1C is an easy-use laboratory marker compared to the time consuming OGTT [1]. This makes this test fast and cost effective.

Out of all the included patients for this study, the majority of the patients are of the male gender (84.3%), which is consistent with the findings of this other study [1, 5]. This study also showed that most patients who has elevated HbA1c is also associated with hypertension, and this pairing is very commonly observed in patients at risk of cardiovascular disease. There are many postulated pathways that diabetes may cause hypertension, but it all comes down to the vascular changes which is associated with diabetes [3]. Apart from hypertension, hypercholesterolemia is also associated with diabetes. It is consistent in this group of population where the majority of patients who have elevated HBA1c is associated with hypercholesterolemia. Higher BMI is also observed in the HbA1c > 6 group. All of this constellation may be part of the metabolic syndrome [8].

This study showed that there is an increase in incidence of post-operative AKI requiring CRRT in the elevated HbA1C group. As previously mentioned, in diabetes, there are vascular changes in both the micro- and macro-levels, which eventually leads to glomerular dysfunction. This in turn predisposes the patients to developing AKI. In general, 1.7% of patients who developed AKI in previously normal kidney function will require CVVH [5]. This study is consistent with other international studies, where elevated HbA1c may predispose patients into developing AKI [1, 9]. This study provides the additional observation whereby elevated HbA1c predisposes to the use of CRRT post-operatively.

This study also showed that elevated HbA1c may cause a lot of other morbidities including prolonging the length of ICU stay. Comparing the two groups, even though the difference is not massive, but it is statistically significant. This finding is also mirrored in the study by Cevdet *et al*., which also found that their patients with elevated HbA1c were also observed to have prolonged ICU length of stay [9]. On the other hand, however, this study did not show any statistical difference in the rates of chest re-open between the two HbA1c groups.

Most studies show that elevated HbA1C including diabetes is associated with higher mortality [7, 9]. This study showed there is increased mortality in the HbA1c > 6 group. However, this study did not show that this finding to be statistically significant. This may be due a small sample size. Surprisingly, Katie *et al*., reported that elevated pre-operative HbA1c was not definitively associated with increased mortality, particularly on patients who have diabetes [2]. They suggested that they have a small sample size of which this may apply to this study.

The other limitation of this study was that it was conducted from a single centre. To the best of our knowledge, this is the first study of its kind in this region. Another limitation is that this is a retrospective study. This study doesn't independently analyze mortality. This study also does not analyze other aspect of morbidity such as infection, stroke and peripheral vascular disease complications. Future prospective studies will be beneficial to gain more information on this subject.

In conclusion, this study showed that elevated HbA1C may be predictor for AKI requiring CRRT. HbA1c also may be associated with prolonged ICU stay and prolonged length of hospital stay. This study may suggest the importance of glycaemic control preoperatively to reduce morbidity and at the same time to increase cost-effectiveness of the surgery.

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