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Original Article

Impact of Pharmacist-Led Diabetes Program on Glycated Hemoglobin and Diabetes-Related Hospitalizations in a District-Level Hospital: A Pilot Retrospective Cohort Study

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Abstract

Purpose: The purpose of this study is to evaluate the effectiveness of pharmacist-led diabetes program in improving glycated hemoglobin and diabetes-related hospitalizations of patients with type 2 diabetes mellitus in a district level hospital without structured diabetes care model. Thus far, the impact of pharmacist-led diabetes program in hospital settings without endocrinologist, dietitian, nutritionist, diabetes educator and diabetes link nurse is unknown. This study hypothesized that there would be a difference in the aforementioned outcomes among patients with type 2 diabetes mellitus managed primarily by pharmacist.

Methods: A pilot retrospective cohort study was conducted among patients with type 2 diabetes mellitus attending regular follow-up in the medical outpatient department and diabetes medication therapy adherence clinic. Convenience sampling method was used to recruit study subjects who were diagnosed with type 2 diabetes mellitus, aged ≥18 years old and A1C ≥8%.

Results: Twenty-nine study subjects were eligible for both groups respectively. Pharmacist group had study subjects with higher baseline A1C values, more dyslipidemia cases and all prescribed with insulin therapy. A significant mean A1C reductions from the baseline to twelve months after enrollment could be observed in the pharmacist program but not in the usual medical care group. However, there was no significant difference between these two groups in terms of diabetes-related hospitalizations. *Conclusion*: Pharmacist-led diabetes program has a significant impact on glycated hemoglobin reductions among patients with type 2 diabetes mellitus but not diabetes-related hospitalizations.

Keywords: Pharmacist, Diabetes, Glycated hemoglobin, Hospitalization

Introduction

Diabetes is a prevalent non-communicable disease with substantial disease and economic burden (American Diabetes Association 2013; Lozano *et al.* 2013; Png *et al.* 2016; Seuring *et al.* 2015; Yesudian *et al.* 2014). Global Report on Diabetes 2016 had shown that 1.5 million of global death in the year 2012 were directly caused by diabetes (World Health Organization 2016). Higher-than-optimal blood glucose, too, had resulted in additional 2.2 million of deaths related to cardiovascular diseases, chronic kidney disease, and tuberculosis (World Health Organization 2016). It was estimated that the worldwide direct annual cost of diabetes to be approximately 825 billion international dollars, which imposed

a massive economic burden to patients, their families, health system, and nation (NCD Risk Factor Collaboration 2016).

As one of the countries providing the best healthcare in the world, Malaysia health care facilities deliver medical treatment at affordable expenses (International Living 2017). This includes government-funded health care facilities caring for patients with non-communicable diseases such as diabetes mellitus. Although the direct and indirect costs of treating diabetes care for ambulatory patients per year in this country are considerably low, the increasing numbers of diabetic patients treated per year, still, incurs a large financial impact on the overall healthcare expenditure (Pharmaceutical Services Division 2014). This was reflected in the recent Malaysia National Health and Morbidity Surveys, in which it was reported that the prevalence of diabetes had increased from 11.6% in 2006 to 17.5% in 2015 (Institute for Public Health 2015a; Institute for Public Health 2015b; Letchuman *et al.* 2010).

In view of its long-term complications and considerable financial burden, a multidisciplinary approach is required to handle diabetes and its co-morbidities. One of the initiatives started is to include pharmacist into the diabetes care model. Previous studies in hospital settings had reported positive impacts of clinical pharmacists in improving patients' adherence towards medications (Butt *et al.* 2016; Samtia *et al.* 2013), clinical outcomes especially glycated hemoglobin (A1C) (Butt *et al.* 2016; Farsaei *et al.* 2011; Jacobs *et al.* 2012; Rothman *et al.* 2005; Samtia *et al.* 2013; Taveira *et al.* 2010), and quality of life (Adibe *et al.* 2013; Butt *et al.* 2016). Several studies also reported that community pharmacists certified as diabetes pharmacists of diabetes educators have been proven to be able to improve clinical outcomes of patients with diabetes (Castejón *et al.* 2013; Cohen *et al.* 2011; Krass *et al.* 2007; Ladhani *et al.* 2012).

In Malaysia, diabetes medication therapy adherence clinic (DMTAC) is an ambulatory care service provided by the certified DMTAC pharmacists in the Ministry of Health since 2004. Throughout the years, several studies have showed this pharmacist-physician collaboration program was effective (Lim & Lim 2010; Lim *et al.* 2016; You *et al.* 2015). However, it is noteworthy that the impact of DMTAC pharmacists in hospital settings without endocrinologist, dietitian, nutritionist, diabetes educator and diabetes link nurse is unknown.

Hence, this study aimed to evaluate the effectiveness of DMTAC pharmacists in improving clinical outcomes of patients with type 2 diabetes mellitus in a district level hospital without a structured diabetes care model. The primary endpoint was the mean A1C changes in both DMTAC and usual medical care (UMC) groups, while the secondary endpoint was diabetes-related hospitalization among these two groups. This study hypothesized that there would be a difference in the aforementioned outcomes among patients with type 2 diabetes mellitus managed primarily by pharmacist.

Methods

Study Design

This was a pilot retrospective cohort study conducted in a district hospital in Malaysia, Port Dickson Hospital, involving patients with type 2 diabetes mellitus attended regular follow-up in Medical Outpatient Department (MOPD) and DMTAC. The current study was registered with Malaysia National Medical Research Registry (NMRR) and approved by Medical Research and Ethics Committee (MREC) prior to the start of the research.

Study Subjects

Patients with type 2 diabetes mellitus under regular DMTAC and MOPD follow-up were identified using convenience sampling method. The study sampling period included 1 January 2015 through 31 May 2017 to ensure each study subject had an approximately one year of follow-up in the current hospital setting. Proper documentation of an A1C value at baseline (defined as within 3 months before or after the initial appointment with DMTAC pharmacist or UMC) was required. Both DMTAC and UMC patients were selected as study subjects if they were diagnosed with

type 2 diabetes mellitus, aged ≥18 years old and A1C ≥8%. Subjects were excluded if there was insufficient relevant information that could be retrieved from their DMTAC record forms, medical record or electronic computer system. Insufficient information in this context mainly referring to less than four evaluable A1C values for each study subjects.

For patients under regular follow-ups in MOPD, their standard of care was provided by physicians and nurses. Those patients with uncontrolled or complicated type 2 diabetes mellitus would be referred to the pharmacists managing DMTAC if further diabetes management would be required. Pharmacists who provided DMTAC services have been credentialed and privileged to educate patients regarding diabetes control, nutrition restriction and requirement, management of co-morbid conditions, and lifestyle modification. They also collaborated with physicians to make medication adjustment, especially for oral diabetes medications and insulin therapy.

Study Outcomes

The primary outcome of this study was mean A1C changes, while the secondary outcome was diabetes-related hospitalizations. A1C levels for each DMTAC and UMC visits were followed-up, beginning from baseline (index date) until the end of the study duration (approximately one-year post-index). In addition, the International Classification of Diseases, Tenth Edition, Clinical Modification (ICD-10-CM) was used to identify diabetes-related diagnoses for those study subjects admitted in Port Dickson Hospital within the study period. The ICD-10-CM codes were used to identify short-term diabetes complications, including hyperglycemia and hypoglycemia, as well as long-term diabetes complications, such as microvascular and macrovascular conditions. Microvascular complications included, but not limited to, retinopathy, nephropathy, neuropathy, while cardiovascular disease (CVD) included coronary artery disease, history of myocardial infarction, or heart valve disease. A hospitalization was considered to be diabetes-related if one of the designated ICD-10-CM codes was documented in the diagnosis fields.

Data Collection

Relevant data for each cohort was collected using a standardized chart review forms and entered into the research database. For both DMTAC and UMC groups, data from chart review included the dates 1 January 2015 through 31 May 2017. Demographic information (i.e. age, sex, and race), initial clinical characteristics (i.e. years of diabetes, co-morbid conditions, types of diabetes medications), as well as A1C levels, were obtained from DMTAC record forms and medical record as appropriate. On the other hand, history of hospitalizations for both DMTAC and UMC groups within one year of follow-up was retrieved via electronic medical records SPP version 2.6. Data available were extracted to explore the relationship between pharmacists' interventions and the aforementioned clinical outcomes.

Statistical Analysis

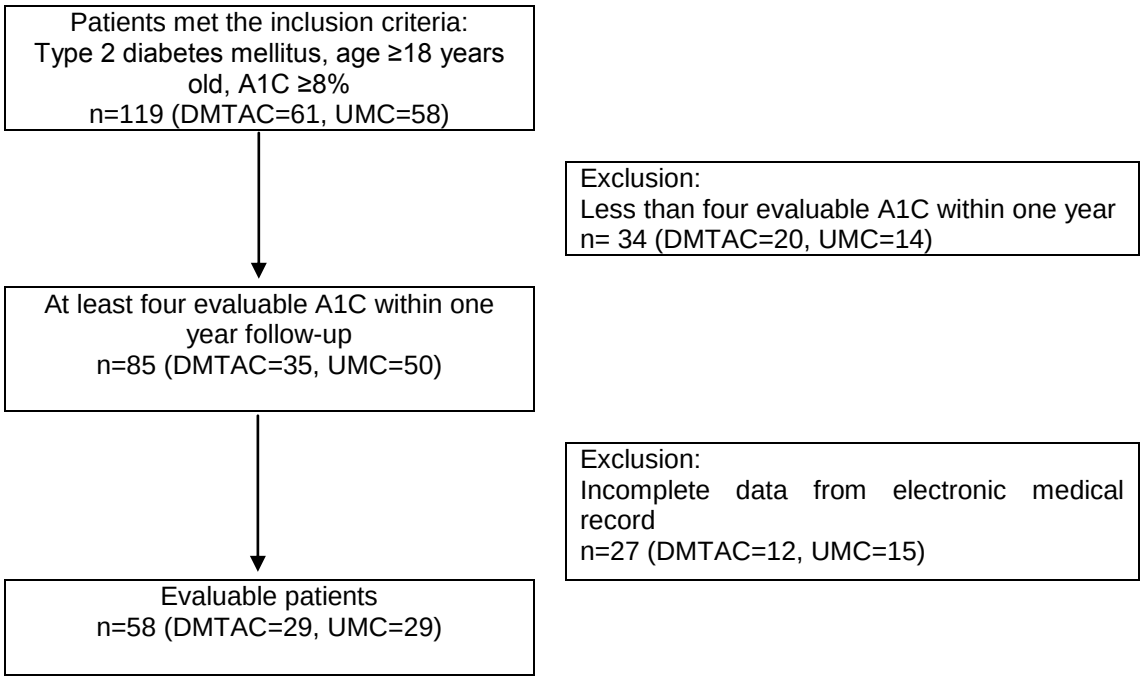
This study was powered with a sample size to detect a difference of 1% A1C reduction with a standard deviation of 1.2% (Kelly & Rodgers 2000). 24 subjects were required for each group with a ratio of 1:1 to obtain a power of 80% and a type I error of 0.05%. (Department of Biostatistics 2009). By accounting for a 20% dropout rate, a total of 29 subjects per group was required for this study.

All statistical analyses were performed by using IBM® SPSS Statistics desktop version 23.0. Continuous data were presented as means and standard deviations or 95% confidence intervals for generalization purposes, while categorical data was presented as frequencies and percentages. The threshold of significance was fixed at 5% level. Distributions of demographic and initial clinical variables were compared by using Pearson's Chi-square and independent t-tests as appropriate. For the primary outcome, mean A1C changes for both DMTAC and UMC groups were computed using repeated measures ANOVA. For the secondary outcome, a time-to-event curve was estimated with the Kaplan-Meier method. The event mentioned was referring to days to the first diabetes-related hospitalization.

Results

Demographics of Study Subjects

Twenty-nine patients from each group were eligible for this study (Figure 1). All these study subjects had complete relevant data to be reviewed and analyzed. Baseline demographic and clinical characteristics of the study subjects are summarized in Table 1. Both groups were comparable, except there were more dyslipidemia cases and more study subjects prescribed with insulin in DMTAC group. In contrary, UMC group had more study subjects prescribed with sulphonylureas.



A1C=glycated hemoglobin, DMTAC=diabetes medication therapy adherence clinic, UMC=usual medical care

Figure 1: Patient Selection Flowchart

Primary Outcome: Mean A1C Changes

Mean A1C changes among DMTAC and UMC study subjects are summarized in Table 2. DMTAC study subjects had significant higher baseline mean A1C value compared to UMC study subjects ($p<0.001$). There was consistent mean A1C reductions in the DMTAC group but not in the UMC group. General linear model analysis with repeated measure ANOVA reported significant mean A1C reduction after 12 months in the program ($p<0.001$). In contrary, no significant mean A1C changes observed in the UMC group. The average mean A1C values in the DMTAC and UMC groups were 10.09% (95% confidence interval 9.541-10.636) and 9.22% (95% confidence interval 8.668-9.763), respectively, with mean A1C changes of 0.87% (95% confidence interval 0.10-1.65) between these two groups. The difference was statistically significant ($p=0.028$). Mean A1C changes in the DMTAC and UMC groups over twelve months is illustrated in Figure 2.

Post hoc tests revealed that A1C reduced by an average of 1.35% (95% confidence interval 0.297-2.392) after being followed-up in the DMTAC for three months ($p=0.006$). Although there were additional A1C reductions between third month and sixth month, as well as between sixth month and twelfth month, the average reduction was not statistically significant ($p=1.000$).

Table 1: Baseline Demographic and Clinical Characteristics of Study Subjects

Variables (N= 58)	**Subjects**		**p-value**
	DMTAC (n=29)	**UMC (n=29)**	
Age, years (SD)	54.24 (9.97)	59.07 (10.25)	0.074
Sex, n (%)			
Male	16 (51.6)	15 (48.4)	0.792
Female	13 (48.1)	14 (51.9)	
Race, n (%)			
Malay	18 (58.1)	13 (41.9)	0.412
Chinese	4 (40.0)	6 (60.0)	
Indian	7 (41.2)	10 (58.8)	
Co-morbidities, n (%)			
Ischemic heart disease	6 (46.2)	7 (53.8)	0.753
Hypertension	27 (50.9)	26 (49.1)	1.000[b]
Dyslipidemia	16 (69.6)	7 (30.4)	0.016[a]
Chronic kidney disease	6 (42.9)	8 (57.1)	0.539
Years of Diabetes Mellitus, years (SD)			
<10 years	19 (52.8)	17 (47.2)	0.588
>10 years	10 (45.5)	12 (54.5)	
Medications, n (%)			
Aspirin	21 (58.3)	15 (41.7)	0.104
Biguanide	18 (47.4)	20 (52.6)	0.581
Sulphonylurea	0 (0)	10 (100)	0.001[b]
DPP4-Inhibitor	3 (33.3)	6 (66.7)	0.470[b]
Insulin	29 (61.7)	18 (38.3)	<0.001[a]
ACEi/ARB	20 (47.6)	2 (52.4)	0.557
Statin	26 (52.0)	24 (48.0)	0.446

[a] p-value < 0.05 is considered statistically significant.
[b] Fisher's exact test.
ACEi = angiotensin-converting-enzyme inhibitor.
ARB = angiotensin II receptor blocker.
DMTAC = diabetes medication therapy adherence clinic.
DPP4-inhibitor = dipeptidyl peptidase-4 inhibitor.
UMC = usual medical care.

Table 2: Mean A1C Changes Among DMTAC and UMC Groups

Variables (N = 58)	**Mean A1C Changes**			
	0 month Mean (SD)	**3 months** Mean (SD)	**6 months** Mean (SD)	**12 months** Mean (SD)
DMTAC (n = 29)	11.16 (1.84)	9.81 (1.66)[a]	9.81 (2.24)[a]	9.57 (2.11)[a]
UMC (n = 29)	9.26 (1.13)	9.30 (1.39)	9.22 (2.25)	9.09 (2.03)

[a] p-value < 0.05 compared to baseline value (repeated measures ANOVA)

A1C = glycated haemoglobin, DMTAC = diabetes medication therapy adherence clinic, SD = standard deviation, UMC = usual medical care.

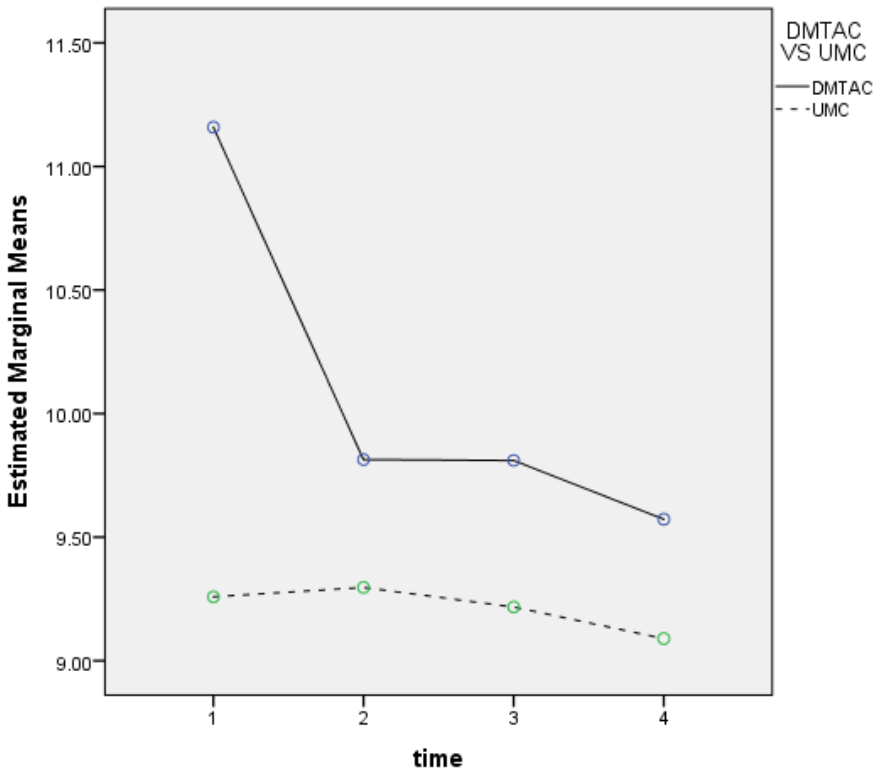


Figure 2: Mean A1C Changes in the DMTAC and UMC Groups over 12 Months
[1]baseline A1C
[2]A1C after three months
[3]A1C after six month
[4]A1C after twelve month

Secondary Outcome: Diabetes-Related Hospitalizations

Figure 3 shows the Kaplan-Meier cumulative event curves for diabetes-related hospitalizations. There were seven events in the DMTAC group compared to two events in the UMC group. The mean time to the first hospitalization in DMTAC group was 385.76 days (95% confidence interval 348.66-422.86). In contrary, the mean time to the first event in UMC was 402.64 days (95% confidence interval 388.78-416.50). A log-rank test was done to determine if there were differences in the diabetes-related hospitalizations for both DMTAC and UMC groups. The distributions for these two groups were statistically not significant, χ^2 (1) = 3.697, p=0.054.

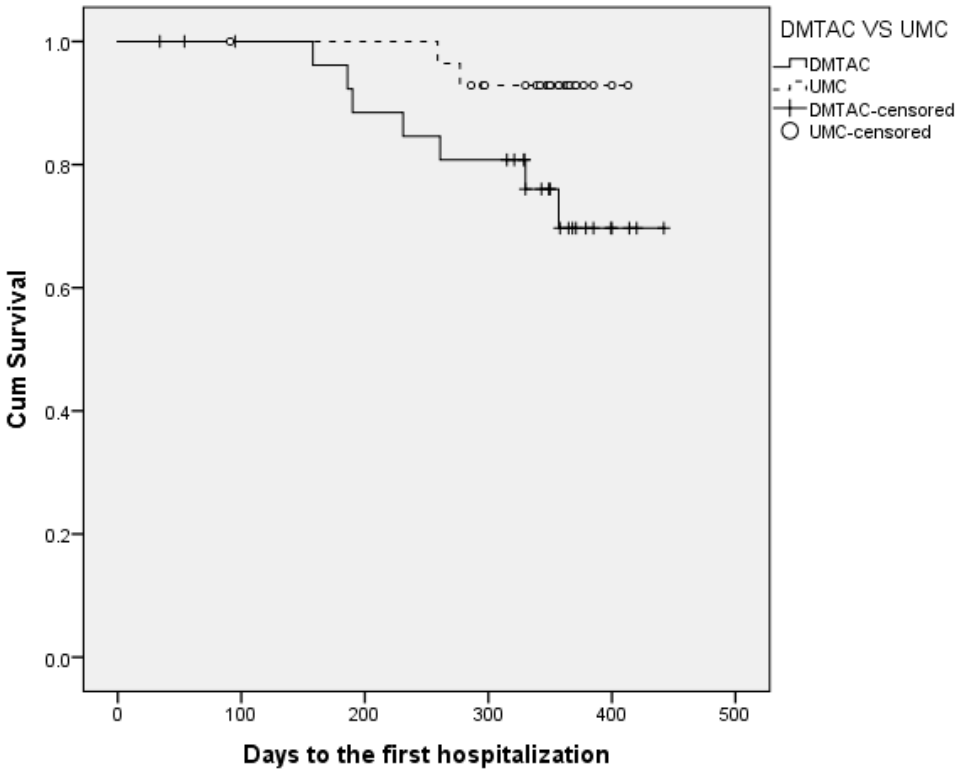


Figure 3: Kaplan-Meier Cumulative Event Curves for Diabetes-Related Hospitalization

Discussion

The findings of this study revealed that patients with type 2 diabetes mellitus managed by pharmacists providing DMTAC service had improved A1C values. There was no significant difference between DMTAC and UMC groups for diabetes-related hospitalizations.

Compared to the UMC group, study subjects enrolled in the DMTAC group had higher baseline A1C because physician usually referred patients to DMTAC program if their diabetes had become uncontrolled or more complicated to manage. A similar scenario was also observed in previous studies, in which pharmacist group tended to have patients with higher baseline A1C levels (Morello *et al.* 2016; Pepper *et al.* 2012). The current study reported a significant 1.35% (95%confidence interval 0.297-2.392) reductions in A1C from the baseline to as early as three months after enrollment in the DMTAC program. Despite the significant improvement in A1C, both DMTAC and UMC groups did not reach the targeted A1C ≤6.5%, which could be attributable to insufficient follow-up duration. In parallel with the current study, a prospective study conducted in a tertiary hospital in Malaysia by Kumar and colleagues (2011) showed a similar reduction in A1C values among DMTAC subjects compared to the control (-1.7% versus -0.6%) over nine months (Kumar *et al.* 2011). Another multi-center retrospective study evaluating the impact of DMTAC services in Malaysia government health clinics revealed a modest yet significant mean A1C reduction improvement of 1.0% (SD=1.70) ($p<0.001$) after having at least four visits with DMTAC pharmacists (You *et al.* 2015). A greater improvement in A1C could probably be achieved with more rigorous and intensive diabetes management. This was demonstrated in a randomized trial conducted by Rothman et al. (2005), in which intervention group able to obtain a significant 2.5% A1C reduction after receiving several intensive management sessions from clinical pharmacists and diabetes care coordinators in one year duration (Rothman *et al.* 2005).

The importance of reducing A1C levels had been ascertained by UK Prospective Diabetes

Study (UKPDS), in which a 35% reduction in the risk of microvascular complications could be observed for every percentage decrease in A1C (UK Prospective Diabetes Study Group 1998). Additionally, outcomes from Action in Diabetes and Vascular Disease: Preterax and Diamicron Modified Release Controlled Evaluation (ADVANCE) trial reported intensive glucose control significantly reduced the combined major macrovascular or microvascular events, mainly as a result of a reduction in nephropathy (ADVANCE Collaborative Group 2008). More diverse treatment strategies are, therefore, essential to ensure patients are able to attain their targeted glycemic goals, with better quality of life and satisfaction, while minimizing the adverse outcomes from the intensive glucose control.

Compared to the pharmacist-led group, there was less improvement in the A1C of study subjects managed by the UMC group. Although it was stated that no convincing association between patient-physician contact time and outcomes of chronic illness (Dugdale *et al.* 1999), the positive outcomes observed in the current study could partly be due to DMTAC pharmacists able to spend more time with their patients to discuss about diabetes management and enforce about compliance to their treatment regimes, in comparison to shorter physician-patient contact time in the outpatient setting. The relationship between healthcare professional-patient contact time and clinical outcomes is out of the scope of this study and can be explored in the future.

Diabetes-related hospitalizations in the current study included microvascular and macrovascular complications as listed in ICD-10-CM codes. This definition varied from previous studies that used ICD-9-CM codes or did not include macrovascular complications as part of the diabetes-related hospitalizations (Chung *et al.* 2014; Menzin *et al.* 2010). The current study showed that both DMTAC and UMC groups had similar outcomes on diabetes-related hospitalizations. Nevertheless, it should be noted that study subjects enrolled in the DMTAC had a shorter interval for the first hospitalization compared to those in the UMC group. This trend was different from that observed in a study conducted by Chung and colleagues (2014) which reported patients treated in the usual care group had a significant increase in hospitalizations but comparable emergency department visits between the clinical pharmacy program and usual care groups (Chung *et al.* 2014). This could be explained via differences in the baseline clinical characteristics of study subjects between these two studies. The current study enrolled DMTAC study subjects with higher A1C levels compared to UMC study subjects, while the former study had both cohorts started with similar A1C levels. Menzin and colleagues (2010) identified that patients with higher A1C levels had higher hospitalization rates, i.e. mean A1C ≥10% had increased odds of having diabetes-related hospitalizations compared to those with mean A1C <7% (Menzin *et al.* 2010). This finding was consistent with the results of the current study.

Evidence of tight glycemic control to reduce diabetes-related complications were contradicting. A large meta-analysis showed that intensive glucose control might lower coronary heart disease but not stroke and overall mortality (Ray *et al.* 2009). Conversely, there was evidence showing no benefit for cardiovascular death and overall mortality outcomes with tight glycemic control (Kelly *et al.* 2009). The conflicting data indicated that more research are required to verify the benefit of tight glycemic control for patients with diabetes.

Limitations

This study was one of the few researches assessing the impact of pharmacist-managed diabetes program on patients' glycemic control and diabetes-related hospitalizations. The findings in this study must be interpreted with caution. Firstly, it was retrospective in design which restricted cause and effect inferences. Selection bias was almost inevitable due to the lack of randomization, as presented through the differences in A1C baseline values between two groups. Secondly, this study was conducted in a single-center without multidisciplinary diabetes care team. The results and findings, therefore, might not be generalized to other settings such as primary health care or tertiary care hospital with

different diabetes care model. Thirdly, study subjects in the DMTAC group were concurrently managed by physicians in the UMC group. Likewise, diabetes management of study subjects in the UMC group might also be affected by pharmacists' interventions because physician might consult with DMTAC pharmacists regarding their diabetes management. Hence, this could be one of the confounding factors being introduced into the study. The better A1C reductions in the pharmacist-led group, hence, could be attributed to better compliance rate among patients with type 2 diabetes mellitus enrolled in that group. In addition, the data regarding numbers of hospitalization was retrieved retrospectively from the local electronic database. Thus, the records of study subjects being hospitalized or treated in other health centers could not be captured. Longer follow-up duration is also necessary to detect significant differences in hospitalization rates among type 2 diabetes mellitus patients managed by the DMTAC and UMC program.

Conclusion

Pharmacist-led diabetes medication therapy adherence clinic in this district hospital has a significant impact on A1C reductions among patients with type 2 diabetes mellitus, especially within the first 3 months of enrolment into the program. Nonetheless, there was no significant difference in terms of diabetes-related hospitalization between DMTAC and UMC groups. Through the current study, it was showed that pharmacists trained in managing patients with type 2 diabetes mellitus is important to improve patients' clinical outcome, especially in a hospital setting without a structured diabetes care model. More studies with longer duration may be necessary to assess the optimum time-frame of this program and also the long-term effects of pharmacist interventions on diabetes-related clinical outcomes in the future.

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References

Adibe, M.O., Ukwe, C.V., & Aguwa, C.N. (2013). The impact of pharmaceutical care intervention on the quality of life of Nigerian patients receiving treatment for type 2 diabetes, *Value in Health Regional Issues*. 2(2), 240-7.

ADVANCE Collaborative Group. (2008). Intensive blood glucose control and vascular outcomes in patients with type 2 diabetes, *New England Journal of Medicine*. 358(24), 2560-72.

American Diabetes Association. (2013). Economic costs of diabetes in the US in 2012, *Diabetes Care.* 36(4), 1033-46.

Butt, M., Ali, A.M., Bakry, M.M., & Mustafa, N. (2016). Impact of a pharmacist led diabetes mellitus intervention on HbA1c, medication adherence and quality of life: A randomised controlled study, *Saudi Pharmaceutical Journal*. 24(1), 40-8.

Castejón, A.M., Calderón, J.L., Perez, A., Millar, C., McLaughlin-Middlekauff, J., Sangasubana, N., Alvarez, G., Arce, L., Hardigan, P., & Rabionet, S.E. (2013). A community-based pilot study of a diabetes pharmacist intervention in Latinos: Impact on weight and hemoglobin A1c, *Journal of Health Care for the Poor and Underserved*. 24(4), 48-60.

Chung, N., Rascati, K., Lopez, D., Jokerst, J., & Garza, A. (2014). Impact of a clinical pharmacy program on changes in hemoglobin A1c, diabetes-related hospitalizations, and diabetes-related emergency department visits for patients with diabetes in an underserved population, *Journal of Managed Care Pharmacy*. 20(9), 914-9.

Cohen, L.B., Taveira, T.H., Khatana, S.A.M., Dooley, A.G., Pirraglia, P.A., & Wu, W.C. (2011). Pharmacist-led shared medical appointments for multiple cardiovascular risk reduction in patients with type 2 diabetes, *The Diabetes Educator*. 37(6), 801-12.

Department of Biostatistics, 2009. PS: Power and sample size calculation version 3.0. Software. Nashville: Vanderbilt University.

Dugdale, D.C., Epstein, R., & Pantilat, S.Z. (1999). Time and the patient–physician relationship, *Journal of General Internal Medicine*. 14(S1), 34-40.

Farsaei, S., Sabzghabaee, A.M., Zargarzadeh, A.H., & Amini, M. (2011). Effect of pharmacist-led patient education on glycemic control of type 2 diabetics: A randomized controlled trial, *Journal of Research in Medical Sciences: The Official Journal of Isfahan University of Medical Sciences*. 16(1), 43.

International Living, 2017. 4 Countries with the best healthcare in the world. Baltimore, MD: International Living, viewed 14 June 2017, from: https://internationalliving.com/2017/01/4-countries-best-healthcare-world/

Institute for Public Health, 2015a. National health and morbidity survey 2011 (NHMS 2011) volume II: Non-communicable diseases. Kuala Lumpur, viewed 14 June 2017 from: http://www.iku.gov.my/index.php/research-eng/list-of-research-eng/iku-eng/nhms-eng/nhms-2011-eng

Institute for Public Health, 2015b. National health and morbidity survey 2015 (NHMS 2015) volume II: Non-communicable diseases, risk factors & other health problems. Kuala Lumpur: Institute for Public Health, viewed 14 June 2017 from: http://www.iku.gov.my/index.php/research-eng/list-of-research-eng/iku-eng/nhms-eng/nhms-2015

Jacobs, M., Sherry, P.S., Taylor, L.M., Amato, M., Tataronis, G.R., & Cushing, G. (2012). Pharmacist assisted medication program enhancing the regulation of diabetes (PAMPERED) study, *Journal of the American Pharmacists Association*. 52(5), 613-21.

Kelly, C., & Rodgers, P.T. (2000). Implementation and evaluation of a pharmacist-managed diabetes service, *Journal of Managed Care Pharmacy*. 6(6), 488-93.

Kelly, T.N., Bazzano, L.A., Fonseca, V.A., Thethi, T.K., Reynolds, K., & He, J. (2009). Systematic review: Glucose control and cardiovascular disease in type 2 diabetes, *Annals of Internal Medicine.* 151(6), 394-403.

Krass, I., Armour, C.L., Mitchell, B., Brillant, M., Dienaar, R., Hughes, J., Lau, P., Peterson, G., Stewart, K., Taylor, S., & Wilkinson, J. (2007). The Pharmacy diabetes care program: Assessment of a community pharmacy diabetes service model in Australia, *Diabetic Medicine*. 24(6), 677-83.

Kumar, L.N., Chin, S.T., Rachet, T., Lim, K.Y., & Fudziah, A. (2011). Clinical and economic impact of pharmacist-run medication therapy adherence clinic service on patients with type 2 diabetes, *Malaysian Journal of Public Health Medicine*. 5(11), 42.

Ladhani, N.N., Majumdar, S.R., Johnson, J.A., Tsuyuki, R.T., Lewanczuk, R.Z., Spooner, R., & Simpson, S.H. (2012). Adding pharmacists to primary care teams reduces predicted long-term risk of cardiovascular events in Type 2 diabetic patients without established cardiovascular disease: Results from a randomized trial, *Diabetic Medicine.* 29(11), 1433-9.

Letchuman, G.R., Wan Nazaimoon, W.M., Wan Mohamad, W.B., Chandran, L.R., Tee, G.H., Jamaiyah, H., Isa, M.R., Zanariah, H., Fatanah, I., & Ahmad Faudzi, Y. (2010). Prevalence of diabetes in the Malaysian national health morbidity survey III 2006, *Medical Journal of Malaysia*. 65(3), 180-6.

Lim, P.C., & Lim, K. (2010). Evaluation of a pharmacist-managed diabetes medication therapy adherence clinic, *Pharmacy Practice*. 8(4), 250.

Lim, P.C., Lim, K., Embee, Z.C., Hassali, M.A., Thiagarajan, A., & Khan, T.M. (2016). Study investigating the impact of pharmacist involvement on the outcomes of diabetes medication therapy adherence program Malaysia, *Pakistan Journal of Pharmaceutical Sciences.* 29(2).

Lozano, R., Naghavi, M., Foreman, K., Lim, S., Shibuya, K., Aboyans, V., Abraham, J., Adair, T., Aggarwal, R., Ahn, S.Y., & AlMazroa, M.A. (2012). Global and regional mortality from 235 causes of death for 20 age groups in 1990 and 2010: A systematic analysis for the Global Burden of Disease Study 2010, *The Lancet*. 380(9859), 2095-128.

Menzin, J., Korn, J.R., Cohen, J., Lobo, F., Zhang, B., Friedman, M., & Newmann, P.J. (2010). Relationship between glycemic control and diabetes-related hospital costs in patients with type 1 or type 2 diabetes mellitus, *Journal of Managed Care Pharmacy*. 16(4), 264-75.

Morello, C.M., Christopher, M.L., Ortega, L., Khoan, J., Rotunno, T., Edelman, S.V., Henry, R.R., & Hirsch, J.D. (2016). Clinical outcomes associated with a collaborative pharmacist-endocrinologist diabetes intense medical management "tune up" clinic in complex patients, *Annals of Pharmacotherapy.* 50(1), 8-16.

NCD Risk Factor Collaboration. (2016). Worldwide trends in diabetes since 1980: A pooled analysis of 751 population-based studies with 4·4 million participants, *The Lancet*. 387(10027), 1513-30.

Pepper, M.J., Mallory, N., Coker, T.N., Chaki, A., & Sando, K.R. (2012). Pharmacists' impact on improving outcomes in patients with type 2 diabetes mellitus, *The Diabetes Educator*. 38(3), 409-16.

Pharmaceutical Services Division. (2014). The cost of diabetes care for ambulatory patients in Malaysian ministry of health facilities. Malaysia.

Png, M.E., Yoong, J., Phan, T.P., & Wee, H.L. (2016). Current and future economic burden of diabetes among working-age adults in Asia: Conservative estimates for Singapore from 2010-2050, *BMC public health*. 16(1), 153.

Ray, K.K., Seshasai, S.R.K., Wijesuriya, S., Sivakumaran, R., Nethercott, S., Preiss, D., Erqou, S., & Sattar, N. (2009). Effect of intensive control of glucose on cardiovascular outcomes and death in patients with diabetes mellitus: A meta-analysis of randomised controlled trials, *The Lancet*. 373(9677), 1765-72.

Rothman, R.L., Malone, R., Bryant, B., Shintani, A.K., Crigler, B., Dewalt, D.A., Dittus, R.S., Weinberger, M., & Pignone, M.P. (2005). A randomized trial of a primary care-based disease management program to improve cardiovascular risk factors and glycated hemoglobin levels in patients with diabetes, *The American Journal of Medicine*. 118(3), 276-84.

Samtia, A.M., Rasool, M.F., Ranjha, N.M., Usman, F., & Javed, I. (2013). A multifactorial intervention to enhance adherence to medications and disease-related knowledge in type 2 diabetic patients in Southern Punjab, Pakistan, *Tropical Journal of Pharmaceutical Research*. 12(5), 851-6.

Seuring, T., Archangelidi, O., & Suhrcke, M. (2015). The economic costs of type 2 diabetes: A global systematic review, *Pharmacoeconomics*. 33(8), 811-31.

Taveira, T.H., Friedmann, P.D., Cohen, L.B., Dooley, A.G., Khatana, S.A.M., Pirraglia, P.A., & Wu, W.C. (2010). Pharmacist-led group medical appointment model in type 2 diabetes, *The Diabetes Educator*. 36(1), 109-17.

UK Prospective Diabetes Study (UKPDS) Group. (1998). Intensive blood-glucose control with sulphonylureas or insulin compared with conventional treatment and risk of complications in patients with type 2 diabetes (UKPDS 33), *The Lancet*. 352(9131), 837-53.

World Health Organization. (2016). *Global report on diabetes*. World Health Organization.

Yesudian, C.A., Grepstad, M., Visintin, E., & Ferrario, A. (2014). The economic burden of diabetes in India: a review of the literature, *Globalization and health*. 10(1), 80.

You, L.X., Selvadurai, S., Yee, C.K., Noh, N.B., Bao, G.C., Joyce, T., Hamdi, A.H., & Haron, N. (2015). Impact of pharmacist-managed diabetes medication therapy adherence clinic (DMTAC) in government health clinics, *Malaysian Journal of Pharmaceutical Sciences*. 13(1), 43.