Impact of Pharmacist-led Educational Intervention on Predictors of Diabetic Foot at Two Different Hospitals of Malaysia

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Objective: Diabetes mellitus (DM) is a chronic metabolic disorder that can initiate organ damage inside the body if not treated appropriately. Apart from tight glycemic control, a suitable educational intervention is also needed from health-care providers to stop or decrease the progression of organ damage in diabetic patients. This study intended to measure the impact of pharmacist-led educational intervention on improvement in predictors of diabetic foot in two different hospitals in Malaysia.

Materials and Methods: In two tertiary care selected hospitals, the included diabetic patients were randomly divided into two study arms. In the control group, 200 patients who were receiving usual treatment from hospitals were included. However, in the intervention group, those 200 patients who were receiving usual treatment along with counseling sessions from pharmacists under the Diabetes Medication Therapy Adherence Clinic (DMTAC) program were included. The study continued for 1 year, and there were four follow-up visits for both study arms. A prevalidated data collection form was used to measure the improvement in predictors of diabetic foot in included patients. Data were analyzed by using the Statistical Package for the Social Sciences (SPSS) software program, version 24.0.

Results: With the average decrease of 1.97% of HbA1c values in the control group and 3.43% in the intervention group, the univariate and multivariate analysis showed a statistically significant difference between both of the study arms in the improvement of predictors belonging to the diabetic foot ($P < 0.05$). The proportion of patients without any signs and symptoms of the diabetic foot in the intervention group was 91.7%, which increased from 42.3% at baseline ($P < 0.05$). However, this proportion in the control group was 76.9% at the fourth follow-up, from 48.3% at baseline ($P < 0.05$).

Conclusion: A statistically significant reduction in the signs and symptoms of diabetic foot was observed in the intervention group at the end of 1 year. The progression of diabetic foot was significantly decreased in the pharmacist intervention group.

Keywords: Control group, diabetes mellitus, diabetic foot, DMTAC program, intervention group, pharmacist intervention, tertiary care hospitals

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IntroduCtion

Diabetes mellitus (DM) is among one of the oldest diseases known to the human population. It initially appeared in the Egyptian manuscript about...
is still undiagnosed in Malaysia. The highest prevalence is in Kedah, Perlis, and Johor states of Malaysia. At the age of 30, approximately 90% of the population in the world who can provide patient education. In Malaysia, the prevalence of DM is continuously increasing, and the majority of the Malaysian population is still undiagnosed. The overall percentage of undiagnosed diabetes is more in the Malay race, which is 53%, followed by the Chinese, approximately 49%, and then in Indians, approximately 42%. Regarding the control of diabetes, only 23.8% of total diabetic patients in primary care, whereas about 12.7% in tertiary institutions were able to achieve glycemic targets.

Uncontrolled T2DM will result in short- and long-term complications, including hypoglycemia, heart problems, neuropathy, nephropathy, retinopathy, and diabetic foot. Poor control of diabetes is a major public health problem and a considerable hazard aspect for the progression of its complications. Thus, good glycemic control remains the key therapeutic goal for the stoppage of organ damage and any other problems due to diabetes. The HbA1c has become a benchmark for determining the control of diabetes and is helping in predicting short- or long-term diabetic complications, whereas the other outcome measure parameters can only predict the control of DM during a specific time interval.

DM is a chronic illness and requires proper medical care along with patient education about self-management to avoid its short- and long-term complications. The ultimate goal of patient education about DM is to achieve the changes in human behavior by providing knowledge, understanding, and consequences of the uncontrolled disease. After physicians and nurses, pharmacists are the third largest health-care providers in the world who can provide patient education. In pharmacies, pharmacists are providing services to diabetic patients with prescription and nonprescription medication, blood glucose meters, and testing strips, dietary supplements, and some other services such as medication review, needle exchange, and disposal of unwanted medicines. Community pharmacists are believed to be the utmost reachable health-care providers, because usually, no appointments are needed to meet them, and they have a good level of patient interactions. Ultimately, they are available to play a significant role in the care of diabetic patients.

In the past, numerous studies have proven that the contribution of pharmacists in achieving a better control of diabetes is significant. In Malaysia, pharmacists are collaborating with physicians in all tertiary hospitals with the help of the Diabetes Medication Therapy Adherence Clinic (DMTAC) program. The DMTAC program is an ambulatory and value-added service provided by pharmacists in alliance with physicians to help diabetic patients for the accomplishment of better medication adherence and good glycemic control. Patients enrolled under the DMTAC program were followed up for a minimum of eight visits, where they receive medication adherence evaluation, identification and solving of drug-related problems, counseling for prescribed medication, evaluating the clinical outcomes, and diabetes education by the pharmacist. In this program, the patients are also taught about the disease progression with its complications. This observational study was conducted to assess the influence of pharmacist-led educational interventions on the different predictors of diabetic foot complications.

Materials and Methods

Sample size calculation and study approvals

This study was an observational, multicenter, randomized control study that was conducted in two hospitals in Malaysia. The Medical Research and Ethics Committee (MREC), Ministry of Health Malaysia, approved the study with reference number [KKM/ NIHSEC/ P18-1307 (13)]. The required sample size was calculated by the previous data from a study conducted by Butt et al. to compare the mean of HbA1c between the intervention and control group. A total of a minimum of 65 patients in each study arm were needed to distinguish the difference of 0.79% (8.47% versus 9.26% HbA1c) with 80% certainty (power) and by using an alpha level of 0.05, and SD is $\sigma = 1.61$. The type I error probability associated with the test of this null hypothesis was 0.05. With an additional 20% dropout, the minimum sample size required was 80 samples per arm.

Study procedure

Depending on the inflow of patients in each hospital, a 3-4-month capsule frame was set for recruitment of estimated sample size from study locations. Initially, the informed consent form was distributed and was signed from a total of 150 patients in each hospital. Then, the hospital identification of patients from each
selected hospital was listed as a control group and similarly, an interventional group. On the completion of 150 record numbers of patients in each group in each hospital, that list was entered into Microsoft Excel, and randomization was carried out to randomly select 100 patients from each 150 record numbers to consider them as final participants of this study in each hospital.

The control group consists of adult outpatients with DM who were receiving usual treatment from diabetic clinics in selected hospitals. The intervention group included adult outpatients with DM who were receiving treatment from diabetic clinics with the intervention of pharmacists from selected hospitals. All the included T2DM patients had been having type 2 diabetes mellitus (T2DM) for at least 5 years and HbA1c more than 8%.

Baseline data were collected for the control group and intervention group from each selected hospital. Then, four follow-ups were made for these patients every 3–4 months in both control and intervention groups. After baseline, a total of four follow-ups were made for both control and intervention groups in each hospital. At every follow-up, the laboratory outcomes and the selected predictors of diabetic foot were noted on prevalidated data collection forms. All the laboratory investigations, including HbA1c, were determined by laboratories of hospitals; the researchers only collected data in the form of information from patients.

Study tool
The patient information was collected by a prevalidated data collection tool; this prevalidated data collection tool was validated before the start of this research. The content validity of the data collection form was done by experts consisting of members of diabetic clinic specialists and pharmacists at both study sites. Face validation was conducted by giving the data collection form to the group composed of 15 members, consisting of academicians and endocrinologists of other hospitals in Malaysia. This tool contained demographic details and clinical outcomes in the form of HbA1c of patients. In addition, this tool also contained information on the list of various signs and symptoms as predictors of the diabetic foot to observe the improvements in selected patients.

Statistical analysis
Data were analyzed by using the Statistical Package for the Social Sciences (SPSS) software program, version 24.0. Descriptive data were expressed as mean ± standard deviation (SD). The normality of the data was checked by SPSS using skewness and kurtosis testing. The univariate and multivariate regression analysis was used to evaluate the association between independent variables and pharmacist intervention in this study. A value of $P < 0.05$ was considered statistically significant.

RESULTS
Of 400 eligible recruited patients, 299 patients had completed four required follow-ups after baseline for the total 1x2-year duration. Overall, 29.5% of patients from the intervention arm, and 23.5% of patients from the control arm, dropped out from study due to various reasons. On the validated data collection tool, data in the form of information were collected from the patients. The first follow-up was taken after 3–4 months of baseline and followed by every 3–4 months. A total of four follow-ups was made in one year from the date of patient recruitment in this study.

The sociodemographic features of the included 299 patients are presented in Table 1. Of these 299 patients, 149 belonged to hospital A, and 150 patients belonged to hospital B. Overall, the portion of Malay ethnicity patients was more at both the study locations.

At baseline, the predictors belonging to the diabetic foot were checked for statistical significance to observe the differences in both of the study arms at baseline [Tables 2 and 3]. Statistically, nonsignificant differences were observed between all the predictors that belonged to the diabetic foot. The number and percentage of patients among study groups having each sign and symptom of the diabetic foot were measured by cross-tabulation. Regression analysis was performed to examine the effect of a pharmacist-led education intervention on each diabetic foot predictor improvement on every follow-up visit.

The baseline characteristics of the intervention and control group for different predictors can be seen in Table 2.

The HbA1c changes among both the study groups can be seen in all follow-ups of this study. At baseline, the levels were statistically equal but after that they started improving more dramatically in the intervention group of this study, as shown in Figure 1.

All the statistical differences at every follow-up from baseline for each study group can be seen in Table 3.

At follow-up 1, changes were noticed in both the study groups in the diabetic foot complication. The improvements were noted in all the predictors of the diabetic foot, but these improvements were more prominent in the intervention group in the presence of pharmacist intervention. In the control group, the patients without any signs and symptoms were 54.5%
at follow-up, one of whom was improved up to 62.9% at the second follow-up. In contrast, in the intervention group, at the first follow-up this percentage was 53.2%, which was improved at the second follow-up by up to 67.3%. At the third follow-up, regression analysis showed significant improvement changes between both the study groups in “ulceration” \( (P = 0.052) \) and “infection” \( (P = 0.087) \). At the fourth follow-up, regression analysis showed statistically significant improvement changes between both the study groups in “ulceration” \( (P = 0.038) \). However, statistically nonsignificant differences were observed in other symptoms of diabetic foot complication in both the study groups at the fourth follow-up. Deliberately, the proportion of patients without any signs and symptoms of the diabetic foot in the intervention group was 91.7%, and it increased from 42.3% at baseline. However, this proportion in the control group was 76.9% at the fourth-follow up, which was from 48.3% at baseline.

**DISCUSSION**

This study was novel among its types, as there has been no study evident so far on the diabetic foot, and that measured the effect of pharmacist-led educational intervention on the diabetic foot as a complication of diabetes mellitus in Malaysia. The signs and symptoms of the diabetic foot were significantly improved in the intervention group as compared with the control group at the end of the study. In this study, the improvement of glycemic control in study groups resulted in the improvement of signs and symptoms belonging to the diabetic foot. The improvement in all the predictors of the diabetic foot started progressing from the first follow-up.

At baseline, the patients without signs and symptoms of the diabetic foot were 48.3% in the control group, which was improved up to 54.5% at the first follow-up. In contrast, in the intervention group, at baseline, this percentage was 42.3%, which was improved up to 53.2% at the first follow-up. Similarly, the improvements were noted in other predictors of the diabetic foot. Still, none of the predictors was found to be significant among both the study groups at the end of the first follow-up.

**Table 1: Demographics and clinical characteristics of patients at baseline**

| Variables             | Frequency (%) |
|-----------------------|---------------|
| Hospital name         |               |
| Hospital A            | 150 (50.2)    |
| Hospital B            | 149 (49.8)    |
| Gender                |               |
| Male                  | 144 (48.2)    |
| Female                | 155 (51.8)    |
| Ethnicity             |               |
| Malay                 | 231 (77.3)    |
| Chinese               | 48 (16.1)     |
| Indian                | 20 (6.7)      |
| Age (mean, SD)        | 60.25±6.31    |
| Gender                |               |
| Male                  | 144 (48.2)    |
| Female                | 155 (51.8)    |
| Ethnicity             |               |
| Malay                 | 231 (77.3)    |
| Chinese               | 48 (16.1)     |
| Indian                | 20 (6.7)      |
| Age (mean, SD)        | 60.25±6.31    |
| Residence status      |               |
| Urban                 | 145 (48.5)    |
| Rural                 | 154 (51.5)    |
| Employment status     |               |
| Unemployed            | 145 (48.5)    |
| Employed              | 154 (51.5)    |
| Educational status    |               |
| No education          | 96 (32.1)     |
| Primary               | 97 (32.4)     |
| Secondary             | 78 (26.1)     |
| College/University    | 28 (9.4)      |
| Type of daily diet    |               |
| Vegetarian            | 159 (52.2)    |
| Nonvegetarian         | 140 (46.8)    |
| Smoking status        |               |
| Yes                   | 53 (17.7)     |
| No                    | 246 (82.3)    |
| Exercise status       |               |
| Yes                   | 78 (26.1)     |
| No                    | 221 (73.9)    |
| Type of antidiabetic therapy |     |
| Oral only             | 116 (38.8)    |
| Insulin               | 129 (43.1)    |
| Oral + insulin        | 54 (18.1)     |

**Table 2: Diabetic complication predictors at baseline (n = 299)**

| Predictors               | Study groups frequency (%) | Univariate analysis |
|--------------------------|----------------------------|---------------------|
| Diabetic Foot            | Control | Intervention | Crude OR (95% CI) | p-value |
| No symptoms              | 69 (48.3) | 66 (42.3)    | Referent          |
| Numbness in the toes     | 22 (15.4) | 29 (18.6)    | 1.378 (0.720–2.637) | 0.333 |
| Ulceration               | 20 (14.0) | 22 (14.1)    | 1.150 (0.575–2.300) | 0.693 |
| Infection                | 17 (11.9) | 19 (12.2)    | 1.168 (0.560–2.440) | 0.679 |
| Ischemic foot            | 15 (10.5) | 20 (12.8)    | 1.394 (0.659–2.950) | 0.385 |

**Assumption:** Simple logistics regression assumed that there must be at least two cases for each category of the dependent
The statistically nonsignificant difference among both the study arms of this study could be due to two possible reasons. First, the preference of the DMTAC pharmacist was to regulate the glycemic level of the patients. Their priorities were not to treat or decrease the progression of diabetic complications. According to various studies, the continuous increase in glycemic levels in patients could result in more damage of other body organs.\textsuperscript{[22-24]} Due to this reason, the diabetic complications did not show any significant differences among both the study groups. The second possible reason could be the recommendations of protocols of the DMTAC program for Malaysia. According to this protocol, the DMTAC pharmacist on initial follow-ups should educate the patients on regulating the blood glucose level and diet modification only. In this way, glycemic control can be achieved.\textsuperscript{[25]}

At the second follow-up, mean HbA1c of the control group patients was decreased by 0.93% from the baseline; whereas in the intervention group, this decrease in HbA1c was 1.59%. As a result of the reduction in HbA1c, the signs and symptoms of the diabetic foot started improving in study arms. In the control group, the patients without any signs and symptoms were 54.5% at the first follow-up, which was improved up to 62.9% at the second follow-up. On the other hand, in the intervention group at the first follow-up, this percentage was 53.2%, which was improved up to 67.3% at the second follow-up. All the changes were noticeable, but they were statistically nonsignificant among both the study groups. These improvements in diabetic foot predictors were perhaps due to the reduction of HbA1c levels in patients. Consistent with other studies, if the HbA1c in diabetic patients decreases consistently, it results in the improvement of diabetic complications in diabetes mellitus.\textsuperscript{[26-29]} In this study, the improvement of glycemic control was more in the intervention group in the presence of diet and lifestyle modification with the help of the pharmacist’s intervention. Alternatively, the improvement of signs and symptoms belonging to the control group was less as compared with the intervention group due to the poor glycemic control in this study arm.

At the third follow-up, the mean HbA1c of the control group of the patients was reduced to 1.53% since baseline data, whereas this mean reduction was around

### Table 3: Diabetic foot predictors at different follow-ups (n = 299)

| Predictors       | Study groups frequency (%) | Univariate analysis | Multivariate analysis |
|------------------|---------------------------|---------------------|----------------------|
|                  | Control | Intervention | Crude OR (95% CI) | p-value | Adjusted OR (95% CI) | p-value |
| No symptoms      | (15.3)  | (24.154)     | 1.187 (0.603–2.335) | 0.619   | -                    | -       |
| Numbness in the toes | (12.6)  | (24.154)     | 0.940 (0.456–1.936) | 0.866   | -                    | -       |
| Ulceration       | (10.5)  | (270.3)      | 1.002 (0.464–2.163) | 0.995   | -                    | -       |
| Infection        | (9.1)   | (270.96)     | 1.084 (0.485–2.424) | 0.844   | -                    | -       |
| Ischemic foot    | (15.3)  | (24.154)     | Referent            | Referent| -                    | -       |
| No symptoms      | (15.3)  | (24.154)     | 0.971 (0.459–2.005) | 0.940   | -                    | -       |
| Numbness in the toes | (12.6)  | (24.154)     | 0.589 (0.260–1.335) | 0.205   | -                    | -       |
| Ulceration       | (8.4)   | (270.64)     | 0.714 (0.295–1.731) | 0.456   | -                    | -       |
| Infection        | (7.0)   | (270.3)      | 1.114 (0.466–2.663) | 0.808   | -                    | -       |
| Ischemic foot    | (7.0)   | (270.3)      | Referent            | Referent| -                    | -       |
| No symptoms      | (17.0)  | (270.64)     | 0.713 (0.292–1.745) | 0.459   | -                    | -       |
| Numbness in the toes | (12.6)  | (24.154)     | 0.392 (0.153–1.008) | 0.052   | 0.185 (0.096–0.963)  | 0.073   |
| Ulceration       | (9.3)   | (270.3)      | 0.349 (0.104–1.165) | 0.087   | 0.185 (0.083–0.938)  | 0.114   |
| Infection        | (8.4)   | (270.64)     | 0.560 (0.173–1.818) | 0.335   | -                    | -       |
| Ischemic foot    | (12.6)  | (24.154)     | 0.342 (0.103–1.139) | 0.081   | 0.216 (0.087–1.072)  | 0.114   |
| No symptoms      | (12.6)  | (24.154)     | 0.321 (0.110–0.937) | 0.038   | 0.182 (0.092–0.579)  | 0.053   |
| Numbness in the toes | (9.3)   | (270.3)      | 0.220 (0.045–1.079) | 0.062   | 0.127 (0.021–0.987)  | 0.068   |
| Ulceration       | (8.4)   | (270.64)     | 0.308 (0.059–1.616) | 0.164   | -                    | -       |

OR = odds ratio, 95% CI = 95% confidence interval
Assumption: Simple logistics regression assumed that there must be at least two cases for each category of the dependent
Inclusion criteria in adjusted OR was >0.09
resulted in improvement in the progression of the diabetic foot. This study shows that the improvement in the signs and symptoms of the diabetic foot was started from “ulceration” and “infection” predictors at the third follow-up. At the third follow-up, the results of univariate and multivariate analysis showed that “ulceration” and “infection” became statistically significant in all diabetic foot signs and symptoms in the pharmacist-led intervention group as compared with the control group. The improvement was maximum at the fourth follow-up of this study in the signs and symptoms of diabetic foot complication. These findings of this study are supported by a retrospective study by Julie Stading et al. [30] which proved the impact of the pharmacist on diabetic foot complication. The cited study was retrospective in nature; in retrospective studies, we only can see the total effect on the outcomes but we cannot predict that this was due to the educational intervention by pharmacists. A better effect in intervention groups could be the difference in the treatment plans that could have given that time to the patients. However, in our study, the effect was due to the educational intervention by the DMTAC pharmacists only, because the only difference in both the study groups of this study was the involvement of pharmacists. In this study, no other difference was present in both the study groups. All medication, laboratory investigations, and the physician involved in the treatment of DM in both the study groups were the same; moreover, the treatment given was also as per the recommendations of the Malaysian guidelines for DM.

Similarly, the findings are supported with two randomized controlled trials by Hae Mi Choe et al. [31] and Porselvi et al. [32] respectively. The randomized controlled trials by Hae Mi Choe and colleagues as well as the one by Porselvi and colleagues were general in nature. They conducted trials on all diabetic complications and reported that the effect of pharmacists on diabetic complications is positive in nature; however, in this study, we reported the specific effect of pharmacists on the diabetic foot, which is a common complication of DM. Further, this study reported that certain predictors of the diabetic foot were improved in the presence of pharmacists during the four follow-ups. This study was not on the general complications but it focuses on the diabetic foot particularly, which was not covered in the randomized controlled trials by Hae Mi Choe and colleagues as well as the one by Porselvi and colleagues.

**Conclusion**

Pharmacist-led educational intervention has a positive impact on the progression of diabetic complications. The signs and symptoms of the diabetic foot were 2.61% in the intervention group since baseline. In predictors of the diabetic foot, noticeable improvement changes among both the study arms in “ulceration” \((P = 0.052)\) and “infection” \((P = 0.087)\) predictors were observed in univariate analysis. However, a statistically nonsignificant difference was observed in other predictors of the diabetic foot among both the study arms at the third follow-up. This noticeable improvement in the predictors of the diabetic foot in both the study arms could be due to the significant reduction in the glycemic levels of the patients. Various studies reported that the reduction in glycemic levels in diabetic patients results in the improvement of diabetic complications. The reduction in the HbA1c level was higher in the intervention group with the presence of diet and lifestyle modification compared with the control group, and this indicated the improved treatment outcomes with pharmacist intervention in this study. This outcome could also be due to the recommendations of the DMTAC protocol that was provided by the Ministry of Health Malaysia. According to this protocol, when the patients are in the fourth module of DMTAC, then the pharmacist expands on all the diabetic complications to the patients. [24] The pharmacist explains to patients in the DMTAC about the precautions, diet, and particular recommendations for diabetic complications and their management. At the third follow-up, the patients would have already gone through the fourth module of DMTAC; thus, the patients were already aware of the lifestyle and diet modifications as well as the pros and cons for diabetic complications.

At the fourth follow-up, in diabetic foot predictors, statistically significant improvement changes were observed between both the study arms in “ulceration” \((P = 0.038)\). However, statistically nonsignificant differences were observed in other symptoms of diabetic foot complications in both the study groups. The results of this study showed that the pharmacist intervention resulted in improvement in the progression of the diabetic foot.
significantly improved in the intervention group as compared with the control group. Further studies on all diabetic complications should be initiated throughout the country to observe the effect of pharmacists on all diabetic complications in the country.

Limitations of the study
There are some limitations accompanying this study. This study was conducted in two major hospitals in Kedah state of Malaysia; the findings cannot be generalized to the whole of Malaysia. Some discrepancies can be anticipated from different states of the country.

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Conflicts of interest
There are no conflicts of interest.

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