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Initiation of the pharmacist-delivered antidiabetic medication therapy management services in a tertiary care hospital in Nepal

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Abstract

The medication therapy management (MTM) pharmacists follow the philosophy of pharmaceutical care to address individualistic medication therapy requirements in their practice settings.

The present study aimed to introduce the pharmacist-delivered MTM services among type 2 diabetes mellitus patients at a tertiary care hospital in Nepal.

Cross-sectional study was conducted at Patan Hospital, Lalitpur, Nepal, among 200 patients with type 2 diabetes mellitus from July to December 2019. The intervention included maintenance of medication profile for individual patients, and then MTM service was proposed based on 5 core elements of MTM services proposed by the American Pharmacists Association. Both antidiabetic and non-antidiabetic medicines were coded as per the anatomic, therapeutic, and chemical classification and defined daily dose assignment 2020 for documentation. The Charlson Comorbidity Index was used to index comorbidities. The drug interaction profile was checked with the Medscape Drug Interaction Checker.

Both fasting and postprandial blood sugar levels were significantly associated with age (*P*-values <.000 for both), baseline symptom (*P*-values .012 and .003 respectively), and diet plan proposed (*P*-values .049 and .011 respectively). Maximum cases of drug interactions requiring close monitoring were between metformin and insulin regular (i.e., 11, 5.5%).

This was a novel initiative of the MTM services in a resource constraint country like Nepal and can show a clue for the pharmacists targeting such services in other similar settings.

Abbreviations: CCI = Charlson Comorbidity Index, FBG = fasting blood glucose, HCCs = health care costs, MTM = medication therapy management, OHAs = oral hypoglycemic agents, PBG = postprandial blood glucose, T2DM = type 2 diabetes mellitus.

Keywords: antidiabetic medications, Charlson Comorbidity Index, medication therapy management, medication-related problems, type 2 diabetes mellitus

1. Introduction

Type 2 diabetes mellitus (T2DM) is one of the serious public health problems worldwide, leading to health complications such as nephropathy, neuropathy, retinopathy, atherosclerotic cardiovascular disease, and economic burden, if not appropriately managed.[1] Globally, USD 471 billion was spent on managing diabetes mellitus in 2012 alone.[2] The worldwide prevalence of diabetes for all age groups has been estimated to rise to 4.4% in

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2030 from 2.8% in 2000.[3] Globally, T2DM took lives of 171 million in 2000 and is expected for 366 million deaths in 2030, and >642 million by 2040, mainly from kidney failure and it has also raised healthcare costs (HCCs) by 5% to 15%.[3,4] Providing high-quality care for diabetics is still challenging for healthcare systems worldwide despite advances in technology and medical care.[5]

Medication therapy management (MTM) has been introduced by the American Pharmacists Association as the service(s) to optimize therapeutic outcomes for the patients to prevent or resolve medication-related problems and to provide health and wellness education to the patients.[1,6] Pharmacists were recognized as the MTM service providers in January 2006, 2 years after its proposed definition.[7] The MTM pharmacists follow the philosophy of pharmaceutical care, and provide relevant services at a clinic in a confidential environment and assess individualistic medication therapy requirements in context-specific patterns.[8] Their involvement in the MTM services may reduce adverse reactions and unnecessary HCCs, optimize pharmacotherapy and adherence plans, and ultimately improve patients' therapeutic outcomes.[9]

The Asheville Project[10] and the Diabetes Ten City Challenge[11] reported that patients with diabetes who were receiving community pharmacists' care had reductions of USD 1200[10] and USD 1079,[11] respectively in their mean total direct medical costs per patient per year and also achieved desired clinical outcomes in terms of HbA1c over a 5-year follow-up period.[10,11] In addition, community pharmacists who provided diabetes care service in the former project received positive responses of their involvement in the care team by the community people.[12]

Health care delivery process is 3-tier in Nepal with primary health care centers and health posts; district hospitals as the secondary service centers; and tertiary hospitals being specialized service delivery points. However, bed capacities, skilled human resources (e.g., physicians, nurses, pharmacists, and other health professionals), health budgets, equipment and diagnostic facilities (e.g., laboratory and radiologic), and others are not optimum. Also, there is no full-fledged health insurance system in the country (except insurance of a maximum of 0.1 million Nepalese rupees [i.e., about USD 885] per year for a family of up to 5 members). Since such a miniature insurance provision does not cover all the diseases and HCCs of the patients, they are forced to spend out-of-pocket. Hence, chronic diseases like diabetes, hypertension, hyperlipidemia, cancer, and many others have been aggravating the economic conditions of the patients owing to their vicious circle. Moreover, the pharmacist-delivered MTM services are still new in Nepal for any diseases, including T2DM because hospital or community pharmacists are still busy assuming the traditional dispensing and inventory management roles in the country. They are still struggling for their appropriate placements in the policy and real practice settings. Hence, the present study was aimed to initiate the MTM services for patients with T2DM at a tertiary care hospital in Nepal to minimize the potential unwanted drug interactions and adverse effects with their anti-diabetic medications.

2. Methods

2.1. Study design and site

The hospital-based cross-sectional study was conducted among 200 patients with T2DM taking anti-diabetic medications at Patan Hospital, Lalitpur, one of the tertiary care hospitals providing super-speciality services in Nepal, from July to December 2019. The hospital has been providing general and specialized patient care and treatment to 320,000 outpatients and 20,000 inpatients per year.

2.2. Ethics approval and consent to participate

Administrative approval to conduct the research was received from the Administration of Patan Academy of Health Sciences, the parent organization governing the hospital, and the ethics approval was obtained from Nobel College Institutional Review Committee (NIRC), Sinamangal, Kathmandu (NIRC: BPY IRC 216/2019).

2.3. Study participants and public involvement

The patients were involved from the data collection stage but were subject to no invasive interventions. Data collection sheets were disseminated to the patients with the details of the research objectives and they were requested to fill out the consent form prior to data collection. Their privacy and confidentiality were maintained throughout the research period and they were informed about the outcome measures. Patients were involved in the study to retrieve their MTM issues on antidiabetic medications, but the researchers followed up with no patients. However, they were followed up by the prescribing physicians every 6 months as per their scheduled treatment plans. Results were disseminated to the participants via reports submitted to the study site, hoping they would be informed on their regular follow-up.

2.4. Sampling technique and sample size

Simple random sampling was followed for data collection using the Cochran's formula for calculating the population proportion with the specified absolute precision:

$$\frac{z_2 \mathrm{p}(1-\mathrm{p})}{\mathrm{d}^2}$$

where, $z = 1.96$ (standard normal variate); $p = 0.05$ (expected portion in population); $d = 0.03$ (absolute error or precision).

Thus, 200 patients with T2DM, who were on antidiabetic therapy, were recruited for the study.

2.5. Inclusion and exclusion criteria

Patients who were taking antidiabetic medications newly or since the last 6 months of the study were included, and those who were not willing to participate were excluded from the study. First, the medication profile was maintained for the individual patient with T2DM, the MTM services proposed for them were discussed with the prescriber.

2.6. Medication therapy management approach

The MTM model was adopted as below:

- First, patients' medication profiles for all the prescribed medications, including over the counter ones were collected from their prescriptions.
- Patients' detailed laboratory test results (mainly fasting blood glucose [FBG] and postprandial blood glucose [PBG] levels, and sodium, potassium, calcium levels) along with the comorbidities were documented.

- Each medication was assessed for its appropriateness, effectiveness, and safety (including drug interactions and adverse drug reactions) based on the guidance of the British National Formulary 80.[13]
- The patients perceived MRPs based on symptoms were consulted with them. Then, pharmaceutical care plan was developed for an individual patient to achieve optimal therapeutic outcomes, and the plan was discussed with them and the ultimate report with the prescriber later on.

2.7. Research instrument, reliability and validity, and data collection

The MTM-related data were collected on the format proposed by Doe[14] to incorporate the following 5 core elements of the MTM services, as proposed by the American Pharmacists Association and National Association of Chain Drug Stores Foundation,[15] which were further agreed upon by other evidence as well.[6]

i. Medication therapy review;
ii. Personal medication record;
iii. Medication-related action plan;
iv. Intervention and/or referral;
v. Documentation and follow-up.

Comorbidities of the patients were coded as per the International Statistical Classification of Diseases and Related Health Problems-11 coding system.[16] Both antidiabetic and non-antidiabetic medicines were coded as per the WHO Guidelines for anatomic, therapeutic, and chemical classification and defined daily dose assignment 2020.[17] The Charlson Comorbidity index (CCI), computed from the CCI online calculator, was used to index the comorbidities and explore the 10-year survival percentage.[18] Drug interaction profile was later checked with the Medscape Drug Interaction Checker,[19] and the report was discussed later with the physicians where the study was conducted.

2.8. Statistical analysis

Data were entered into and analyzed with the statistical package for the social sciences (SPSS) software version 26 (International Business Machine (IBM), New York, USA) and were analyzed with the R programming version 4.0.3, (R Foundation for Statistical Computing, Vienna, Austria)[20] considering a confidence interval of 95% as statistically significant. Chi-square test was applied to test for the association between the categorical variables (e.g., age, gender, symptoms experienced by the patients, and diet plan suggested for them), and their respective strength of association was measured with the Cramer V. Degree of association with the Cramer V was interpreted based on the guidelines by Akoglu.[21]

3. Results

The raised FBG level (i.e., >110 mg/dL) and raised PBG level (i.e., >153 mg/dL) were found among 64 (32%) and 60 (30%) patients aged 50 to 59 years, 86 (43%) and 81 (40.5%) men, and 39 (19.5%) and 40 (20%) patients who were experiencing increased thirst and frequent urination, respectively. Both FBG and PBG levels were significantly associated with age (*P*-values <.001 for both), baseline symptoms (*P*-values .012 and .003, respectively), and diet plans proposed (*P*-values .049 and .011, respectively). The values of effect sizes (i.e., Cramer V) indicated that both FBG and PBG levels had very strong strength of association with symptoms (Cramer V 0.388 and 0.409, respectively) and diet plans (Cramer V 0.269 and 0.294, respectively). In contrast, they had a weak and moderate association with their age (Cramer V 0.096 and 0.119, respectively) (Table 1).

There were 70 (35%) cases of metformin 500 mg tablet use, followed by 66 (33%) insulin injection 30/70 (i.e., insulin injection 30 units/mL and insulin isophane suspension 70 units/mL). Therapeutic category-wise, biguanides were prescribed in 134 (67%) patients (Table 2). Maximum cases of drug interactions requiring close monitoring were between metformin and insulin regular (11, i.e., 5.5%) and between amlodipine and metformin (10, i.e., 5%) (Table 3).

There were 83 (41.5%) patients with hypertension. The CCI of 0 and 1 were maximum among 61 (30.5%) and 60 (30%) patients, respectively. Estimated 10-year survival of 98% and 96% were seen among 61 (30.5%) and 60 (30%) patients, respectively (Supplemental Digital Content [Annex 1], http://links.lww.com/MD/G679). Pantoprazole tablet 40 mg and atorvastatin tablet 10 mg were the most commonly used non-antidiabetic medications which were consumed by the study patients 30 (15%) and 17 (8.5%) times, respectively (Supplemental Digital Content [Annex 2], http://links.lww.com/MD/G680). Maximum patients (99, i.e., 49.5%) had monotherapy (i.e., only one antidiabetic medicine) during the study period (Supplemental Digital Content [Annex 3], http://links.lww.com/MD/G681).

4. Discussion

Based on the extensive literature reviews, the present study was the leading research of its kind in a resource constraint country Nepal. The study showed that the raised FBG and PBG levels were found among 64 (32%) and 60 (30%) patients, respectively, who were aged 50 to 59 years. The age distribution was nearly similar to those reported by various studies, such as 61.3 years in the MTM group,[5] and 67.8 years in the MTM cohort.[22] However, other researchers also reported a wide age range of 22 to 92 years (mean age of 49 years) in the intervention group.[23] Different researches reported differently in case of gender-wise distribution such as men (30, i.e., 55.5%) in the MTM group,[5] and female (48, i.e., 59.3%) in the MTM cohort.[22] Such diversity in the demographics among patients with T2DM might be one of the beauties of epidemiological research owing to the population diversity. Moreover, both FBG and PBG levels were significantly associated with age (*P*-values <.001 for both), as predicted with ageing. This also supported that the risks of T2DM increase with age, obesity, and sedentary lifestyle[24] because obesity alone may increase the risks of hypertension, diabetes, dyslipidemia, cardiovascular diseases, cancer, and musculoskeletal pains.[25]

Another study also reported different comorbidity profiles among the patients with T2DM—85 (91%) with dyslipidemia and 72 (77%) hypertensive in the intervention group,[26] which were similar to hypertensive cases in the present research (83, i.e., 41.5%), and only 3 (1.5%) patients had hyperlipidemia. Similar comorbidity patterns indicate that hypertension may be one of the serious concerns among patients with T2DM almost everywhere. The CCI of 0 and 1 were maximum among 61 (30.5%) and 60 (30%) patients, respectively, but CCI was ≥2 among 49 (54.4%) patients in another research.[9] Patients with

Table 1

Association of fasting and postprandial blood sugar with demographic characteristics of the study population (n = 200).

Variables	Fasting blood sugar, (mg/dL) (mean ± SD: 117.58 ± 74.18)				χ^2; *P*-value, and [Cramer V]	Postprandial blood sugar (mg/dL) (mean ± SD: 180.08 ± 103.95)				χ^2; *P* value and [Cramer V]
	Not taken	70–110	>110	Total		<110	110–153	>153	Total	
Age (in yrs) (mean ± SD: 51.25 ± 11.86)										
<=19	1 (0.5)	0	0	1 (0.5)	χ^2 (14) = 56.59; <.000	1 (0.5)	0	0	1 (0.5)	χ^2 (14) = 38.25; <.000
20–29	5 (2.5)	0	1 (0.5)	6 (3)		4 (2)	1 (0.5)	1 (0.5)	6 (3)	
30–39	8 (4)	1 (0.5)	9 (4.5)	18 (9)		8 (4)	1 (0.5)	9 (4.5)	18 (9)	
40–49	4 (2)	4 (2)	53 (26.5)	61 (30.5)		5 (2.5)	5 (2.5)	51 (25.5)	61 (30.5)	
50–59	6 (3)	2 (1)	64 (32)	72 (36)		6 (3)	6 (3)	60 (30)	72 (36)	
60–69	5 (2.5)	3 (1.5)	16 (8)	24 (12)		5 (2.5)	1 (0.5)	18 (9)	24 (12)	
70–79	5 (2.5)	4 (2)	8 (4)	17 (8.5)		4 (2)	3 (1.5)	10 (5)	17 (8.5)	
80+	0	0	1 (0.5)	1 (0.5)		0	0	1 (0.5)	1 (0.5)	
Sex										
Male	15 (7.5)	7 (3.5)	86 (43)	108 (54)	χ^2 (2) = 1.83; .400 [0.096, weak]	15 (7.5)	12 (6)	81 (40.5)	108 (54)	χ^2 (2) = 2.85; .240 [0.119, moderate]
Female	19 (9.5)	7 (3.5)	66 (33)	92 (46)		18 (9)	5 (2.5)	69 (34.5)	92 (46)	
Symptoms experienced										
None experienced	3 (1.5)	1 (0.5)	0	4 (2)	χ^2 (38) = 60.28; .012 [0.388, very strong]	3 (1.5)	0	1 (0.5)	4 (2)	χ^2 (38) = 66.99; .003 [0.409, very strong]
Sweating, dizziness	4 (2)	2 (1)	8 (4)	14 (7)		4 (2)	4 (2)	6 (3)	14 (7)	
Increased thirst, frequent urination	8 (4)	2 (1)	39 (19.5)	49 (24.5)		8 (4)	1 (0.5)	40 (20)	49 (24.5)	
Knee pain	1 (0.5)	1 (0.5)	2 (1)	4 (2)		0	0	4 (2)	4 (2)	
Irritability, nausea	1 (0.5)	0	6 (3)	7 (3.5)		1 (0.5)	1 (0.5)	5 (2.5)	7 (3.5)	
Abdominal pain, dizziness	6 (3)	3 (1.5)	11 (5.5)	20 (10)		6 (3)	6 (3)	8 (4)	20 (10)	
Paresthesia in hands and feet	2 (1)	0	8 (4)	10 (5)		2 (1)	1 (0.5)	7 (3.5)	10 (5)	
COPD, cough	2 (1)	0	4 (2)	6 (3)		2 (1)	1 (0.5)	3 (1.5)	6 (3)	
Slow healing wounds	0	0	5 (2.5)	5 (2.5)		0	0	5 (2.5)	5 (2.5)	
Hunger, blurred vision	1 (0.5)	0	12 (6)	13 (6.5)		1 (0.5)	1 (0.5)	11 (5.5)	13 (6.5)	
Ketonuria	1 (0.5)	1 (0.5)	0	2 (1)		1 (0.5)	0	1 (0.5)	2 (1)	
Glycosuria, weakness	0	0	1 (0.5)	1 (0.5)		0	0	1 (0.5)	1 (0.5)	
Bleeding, infection	2 (1)	0	1 (0.5)	3 (1.5)		2 (1)	0	1 (0.5)	3 (1.5)	
Weakness, anxiety, headache	2 (1)	2 (1)	4 (2)	8 (4)		2 (1)	1 (0.5)	5 (2.5)	8 (4)	
Weight loss	1 (0.5)	1 (0.5)	10 (5)	12 (6)		1 (0.5)	0	11 (5.5)	12 (6)	
Tiredness	0	1 (0.5)	28 (14)	29 (14.5)		0	1 (0.5)	28 (14)	29 (14.5)	
Anorexia	0	0	1 (0.5)	1 (0.5)		0	0	1 (0.5)	1 (0.5)	
Sexual disorder	0	0	4 (2)	4 (2)		0	0	4 (2)	4 (2)	
Body pain	0	0	6 (3)	6 (3)		0	0	6 (3)	6 (3)	
Loose stool	0	0	2 (1)	2 (1)		0	0	2 (1)	2 (1)	
Diet plan										
Low caloric drinks	7 (3.5)	5 (2.5)	31 (15.5)	43 (21.5)	χ^2 (18) = 28.93; .049 [0.269, very strong]	6 (3)	5 (2.5)	32 (16)	43 (21.5)	χ^2 (18) = 34.55; .011 [0.294, very strong]
Raw, cooked or roasted vegetables	5 (2.5)	1 (0.5)	12 (6)	18 (9)		5 (2.5)	4 (2)	9 (4.5)	18 (9)	
Normal diet	15 (7.5)	3 (1.5)	22 (11)	40 (20)		15 (7.5)	2 (1)	23 (11.5)	40 (20)	
Salad, spinach	2 (1)	2 (1)	30 (15)	34 (17)		2 (1)	1 (0.5)	31 (15.5)	34 (17)	
Fruits	1 (0.5)	2 (1)	31 (15.5)	34 (17)		1 (0.5)	2 (1)	31 (15.5)	34 (17)	
Low fat dairy, lean meat	2 (1)	0	15 (7.5)	17 (8.5)		2 (1)	2 (1)	13 (6.5)	17 (8.5)	
High potassium containing foods	1 (0.5)	0	1 (0.5)	2 (1)		1 (0.5)	0	1 (0.5)	2 (1)	
Lemon tea, green tea	0	0	3 (1.5)	3 (1.5)		0	0	3 (1.5)	3 (1.5)	
Fiber containing diet	1 (0.5)	1 (0.5)	5 (2.5)	7 (3.5)		1 (0.5)	1 (0.5)	5 (2.5)	7 (3.5)	
High protein diet	0	0	2 (1)	2 (1)		0	0	2 (1)	2 (1)	

diabetes are susceptible to other comorbidities such as hypertension, stroke and, end-stage renal disease, compromized immunity, all leading to poor prognosis with their supra-additive effects on macro- and microvasculature.[27] However, in the present study, no severe macrovascular and microvascular complications were reported in the patients' prescriptions, and these were also confirmed by communicating with them. Nevertheless, other studies reported serious complications among the patients with

Table 2

Antidiabetic medicines usage by the patients.

Medications	Therapeutic category	ATC classification*	Frequency (%)
Insulin injection 30/70	Hypoglycemic polypeptides (69, 34.5%)	A10AB01	66 (33)
Insulin glargine		A10AE04	2 (1)
Insulin lispro		A10AB04	1 (0.5)
Metformin tablet 500 mg	Biguanides (134, 67%)	A10BA02	70 (35)
Metformin tablet 850 mg			24 (12)
Metformin tablet 1 g			40 (20)
Glimepiride tablet 1 mg	Sulfonylureas (16, 8%)	A10BB12	13 (6.5)
Gliclazide tablet 30 mg		A10BB09	2 (1)
Gliclazide tablet 60 mg			1 (0.5)
Linagliptin tablet 5 mg	DPP-4 inhibitors	A10BH05	1 (0.5)
Acarbose tablet 50 mg	α-Glucosidase inhibitors (2, 1%)	A10BF01	1 (0.5)
Total			221 (110.5)

DPP = Dipeptidyl peptIdase-4.
* WHO Guidelines for ATC classification and DDD assignment 2020 (WHO, 2019).

T2DM such as retinopathy, neuropathy, and nephropathy among 14 (25.9%), 13 (24.1%), and 15 (27.8%) patients in the MTM group,[5] retinopathy, nephropathy or albuminuria, and neuropathy among 14 (15%), 12 (13%), and 26 (28%) patients in the intervention group.[26]

There were 70 (35%) cases of metformin tablet 500 mg use, followed by 66 (33%) insulin injection 30/70 uses. Another study also had similar patterns of medications such as metformin, metformin with glibenclamide and insulin among 22 (40.8%), 26 (48.1%), and 6 (11.1%) patients, respectively in the MTM group.[5] Therapeutic category-wise, biguanides were prescribed in 134 (67%). Insulin was prescribed in 69 (34.5%), which was partially similar to other researches—biguanides and sulfonylureas were prescribed in 29 (31%) and 6 (7%) patients, respectively in the intervention group,[26] Neutral Protamine Hagedorn insulin, glibenclamide with metformin, and metformin were prescribed among 102 (47.2%), 62 (28.7%), and 31 (14.4%) patients, respectively.[28] Diabetes requires long-term medical care with mixed modalities (such as lifestyle adjustments, nutrition therapy, dietary modifications, oral hypoglycemic agents [OHAs], and insulin), and patient empowerment for self-assessment and management of hyperglycemia and medications-induced subsequent hypoglycemic attacks.[1,2] A study reported that >25% of the patients with diabetes use insulin therapy, irrespective of diabetes, despite unsatisfactory effectiveness. The effectiveness of insulin therapy can be improved with regular titrations to overcome intra- and inter-individual variations. However, insulin dosages are rarely adjusted during outpatient clinic visits due to time constraints to both the health care providers and the patients and the lack of medical expertise among the providers.[26]

Maximum cases of drug interactions requiring close monitoring were reported between metformin and insulin regular (11, i.e., 5.5%) and between amlodipine and metformin (10, i.e., 5%). Other studies reported different MRPs such as non-adherence and the need for additional medication therapy among 124 (28.1%), 96 (21.8%) patients, with 441 MRPs, requiring interventions by the prescribers in 252 cases.[9]

Total, 31 (15.5%) and 32 (16%) patients were on the recommended low caloric drinks with the raised FBG and PBG levels. Patel et al[29] found diet control effective among 103 (17%) patients, but 219 (35%) patients required medications, excluding diet control. Hence, T2DM management requires mixed approaches such as screening, medications, regular monitoring of blood glucose, and follow up. The pharmacist-delivered MTM services usually improve adherence and reduce hospitalizations in the case of T2DM.[5]

Previously, 7 studies were found on PubMed search till February 24, 2022, conducted among Nepalese people with diabetes and were related to the topic area of the present research, but only 2 reported anti-diabetic medications. Still, these studies focused on adherence, clinical outcomes, and patients' adherence to medication therapy. For instance, Shrestha et al[30] reported that most patients started discontinuing OHAs after the first 6 months of its initiation and became completely non-adherent after 5 years of its initiation. The prime reason for discontinuing and non-adhering to the therapy among 24% out of 100 study patients was their perceived hypoglycemic attack; however, only 16 patients had an intended concept on hypoglycemic effects of OHAs.

The urban prevalence of ~15% among people over 20 years of age and 19% among people over 40 years of age depicts the serious public health implications of diabetes in Nepal. Still, patients who were prescribed antidiabetic medications were found to have biased perceptions as they perceived that these were harmful and hence, were reluctant to initiate these immediately as suggested by the physicians.[31] Hence, the pharmacists-delivered antidiabetic therapy management services would have assisted the physicians in optimizing their medication therapy.

5. Future prospects

In the future, such MTM services might be expanded to target the adverse events mitigation and management; drug interaction management and switching to non-interacting ones in case the interactions were clinically serious; dosage optimization as per the disease states; antidiabetic medication adherence; and pharmacoeconomic evaluation of the antidiabetic medications in collaboration with the practicing pharmacists at the hospital.

5.1. Strengths and limitations

The findings of the present study would sensitize the hospital policymakers on the necessity of the pharmacists delivered MTM services despite resource constraints. The research was probably the first of its type in Nepal to initiate the MTM

Table 3

Drug interaction profile*.

Medicine1–Medicine2 interactions	Interaction report	Number of patients (prescriptions) (n, %)	
		Minor	Monitor closely
Amlodipine—metformin	Amlodipine decreases effects of metformin by pharmacodynamic antagonism.	–	10 (5)
Aspirin—furosemide	Aspirin increases and furosemide decreases serum potassium.	–	1 (0.5)
Aspirin—insulin glargine	Aspirin increases effects of insulin glargine by pharmacodynamic synergism.	–	1 (0.5)
Aspirin—insulin lispro	Aspirin increases effects of insulin lispro by pharmacodynamic synergism.	–	1 (0.5)
Aspirin—insulin regular	Aspirin increases effects of insulin regular by pharmacodynamic synergism.	–	7 (3.5)
Aspirin—metoprolol	Aspirin decreases effects of metoprolol by pharmacodynamic antagonism.	–	1 (0.5)
Aspirin—prazosin	Aspirin decreases effects of prazosin by pharmacodynamic antagonism.	–	1 (0.5)
Aspirin—spironolactone	Aspirin decreases effects of spironolactone.	–	1 (0.5)
Aspirin—torsemide	Aspirin increases and torsemide decreases serum potassium.	–	1 (0.5)
Calcium carbonate—amlodipine	Calcium carbonate decreases effects of amlodipine by pharmacodynamic antagonism.	–	4 (2)
Calcium carbonate—aspirin	Passive renal tubular reabsorption due to increased pH.	2 (1)	–
Calcium carbonate—ciprofloxacin	Calcium carbonate decreases effects of ciprofloxacin by inhibition of GI absorption.	–	1 (0.5)
Carbamazepine—amlodipine	Carbamazepine will decrease the level or effect of amlodipine by affecting hepatic/intestinal enzyme CYP3A4 metabolism.	–	1 (0.5)
Carbamazepine—losartan	Carbamazepine decreases level or effect of losartan by affecting hepatic enzyme CYP2C9/10 metabolism.	–	1 (0.5)
Ciprofloxacin—insulin regular	Ciprofloxacin increases effects of insulin regular by pharmacodynamic synergism.	–	2 (1)
Ciprofloxacin—thiamine	Ciprofloxacin will decrease the level or effect of thiamine by altering intestinal flora.	1 (0.5)	–
Enalapril—furosemide	Pharmacodynamic synergism.	–	1 (0.5)
Enalapril—glimepiride	Enalapril increases effects of glimepiride by pharmacodynamic synergism.	–	1 (0.5)
Enalapril—insulin regular	Enalapril increases effects of insulin regular by pharmacodynamic synergism.	–	2 (1)
Enalapril—metformin	Enalapril increases toxicity of metformin.	–	2 (1)
Enalapril—spironolactone	Pharmacodynamic synergism.	–	1 (0.5)
Fenofibrate—insulin regular	Fenofibrate increases effects of insulin regular.	–	1 (0.5)
Furosemide—metformin	Furosemide increases levels of metformin.	1 (0.5)	–
Levofloxacin—insulin regular	Levofloxacin increases effects of insulin regular by pharmacodynamic synergism.	–	1 (0.5)
Levofloxacin—metformin	Levofloxacin increases effects of metformin by pharmacodynamic synergism.	–	2 (1)
Losartan—insulin regular	Losartan increases effects of insulin regular.	–	6 (3)
Metformin—cyanocobalamin	Metformin decreases levels of cyanocobalamin.	1 (0.5)	–
Metformin—folic acid	Metformin decreases levels of folic acid.	1 (0.5)	–
Metformin—insulin regular	Either increases effects of the other by pharmacodynamic synergism.	–	11 (5.5)
Metoprolol—aspirin	Metoprolol and aspirin both increase serum potassium.	–	1 (0.5)
Metoprolol—furosemide	Metoprolol increases and furosemide decreases serum potassium. Effect of interaction is not clear, use caution.	–	1 (0.5)
Metoprolol—spironolactone	Metoprolol and spironolactone both increase serum potassium.	–	1 (0.5)
Metronidazole—tamsulosin	Metronidazole increases levels of tamsulosin by affecting hepatic/intestinal enzyme CYP3A4 metabolism.	-	1 (0.5)
Ofloxacin—metformin	Ofloxacin increases effects of metformin by pharmacodynamic synergism.	1 (0.5)	1 (0.5)
Omega 3 fatty acids—heparin	Potential increased risk of bleeding.	–	1 (0.5)
Ondansetron—metformin	Ondansetron increases levels of metformin.	–	1 (0.5)
Pantoprazole—cyanocobalamin	Pantoprazole decreases levels of cyanocobalamin by inhibition of GI absorption.	1 (0.5)	–
Prazosin—amlodipine	Prazosin and amlodipine both increase anti-hypertensive channel blocking.	–	1 (0.5)
Spironolactone—aspirin	Spironolactone and aspirin both increase serum potassium.	–	1 (0.5)
Spironolactone—furosemide	Spironolactone increases and furosemide decreases serum potassium.	–	2 (1)
Sulfamethoxazole—glimepiride	Sulfamethoxazole increases levels of glimepiride by plasma protein binding competition.	–	1 (0.5)
Sulfamethoxazole—metformin	Sulfamethoxazole increases level or effect of metformin by basic (cationic) drug competition for renal tubular clearance.	1 (0.5)	–
Telmisartan—ketorolac	Either increases toxicity of the other.	–	1 (0.5)
Torsemide—calcium carbonate	Torsemide decreases levels of calcium carbonate by increasing renal clearance.	1 (0.5)	–
Trimethoprim—metformin	Trimethoprim increases levels of metformin.	–	1 (0.5)

GI = gastrointestinal.

* All drug interaction profile was later checked with the Medscape Drug Interaction Checker.

services among patients with T2DM. However, since the sustainability of the MTM services is still challenging in resource-constrained settings due to budgetary limitations, more generalizations with large-scale cohort studies are warranted in the future.

6. Conclusion

The present study was a novel initiative of the medication therapy management services in a resource constraint country Nepal, and it can show a clue for pharmacists targeting such services in other similar settings. Furthermore, this initiative helped explore and manage medication-related problems such as drug interactions among patients taking antidiabetics and other medications to promote patients' safety, ensuring appropriate medicines and regimens.

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Binaya Sapkota conceptualized and designed the study, performed a literature review, analyzed and interpreted data, and prepared the final manuscript. Priyanka Bokati, Salina Dangal, and Pooja Aryal designed the study, performed literature review, did necessary fieldwork including data collection, performed literature review, drafted and revised the manuscript. Sunil Shrestha critically reviewed the manuscript. All authors read and approved the final manuscript.

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