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Posted Date: 6 August 2024

doi: 10.20944/preprints202408.0382.v1

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Article

Assessment of the Impact of Medication Regimen Complexity on Medication Adherence and Glycemic Control in Management of Type-2 Diabetes

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Abstract: Background and Aim: Patients with Type 2-diabetes condition tend to have multiple medications in various dosage which leads to complex medication regimens. Complexity of regimen results in poor adherence, uncontrolled glycemic value and treatment failure. The research aimed to investigate medication regimen complexity index, medication adherence, and impact of medication regimen complexity on glycemic control and medication adherence. **Materials and Methods:** A Crossectional Study methods was conducted at Bheri Hospital Nepalgunj, among 145 Diabetes patients. Medication adherence was assessed by using a General Medication Adherence Scale (GMAS Nep-Tool). Medication regimen complexity was assessed by using a Medication Regimen Complexity Index (MRCI) tool. Chi-square test, One-way ANOVA, Paired t-test, and binary logistic regression were used for inferential statistics. **Results:** This study shows that most of the participants were female and aged group 50-59 years. Hypertension was the most common comorbidity, followed by hypothyroidism. The majority of participants exhibited partial adherence 90 (62.1%) to their medication regimen. It was seen that medications prescribed for diabetes were more complex than non-diabetes medications (Mean±SD MRCI: 8.28±3.155 vs. 4.57±2.107). The negative correlation was seen with diabetes MRCI and medication adherence (r=-0.090). There was statistically significant association between diabetes MRCI and glycemic control, ($p<0.05$). Binary logistic regression revealed that females had lower odds of high MRCI compared to males (multivariate p-value: 0.014, AOR: 0.403, 95% CI: 0.195-0.832), while sedentary lifestyle showed high Diabetes MRCI (COR: 4.709, 95% CI: 0.962-23.05) and abnormal BMI were associated with higher MRCI (binary p-value: 0.067, COR: 2.30, 95% CI: 0.942-5.65; multivariate p-value: 0.092, AOR: 2.323, 95% CI: 0.878-5.67). **Conclusion:** Diabetes medications are more complex, reducing adherence and worsening A1C outcomes. Simplifying regimens improves results, with MRCI being valuable for healthcare providers. The medication adherence and therapeutic outcomes can be improved by the improved by the involvement of clinical pharmacist using MRCI.

Keywords: diabetes; glycemic control; medication adherence; medication regimen complexity

Introduction

Diabetes is a chronic condition characterized by inadequate insulin production or inefficient insulin usage, resulting in hyperglycemia that destroys blood vessels and neurons [1].

The global growth of type 2 diabetes (T2DM) complicates therapy by requiring complex medication regimens that challenge patient adherence. This rise, spurred by urbanization, aging, inactivity, and obesity, results in high death rates from linked illnesses such ischemic heart disease and stroke, particularly in low- and middle-income countries [2,3]

In Nepal, diabetes affects 15% of urban individuals over the age of 20 and 19% over the age of 40, with many people being ignorant of their illness. Poor medication adherence results in suboptimal glycemic control in T2DM, which contributes to higher morbidity, mortality, and healthcare expenditures [4]. Despite treatment choices, barely half attain HbA1c levels below 7% [5].

 doi:10.20944/preprints202408.0382.v1

Adherence is influenced by socioeconomic level, age, gender, race, health literacy, pharmacy convenience, and regimen complexity [5]. The Medication Regimen Complexity Index (MRCI) assesses regimen complexity based on dose forms, dosing frequency, and supplementary directions, which influences adherence and results [6]. Collaboration between pharmacists and healthcare professionals can simplify regimens, improving adherence and clinical results [4].

Complex medication regimens are considered as predictive of Poor adherence results in increased morbidity, mortality, hospitalizations, healthcare expenses, waste of medication and reduced quality of life [7]. Studies regarding treatment practices and medication adherence are limited in Nepal. Likewise, and the impact of medication regimen complexity on medication adherence is largely unexplored. The study aims to bridge existing research gaps, specifically in the context of Nepal, providing nuanced insights into treatment practices, medication adherence, and the impact of medication regimen complexity on diabetes outcomes. The findings of this study will help healthcare professionals, policymakers, and researchers create targeted interventions and strategies to improve treatment outcomes and adherence among patients, as well as reduce the burden associated with this condition.

Objectives

The general objective of this research is aimed at finding out whether the regimen complexity and patient's adherence to medication and glycemic control are correlated among patients with Diabetes Mellitus Type 2. The specific objectives of this research is to access the demographic characteristics of T2DM patients, evaluate their prescribed medications Medication Regimen Complexity Index (MRCI), and observe their adherence to their medications. Moreover, the study aim to measure HbA1c levels for glycemic control and explore the relationship between medication regimen complexity, medication adherence, and glycemic control. Through an understanding of a correlation among these variables, the study aim to provide a new insight into the impact of medication regimen complexity on patient outcomes in T2DM management.

Method and Methodology

Study Design, site, duration

A hospital based cross-sectional study was conducted at Bheri Hospital Nepalgunj with the patient visiting the general medicine section outpatient department of the hospital from November 2023 to May 2024.

Selection criteria

Eligible adults are insured, diagnosed with Type II diabetes for over a year, and on medication. Those who refuse, are uncooperative, have incomplete records, have severe cognitive impairment, or have psychiatric conditions are excluded.

Sample size and technique

A sample size of 145 was calculated using Cochrane's calculation, assuming an 8.5% prevalence and a 10% non-response rate. Purposive sampling identified eligible persons with type 2 diabetes who attended the outpatient department over the course of three months.

Operational Definition

Age: It refers to the age of patients in completed years during the interview period.

Gender: Gender refers to the social and cultural roles, behaviors, and identities of patients.

Education status: It refers to the highest education level completed by the patients categorized as Primary, Secondary, Higher secondary, Graduate.

Primary Education: Foundational education up to elementary school (Grade 5).

Secondary Education: Middle level education from grade 6 –Grade 10.

Higher Secondary Education: Education beyond secondary school, typically grades 11 and 12 or equivalent.

Graduate Education: Completion of a bachelor's degree or equivalent undergraduate program.

 doi:10.20944/preprints202408.0382.v1

Ethnicity: In this study, ethnicity refers to the ethnic group of people as per the Ministry of Foreign Affairs categorization as Brahmin, Chhetri, Dalit, Janajati (Gurung, Rai, Limbu, Newar, Thakali, Tamang) and others (Muslim, Madhesi).

Religion: It refers to the system of faith and worship followed by patients categorized as Hinduism, Buddhism, Christianity, Islam, and others.

Occupation: It represents any kind of job in which participants are engaged for earning and livelihood purposes. It will be categorized as Government jobs, non-government jobs, Agriculture, Homemakers, Retired and Unemployed.

- Homemakers: Homemakers are individuals who manage household tasks and activities such as cleaning, cooking, child-rearing, and budgeting. This role is often unpaid and traditionally associated with domestic responsibilities [8].

Medication regimen complexity: Medication regimen complexity is the quantification of the medication prescribed based on dosage form (Section A), Dosing frequency (section B) and additional directions (section C).

Diabetes-specific MRCI: Refers to medication regimen complexity of medication taken for Diabetes only categorized as (≤8 as low, >8 as high).

Non-Diabetes MRCI: It refers to the medication regimen complexity of medication taken for comorbid conditions and other over-the-counter drugs categorized as (≤ 4 as low, >4 as high).

Patient Level MRCI: Refers to MRC of overall medication taken by the patient including OTC. Categorized as (≤12 as low, > 12 as high).

Level of Medication adherence: Medication adherence is defined as the extent to which patients' behavior matches with the health care providers recommendations categorized as (0-10) as poor, (11-16) as low, (17-26) as Partial, (27-29) as good and (30-33) as High Adherence.

Glycemic Control: The American Diabetes Association (ADA) defines glycemic control primarily through hemoglobin A1c (HbA1c) targets. The Cut off Values for HbA1C is less than 7% termed as Controlled.

Smoking: Smoking is defined as the inhalation of smoke from burning tobacco encased in cigarettes, cigars, or pipes. Participants will be categorized based on their smoking status.

- Current Smokers: Individuals who have smoked any tobacco products daily or occasionally in the past month.
- Former Smokers: Individuals who have smoked tobacco products in the past but have quit smoking for at least one month.
- Non- Smokers: Individuals who have never smoked or have smoked fewer than 100 cigarettes in their lifetime.

Alcohol consumption: It is defined as the intake of beverages containing ethanol. Participants will be categorized based on their alcohol consumption status:

- **Current Drinkers**: Individuals who have consumed any alcoholic beverage (beer, wine etc.) within the past month.
- **Non-Drinkers**: Individuals who have never consumed alcoholic beverages or have abstained from drinking for at least one year.

Data collection tools and technique

Data collection starts with selecting participants based on inclusion criteria and gaining informed consent. Initially, three months of retrospective data were obtained, followed by prospective data. Semi-structured questionnaires for socio-demographic and clinical information were used, as well as a pro forma for prescription drugs. MRCI was calculated by using a 65-item instrument [6] for medication regimen complexity. HbA1C levels were taken from patient records. To measure medication adherence, respondents were interviewed face-to-face using the validated and reliable GMAS-Nep tool [9]. HbA1C levels were checked again three months later. Finally, data was reviewed, revised, and programmed to ensure its completeness.

Statistical Analysis

 doi:10.20944/preprints202408.0382.v1

Data analysis was done using the SPSS 23. Descriptive analysis included the computation of means, standard deviation, frequency, and percentage. Bivariate analysis performed cross-tabulation with Pearson chi-square test; the level of significance was set at $p < 0.05$. Pearson correlation assessed the relation between medication regimen complexity, medication adherence, and glycemic control. One-way ANOVA determined mean distribution of Diabetes MRCI scores across the three adherence levels. A paired t-test method assessed the mean differences in HbA1C values over a period of three months. In multivariate analysis, variables with a significance value less than 0.25 in the bivariate analysis were included and calculated the odds ratio with 95% confidence intervals by binary logistic regression.

Ethical Consideration

The ethical approval was obtained from the institutional review committee of Pokhara University (PUIRC), (Ref no:79/2080/81). The approval for data collection was taken from Bheri Hospital (Ref no: 115/080/081). Permission were taken with author to use GMAS adherence questionnaire scale.

Results

Table 1 shows the socio-demographic characteristics of the participants, where the mean age of participants was (Mean±SD 56.05±10.66) years. Likewise, 10 (6.9%) participants were under the age group of 30-39 years, 26(17.9%) were of 40-49 years, and 32 (22.1%) of participants were of age group 60-69 years. Similarly, most of the participants, 59 (40.7%) were between age group 50-59 years and 18 (12.4%) participants had an age above 70 years. Similarly, 84 (57.9%) of participants were female and 61(42.1%) of participants were male. Regarding occupation, 16 (11%) were engaged in a government job, 40(27.6%) of participant were engaged in non-governmental job, 26 (17.9%) of participants were engaged in agriculture, majority 43 (29.7%) of participants were homemakers, 10 (6.9%) of participants were both retired and unemployed. It was found that 34 (23.4%) of participants were illiterate, 32 (22.1%) obtained primary education, 21 (14.5%) obtained secondary education, 35 (24.1%) obtained higher secondary education and 23 (15.9%) were graduate and post-graduate. Concerning the ethnicity of participants, 32 (22.1%) were Brahmin, 48 (33.1%) were Chettri, 26 (17.9%) were janajati, 18 (12.4%) were dalit and 21 (14.5%) were Muslim and Madhesi. Our Study found that 129 (89%) of participants were Hindu, 13 (9%) were Islam, 2 (1.4%) were Christain, and 1 (0.7%) were Buddhist. Likewise 56(38.6%) of participants had present family history of T2DM and 89 (61.4%) had no family history of T2DM.

Table 1. Sociodemographic Characteristics of Participants (n=145).

Characteristics	Category	n (%)
Age (Years)	30-39	10 (6.9)
	40-49	26 (17.9)
	50-59	59 (40.7)
	60-69	32 (22.1)
	Above 70	18 (12.4)
Gender	Female	84 (57.9)
	Male	61 (42.1)
Occupation	Government Job	16 (11)
	Non-Government Job	40 (27.6)
	Agriculture	26 (17.9)
	Homemakers	43 (29.7)
	Retired	10 (6.9)
	Unemployed	10 (6.9)
Education	Illiterate	34 (23.4)
	Primary Education	32 (22.1)

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	Secondary Education	21 (14.5)
	Higher Secondary Education	35 (24.1)
	Graduate	20 (13.8)
	Post Graduate	3 (2.1)
Ethnicity		
	Brahmin	32 (22.1)
	Chettri	48 (33.1)
	Janajati	26 (17.9)
	Dalits	18 (12.4)
	Others*	21 (14.5)
Religion		
	Hindu	129 (89)
	Buddhist	01 (0.7)
	Christian	2 (1.4)
	Islam	13 (9)
Family History	Present	56 (38.6)
	Absent	89 (61.4)

Others*:Muslim, Madhesi.

Table 2 shows the lifestyle characteristics of the participants where 25 (17.2%) of participants were current smokers, 21 (14.5%) of participants were former smokers and 99 (68.3%) of non-smokers. Regarding the alcohol-taking behavior of participants, 65 (44.8%) participants were alcoholic and 80 (55.2%) of participants were non-alcoholic. Regarding physical activity of the participants, 88 (60.7%) have sedentary activities, 46 (31.7%) have moderate whereas 11 (7.6%) have vigorous Activities.

Table 2. Lifestyle Characteristics of Participants (n=145).

Characteristics	**Category**	**n (%)**
Smoking	Current Smoker	25 (17.2)
	Former Smoker	21 (14.5)
	Non-Smoker	99 (68.3)
Alcohol	Alcoholic	65 (44.8)
	Non-Alcoholic	80 (55.2)
Physical Activity	Sedentary	88 (60.7)
	Moderate	46 (31.7)
	Vigorous	11 (7.6)

Table 3 shows the clinical characteristics of the participants where BMI classification as per WHO, 10 (6.9%) of participants have underweight, 88 (60.7%) have normal weight, 43 (29.7%) of participants have overweight and 4 (2.8%) have obesity. Regarding the comorbidity status of participants, 76 (52.4%) of participants had comorbid conditions while 69 (47.6%) participants had only T2DM without other comorbid conditions. Hypertension was seen as co-morbidity in most of the participants, i.e., 46 (60.52%). Similarly, Mean duration of diagnosis of Type 2 diabetes of participants was (Mean±SD 8.02±4.87) years. 38 (26.2%) of participants have less than 4 years duration of diagnosis of T2DM, 74 (51%) have between 5 – 10 years of duration and 33 (22.8%) have more than 10 years of diagnosis of T2DM.

 doi:10.20944/preprints202408.0382.v1

Table 3. Clinical Characteristics of Participants (n=145).

Characteristics	Category	n (%)
BMI		
	Underweight	10 (6.9)
	Normal	88 (60.7)
	Overweight	43 (29.7)
	Obesity	4 (2.8)
Comorbidity	Present	76 (52.4)
	Absent	69 (47.6)
Types of Comorbidity		
	Hypertension	46 (60.52)
	Hypertension and Hypothyroidism	7 (9.21)
	Hypertension and Hyperlipidemia	4 (5.26)
	Thyroid Disorder	3 (3.94)
	Hyperlipidemia	3 (3.94)
	Hypertension and COPD	2 (2.63)
	COPD	2 (2.63)
Duration of Diagnosis	Less than 4 years	38 (26.2)
	5-10 years	74 (51)
	More than 10 Years	33 (22.8)

Table 4 shows the prescribed drugs in 145 diabetes patients, where most of the participants i.e., 67(46.20) used medication is Metformin Hydrochloride (Biguanides), followed closely by a combination of Metformin and Glimipride (Biguanides + Sulfonylureas) at 45.5%. linagliptin (DPP-4 inhibitors) is used by 37.9% of patients, while Dapagliflozin (SGLT-2 inhibitors) is used by 33.1%. Voglibose (Alpha-Glucosidase inhibitors) has a usage rate of 29.7%, and Empagliflozin (SGLT-2 inhibitors) is used by 20.7% of patients. Combinations of Metformin with Sitagliptin and Linagliptin (Biguanides + DPP-4 inhibitors) are used by 20.7% and 20% of patients, respectively. Insulin preparations are used by 15.9% of patients, and Acarbose (Alpha-Glucosidase inhibitors) is used by 10.3%.

Table 4. Medication Prescribed for Diabetes (n=145).

Classification	Medication	ATC code	n (%)
Biguanides	Metformin Hydrochloride	A10BA02	67 (46.20)
Biguanides+ Sulfonylureas	Metformin +Glimipride	A10BD02	66 (45.5)
DPP-4 inhibitors	Linagliptin	A10BH05	55 (37.9)
SGLT-2 inhibitors	Dapagliflozin	A10BK01	48 (33.1)
Alpha-Glucosidase inhibitors	Voglibose	A10BF03	43 (29.7)
SGLT-2 inhibitors	Empagliflozin	A10BK03	30 (20.7)
Biguanides + DPP-4 inhibitors	Metformin+Sitagliptin	A10BD07	30 (20.7)
Biguanides + DPP-4 inhibitors	Metformin+Linaglipin	A10BD11	29 (20)
Insulin	Insulin preparation	A10A	23 (15.9)
alpha-glucosidase inhibitors	Acarbose	A10BF01	15 (10.3)

Table 5 shows the Mean±SD of MRCI scores, MRCI sub-scores, and total medicine count, where the mean score of diabetes specific MRCI i.e., 8.28±3.155 is found to be more than that of non-diabetes MRCI i.e., 4.57±2.107. Similarly, Dosing frequency MRCI has the highest contribution to diabetes specific MRCI followed by medicine count, additional directions and dosage form MRCI. Likewise, for Non-diabetes MRCI, dosing frequency has the highest contributions followed by medicine count, additional directions and dosage form MRCI.

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Table 5. Mean±SD of MRCI Score and Sub-scores n (145).

Variables	Mean±SD
Diabetes MRCI Score	8.28±3.155
Dosage form MRCI	1.48±1.100
Dosing frequency MRCI	4.23±1.728
Additional Directions MRCI	2.66±0.937
Diabetes Medicine Count	2.82±0.955
Non-Diabetes MRCI Score	4.57±2.107
Dosage form MRCI	1.16±0.833
Dosing frequency MRCI	2±1.115
Additional directions MRCI	1.41±0.785
Non-Diabetes medicine Count	1.90±0.979
Patient-level MRCI Score	12.38±3.786
Total medicine count	4.52±1.370

Table 6 shows the medication regimen complexity of patients, it is found that 59.3% of participants had low diabetes complexity, and 40.7% had high diabetic complexity. Likewise, for patients having comorbid conditions, 53.8% had low non-diabetes complexity and 35.9% had high non-diabetes complexity. The patient-level regimen complexity was found to be low in 57.2% of patients and high in 42.8% of patients.

Table 6. Medication Regimen Complexity (n=145).

Variables	**n (%)**
Diabetes MRCI	
Low	86 (59.3)
High	59 (40.7)
Non-Diabetes MRCI	
Low	78 (53.8)
High	52 (35.9)
Patient level complexity	
Low	83 (57.2)
High	62 (42.8)

Table 9 shows the level of medication adherence where 15.9% of participants had high adherence with a mean of 31.086±0.900. 22.1% of participants had good adherence with a mean of 27.75±0.803 and 62.1% of participants had partial adherence with a mean of 24.05±2.240. The association between medication adherence and diabetes MRCI is found to be significant, (p<0.05).

Table 8 shows the glycemic control (Hemoglobin A1C) among diabetic patients, where Baseline hemoglobin A1C, Mean of 7.73±1.21 found statistically significant with A1C after 3 month mean 6.62±0.0727 (p<0.05).

Table 7. Level of Medication Adherence (n=145).

Level of adherence	**Grading (cumulative)**	**n (%)**	**Mean ±SD**	***p* value**
High adherence	30 – 33	23 (15.9)	31.086±0.900	
Good Adherence	27 – 29	32 (22.1)	27.75±0.803	<0.001*
Partial adherence	17 – 26	90 (62.1)	24.05±2.240	

*One-way ANOVA, p<0.05.

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Table 8. Glycemic Control (n=145).

Hemoglobin A1C	Mean ±SD	*p* value
Baseline	7.73±1.21	
After 3 month	6.62±0.0727	<0.001*
Difference	1.11±0.730	

Paired t-test p <0.05.

Table 9. Association of demographic variable with diabetes MRCI and Medication Adherence.

Variable	Diabetes MRCI n (%)		P value	Medication Adherence n (%)			P value
Age	**Low**	**High**		**High**	**Good**	**Partial**	
30-39	10(11.6)	0(0)		1(4.3)	2(6.3)	7(7.8)	
40-49	18(20.9)	8(13.6)		8(34.8)	6(18.8)	12(13.3)	
50-59	30(34.9)	29(49.2)	0.002*	6(26.1)	11(34.4)	42(46.7)	0.0626
60-69	21(24.4)	11(18.6)		5(21.7)	12(37.5)	15(16.7)	
Above 70	7(8.1)	11(18.6)		3(13)	1(3.1)	14(15.6)	
Gender							
Male	30(34.9)	31(52.5)	0.034*	7(30.4)	18(56.3)	36(40)	0.130
Female	56(65.1)	28(47.5)		16(69.6)	14(43.8)	54(60)	
Occupation							
Government job	1(1.01)	2(4.34))		0(0)	2(5.3))	14 (15.6)	
Non-Gov. Job	14(14.14))	11(23.91)		9(39.1)	12(31.6)	19(21.1)	
Agriculture	23 (23.23))	18(39.13)	0.768	6(26.1)	3(7.9)	17(18.9)	0.006*
Homemakers	26(26.26))	19(41.30)		7(30.4)	11(28.9)	25(27.8)	
Retired	9(9.09))	3(6.52)		1(4.3)	10(26.3)	5(5.6)	
Unemployed	26(26.26)	22(47.82)		0(0)	0(0)	10(11)	
Education Level							
Illiterate	23(26.7)	11(18.7)		5(21.8)	8(25)	21(23.3)	
Primary	16(18.6)	16(27.1)		6(26)	6(18.8)	20(22.2)	
Secondary	11(12.8)	10(16.7)	0.061	4(17.4)	2(6.2)	15(16.7)	0.094
Higher Secondary	25(29)	10(16.7)		4(17.4)	10(31.2)	21(23.3)	
Graduate	11(12.8)	12(20.3)		4(17.4)	6(18.8)	13(14.5)	
Physical Activity							
Sedentary	43(50)	45 (76.3)		5(21.7)	20(62.5)	63(70)	
Moderate	34(39.5)	12(20.3)	<0.05*	18(78.3)	7(21.9)	21(23.3)	<0.001*
Vigorous	9(10.5)	2(3.4)		0(0)	5(15.6)	6(6.7)	
Smoking Habit							
Current smoker	10(28.6)	25(71.4)		0(0)	5(15.6)	20(22.2)	
Former smoker	47(56)	37(44)	<0.001*	1(4.3)	6(18.8)	14(15.6)	0.006*
Non- smoker	42(46.4)	13(23.6)		22(95.7)	21(65.6)	56(62.2)	
Alcohol habit							
Alcoholic	47(54.7)	33(55.9)	0.879	13(56.5)	16(50)	54(60)	0.292
Non-Alcoholic	39(45.3)	26(44.1)		10(43.5)	16 (50)	36(40)	
Co-morbidity							
Present	43(50)	26(44.1)	0.482	11(47.8)	13(40.6)	45(50)	0.658
Absent	43(50)	33(55.9)		12(52.2)	19(59.4)	45(50)	
BMI							
Underweight	6(7)	4(6.8)		0(0)	0(0)	10(11.1)	
Normal	60(69.9)	28(47.5)	0.001*	14(60.9)	14(60.9)	59(65.6)	<0.01*
Overweight	16(18.6)	27(47.5)		8(34.8)	8(34.8)	21(23.3)	
Obesity	4(4.7)	27(45.8)		1(4.3)	1(4.3)	0(0)	

 doi:10.20944/preprints202408.0382.v1

Table 10 shows the association between medication regimen complexity and adherence, where there was no significant association between Diabetes-specific MRCI and adherence. There was significant association between non-Diabetes MRCI and medication adherence (p<0.05). Similarly, there was no significant association between patient-level complexity and medication adherence.

Table 10. Association between MRCI and Medication Adherence (n=145).

Medication regimen complexity	Medication Adherence n(%)			p value
	High	Good	Partial	
Diabetes MRCI				
Low	12 (52.2)	20 (62.5)	54(60)	0.729
High	11 (47.8)	12 (37.5)	36(40)	
Non-diabetes MRCI				
Low	8 (42.1)	12 (44.4)	58(69)	0.018*
High	11 (57.9)	15 (55.6)	26(31)	
Patient level MRCI				
Low	11 (47.8)	17 (53.1)	55(61.1)	0.450
High	12 (52.2)	15 (46.9)	35(38.9)	

*Chi-square test, (p<0.05).

Table 11 shows the association between medication regimen complexity and Glycemic Control, where there was significantly association between Diabetes-specific MRCI and adherence (<0.05).

Table 11. Association between MRCI and Glycemic Control (n=145).

Medication regimen complexity	Glycemic Control n(%)		p value
	Controlled	Uncontrolled	
Diabetes MRCI			
Low	74 (70.5)	31 (29.5)	**<0.01***
High	12 (30)	28 (70)	

*Chi-square test, (p<0.05).

Table 12 depicts the correlation matrix between medication adherence and Diabetes MRCI, non-Diabetes MRCI, and patient-level MRCI. The Pearson correlation coefficient between Diabetes MRCI and medication adherence is (r=-0.090), indicating a weak negative correlation between Diabetes medication regimen complexity and medication adherence, which reveals that with an increase in medication regimen complexity, medication adherence decreases. Similarly, with Pearson correlation coefficient between patient-level MRCI and medication adherence is (r=-0.050) which shows a negative correlation while there is a strong negative correlation, (r=-0.766), between non-Diabetes MRCI and medication adherence, which reveals that comorbidity may influence on it.

Table 12. Correlation Matrix Between Medication Adherence and MRCI (n=145).

Variable	Medication adherence	Diabetes MRCI	Non-Diabetes MRCI	Patient level MRCI
Medication adherence	1			
Diabetes MRCI	-.090	1		
Non-Diabetes MRCI	-.766**	.515**	1	
Patient level MRCI	-.050	.114	.802	1

*Pearson correlation (p<0.05).

Table 13 features both binary and multivariate logistic regression analyses, gender had been found to be connected significantly to the outcome where females had the odds in their favor over

 doi:10.20944/preprints202408.0382.v1

males (binary p-value: 0.0011, COR: 0.395, 95% CI: 0.194-0.804; multivariate p-value: 0.014, AOR: 0.403, 95% CI: 0.195-0.832). Nonactive, even whether sedentary or moderately, compared to vigorous activity, did not display the main effects in either regression model, though the odd ratios for the three modes were convincingly large (e.g., sedentary in binary: COR: 4.709, 95% CI: 0.962-23.05). Smoking status, indicated higher odds for ongoing smokers compared to non-smokers, but, it was statistically non-significant at the same time when it was compared with the normal (binary p-value: 0.067, COR: 2.30, 95% CI: 0.942-5.65; multivariate p-value: 0.092, AOR: 2.323, 95% CI: 0.878-5.67). Moreover, an abnormal BMI was more likely to be associated with the odds of the abnormal BMI in the both models, which were binary and multivariate, separately (binary p-value: 0.008, COR: 2.55, 95% CI: 1.284-5.082; multivariate p-value: 0.017, AOR: 2.355, 95% CI: 0.195-0.832).

Table 13. Factors Affecting Diabetes MRCI (n=145).

Characteristics	Binary logistic regression			Multivariate logistic regression		
	p value	COR	95% CI	*p* value	AOR	95 % CI
Gender						
Male	**Reference**			**Reference**		
Female	0.0011	0.395	(0.194-0.804)	0.014	0.403	(0.195-0.832)
Physical Activity						
Vigorous	**Reference**			**Reference**		
Sedentary	0.56	4.709*	(0.962-23.05)	0.67	4.66*	(0.899-24.160)
Moderate	0.587	1.588*	(0.300-8.416)	0.523	7.76*	(0309-10.02)
Smoking						
Current Smoker	0.067	2.30	0.942-5.65	0.092	2.323	0.878-5.67
Former Smoker	0.185	0.481	0.163-1.41	0.312	0.56	0.183-1.713
Non-smokers	**Reference**			**Reference**		
BMI						
Normal	**Reference**			**Reference**		
Abnormal	0.008	2.55*	(1.284-5.082)	0.017	2.355*	(0.195-0.832)

Discussion

Sociodemographic and clinical characteristics

It was found that most of the participants were female, the female: male ratio was (1.37). The result was consistent with study conducted by [8], where half of patients were female. Finding was in contrast with study conducted by [10] where more than half participants were male. The reason behind female predominance might be due to hormonal changes and increased risk factors like obesity and cardiometabolic changes due to menopause. The study showed that most of the participants were aged (50-59) years. Similar findings were obtained in a study conducted [11] where most of the participants were of age group (40-50) This might be due to reason that the onset of type 2 diabetes is most common in people aged 45–64 years. Hypertension was most prevalent comorbidity seen in about one fourth of participants, while other comorbidities were thyroid disorder, heart diseases which was consistent with study conducted by [12] where hypertension was most prevalent comorbidity.

Medication regimen complexity

It was seen that Diabetes-specific medications were more complex than those of non-Diabetes medication (Mean MRCI: 8.28±3.155 versus 4.57±2.107 respectively). Findings from this study are supported by the study conducted by [2] in Malaysia where the complexity of Diabetes medication regimens was higher than those of non-diabetes medications (median MRCI: 14.5 vs. 9). In this study, complex dosing frequency contributed to higher Diabetes MRCI scores which was similar with a study conducted by [13] where dosing frequency score contributed the most to higher MRCI scores of Diabetes medication. This study showed that the average number of medications per prescription was (Mean±SD 2.82±0.955) which was associated with medication regimen complexity and glycemic control, which is consistent with a study conducted by [14] where most of the patients with a greater

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number of medications shows Regimen complexity was high. Based on overall medications (mean = 6.6 medications, SD: 3.09). This association suggests that as the number of prescribed medications increases, so does the complexity, which can negatively impact glycemic control. The correlation of Diabetes MRCI and medication adherence showed a negative correlation (Pearson correlation coefficient, -.050) between Diabetes MRCI and medication adherence which is consistent with the study conducted by [4] where complexity led to a decrease in adherence. However, There is no statistically significance between Diabetes MRCI and Medication Adherence, which is contrast with the study done by [15]. One reason for the different results could be variability in prescribing practices among healthcare providers. Prescribing factors such as the choice of medication, dosing frequency, and the inclusion of combination therapies can influence regimen complexity. Variations in these factors across different studies could lead to discrepancies in the observed relationship between complexity and adherence.

Medication adherence

The study showed that more than half of participants had partial medication adherence which is similar to study conducted by [3] which showed more than half participants had fair adherence. The finding was in contrast with study conducted by [16] in tertiary care hospital, Nepal where that 61% of respondents had high medication adherence. Similarly, a study conducted in a tertiary care hospital, Nepal found that the self-reported medication adherence was high (97.3%). The reason behind partial adherence in our study might be due to Medication regimen complexity, occupation and other characteristics of patients. Findings from this study are supported by study conducted by [8] where medication was medium in 55.81% patients.

Glycemic Control

The current study offers a comprehensive look at the relationship between glycemic control and medication regimen complexity among patients with type 2 diabetes mellitus (T2DM). It reveals that more than half of the patients had good glycemic control, a finding that aligns with the results of [8], who also reported that over half of their study participants achieved good glycemic control. This consistency suggests a reassuring trend that a significant portion of patients are managing their blood glucose levels effectively.

However, the study also highlights a critical insight: there is a statistically significant relationship between medication regimen complexity and glycemic control. Specifically, as the complexity of diabetes-specific medication regimens increases, glycemic control tends to worsen. This negative correlation was corroborated by [4], who found that high medication regimen complexity was associated with poor glycemic control. Similarly, [15] supported these findings, showing that patients with greater medication regimen complexity exhibited poorer glycemic control.

Conclusion

This study indicated that women were the most frequently encountered among the patients, mainly those of whom had high blood pressure. MRCI for diabetes was statistically higher (8.28 ± 2) than for non-diabetes medications (4.57 ± 2). We found that an increased Diabetes MRCI score and drug treatment compliance resulted in a negative relationship, which means that the more complicated regimens will lead to the lower adherence of patients. Elements like dosing frequency, occupation, BMI, and physical activity had a statistically significant effect on adherence. This study shows that patients with more medication regimen and difficult to adherence on that, have the highest hemoglobin A1c levels. The results of this study demonstrate that the Medication Regimen Complexity Index (MRCI) is a useful tool for the identification of regimen complexities. Simplifying regimens in the form of deprescribing, better insurance coverage and the encouragement of healthcare engagement can increase adherence and glycemic control in the T2DM patients.

Limitation

- There was possibility of recall bias.
- There was change of Selection Bias

 doi:10.20944/preprints202408.0382.v1

- This study focused only on identifying MRCI and not on applying interventions, especially in the country where the role of the clinical pharmacist has not yet been fully implemented.

Recommendations

- This study recommends that utilizing the MRCI tool regularly to evaluate the complexity of medication regimens for patients with Type 2 Diabetes Mellitus (T2DM) can help healthcare providers identify and mitigate factors contributing to regimen complexity.
- Smoking, alcohol and Physical activities were associated with low medication adherence, Uncontrolled Glycemic Control as well as medication complexity. So, non-pharmacological interventions like alcohol limitations, smoking cessation programs and maintaining healthy BMI with active physical activity are strongly recommended.
- This study recommends to implement MRCI in clinical practice to assess complexity and also train providers for better adherence outcome and interventions.

Author Contributions: SP and RK supervised and reviewed draft manuscript. AA participated as a principle investigator in the collection of data, arranged in tubular form, and carried out the literature review and make ready for draft. All authors read and approved the final manuscript.

Funding: Nil.

Conflicts of Interest: there are no conflicts of interest for all authors.

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