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Original Article

Medication Adherence of DPP-4 Inhibitors in Type 2 Diabetic Management: A Hill Bone Medication Adherence Scale Analysis

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ABSTRACT

Background: The management of diabetes is a global health challenge. Non-adherence to medication in chronic diabetics is a severe issue that is linked to negative consequences, which can be related to various factors. The present study aims to evaluate the proportion of adherence to DPP-4 inhibitors with other Oral Hypoglycemic Agents (OHA) in type 2 diabetic management using hill bone medication adherence scale analysis. **Materials and Methods:** In this prospective interventional study, out of 1000 patients, 974 fulfilled the inclusion criteria and considered for the study. A Nine-item Hill Bone Medication Adherence Scale (HBMAS) was used for data collection. Adherence was classified as 'poor or high' based on the patient's mean score. The data was analyzed using student t-tests and ANOVA. **Results:** At the beginning of the study, 49.85% patients had low adherence to DPP-4 inhibitors, while 50.2% had high adherence. Following counseling, the medication adherence increased to 69.6% at the end of the study. Based on demographic data such as sex, occupation and social habit, statistically did not have any impact on medication adherence, but other data like age, duration of diabetic history, family history, personal history, BMI and treatment regimen had a huge impact on the adherence to DPP4 inhibitors. **Conclusion:** It was found that various factors contributed to non-adherence towards the diabetic medication with DPP4 inhibitors, while the result of present study indicates that counseling of patients for adherence to their diabetic medication improves understanding of disease status and positive impact on medication adherence which eventually enhances quality of life.

Keywords: Gliptin, Non-adherence, Hill-Bone scale, Medication adherence, Type 2 diabetic patients.

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INTRODUCTION

Management of diabetes is a global health challenge. Globally 422 million people have diabetes as stated by World Health Organization (WHO), with the Eastern Mediterranean nations having the highest prevalence (43 million).[1] Over 74 million adults in India, or one in every 12, have diabetes, according to the 10th Edition of the IDF Diabetes Atlas.[2]

Non-adherence to medication in chronic diabetics is a serious issue linked to negative consequences and may also be considered as the reason for the constant rise in the number of diabetic patients. Medication Adherence (MA) is a behavioral process that includes taking prescriptions, adhering to a diet and leading a healthy lifestyle that is consistent with healthcare providers, as described by WHO. MA includes the avoidance of complications and efficient management of diabetes, both of which can only be accomplished with patient participation in their medication regimens as advised by the healthcare provider.[3]

In the treatment of diabetes, to achieve glycemic control, patients are prescribed with multiple Oral Hypoglycemic Agents (OHA) and/or sulfonylurea and/or metformin therapy as the disease progresses. The gliptins are new group of DPP-4 inhibitors which have been included in diabetes therapy. These Oral Antidiabetic medications (OADs) have a low intrinsic risk of hypoglycemia, sustain beta-cell activity, are weight-neutral or even cause weight loss.[4,5] Gliptin promotes insulin secretion while inhibiting glucagon release by inhibiting the enzymatic breakdown of Glucagon-Like Peptide-1 (GLP-1). Despite the efficiency that gliptins can provide in the treatment of diabetes along with other drugs, MA has a direct impact on the glycemic control and clinical outcome. MA-related factors are typically complex due to

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interactions between the patient, physician, healthcare team and medication factors.[6]

There is a paucity of data in India, particularly in the southern part of the country, on the MA towards antidiabetic medications in patients with T2DM. We proposed to study the MA in patients at a diabetic center in Erode, Tamil Nadu and India. The present study was intended to determine medication adherence of gliptins with other OHA in type 2 diabetic management by using the hill bone medication adherence scale.

MATERIALS AND METHODS

This prospective interventional study was conducted among 974 T2DM patients attending a diabetic care centre in Erode, Tamil Nadu between March 2021 and June 2022. Patients' data were collected by using a well-structured form attached with medication adherence relevant questionnaire. The Hill bone adherence scale, a Nine-item questionnaire with widespread application across numerous long-term diseases and condition for self-evaluation of MA, was utilized for the assessment. Measuring medication adherence in individuals with conditions like hypertension, diabetes, chronic obstructive pulmonary disease and stroke is made easier with the Medication Adherence Scale. The questionnaires (Table 2) were collected once every six months for a review and individual patient score was calculated. Each patient's overall score was determined by adding the total points provided, with the minimum and highest scores being 4 and 36, respectively. The averages of patients' total points were calculated. Based on the average value, the patients were classified as having high or low adherence to the prescribed medication; above the average value, higher the adherence and below the average value, lower the adherence. Adherence levels also improved at the end of the study due to the provision of leaflets explaining the importance of medication adherence to individual patients.

Inclusion Criteria

Out patients with one year of diabetes diagnosis.

Non-insulin dependent diabetic mellitus patients.

Age group 18-90 years.

Patients with regular follow up.

Exclusion Criteria

T1DM patients.

Paediatric patients and pregnant women with gestational diabetes.

Patients without regular follow up and irregular with prescribed medication.

Ethical Consideration

The study was performed with the approval of the institutional ethical committee (Approval ID DCC/IEC/026/2021). Participants were informed about the goal of the study and were assured of the confidentiality and secrecy of the data. Each study participant signed a written informed voluntary participation permission form.

Statistical Analysis

For statistical analysis, the SPSS statistical software (version 22.0) was utilized. For data analysis, descriptive and inferential statistics were utilized. Frequencies (n) and percentages (%) were used to report socio-demographic information. Medication adherence was given as a mean and Standard Deviation (SD). ANOVA and *t* test was done. A *p* value of <0.05 was seen as statistically significant.

RESULTS

A total of 974 patients were included in the data analysis and an observational study has been conducted to determine the medication adherence. Table 1 represents the baseline information collected from these patients; Table 2 shows the individual data of first review and end of the study period in comparison with baseline values.

MA of DPP-4 inhibitors with other OHA in type 2 diabetic management was determined by using the hill bone scale from the data collected from 974 patients and the results are as follows:

The association of OHA taking medication adherence in type 2 diabetic patients was compared with the demographic characteristics. In this age group, duration of diabetes, family history, personal history, BMI and treatment regimen is found to be statistically significant ($p<0.05$). The patient's sex, occupation and social history have shown that statistically not significant ($p>0.05$) (Table 1).

The mean score value of individual questionnaire of first review and end of the study period in comparison with baseline values. The MSBV (Mean Score Baseline Value), MSFRV (Mean Score First Review Value) and MSEV (Mean Score End Value) of Q1 were found to be 2.5, 3 and 3.5, respectively. The MSBV, MSFRV and MSEV of Q2 were found to be 3.3, 2.8 and 3.2, respectively. The MSBV, MSFRV and MSEV of Q3 were found to be 2.8, 3.4 and 3.6, respectively. The MSBV, MSFRV and MSEV of Q4 were found to be 2.7, 3.1 and 3.5, respectively. The MSBV, MSFRV and MSEV of Q5 were found to be 2.5, 3.3 and 3.6, respectively. The MSBV, MSFRV and MSEV of Q6 were found to be 2.6, 4.2 and 4.5, respectively. The MSBV, MSFRV and MSEV of Q7 were found to be 2.6, 3.2 and 3.4, respectively. The MSBV, MSFRV and MSEV of Q8 were found to be 2.7, 3.3 and 3.7, respectively. The MSBV, MSFRV and MSEV of Q9 were found to be 2.8, 3.3 and 3.5, respectively. Based on the above mean score values,

the ANOVA test was done. The obtained mean score values of MSFRV and MSEV were statistically and significantly improved in comparison with MSBV with respect to medication adherence in the patients (Table 2).

The hill bone medication adherence scale was used to assess medication adherence. The baseline Adherence levels were compared with and between the initial and end of the study period. Based on the HBMAS, the medication adherence was found to be 23.49 of average baseline value. 485 (49.8%) patients were less adherence and 489 (50.2%) patients were more adherence towards the medication based on the average baseline value. At first review, 446 (46%) patients were found to be less adherence and 526 (54%) patients were more adherence. At the end of the study period, 296 (30.4%) patients were found to be less adherence and 678 (69.6%) patients were found to be more adherence (Table 3).

We performed student *t* test for the data obtained. The result showed that the first review and end of the study value was statistically significant when compared with the baseline value of adherence. The results showed that the medication adherence value substantially improved at first and end of our study period in comparison with baseline value.

DISCUSSION

Type 2 diabetes is a chronic disease that frequently results in higher pharmaceutical requirements, risks to one's health, complications and higher medical expenses.[7] Adherence is very crucial to the management of diabetes since non-adherence and/or poor adherence not only slows the treatment process but also has the potential to cause problems in diabetic patients. Compliance is crucial since data shows that diabetes and hypertension regularly coexist and that one illness frequently precedes the other, increasing the risk of fatal cardiovascular events.[8] There is a notable lack of data from developing countries on the prevalence and correlates of adherence in diabetes patients, which is why the current study was initiated. The prevalence of medication non-adherence was examined in a recent study by Ghosh *et al*., among 178 type 2 diabetes patients who were enrolled in a lifestyle clinic at a tertiary care hospital in West Bengal, India which showed a low rate of OHA adherence.[9] Self-care and medication adherence were difficult for all socioeconomic categories. Moreover, according to Venkatesan *et al*., it concluded that 45.4% of diabetics are projected to have low medication adherence, based on a significant community-based study from the south of the country.[10]

The present study determined medication adherence in 974 T2DM patients taking OHA including DPP-4 inhibitors, using the hill bone scale. Basic demographic details and adherence to the prescribed medication were evaluated in these patients. The measurement of the adherence from the baseline to first review and the end of the study showed that there is no significant difference between adherence and gender.

In our study, the highest numbers of patients were in the age group 50-59, who tend to have high work pressure, less financial support and family problems. The measurement of the mean score value of adherence from baseline to end of the study shows that the adherence levels improved at the end of the study period indicating that the age group does not alter medication adherence.

Duration of the disease, smoking, alcoholism, choice of vegetarian food, did not affect medication adherence to OHAs. Based on the questionnaire, it was identified that forgetfulness, not deciding to take medication, carelessness, side effects, running out of diabetes pills, skipping the medication, feeling sick led to non-adherence to diabetic medication, which significantly improved after appropriate patient counseling and knowledge transfer by providing patient information leaflets. Malik *et al*., also concluded that Community pharmacist counseling aided patients in attaining their intended blood glucose goals and improved medication adherence, which improved diabetes management.[11]

Highest numbers of study population were employed, but due to lack of the family members support, patients didn't properly follow the adherence, so medication adherence levels were not statistically significant.

In our study, all the patients were under gliptins along with other OHA including monotherapy, three drug regimens and four drug regimens. All the groups were baseline statistically significant with initial and end of the study period, stating that patient's adherence also improved. In contrast, Lee*et al*., concluded that the adherence to DPP4 inhibitors once-daily regimens (such as Teneligliptin and sitagliptin) was higher when compared to other multi-dose OHA.[6]

When DPP-4 inhibitors were included in polytherapy, this class of medication out performed sulfonylureas and other OHA in terms of the MA. In the study, all 974 patients were prescribed with gliptin to minimize the hypoglycemic effect and maintain weight neutral effect to avoid the multiple doses. So, use of DPP-4 inhibitors single dose and single tablet formulation (combination of gliptins plus metformin) improves the medication adherence.

The implementation of Hill bone scale for measuring medication adherence for the pattern of DPP-4 inhibitors along with other OHA's in a diabetic centre have resulted in statistically improved adherence to the regimen from the baseline to the first review and end of the study period. The results are supported by Gholamalies *et al*., who performed similar study which proves that Hill bone medication adherence instrument was useful in planning and implementing effective individualized hill bone diabetic scale at each visit.[3] Nurses, physicians and community health personnel working in clinics and communities may find the tool useful from

Table 1: Association between Adherence and Demographic Variables.

Demographic details	N (%) 974	Hill bone Scale			*p* value
		Mean Base line Score	Mean first review value	Mean End of the study period Score	
Sex					
Male	513 (52.7)	23.38	28.53	31.50	t=4.261
Female	461 (47.3)	23.61	28.35	31.40	0.187>0.05 Not Significant
Age group					
< 30	11 (1.1)	23.45	28.45	30.10	f=8.715
30-39	81 (8.3)	23.36	28.32	31.30	0.017<0.05
40-49	281 (28.9)	24.01	28.39	31.40	Significant
50-59	314 (32.2)	23.44	28.45	31.54	
60-69	208 (21.4)	22.89	28.61	31.39	
70-79	74 (7.6)	23.28	28.29	31.24	
>80	5 (0.5)	27.00	29.6	32.00	
Duration of diabetes					
1-5 yrs	532 (54.6)	23.35	28.40	31.38	f=11.241
6-10 yrs	286 (29.4)	23.94	28.51	31.48	0.003<0.05
11-15 yrs	90 (9.2)	22.93	28.76	31.34	Significant
16-20 yrs	51 (5.2)	23.33	28.37	31.86	
21-25 yrs	11 (1.1)	21.82	27.55	31.73	
26-30 yrs	4 (0.004)	27.75	26.5	31.00	
Family History					
Yes	504 (51.7)	23.80	28.46	31.27	f=5.452
No	470 (48.3)	23.14	28.43	31.60	0.009<0.05 Significant
Personal History					
Alcohol	5 (0.5)	16.20	27.2	31.80	f=13.468
Smokers	89 (9.1)	24.24	28.47	31.55	0.007<0.05
Alcohol, Smokers	62 (6.4)	22.71	29.24	31.84	Significant
Non-Smokers Non-Alcoholic	818 (84)	23.51	28.39	31.39	
BMI					
Under Weight	40 (4.1)	23.55	27.6	31.65	f=13.187
Normal Weight	457 (46.9)	23.20	28.3	31.37	0.001<0.05
Over Weight	332 (34.1)	23.73	28.60	31.52	Significant
Obese	145 (14.9)	23.83	28.81	31.37	
Occupation					
Employed	579 (59.4)	23.46	28.49	31.48	t=2.672
Unemployed	395 (40.6)	23.53	28.39	31.36	0.342>0.05 Not Significant

Demographic details	N (%) 974	Hill bone Scale			*p* value
		Mean Base line Score	Mean first review value	Mean End of the study period Score	
Social Habit					
Vegetarian	493 (50.6)	23.72	28.41	31.34	t=2.697 0.261>0.05 Not Significant
Non-Vegetarian	481 (49.4)	23.27	28.48	31.53	
Treatment					
Teneligliptin	124 (12.7)	23.77	28.74	31.32	f=14.957 0.000<0.05 Significant
Teneligliptin+SU+Metformin	414 (42.5)	23.38	28.47	31.42	
Teneligliptin+SU+Metformin +Insulin	165 (16.9)	23.68	28.45	31.57	
Vildagliptin+SU+Metformin	172 (17.6)	23.55	28.16	31.38	
Sitagliptin+SU+Metformin	99 (10.2)	23.17	28.49	31.47	

* Student *t* test and one way ANOVA test $p<0.05$ Significant.

Table 2: Mean Score Value of Individual Questionnaire Compared with Baseline, First Review and End of the Study Period.

Sl. No.	Son Hill bone scale questionnaire	Mean Score Baseline Value (MSBV)	Mean Score First Review Value (MSFRV)	Mean Score End of the study period Value (MSEV)	*p* value
Q1.	How often do you forget to take your Diabetes medicine?	2.5	3.0	3.5	f=13.654 0.001<0.05 Significant
Q2.	How frequently do you choose not to take your Diabetes medication?	3.3	2.8	3.2	
Q3.	How frequently do you forget to fill your prescriptions?	2.8	3.4	3.6	
Q4.	How often do you run out of Diabetes pills?	2.7	3.1	3.5	
Q5.	How often do you skip your high Diabetes medicine before you go to the doctor?	2.5	3.3	3.6	
Q6.	When you feel better, how frequently do you forget to take your Diabetes medication?	2.6	4.2	4.5	
Q7.	How often do you miss taking your Diabetes pills when you feel sick?	2.6	3.2	3.4	
Q8.	How frequently do you take someone else's Diabetes medication?	2.7	3.3	3.7	
Q9.	How often do you miss taking your diabetes pills when you are careless?	2.8	3.3	3.5	

*One way ANOVA test $p<0.05$ significant.

Table 3: Hill Bone Scale.

Sl. No.	Hill bone scale	No. of patients (%) (*n*=974)	Mean Score Value	*p* value
1	**Baseline**			
	Less Adherence	485 (49.8)	18.08	t=11.274 0.031<0.05 Significant
	More Adherence	489 (50.2)	28.85	
2	**First review**			
	Less adherence	448 (46	25.81	t=13.467 0.016<0.05 Significant
	More adherence	526 (54)	30.70	
3	**End of the study period**			
	Less adherence	296 (30.4)	29.33	t=11.917 0.041<0.05 Significant
	More adherence	678 (69.6)	32.35	

Student '*t*' test $p<0.05$ statistically significant.

teaching to guiding the behavior modification leading to diabetic control.[12]

One of the most important concerns causing diabetic-related mortality and morbidity in T2DM patients is non-adherence to anti-diabetic treatment. At the beginning of this study, 49.85% patients had low adherence to diabetic medication including DPP-4 inhibitors while 50.2% had high adherence. Following counseling, the medication adherence increased to 69.6% at the end of the study. The demographic data, sex, occupation and social habit, statistically did not have any impact on medication adherence, but age group, duration of diabetic history, family history, personal history, BMI and treatment regimen had a huge impact on the MA.

To the best of our knowledge, this is the first study reporting the MA in T2DM patients in Tamil Nadu with a large study population (>900), which strengthens the credibility of the data obtained.

CONCLUSION

The outcome of the present study indicates that counseling of patients improves adherence to diabetic medication including gliptins as one of the regimens. Various factors were identified as being related to MA in these patients, however, a structured counseling was successful in encouraging the patients to understand the benefits of MA, which can eventually enhance their quality of life.

Our findings will assist physicians and public health workers in identifying additional factors that contribute to poor adherence and developing innovative interventions to address these and, ultimately, improve medication adherence.

CONFLICT OF INTEREST

The authors declare that there is no conflict of interest.

ABBREVIATIONS

T2DM: Type 2 diabetes mellitus; **HBMAS:** Hill Bone Medication Adherence Scale; **OHA:** Oral Hypoglycemic Agent; **MA:** Medication Adherence; **WHO:** World Health Organization; **OADs:** Oral Antidiabetic Medications; **GLP-1:** Glucagon-like Peptide-1; **SPSS:** Statistical Package Social Sciences; **BMI:** Body Mass Index; **MSBV:** Mean Score Baseline Value; **MSFRV:** Mean Score First Review Value; **MSEV:** Mean Score End of the study period Value; **SD:** Standard Deviation; **ANOVA:** Analysis of variance.

SUMMARY

The purpose of conducting and undertaking this study was to truly assess and analyze the medication adherence of patients in T2DM. This is very useful tool improve the efficacy and quality of life in type 2 diabetic patients. Nurses, physicians and community health personnel working in clinics and communities may find the tool useful from teaching to guiding the behavior modification leading to diabetic control.

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