ORIGINAL ARTICLE

Usage of vildagliptin among patients with type 2 diabetes mellitus attending a public primary healthcare clinics in Kuala Selangor District, Selangor

Farhani Samat, Mmed.FamMed[1], Sulizah Samad, MD[2], Siti Khalimah Rosnan, MBBS[3], Jasrinjeet Kaur, BPharm[1], Nur Hidayah Zulkefli, BPharm[2], Nur Athirah Rosli, Mmed.FamMed[1], Fateen Nadhira Ismail, MBBS[1], Noor Rafizah Aminah Aziz, MPH[4]

[1]Klinik Kesihatan Tanjung Karang, Jalan Sungai Kajang, Tanjung Karang, Selangor, [2]Klinik Kesihatan Kuala Selangor, Jalan Klinik, Kuala Selangor, [3]Klinik Kesihatan Sungai Tengi Kanan, Jalan Kiai Moid, Tanjung Karang, Selangor, [4]Pejabat Kesihatan Daerah Kuala Selangor, Jalan Semarak, Kuala Selangor

ABSTRACT

Introduction: Studies showed that vildagliptin can lower HbA1c levels by 0.8%–1%. However, there is limited data looking at vildagliptin use among suburban populations. The efficacy of vildagliptin use may differ among different populations, especially those with low socio-economic status. Thus, this study aimed to assess the HbA1c reduction after vildagliptin initiation, treatment patterns and the reason for its initiation among patients with type 2 diabetes mellitus attending outpatient clinics in Kuala Selangor District, Selangor.

Materials and Methods: This is a cross-sectional, retrospective study design. All patients who received vildagliptin in the Pharmacy Integrated Health System (PHIS) registry database from 2016 to 2021 were included as study samples. The exclusion criteria were being less than 18 years old and having type 1 diabetes mellitus. Patients' medical records were retrieved after sampling, and data were collected. One medical record was missing, thus SPSS analysis were performed on 144 vildagliptin users.

Results: In total, 84 females (58.3%) and 60 males (41.7%) with a mean age of 62.1 (±10.1) years were analysed in this study. Mean HbA1c pre-therapy was 8.5 ± 2.1%; while post-therapy 6 months demonstrated a mean HbA1c of 7.9 ± 1.8%. Use of vildagliptin alone or as an adjunct was associated with a mean reduction of 0.6% in HbA1c (p = 0.01). Factors influencing this HbA1c reduction were advancing age, specifically individuals aged 62 years and older (p = 0.02), patients who are already receiving insulin therapy (p=0.00) and those who express a willingness to commence insulin treatment during the counselling session prior to initiating the treatment plan (p = 0.00). Reasons for vildagliptin initiation documented by prescribers were non-insulin acceptance (n = 59, 40.97%), frequent hypoglycaemia (n = 6, 4.1%) and non-compliance with medications (n = 23, 15.9%). There was no association between demographic, medical background and reason for starting vildagliptin variables and HbA1c reduction (p < 0.001).

Conclusion: This study showed that initiating vildagliptin alone or as an adjunct therapy significantly reduced HbA1c and is beneficial for uncontrolled diabetes patients. While advancing age, concurrent administration of insulin and the patients' willingness to accept insulin treatment prior to the commencement of therapy were the factors that influenced HbA1c reduction among patients receiving vildagliptin therapy, we recommend primary care providers prioritise all of the significant variables discovered before initiating vildagliptin for their patients.

KEYWORDS:
vildagliptin; DPP-4 inhibitor; type 2 diabetes mellitus; T2DM

INTRODUCTION

The prevalence of patients with type 2 diabetes mellitus (T2DM) in Malaysia is increasing, from 13.4% in 2015 to 18.3% in 2019.[1] Remarkably, recent data from the National Diabetes Registry found that the prevalence of uncontrolled HbA1c is high compared to the controlled group, with a cut-off HbA1c level of 6.5% and below defined as controlled.[2] Studies showed that poor health literacy, low income and a poor social support population make them more likely to have poor glycemic control.[3,4] Kuala Selangor lies in a suburban area, and the majority of the people work as fishermen, self-employed, hawkers or government servants. The populations represent low to moderate socio-economic status. Data from an internal clinical audit showed that HbA1c levels in Kuala Selangor district mainly range from 7.5% to 8.5%, which is far from the Malaysian glycemic target of HbA1c 6.5%.[5] Thus, different measures are being taken to tackle this issue. These include using a multidisciplinary team approach and frequent audits and quality assurance to ensure the treatment modalities used are cost-effective and valuable to patients making the best use of common oral glucose-lowering drugs (OGLD). Treatment modalities used include metformin, sulphonylurea, Sodium-Glucose Cotransporter-2 inhibitors (SGLT2-i), insulin and DPP-4 inhibitors.

DPP-4 inhibitors prevent the hormone GLP-1 from degrading, which boosts the release of insulin right after a meal. Researchers have found that DPP-4 inhibitors help people reach their treatment goal of a 0.8%–1.0% drop in HbA1c

This article was accepted: 10 January 2024
Corresponding Author: Nur Athirah Rosli
Email: trahrosli@yahoo.com

with fewer hypoglycaemic side effects and better tolerance in older people.[6,7] With patients receiving a higher dose, the reduction in HbA1c is greater.[7,8] Due to its limited availability in Malaysia, especially in primary care settings, its use is mainly reserved as a second-line therapy among patients inadequately controlled on the maximal tolerated dose of sulphonylurea and contraindicated for metformin therapy or inadequately controlled with dual combination therapy with sulphonylurea and metformin.[8] Since the introduction of DPP-4 inhibitors in Kuala Selangor in 2016, only vildagliptin has been made available to our district health clinics. Other DPP-4 inhibitors have been introduced, but in view of vildagliptin's feasibility of use in terms of drug dosing and needing no-renal dose adjustment, it is still the preferred agent in our local settings. It has been in use up until the completion of this study.

The clinical efficacy of vildagliptin use among diabetic patients has been demonstrated in several studies in the literature review,[9,10] but is limited in Malaysia, especially in suburban populations with low to moderate socio-economic status in Kuala Selangor. Thus, exploring the usage of vildagliptin and its effect on HbA1c reduction, factors that influenced HbA1c reduction among vildagliptin users, treatment pattern and reason for its' initiation among prescribers is important for future reference and guidelines.

MATERIALS AND METHODS

This study is a cross-sectional, retrospective study involving patients' attending public primary healthcare clinics in Kuala Selangor district. All patients who received vildagliptin therapy registered under the Pharmacy Integrated Health System (PHIS) database under Kuala Selangor district from 2016 to 2021 were included in the study sample, while those below the age of 18 and having type 1 diabetes mellitus were excluded. A total of 145 patients were recruited in the sampling frame. Retrieval of patients' records was done from the PHIS database after sampling. Outpatient clinics that were involved during the retrieval of patients' records include Tanjung Karang Health Clinic, Kuala Selangor Health Clinic, Bukit Cerakah Health Clinic, Bestari Jaya Health Clinic, Ijok Health Clinic, Jeram Health Clinic and Sungai Tengi Kanan Health Clinic. Data on demographic and medical parameters, prescribers' documentation on the reason for vildagliptin initiation and changes in HbA1c were collected from the patients' record using a data collection sheet. One record was missing, so 144 patients were entered into the analysis.

Variables and Outcomes

Study variables were demographic characteristics, medical characteristics and the reason for vildagliptin initiation in the study population. The outcomes measured were mean HbA1c reductions post-therapy and variables that influenced HbA1c differences post-therapy for 6 months. Treatment patterns were also described in the analysis.

Data Management and Analysis

IBM SPSS version 26.0 was used for data analysis. Categorical data were analysed using descriptive statistics and reported as frequencies and percentages, while continuous data were reported as mean ± standard deviation (SD). A multivariate analysis (one-way MANOVA test) was used to compare the HbA1c difference between the groups (pre- and post-therapy). Post-hoc analysis (least significant differences) was conducted for significant ANOVA outcomes. A p-value of <0.05 was considered statistically significant.

RESULTS

Demographic Description and Treatment Patterns

In total, 145 patients received vildagliptin during the study period. One patient's record was missing, thus 84 females (58.3%) and 60 males (41.7%) were analysed (n = 144). The mean age was 62.1 ± 10.1 years old, while the mean duration of diabetes was 12.25 ± 6.7 years. One-third of them were obese (BMI ≥ 30 kg/m^2), while 94.4% had hypertension as a comorbidity. 75.7% have renal impairment, defined as a glomerular filtration rate less than 90 ml/min. The baseline characteristics of patients who were treated with vildagliptin, as well as the relationship between these characteristics and the difference in HbA1c after 6 months of vildagliptin therapy, are described in Table I. Paired t test were conducted to assess HbA1c reduction pre- and post-therapy. The mean HbA1c pre-therapy was 8.5 ± 2.1%, while post-therapy 6 months demonstrated a mean HbA1c of 7.9±1.8%. Use of vildagliptin as alone or as an adjunct was associated with a mean reduction of 0.6% in HbA1c; mean difference –0.6 ± 0.23 SD (–1.05, –0.15 95% CI) (p = 0.01). Factor analysis demonstrated three statistically significant values, which were advancing age, specifically individuals aged 62 years and older (p = 0.02), patients who are already receiving insulin therapy (p = 0.00) and those who express a willingness to commence insulin treatment during the counselling session prior to initiating the treatment plan (p = 0.00). Looking at treatment patterns, 85.5% received dual or triple agents, either in combination with metformin or together with sulphonylureas. Half of them were already on insulin at baseline (54.9%), while others remained on vildagliptin with combination with other agents or alone.

Figure 1 showed mean HbA1c reductions pre- and post-therapy while reasons for vildagliptin initiation were described in Figure 2. Looking at Figure 1, mean age (62.1 ± 10.1 years old) showed a lesser reduction in HbA1c during post-therapy compared to other factors, such as concomitant insulin therapy and patients who can accept insulin prior to initiation of vildagliptin. On the other hand, Figure 2 depicts prescribers' reasons for vildagliptin initiation. The most common reasons given were refusal of insulin therapy (40.9%), noncompliance with medication (15.9%) and frequent hypoglycaemia (4.1%).

DISCUSSION

Local guidelines recommend use of DPP4-inhibitor among patients with HbA1c 6.5%–10% as an alternative or with combination with other oral hypoglycaemic agent like metformin and sulphonylureas.[11] Some patients in this study have HbA1c of more than 10% prior to initiation of vildagliptin. While half of patients in this study refused insulin as stated by prescribers in their medical records, further reason for this issue need to be explored in future research. Many patients were overweight (BMI 23–27.4 kg/m^2), and these findings similar with studies done among

Table I: Demographics, medical characteristics and treatment pattern of study participants and difference in HbA1c level (n = 144)

Demographic characteristics	n (%)	HbA1c (%) pre-therapy	HbA1c (%) post 6 months	p value
Age, years (mean)	62.1 (±10.1)	8.471 ± 2.14	7.87 ± 1.89	0.02*
Weight, kg (mean)	73.4 (±15.5)	8.471 ± 2.14	7.87± 1.89	0.45
BMI, kg/m^2 (mean)	28.6 (±5.6)	8.471 ± 2.14	7.87± 1.89	0.91
Gender				
Male	60 (41.7)	8.05 ± 1.7	7.44 ± 1.5	0.06
Female	84 (58.3)	8.78 ± 2.07	8.19 ± 2.0	
Ethnicity				
Malay	108 (75)	8.52 ± 2.12	7.71 ± 1.67	0.91
Chinese	16 (11.1)	7.36 ± 0.91	7.27 ± 1.73	
Indian	20 (13.9)	9.06 ± 2.65	9.22 ± 2.54	
Employment				
Employed	41 (28.5)	8.493 ± 0.34	7.922 ± 0.3	0.98
unemployed	103 (71.5)	8.463 ± 0.21	7.86 ± 0.19	
Medical characteristics				
Duration of diabetes, years (mean)	12.25 (±6.7)	8.47 ± 2.15	7.87 ± 1.89	0.54
Polypharmacy (five and more drugs)				
Yes	136 (94.4)	8.49 ± 2.15	7.92 ± 1.89	0.46
No	8 (5.6)	8.14 ± 2.21	7.15 ± 1.76	
Renal impairment (eGFR<90 ml/min)				
Yes	109 (75.7)	8.406 ± 2.22	7.75 ± 1.88	0.35
No	35 (24.3)	8.67 ± 1.93	8.26 ± 1.91	
History of stroke				
Yes	1 (0.7)	9.0 ± 0.0	7.6 ± 0.0	0.86
No	143 (99.3)	8.47 ± 2.15	7.88 ± 1.90	
History of coronary artery disease				
Yes	17 (11.8)	8.05 ± 1.89	7.91 ± 2.06	0.39
No	127 (88.2)	8.53 ± 2.18	7.87 ± 1.88	
Obesity (BMI ≥30 kg/m2)				
Yes	49 (34.0)	8.26 ± 1.73	7.79 ± 1.66	0.64
No	95 (66.0)	8.58 ± 2.33	7.92 ± 2.01	
Hypertension				
Yes	136 (94.4)	8.49 ± 2.19	7.93 ± 1.92	0.29
No	8 (5.6)	8.21 ± 1.18	7.04 ± 1.09	
Dyslipidaemia				
Yes	0.29	8.53 ± 2.17	7.93 ± 1.91	0.23
No	6 (4.2)	7.23 ± 0.58	6.59 ± 0.46	
Treatment patterns				
Usage of oral hypoglycaemic agent				
vildagliptin alone	21 (14.6)	8.57 ± 2.51	7.97 ± 2.2	0.07
vildagliptin and metformin	63 (43.8)	9.005 ± 2.55	8.2 ± 2.05	
vildagliptin, metformin and sulphonylureas	60 (41.7)	7.89 ± 1.24	7.51 ± 1.55	
Insulin therapy				
Yes	79 (54.9)	9.25 ± 2.5	8.48 ± 2.06	0.00*
no	65 (45.1)	7.54 ± 1.03	7.15 ± 1.37	
Reason for vildagliptin initiation				
History of non-compliance pre-initiation				
Yes	23 (16.0)	8.78 ± 2.09	8.41 ± 1.72	0.29
No	121 (84.0)	8.41 ± 2.16	7.77 ± 1.92	
History of hypoglycaemia pre-initiation				
Yes	6 (4.2)	8.95 ± 2.53	7.85 ± 0.91	0.69
No	138 (95.8)	8.45 ± 2.14	7.88 ± 1.89	
Insulin acceptance pre-initiation				
Yes	85 (59.0)	9.18 ± 2.42	8.43 ± 2.03	0.00*
No	59 (40.9)	7.49 ± 0.97	7.08 ± 1.38	

*p value <0.05 (significant).

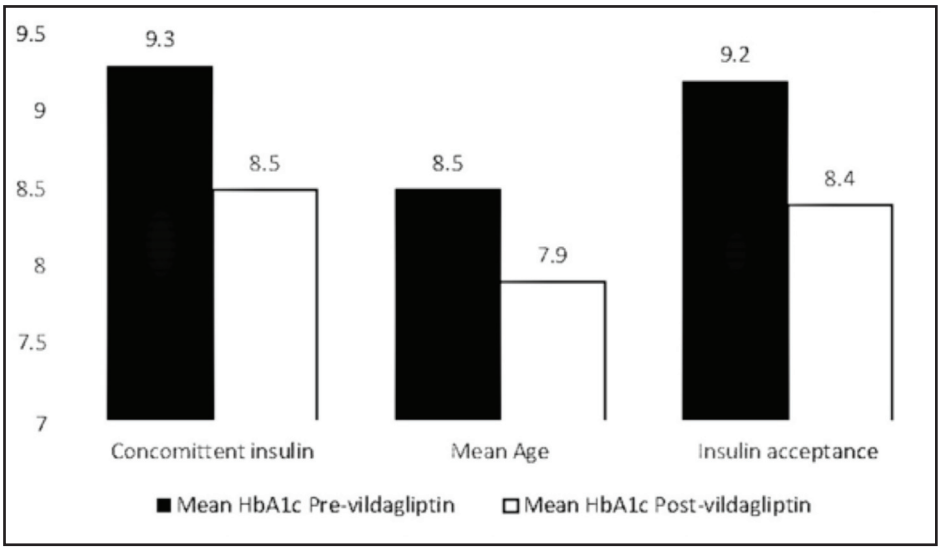

Fig. 1: HbA1c reduction pre- and post-vildagliptin therapy based on factors found on statistical analysis.

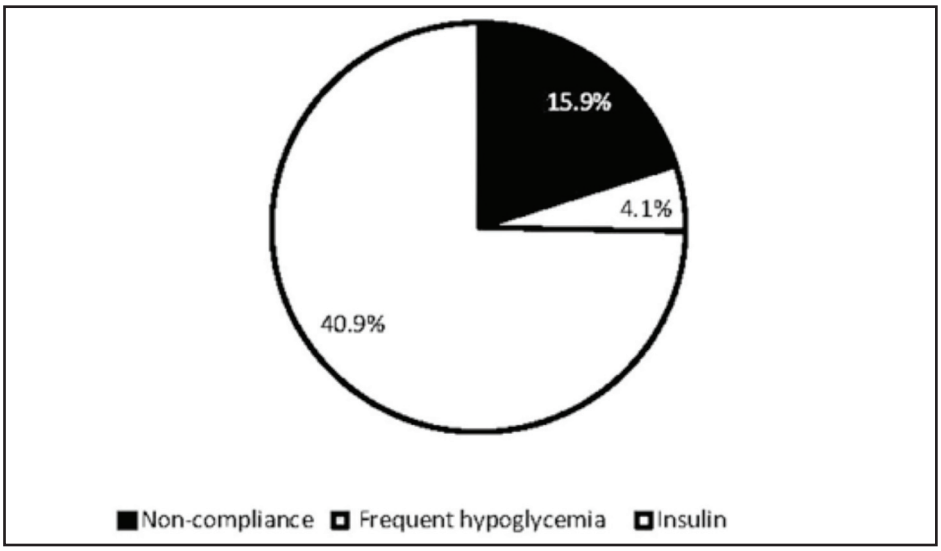

Fig. 2: Reasons for vildagliptin initiation (n = 144).

DPP4-inhibitor users in hospital settings in Malaysia.[12] Dyslipidaemia, followed by hypertension and coronary artery disease (CAD), is most common in our study population. Majority of patients have renal impairment at the start of therapy, probably due to long-standing years of diabetes; mean duration of 12 years. DPP4-inhibitor effectively lowers HbA1c, and meta-analysis have shown its safety among diabetes patients at various stages of renal insufficiency.[13]

The HbA1c reduction rate found in this study is lower compared to other studies done in different populations worldwide. Overall, the reduction rate reported from other studies ranged from 0.8% to 1.0%.4–6 Interestingly, we found that other than age, gender, ethnicity and employment status, they did not have a significant impact on HbA1c, as well as the patients' medical background in this study. There are many factors, like health literacy, that could possibly influence these findings and hence need to be explored. During the analysis, we found that three factors may influence HbA1c reduction after 6 months of vildagliptin initiation: increasing age, patients on concurrent insulin therapy and insulin acceptance prior to treatment.

Increasing Age

According to a study conducted by Hong, Jung[14], was determined that advancing age is an indicator of HbA1c reduction in patients on DPP-4 inhibitor therapy, with a mean age of 53 years. However, the group under study exhibits a contrasting perspective; specifically, the advantages were observed to vary significantly with a 10-year difference in age compared to our study. A systematic analysis also found that a reduction of HbA1c of 8.4% was seen among elderly patients receiving vildagliptin 50 mg bd dosing (65 years old and older) compared to other age ranges.[11] In addition, randomised controlled trials have reported that the elderly significantly reduced HbA1c

compared to the placebo group among those treated with vildagliptin,[12] and they demonstrated fewer hypoglycaemic events during the treatment. Thus, the reduction of HbA1c in this study cannot be negligible and needs to be emphasised during future consultations. Additional variables such as body mass index (BMI) and gender were shown to be statistically insignificant, aligning with the findings reported in the aforementioned study by Mathieu and Degrande.[11]

Patients with Concomitant Insulin Therapy

Most diabetic patients in this study were on insulin therapy (54.9%) concurrent with their vildagliptin treatment. Significant reductions in HbA1c were observed among them after 6 months of initiation compared to those without insulin therapy. Even though a study by Mak, Nagarajah[15] found that adding DPP-4 inhibitors to patients with or without insulin therapy will have a significant impact on the HbA1c level, our study found it differently. However, the specific type of insulin therapy was not addressed in the study, and the HbA1c outcomes were also obtained at varied durations of DPP-4 inhibitors used. Nevertheless, if cost is a concern, it may be advantageous to concentrate on this particular demographic, as previous research has demonstrated its efficacy. Based on systematic studies, using a combination of DPP-4 inhibitors, specifically vildagliptin, along with insulin was suggested as a safe and effective way to improve blood sugar control. In addition, it was shown in the study that vildagliptin reduced HbA1c by 0.8%, with a between-group difference of −0.7% compared with placebo. This method minimises the likelihood of hypoglycaemia or excessive weight gain.[16] In addition, according to Ebrashy et al.[17], adding vildagliptin to insulin reduced HbA1c, body weight and insulin dosage in a clinically significant way without exposing T2DM patients at risk for hypoglycaemia. Additionally, Li et al.[18] found that patients receiving vildagliptin add-on insulin therapy had a significantly lower HbA1c (by 0.9%) than those receiving placebo at the endpoint.

Insulin Acceptance

Interestingly, according to the analysis, a subset of patients was initiated on vildagliptin due to their refusal of insulin. However, the statistical findings revealed the opposite outcome. The results of our investigation indicate that patients who demonstrated a willingness to initiate insulin therapy experienced a notable decrease in HbA1c levels, with a mean reduction from 9.1% to 8.4% (–0.7). Nevertheless, certain individuals who expressed their willingness to initiate insulin therapy after the initial consultation ultimately commenced insulin treatment during the subsequent follow-up session. A qualitative study showed that belief and insulin acceptance do have an impact on medication adherence and glycemic control in the long term run.[19] Insulin acceptance has become one of the major factors for determining target glycemic control among many countries worldwide.[20] However, studies have shown that DPP-4 inhibitors can only lower HbA1c levels by up to 0.8% when used alone.[5] In addition, when taken with insulin, the reduction in insulin requirement is more significant. Hence, the selection of an optimal patient profile and the assessment of readiness for insulin administration are crucial considerations in the context of follow-up care among patients planning to start on vildagliptin therapy.

STUDY LIMITATIONS

This study is a cross-sectional study design; thus, it cannot determine a true causal-effect relationship. As it was done retrospectively, many factors could not be assessed that may have influenced the study findings, such as monthly income of patients (to determine their socio-economic status), and their reasons for insulin refusal. Additionally, there are potential sources of error in the process of transcribing manual prescriptions from the patients' record into the PHIS, which could result in the omission of data. Furthermore, there were other confounding factors that contributed to the decrease in HbA1c levels, apart from the use of pharmaceutical therapy. These factors may have potentially impacted the accuracy of the data reported in the present investigation. Additional variables that could potentially influence the results, such as levels of physical activity, dietary habits and the occurrence of surgical interventions, were not included in the study's measurements.

RECOMMENDATIONS

Despite its several limitations, this study's findings showed that there was a reduction in HbA1c after 6 months of its initiation among vildagliptin users. Therefore, its usage is beneficial and should be recommended to improve glycemic control among people with type 2 diabetes. Addressing age and willingness to start insulin influence positive outcomes, which should be emphasised during clinical consultation. Despite that, we recommend future research with a better study design, such as randomised controlled trials to look for the true effect of vildagliptin on HbA1c reduction and case–control studies to look for the true odds ratio among factors that we found during this analysis. In additon, a qualitative study looking at the reasons for insulin refusal among this population is highly recommended.

CONCLUSIONS

This study showed that initiating vildagliptin alone or as an adjunct therapy significantly reduced HbA1c and is beneficial for uncontrolled diabetes patients. While advancing age, concurrent administration of insulin, and the patients' willingness to accept insulin treatment prior to the commencement of therapy were the factors that influenced HbA1c reduction among patients receiving vildagliptin therapy, and we recommend primary care providers prioritise all of the significant variables discovered before initiating vildagliptin for their patients.

ACKNOWLEDGEMENTS

This study had received approval from the Medical research and Ethics Committee (MREC). The researchers also would like to express their gratitude to everyone who helped with this study, whether directly or indirectly.

REFERENCES

1. Institute for Public Health (IPH) 2021. National Health and Morbidity Survey (NHMS) 2020.
2. Arunah Chandran PHP, Disease Control Division, Mohd Nazri Abdullah AMO, Disease Control Division, Fathilah Abdul PHM, Disease Control Division. Ministry of Health Malaysia 2020. National Diabetes Registry Report 2013-2019. 2020.

3. Gomes MB, Tang F, Chen H, Cid-Ruzafa J, Fenici P, Khunti K, et al. Socioeconomic Factors associated with glycemic measurement and poor hba1c control in people with type 2 diabetes: The Global DISCOVER Study. Front Endocrinol (Lausanne). 2022; 13: 831676.
4. Ong-Artborirak P, Seangpraw K, Boonyathee S, Auttama N, Winaiprasert P. Health literacy, self-efficacy, self-care behaviors, and glycemic control among older adults with type 2 diabetes mellitus: a cross-sectional study in Thai communities. BMC Geriatr. 2023; 23(1): 297.
5. Malaysia MoH. Clinical Practice Guideline Management of Type 2 Diabetes Mellitus.6th edn; 2020.
6. Schweizer A, Dejager S, Bosi E. Comparison of vildagliptin and metformin monotherapy in elderly patients with type 2 diabetes: a 24-week, double-blind, randomized trial. Diabetes Obes Metab. 2009; 11(8): 804-12.
7. Pan C, Xing X, Han P, Zheng S, Ma J, Liu J, et al. Efficacy and tolerability of vildagliptin as add-on therapy to metformin in Chinese patients with type 2 diabetes mellitus. Diabetes Obes Metab. 2012; 14(8): 737-44.
8. Waugh N, Cummins E, Royle P, Clar C, Marien M, Richter B, et al. Newer agents for blood glucose control in type 2 diabetes: systematic review and economic evaluation. Health technology assessment (Winchester, England). 2010; 14(36): 1-248.
9. De P, Mozdiak E, Andrews C, Geransar P. Vildagliptin as an add-on agent in type 2 diabetes in a multi-ethnic UK clinic: a single-centre audit. Br J Diab Vasc Dis. 2011; 11(2): 99–102.
10. Das S, Gupta AK, Bandyopadhyaya B, Darla BH, Arya V, Abhyankar M, et al. Data on vildagliptin and vildagliptin plus metformin combination in type-2 diabetes mellitus management. Bioinformation. 2021; 17(3): 413-23.
11. Mathieu C, Degrande E. Vildagliptin: a new oral treatment for type 2 diabetes mellitus. Vasc Health Risk Manag. 2008; 4(6): 1349-60.
12. Schweizer A, Dejager S. Experience with vildagliptin in patients ≥75 years with type 2 diabetes and moderate or severe renal impairment. Diabetes Ther. 2013; 4(2): 257-67.
13. Chen Y, Men K, Li X-F, Li J, Liu M, Fan Z-Q. Efficacy and safety of dipeptidyl peptidase-4 inhibitors in the treatment of type 2 diabetes mellitus patients with moderate to severe renal impairment: a meta-analysis. Eur Rev Med Pharmacol Sci. 2018;11:3502–14.
14. Hong S, Jung CH, Han S, Park CY. Increasing age associated with higher dipeptidyl peptidase-4 inhibition rate is a predictive factor for efficacy of dipeptidyl peptidase-4 inhibitors. Diab Metab J. 2022; 46(1): 63-70.
15. Mak WY, Nagarajah JR, Abdul Halim H, Ramadas A, Mohd Pauzi Z, Pee LT, et al. Dipeptidyl peptidase-4 inhibitors use in type ii diabetic patients in a tertiary hospital. J Pharm Policy Practice. 2020; 13(1): 34.
16. Gomez-Peralta F, Abreu C, Gomez-Rodriguez S, Barranco RJ, Umpierrez GE. Safety and efficacy of DPP4 inhibitor and basal insulin in type 2 diabetes: an updated review and challenging clinical scenarios. Diabetes Ther. 2018; 9(5): 1775-89.
17. El Ebrashy I, El Kafrawy N, Raouf R, Yousry D. Effectiveness, safety, and tolerability of vildagliptin or vildagliptin/metformin combination in patients with type 2 diabetes uncontrolled on insulin therapy in a real-world setting in Egypt: The OMEGA study. Diabetes Res Clin Practice. 2020; 162: 108042.
18. Li F-f, Shen Y, Sun R, Zhang D-f, Jin X, Zhai X-f, et al. Effects of vildagliptin add-on insulin therapy on nocturnal glycemic variations in uncontrolled type 2 diabetes. Diab Ther. 2017; 8(5): 1111-22.
19. Liu C, De Roza J, Ooi CW, Mathew BK, Elya, Tang WE. Impact of patients' beliefs about insulin on acceptance and adherence to insulin therapy: a qualitative study in primary care. BMC Primary Care. 2022; 23(1): 15.
20. Boels AM, Koning E, Vos RC, Khunti K, Rutten GE. Individualised targets for insulin initiation in type 2 diabetes mellitus-the influence of physician and practice: a cross-sectional study in eight European countries. BMJ Open. 2019; 9(8): e032040.