The Usage of Vildagliptin as an Adjuvant Therapy in Patients with Type 2 Diabetes Mellitus in Public Health Clinics in Penang

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Abstract

Introduction: Diabetes mellitus is an increasing public health burden in Malaysia, with type 2 diabetes mellitus (T2DM) accounting for most adult cases. Vildagliptin, a dipeptidyl peptidase-4 (DPP-4) inhibitor, is widely used as adjunctive therapy for T2DM in public primary care settings. However, local real-world evidence on its effectiveness in routine primary care remains limited, with demographic factors potentially influencing the glycaemic response.

Objectives: To compare glycated haemoglobin (HbA1c) and fasting blood glucose (FBG) levels in patients with T2DM before and after addition of vildagliptin to existing antidiabetic regimen, and to identify demographic factors associated with changes in HbA1c levels.

Methods: A retrospective study was conducted from 1st January 2019 to 31st December 2022 to observe the changes of HbA1c and FBG in T2DM patients treated with vildagliptin in six public health clinics in South Seberang Perai. Demographic and clinical data were extracted from medical records. Changes in HbA1c and FBG following vildagliptin initiation were evaluated using paired t-tests, while independent t-tests and one-way analysis of variance (ANOVA) were used to assess associations between demographic factors and HbA1c changes.

Results: A total of 325 patients were included. The majority were female (64.6%, n=210) and 66.8% were receiving concomitant vildagliptin and insulin therapy (n=217). The mean age was 60.6 ± 10.9 years, and the mean duration of T2DM was 13.19 ± 6.70 years. At baseline, more than half of the patients (54.4%) had HbA1c more than 10.0% with a mean of 10.2 ± 2.2%. The mean FBG was 10.0 ± 4.3 mmol/L before the initiation of vildagliptin. Following vildagliptin initiation, mean HbA1c decreased by 0.61% ($p<0.001$) and mean FBG decreased by 1.08 mmol/L ($p<0.001$). Male patients demonstrated a significantly greater reduction in HbA1c than female patients ($p=0.022$).

Conclusion: Vildagliptin, when added to existing antidiabetic therapy, was associated with significant improvements in glycaemic control among patients with inadequately controlled T2DM in public primary care settings. These findings support its role as an effective add-on treatment option in routine clinical practice, while further studies are warranted to determine whether the observed sex-related difference in HbA1c reduction persists after adjustment for potential confounding factors.

Keywords: Vildagliptin, DPP-4 inhibitors, HbA1c, FBG, type 2 diabetes mellitus

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Introduction

Diabetes mellitus continues to pose a major global health challenge, with its prevalence rising sharply in many countries, including Malaysia. Within the Western Pacific region, Malaysia is among the nations with the fastest-growing burden of diabetes (1). According to the National Health and Morbidity Survey (NHMS) 2019, the prevalence of diabetes among Malaysians aged 18 years and above was 18.3%, representing a 4% increase compared with year 2015. Furthermore, 48.6% of individuals with diabetes remained undiagnosed while the prevalence among young adults aged 18-29 years increased by approximately 5% (2). Type 2 diabetes mellitus (T2DM) remains the predominant form of diabetes, accounting for almost all cases of newly diagnosed adult diabetes according to the National Diabetes Registry Report 2023.

Globally, an estimated USD 727 billion was spent on diabetes management in 2017 with healthcare expenditure expected to increase further in the future (1). Effective management of T2DM is therefore essential to mitigate its growing public health burden. It requires sustained lifestyle modification and long-term pharmacotherapy when indicated to achieve and maintain optimal glycaemic control. Oral antidiabetic drugs (OADs) such as metformin and sulfonylureas are commonly used as first-line treatments in primary care, with dipeptidyl peptidase-4 (DPP-4) inhibitors generally prescribed as an adjunct to existing glucose-lowering therapy when glycaemic targets are not achieved. In fact, DPP-4 inhibitors have been increasingly valued for their glucose-dependent mechanism, low incidence of hypoglycaemia, and weight-neutral profile, making them suitable for a broad range of patients in routine clinical practice (2).

DPP-4 inhibitors, particularly vildagliptin, have been widely prescribed as part of routine diabetes management in South Seberang Perai public health clinics since 2019. However, local data on glycaemic outcomes following addition of vildagliptin to the existing antidiabetic regimen remains limited. Meanwhile, studies have reported that glycaemic response to OADs including DPP-4 inhibitors may vary among individuals with distinct demographic characteristics such as age, sex, ethnicity and duration of diabetes (3-6). Given the multi-ethnic population of South Seberang Perai, this setting provides an ideal opportunity to examine whether demographic factors influence treatment response to OADs including vildagliptin in addition to its primary objective to evaluate changes in glycated haemoglobin (HbA1c) and fasting blood glucose (FBG) with the use of vildagliptin as adjunctive therapy among individuals with T2DM attending public health clinics in South Seberang Perai.

Method

A retrospective study was designed to evaluate changes in glycaemic parameters among patients who were initiated on vildagliptin in addition to existing OADs between 1st January 2019 and 31st December 2022. This study was conducted across six public health clinics in the South Seberang Perai District, which included Bukit Panchor, Bandar Tasek Mutiara, Sungai Bakap, Sungai Acheh, Nibong Tebal, and Valdor. The study received approval from the Medical Research Ethics Committee (MREC), Ministry of Health Malaysia, and was registered with the National Medical Research Registry (NMRR ID-23-03281-SJX).

Universal sampling was employed, whereby all patients who fulfilled the inclusion criteria during the study period were included. Therefore, no sample size calculation was performed for this study. Patients were eligible for inclusion if they had a diagnosis of T2DM, aged 18 years or older, had been receiving first-line antidiabetic therapy prior to the initiation of vildagliptin, received follow-up care at any of the participating clinics during the study period, and had vildagliptin added to their usual diabetes regimen within the specified timeframe of this study. Patients were excluded if they discontinued vildagliptin due to intolerance, had incomplete or missing clinical records, or defaulted follow-up during the three-month post-initiation period.

Patient records were retrieved manually from medical records maintained at the participating clinics. A structured data collection form was developed to ensure standardised data extraction, which consisted of three sections. The first section captured demographic information, including age, sex, ethnicity, height, and duration of diagnosed T2DM. The second section collected baseline information of the participants and three-month post-vildagliptin measurements, including HbA1c, FBG, body

weight, and body mass index (BMI). The third section documented concurrent medication regimen such as metformin, sulfonylureas, insulin, sodium-glucose cotransporter 2 (SGLT2) inhibitors. All data were obtained directly from physician-documented clinical records to ensure accuracy and consistency.

Statistical analyses were performed using Statistical Package for the Social Sciences (SPSS) version 20.0. Descriptive statistics were used to summarise patient characteristics. Categorical variables were presented as frequencies and percentages, whereas numerical variables were reported as means with standard deviations (SD) for normally distributed data or medians with interquartile ranges (IQR) for skewed data. Paired t-tests were used to compare HbA1c and FBG values before and three months after vildagliptin initiation. Independent t-tests were employed to assess differences in HbA1c reduction between dichotomous variables, such as sex and insulin use. One-way analysis of variance (ANOVA) was used to evaluate differences across variables with more than two categories, including ethnicity and duration of diabetes. A p-value of less than 0.05 was considered statistically significant (7).

Results

Of the 460 patients who received vildagliptin during the study period, 135 were excluded due to incomplete or missing clinical data, discontinuation due to intolerance, or defaulted follow-up. Consequently, 325 patients were included in the final analysis. Among these patients, 35.4% (n=115) were male and 64.6% (n=210) were female. The age of patients ranged from 22 to 90 years, with a mean age of 60.6 ± 10.9 years. More than half of the study population (56.6%) were aged 60 years or older. The mean duration of T2DM was 13.19 ± 6.70 years, with 60.7% of patients having lived with diabetes for more than 10 years. Concurrent insulin therapy was prescribed in 66.8% (n=217) of patients receiving vildagliptin (Table 1).

Table 1: Demographic factors associated with changes in HbA1c with adjunctive vildagliptin usage, n=325

Variable	n (%)	Mean HbA1c changes (SD)	p-value
Age[a] (years old)			
< 60	141 (43.4)	-0.53 (2.03)	0.550
⩾ 60	184 (56.6)	-0.67 (2.21)	
Gender[a]			
Male	115 (35.4)	-0.98 (2.20)	**0.022**
Female	210 (64.6)	-0.41(2.07)	
Ethnicity[b]			
Malay	138 (42.5)	-0.46(2.34)	0.533
Chinese	39 (12.0)	-0.79 (1.72)	
Indian	148 (45.5)	-0.71 (2.03)	
Duration of T2DM[b] (years)			
⩽10	128 (39.4)	-0.47 (2.23)	0.689
11 - 20	164 (50.5)	-0.66 (2.05)	
21 - 30	26 (8.0)	-0.80 (2.25)	
> 30	7 (2.2)	-1.26 (2.04)	
Insulin[a]			
No	108 (33.2)	-0.46 (1.85)	0.343
Yes	217 (66.8)	-0.69 (2.26)	

[a]Independent t -test was conducted to compare age, gender and insulin usage between the groups.
[b]One-way ANOVA was conducted to compare the ethnicity and duration of T2DM between the groups.
Abbreviation: HbA1c = glycated haemoglobin; SD = standard deviation; CI = confidence interval; df = degrees of freedom; T2DM = type 2 diabetes mellitus

Inspection of histograms revealed that HbA1c differences were normally distributed for both gender groups. The assumption of homogeneity of variances was met, as assessed by Levene's test for equality of variances. Therefore, an independent t-test was run to compare the mean change in HbA1c between males and females, and 95% confidence interval (CI) for the mean difference were calculated.

On average, males showed a greater mean reduction in HbA1c (-0.98 ± 2.20) compared with females (-0.41 ± 2.07), with a mean difference of -0.56 (95% CI: -1.05 to -0.08) and p=0.022 (Table 1). These findings suggest a significant association between HbA1c reduction and gender. Independent t-tests were also run to evaluate the associations between HbA1c change and age group as well as concurrent insulin use. However, neither analysis demonstrated a statistically significant difference. Similarly, one-way ANOVA was used to assess differences in HbA1c reduction across ethnic groups and categories of diabetes duration, but no significant associations were identified (Table 1).

Table 2: HbA1c categories distribution before and after vildagliptin use, n=325

HbA1c	Pre vildagliptin, n (%)	Post vildagliptin, n (%)
< 6.5%	7 (2.2)	19 (5.8)
6.5 - 9.9%	141 (43.4)	177 (54.4)
⩾10.0%	177 (54.5)	129 (39.7)

Abbreviation: HbA1c = glycated haemoglobin

Table 3: Changes in HbA1c and FBG following vildagliptin initiation, n=325

Parameters[a]	Pre vildagliptin	Post vildagliptin	Mean difference (95% CI)	p-value
HbA1c (%)	10.15 ± 2.20	9.54 ± 2.30	-0.61 (0.38, 0.84)	**<0.001**
FBG (mmol/L)	10.00 ± 4.30	8.92 ± 3.60	-1.08 (0.60, 1.56)	**<0.001**

[a] Paired T-test was conducted.
Values reported as mean ± SD
Abbreviation: CI = confidence interval; HbA1c = glycated haemoglobin; FBG = fasting blood glucose

More than half of the patients (54.5%) had a baseline HbA1c of more than 10% (Table 2). Prior to the initiation of vildagliptin, the mean HbA1c was 10.15 ± 2.20%, whereas the mean FBG was 10.00 ± 4.30 mmol/L (Table 3). Histogram inspection confirmed that the changes in HbA1c and FBG were normally distributed. Therefore, paired-t tests were performed to compare glycaemic parameters before and after vildagliptin initiation. Mean HbA1c decreased significantly to 9.54 ± 2.30% after treatment, representing a mean reduction of 0.61% (p<0.001). Similarly, mean FBG decreased significantly to 8.92 ± 3.60 mmol/L, corresponding to a mean reduction of 1.08 mmol/L (p<0.001) (Table 3).

Discussion

Prior to treatment, more than half of the cohort presented with markedly elevated HbA1c values (≥10.0%), reflecting poor glycaemic control and the need of treatment modification. After three months of adjunctive therapy with vildagliptin, significant reductions were observed in both HbA1c and FBG, demonstrating the clinical benefit of adding vildagliptin to existing treatment regimens which typically included metformin, gliclazide and insulin. This finding was consistent with previous observational studies and clinical trials demonstrating improvements in glycaemic control following the addition of vildagliptin to existing treatment regimens, including metformin-based combinations (8–11). Similar benefits have also been reported when DPP-4 inhibitors were added to insulin therapy, with improvements in glycaemic control without a substantial increase in hypoglycaemia or weight gain (12). Fonseca et al. likewise demonstrated the efficacy of vildagliptin in patients with inadequately controlled HbA1c despite insulin therapy (13). Collectively, these findings support the effectiveness of vildagliptin as an adjunctive therapy for improving glycaemic control among patients with T2DM receiving existing antidiabetic treatment in routine primary care.

The clinical relevance of these findings may be considered in the context of the progressive nature of T2DM. The Malaysian Clinical Practice Guidelines recommend an HbA1c target of <7% for most adults with individualised goals based on age, comorbidities, and hypoglycaemia risk (2). As beta cell function progressively declines in T2DM, treatment intensification may be necessary when glycaemic targets are no longer achieved with existing therapy (14). This may involve adding another OAD or initiating injectable therapy. In this context, vildagliptin offers an alternative oral option, particularly for patients reluctant to use injectables due to needle anxiety or self-administration challenges. Its glucose-dependent mechanism, low risk of hypoglycaemia, and weight-neutral profile may also support treatment acceptance and adherence (15–18). Overall, the glycaemic benefits and established safety profile of vildagliptin support its role as a potential option for treatment intensification in patients with suboptimal glycaemic control.

A notable finding of this study was the significantly greater reduction in HbA1c observed among male patients compared with female patients when vildagliptin was used in adjunct with other OADs. This aligns with previous reports by Hassan et al. and Choe et al., which suggested that men were more likely to achieve glycaemic targets than women when vildagliptin is used as part of the OADs regimen (19-20). Biological differences may potentially contribute to variation in treatment response. Differences in body fat distribution, insulin sensitivity, β-cell function, and sex hormones may influence glucose metabolism and potentially modify the response to incretin-based therapies (21-22). Nevertheless, these mechanisms remain speculative in the absence of direct measurements of hormonal status, insulin sensitivity, or β-cell function in the present study. As vildagliptin was used as an adjunct with other OADs, the observed reduction in HbA1c cannot be attributed to vildagliptin alone, and the potential contribution of concomitant therapies to the observed sex-related difference cannot be excluded. Overall, while the observed sex-related difference in glycaemic response warrants further investigation, it should be interpreted as a difference in HbA1c reduction among patients receiving vildagliptin-containing regimens rather than as evidence of a sex-specific difference in the efficacy of vildagliptin. From a clinical perspective, gender alone should not be used as a determinant for prescribing vildagliptin, and treatment selection should continue to be guided by individual patient characteristics, treatment goals, comorbidities, and the overall suitability of the therapeutic regimen.

Several limitations must be acknowledged when interpreting the findings of this study. First, the impact of different combinations of OADs was not evaluated separately because of the substantial heterogeneity and large number of possible treatment regimens. Hence, this may have limited the ability of this study to determine whether treatment response varied according to concomitant therapy. Differences in concomitant therapy may also have contributed to the observed sex-related difference in HbA1c reduction and cannot be excluded. Second, the retrospective study design limited the availability of potentially important clinical information, particularly medication adherence, which may have influenced the observed changes in HbA1c and FBG and introduced potential bias. Other factors that may affect glycaemic response, such as lifestyle-related factors, may also not have been consistently captured in this study. Third, although universal sampling was employed, the relatively small number of eligible patients may have reduced the statistical power and limited the generalisability of the findings in this study. Fourth, the follow-up duration was limited to three months, which may not adequately capture the long-term durability of glycaemic improvements or changes in treatment requirements over time. A longer observation period would allow for assessment of HbA1c stability, sustained treatment response, and the need for subsequent therapeutic adjustments.

Given these limitations, future studies should adopt prospective, multicentre designs with larger sample sizes to improve the robustness and generalisability of the findings and assess the sustained effectiveness of vildagliptin. Treatment response should be evaluated according to concomitant antidiabetic regimens, with adjustment for potential confounding factors, including medication adherence, lifestyle factors, and subsequent treatment modifications. Serial assessments of HbA1c and FBG, together with systematic evaluation of medication adherence, adverse events, and patient-reported outcomes, would provide a more comprehensive assessment of treatment response. Longer follow-up would also allow evaluation of the durability of glycaemic improvement and subsequent treatment intensification or modification. In addition, adequately powered analyses should further investigate the observed sex-related difference in HbA1c reduction and determine whether this association persists after adjustment for potential confounding factors.

Conclusion

The addition of vildagliptin to existing antidiabetic therapy was associated with significant reductions in HbA1c and FBG over three months among patients with T2DM attending public health clinics in South Seberang Perai. These findings suggested a potential benefit of vildagliptin as an adjunctive therapy for patients requiring additional glycaemic control. Male patients demonstrated greater HbA1c reductions than female patients, although this finding should be interpreted cautiously given the potential influence of unmeasured factors. Larger prospective studies and longer follow-up are warranted to confirm these findings and assess the durability of treatment response.

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Conflict of Interest

The authors declare that they have no conflicts of interest and they did not receive any financial support or funding that is relevant to this study.

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