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Original Research Article

Prescribing patterns of antidiabetic drugs and glycaemic control in type 2 diabetes patients visiting tertiary care hospital based in Karachi, Pakistan

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ABSTRACT

Background: Diabetes mellitus (DM) is a global health concern with elevated blood glucose levels and insulin dysfunction. Our study analyzed antidiabetic drug prescriptions and their effectiveness in managing type 2 diabetes (T2DM) with or without comorbidities. We aimed to gain insights into prescribing practices and efficacy in diverse patient populations.
Methods: This retrospective study was conducted at The Aga Khan University in Karachi, Pakistan, over a three-month period. It analysed prescriptions of anti-diabetic drugs for male and female patients aged 18 years and above with type 2 diabetes mellitus. Patient data, including prescribed drugs, diabetes duration, co-morbid conditions, and HbA1c levels, were reviewed using the hospital's Health Information Management System (HIMS).
Results: Data from 552 diabetic patients were analysed. The mean age of participants with type-2 DM was 58 years, with 53.3% males and 46.7% females. 25.2% had diabetes for 5-10 years. Good glycaemic control was achieved by 48.7% of patients. Metformin (83.9%), dipeptidyl peptidase 4 inhibitors (DPP4) inhibitors (61.1%), and sodium-glucose transport 2 inhibitors (SGLT2) inhibitors (54.0%) were the most prescribed medications. Three-drug combinations were predominant (41.5%).
Conclusions: Metformin was the most prescribed monotherapy for T2DM, followed by DPP4 inhibitors and SGLT2 inhibitors. Common combinations included DPP4 inhibitors with metformin, three-drug combinations with metformin, DPP4 inhibitors, and SGLT2 inhibitors, and four-drug combinations with metformin, DPP4 inhibitors, SGLT2 inhibitors, and sulfonylurea. DPP4 inhibitors were commonly used after metformin due to availability and cost-effectiveness. Glucagon-like peptide-1 inhibitors (GLP-1) analogs were less commonly prescribed due to cost, patient preference, and concerns about side effects.

Keywords: T2DM, SGLT2, GLP-1, DPP4

INTRODUCTION

Diabetes mellitus (DM) presents a major worldwide public health concern due to its high prevalence. It is a condition characterized by chronically elevated blood glucose levels caused by a malfunction in insulin production or effectiveness, leading to disturbances in carbohydrate metabolism.[1] Globally, it is estimated that approximately 537 million adults experience DM, with type-2 DM constituting around 90% of these cases.[2] According to the 2022 report by the International Diabetes Federation (IDF), around 26.7% of adults in Pakistan were affected by this disease, resulting in an estimated total of approximately 33 million cases.[2] The development of diabetes in individuals, particularly adults, is primarily influenced by genetic factors and lifestyle choices. These factors encompass obesity, a sedentary lifestyle, and the consumption of processed foods with elevated sugar

content. When considering the criteria established by the World Health Organization (WHO) Asia-Pacific cut-offs, Pakistan exhibits an overall weighted prevalence of 57.9% for generalized obesity (42% in males and 58% in females), and 73.1% for central obesity (37.3% in males and 62.7% in females).[3]

According to the 2023 guidelines of the American Diabetes Association (ADA), sodium glucose transport 2 inhibitors and glucagon-like peptide GLP-1 receptor agonists are recommended for patients who are at a high risk of developing atherosclerotic cardiovascular disease, heart failure, or chronic kidney disease (CKD).[4] A research study conducted in Eastern India examined the prescribing patterns of antidiabetic drugs in patients with type-2 diabetes mellitus. The study observed that 5.23% of the cases involved prescriptions for antidiabetic drugs as a single therapy. Alongside monotherapy, combinations of different antidiabetic drugs were prescribed in various combinations: two-drug combinations accounted for 32.36% of cases, three-drug combinations for 38.17% of cases, four-drug combinations for 16.47% of cases, five-drug combinations for 7.17% of cases, and six-drug combinations for 0.58% of cases.[5] Similarly, in another study conducted among type-2 DM patients with hypertension as a comorbidity, metformin was the most frequently prescribed antidiabetic drug as a monotherapy, accounting for 85.19% of such prescriptions.[6]

Therefore, this study aimed to examine the prescription patterns and assess the effectiveness of antidiabetic drugs, both as monotherapy and in combination therapy, in patients with type 2 diabetes mellitus (T2DM), with or without other medical conditions (comorbidities). The study also shed light on how these drugs are prescribed and how effective they are in managing T2DM in different patient populations.

METHODS

Study design and setting

This was a cross-sectional retrospective study conducted over three months (November 2022-January 2023) in the Department of Endocrinology, Aga Khan University (AKU), Karachi, Pakistan. AKUH, is a tertiary care hospital with physicians that specialized in providing compassionate care and treatment to patients with a wide range and severity of illnesses and ailments.

Study population and eligibility

Prescriptions of patients with anti-diabetic drugs from the outpatient department of AKU; diagnosed with type 2 DM; both males and females, aged more than 18 years were included to participate in the study. Patients' data regarding prescribed drugs and details about the duration of diabetes, co-morbid condition, and glycaemic control by checking HbA1c) with type-2 DM for the past three months were reviewed by the Health Information Management system (HIMS) of the hospital. Patients aged less than 18 years and with an incomplete diabetic history were excluded.

Data collection

A Google form designed as a structured questionnaire in the English language was used to collect data. The questionnaire had basic socio-demographic information including conditions and its description, the duration of, type-2 DM, and the medications prescribed.

Data analysis

Frequencies and percentages were reported for age groups, gender, BMI categories, duration of type-2 DM, glycaemic control, and medications prescribed. Mean and SD was reported for age, weight, height, BMI, and HBA1C (%). STATA version 14 is used to conduct all analyses.

Ethical consideration

The research adhered to the guidelines set forth in the Declaration of Helsinki as well as those for good clinical practice (GCP) and all relevant regulatory requirements. The study was approved by the Ethical Review Committee (ERC) of AKU (ERC Ref#: -2022-8081-23101). Telephonic consent was obtained from the study participants before the commencement of the retrospective data extraction. The data was collected through a unique identification number and confidentiality of the data was maintained. Access to the data was password-protected and restricted to the research team to maintain data privacy.

RESULTS

Data from 552 diabetic patients were analyzed for the study. The mean age of study participants with type-2 DM was 58 years, and among them, 294 (53.3%) were males and 258 (46.7%) were females. Diabetic patients were more in the age group 51-70 years (62.7%). Of most of the diabetic patients, 41.9% were obese while 38% were overweight. Only 19.9% of diabetic patients were healthy. Moreover, 25.2% of the patients had diabetes for the past 5-10 years. Furthermore, it was seen that 48.7% of the patients had achieved good glycaemic control (Table 1).

The majority of medication prescriptions had a drug combination of three antidiabetic drugs (41.5%) (Table 1). It was further seen that metformin was the most prescribed medication (83.9%), followed by DPP4 inhibitors and SGLT2 inhibitors i.e., 61.1% and 54.0% respectively. However, only 1.1% of diabetic patients were prescribed Thiazolidinedione as an antidiabetic drug.

Table 2 below indicates the commonly prescribed drug therapies for patients with type-2 DM. Among commonly available monotherapies, metformin was prescribed as the most frequent drug of choice i.e., 6.34%. Likewise, a

combination of DPP-4 inhibitor + Metformin was prescribed commonly among these patients as a two-drug combination regimen (9.96%). The most prescribed three drugs combination was DPP-4 inhibitor + SGLT-2 Inhibitor+ Metformin (12.86%) while among four drugs combination, DPP-4 inhibitor+ SGLT-2 inhibitor+ Metformin+ sulfonylurea (8.33%) was highly prescribed.

Table 3 below describes the duration of diabetes in years and the drug therapies given over these years. Among different drug therapies, the highest percentage of monotherapy and two drug combinations were prescribed in patients who had diabetes for less than 5 years i.e., 21.3% and 35.2% respectively. Whereas a 3-drug combination treatment has been prescribed to patients who had diabetes for more than 20 years (47.2%). Lastly, 29.5% of the study participants have highly prescribed a 4-drug combination and had a duration of diabetes of 10-15 years.

Table 4 (supplemental table) shows that there was a significant association of age with patients having and not having comorbidities. The comorbidities included hypertension, ischemic heart disease and chronic kidney disease. The mean age of the patients having comorbidities was 59.5 ± 10.4. There was a higher number of patients having comorbidities in both the genders, with a significant association of p-value 0.004. The patients who were prescribed three drug combinations had a higher frequency of patients (145, 42.8%). It is also worth noticing that metformin, DPP4 inhibitors and SGLT2 inhibitors were prescribed to more patients who suffered from comorbidities.

Figure 1 shows the most prescribed drugs in monotherapy and combination therapy. Among various combinations, DPP-4 Inhibitor +SGLT-2 Inhibitor+ Metformin (12.86 %) was frequently prescribed by physicians for the treatment of type-2 DM.

Figure 2 below illustrates the gender-wise distribution of anti-diabetic drug therapies depending on their glycaemic control.

Among monotherapy, females had good, poor, and inadequate glycaemic control over males i.e., 19.09%, 9.41%, and 11.11% respectively. On the other hand, 2-drug combination therapy had good and poor glycaemic control in females i.e., 25.45% and 28.24% respectively but inadequate control in males as compared to females i.e., 21.67%. Interestingly, a 3-drug combination had good, poor, and inadequate glycaemic control higher in males as compared to females i.e. 38.99%, 40%, and 53.33% respectively. Lastly, a 4-drug combination anti-diabetic regimen had good (20.13%) and poor glycaemic control (26.67%) in males but inadequate control in females i.e., 22.22%.

Table 1: Demographic data.

Variables	N (%)
Age in years	57.5±11.0
Age groups	
<50	143 (25.9)
51–70	346 (62.7)
>70	63 (11.4)
Gender	
Male	294 (53.3)
Female	258 (46.7)
Weight in kg	76.4±16.0
Height in cm	160.8±9.9
BMI in kg/m^2	29.6±5.6
BMI categories	
Underweight	1 (0.2)
Healthy	110 (19.9)
Overweight	210 (38.0)
Obesity	231 (41.9)
Duration of type 2 DM (years)	
<5	108 (19.6)
5-10	139 (25.2)
10–15	129 (23.4)
15-20	87 (15.8)
>20	89 (16.1)
HBA1C (%)	7.4±1.6
Glycemic control	
Good (<7%)	269 (48.7)
Poor (>8%)	160 (29.0)
Inadequate (7-8%)	123 (22.3)
Medication prescribed	
Drug therapy	
Monotherapy	69 (12.5)
2 drugs combinations	136 (24.6)
3 drugs combinations	229 (41.5)
4 drugs combinations	118 (21.4)
Which of the following medications were prescribed	
Metformin	463 (83.9)
Insulin	207 (37.5)
GLP1 receptor agonists	32 (5.8)
Sulfonylurea	153 (27.7)
SGLT2 inhibitors	298 (54.0)
DPP4 inhibitors	337 (61.1)
Thiazolidinedione	6 (1.1)

Table 2: Generic name.

Generic name	Frequency	Percentage
Monotherapy		
Metformin	35	6.34
Insulin	19	3.44

Continued.

Generic name	Frequency	Percentage
DPP-4 inhibitors	5	0.91
Sulfonylureas	4	0.72
SGLT-2 inhibitors	4	0.72
Thiazolidinedione	1	0.18
GLP-1 receptor agonist	1	0.18
Two drugs combination regimen		
DPP-4 inhibitor + Metformin	55	9.96
Metformin + SGLT-2 inhibitor	27	4.89
SGLT-2 inhibitor + Insulin	19	3.44
Metformin + Insulin	12	2.17
DPP-4 + Insulin	7	1.27
DPP-4 + SGLT-2 inhibitor	5	0.91
Metformin + Sulfonylurea	3	0.54
DPP-4 inhibitor+ Thiazolidinedione	1	0.18
GLP-1 receptor agonist+ Insulin	1	0.18
GLP-1 receptor agonist + Metformin	1	0.18
Sulfonylurea + DPP-4 inhibitor	4	0.72
Sulfonylurea + Insulin	1	0.18
Three drugs combination regimen		
DPP-4 inhibitor + SGLT-2 inhibitor+ Metformin	71	12.86
DPP-4 + Metformin + Sulfonylurea	50	9.06
SGLT-2 inhibitor + Metformin + Insulin	36	6.52
DPP-4 inhibitor + Metformin + Insulin	30	5.43
GLP-1 receptor agonist + SGLT-2 inhibitor+ Metformin	9	1.63
SGLT-2 inhibitor+ Metformin + sulfonylurea	8	1.45
DPP-4 inhibitor + SGLT-2 inhibitor + Insulin	7	1.27
GLP-1 receptors agonist + Metformin + Insulin	5	0.91
DPP-4 inhibitor + SGLT-2 inhibitor+ Sulfonylurea	4	0.72
DPP-4 inhibitor+ SGLT-2 inhibitor + Thiazolidinedione	2	0.36
SGLT-2 inhibitor+ Metformin +thiazolidinedione	1	0.18
GLP-1 receptor agonist+ Metformin + Sulfonylurea	2	0.36
Metformin + Sulfonylurea+ insulin	2	0.36
Metformin + Sulfonylurea+ thiazolidinedione	1	0.18
DPP-4 inhibitor+ Sulfonylurea+ insulin	1	0.18
Four drugs combination regimen		
DPP-4 inhibitor+ SGLT-2 inhibitor+ Metformin+ sulfonylurea	46	8.33
DPP-4 inhibitor+ SGLT-2 inhibitor + Metformin+ insulin	35	6.34
GLP-1 receptor agonist + SGLT-2 inhibitor+ Metformin+ insulin	10	1.81
DPP-4 inhibitor+ Metformin + Sulfonylurea+ insulin	12	2.17
GLP-1 receptors agonist + SGLT-2 inhibitor+ Metformin+ sulfonylurea	4	0.72
SGLT-2 inhibitor + Metformin +sulfonylurea+ insulin	7	1.27
SGLT-2 + Metformin +sulfonylurea+ thiazolidines	1	0.18
DPP-4 inhibitor+ SGLT-2 inhibitor+ Sulfonylurea+ insulin	2	0.36
GLP-1 receptor agonist + SGLT-2 inhibitor + Sulfonylurea+ insulin	1	0.18
Total	552	100

Table 3: Drug therapy.

Drug therapy	Duration of diabetes (in years)				
	< 5	**5-10**	**10-15**	**15-20**	**>20**
Monotherapy	23 (21.3)	16 (11.5)	12 (9.3)	9 (10.3)	9 (10.1)
2 drug combination	38 (35.2)	44 (31.6)	24 (18.6)	13 (14.9)	17 (19.1)
3 drug combination	39 (36.1)	53 (38.1)	55 (42.6)	40 (46.0)	42 (47.2)
4 drug combination	8 (7.4)	26 (18.7)	38 (29.5)	25 (28.7)	21 (23.6)

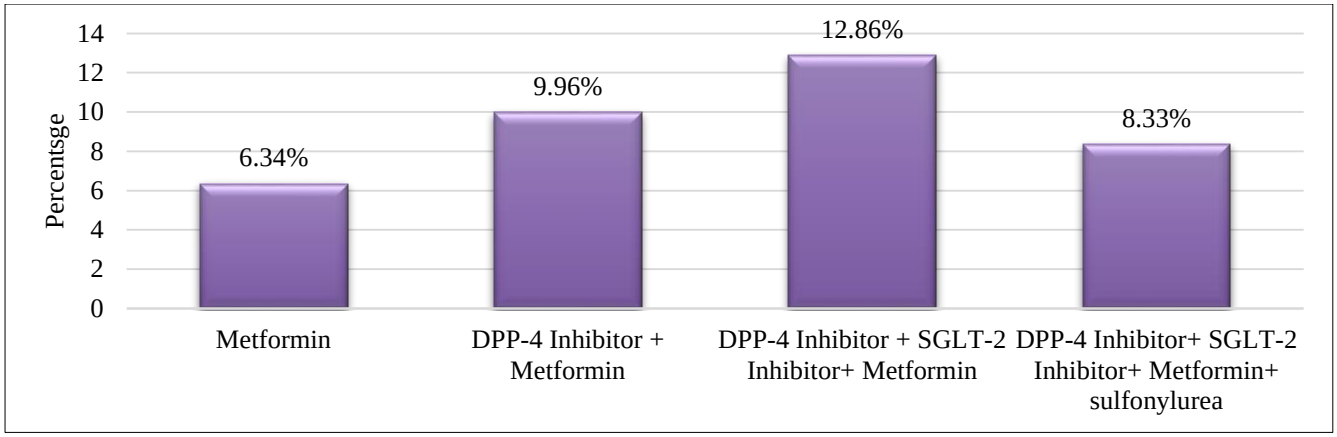
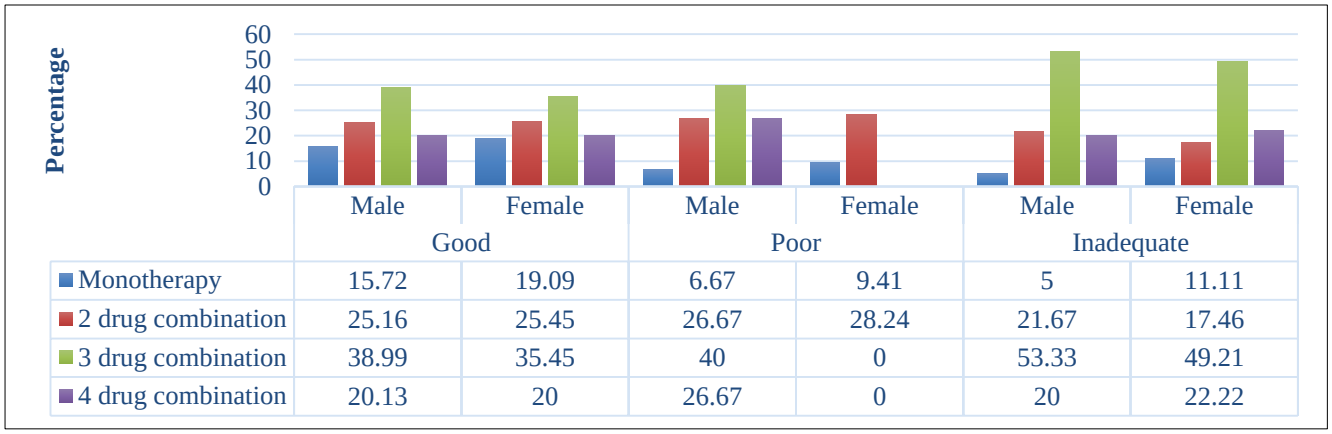


Figure 1: Most common prescribed drugs in monotherapy and combination therapy.



	Good		Poor		Inadequate	
	Male	Female	Male	Female	Male	Female
Monotherapy	15.72	19.09	6.67	9.41	5	11.11
2 drug combination	25.16	25.45	26.67	28.24	21.67	17.46
3 drug combination	38.99	35.45	40	0	53.33	49.21
4 drug combination	20.13	20	26.67	0	20	22.22

Figure 2: Gender-wise distribution of anti-diabetic drug therapies depending on their glycaemic control.

DISCUSSION

Diabetes is the most common endocrine disorder; it is a prevalent disease affecting developed and non-developed nations worldwide.[7] In 2022, IDF reported that 33,000,000 (26.7%) citizens of Pakistan are affected by Diabetes, which makes us rank the third highest country with the prevalence of this disease after China and India.[8] A community-based study conducted in Pakistan reported a prevalence of 17% of T2DM patients in the country, which is why targeting these patients, can help to conquer the progression of this disease.[9] Our study reports the prescribing patterns of antidiabetic drugs and glycaemic control in T2DM patients visiting a Tertiary Care Hospital based in Karachi, Pakistan.

This study reports a mean age and standard deviation of 57.5±11.0. In 2016, a community-based study conducted in the major metropolitan cities of Pakistan reported a mean age of 45.23±13.97.[9] Similar was the case in the study conducted in India, which reported a mean age of 51.87±9.24 years, and the majority fell under the age group of 51-70 which is similar to our study.[10] The risk of T2DM increasing with age is a well-established observation. This is because the specified age group has lifestyle changes that include a lack of physical exercise.[11] The lack of physical exercise can also lead to an increase in weight; obesity is one of the precursors of T2DM.[12] Our study reports that the majority of our participants were obese (231) and overweight (210) with a mean BMI of 29.6±5.6 kg/m2. In 2023, a study conducted in India reported a mean BMI of 26.35±0.21 kg/m^2 in their newly onset diabetic patients with 141 participants being obese and 185 participants being overweight.[13]

The population of males was greater than the females in our study reporting a ratio of 1:1. While the study in India reported a ratio of 0.96 with females being 51.11%.[14] Alternatively, a study conducted in West Bengal, India reported 57% of males and 43% of females.[10] Our study reports 53.3% males and 46.7% females. However, a study conducted in Peshawar, Pakistan reports that the majority of female participants (209, 59%) had been diagnosed with T2DM.[15] Studies report that males are highly susceptible to T2DM than their counterparts because of the larger amount of visceral fat in their bodies.[16,17]

Our study reports that the majority of participants had a diabetes duration of five to ten years (139, 25.2%) followed by ten to fifteen years (129, 23.4%). However, in 2021, a study conducted in Jammu and Kashmir, India reported 49.68% of their participants had less than five

years of diabetes duration.[18] Similar results were reported from a study in Bangladesh that accounts for 51.4% of participants having less than five years of diabetes duration.[11] In another study conducted in Dhaka Bangladesh, 84% of the participants had a history of less than five years of diabetes.[19] This could mean that there is still a lack of awareness regarding diabetes and its treatment in our country as compared to the neighbouring countries as the patients do not present to the doctors immediately after the diagnosis.[11]

The mean HbA1c reported in our study was 7.4±1.6. The Delhi study reports a mean HbA1c of 08.39±2.4.[20] A study conducted in India reported greater than 6.5% of baseline HbA1c in 133 (98.52%) of the patients which significantly reduced to 79 (58.2%) after 18 months of follow-up.[14]

The Delhi study reports that the majority of their participants were using Metformin (406, 32.8%) followed by 318 (25.7%) using Insulin.[20] Similar was the case in our study where 463 (83.9%) of the participants were prescribed Metformin; however, DPP4 inhibitors were the second highest anti-diabetic prescribed in 337 (61.1%) patients. In a study conducted in Mumbai India, metformin was the most popular prescribing anti-diabetic drug in 585 (97.5%) patients whereas the sulfonylureas group was the second highest with 322 (53.6%) patients.[21] Whereas, in our study, Sulfonylureas were the fifth-highest-prescribed drug in 153 (27.7%) patients.

The majority of the patients in our study were on three-drug therapy i.e. 229 patients (41.5%); out of which DPP-4 Inhibitor, SGLT-2 inhibitor and Metformin were the common drugs prescribed in 71 patients (12.86%). It is also worth noticing that the three-drug therapy was majorly utilized in 55 (42.6%) patients with 5-10 years of diabetic history. In the Bangladesh study, the majority of the patients were prescribed 4-6 drugs with Metformin and Sitagliptin being the commonest combination therapy.[11] In another study conducted in Dhaka, Metformin and DPP4i combination was the most commonly prescribed combination.[19]

The common prescription of Metformin is because it is inexpensive, effective, and shows fewer adverse effects. It shows great efficacy when used as a monotherapy producing good glycaemic and weight control with rare events of hypoglycaemia and cardiovascular mortality. It is also reported that DPP4i has a good effect on geriatric patients and patients with mild renal impairment.

The study is the first of its kind in one of the metropolitan cities of Pakistan. In addition, the study is executed in a tertiary care centre where the majority of the population from various lifestyles come for their treatment, which is why the study does give an understanding of the current prescribing patterns of the country. However, a large-scale prospective study is needed where the data from various centres of the city is included to conclude the results.

CONCLUSION

Our study found that the most prescribed antihyperglycemic monotherapy for T2DM was metformin, followed by DPP4 inhibitors and SGLT2 inhibitors. Common two-drug combinations included DPP4 inhibitors with metformin. Three-drug combinations consisted of metformin, DPP4 inhibitors, and SGLT2 inhibitors, while four-drug combinations included metformin, DPP4 inhibitors, SGLT2 inhibitors, and sulfonylurea. DPP4 inhibitors were commonly used after metformin due to their availability and cost-effectiveness, despite lacking cardiorenal benefits. GLP1 analogues, known for their favourable effects, were less commonly prescribed due to cost, patient preference, and concerns about side effects. Adherence to guidelines was not consistently 100%. Continued research is needed to address the challenges in managing Diabetes Mellitus and assess prescription trends over time.

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