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Original Research Article

A study to assess clinical profile of Indian type 2 diabetes mellitus patients treated with Teneligliptin-ASPIRE study

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ABSTRACT

Background: Teneligliptin is a DPP-4 inhibitor with unique chemical structure. Efficacy and safety of Teneligliptin is well established in the patients with type 2 diabetes mellitus (T2DM) in different randomized controlled trials. However, limited real-world data is available for Teneligliptin pertaining to Indian T2DM patient profile such as demographics, duration of disease, currently prescribed anti-hyperglycemic drugs, initiation of Teneligliptin as monotherapy or as an add on therapy.

Methods: A cross-sectional, multicenter, non-interventional study was conducted to understand the demographics and clinical profile of Indian T2DM patients (n=5091) who were prescribed Teneligliptin.

Results: Majority of patients were male (65.2%) with family history of T2DM present in 43.45% of cases. Age at onset of T2DM was 51.1 ± 11.6 years. Among the T2DM patients, 36.2% of patients were newly diagnosed and more than half of them (54.7%) were uncontrolled with current anti-hyperglycemic drugs. Mean HbA1c level among these patients was $8.09\pm1.3\%$. Mean fasting and postprandial blood glucose levels were 170.2 ± 46.9 mg/dl and 255.3 ± 69.3 mg/dl respectively. Teneligliptin was prescribed as monotherapy in 2165 (41.66 %) of patients while as dual, triple and quadruple therapy in 2346 (46.08%) and 551 (10.82%) and 29 (0.56%) respectively. Among the patients on current anti-hyperglycemic treatment, most commonly prescribed drugs along with Teneligliptin were metformin (43.39%) followed by glimepiride (11%) and voglibose (3.42%).

Conclusions: Teneligliptin is preferred as monotherapy and combination with metformin and sulfonylureas (mostly glimepiride) in newly diagnosed and uncontrolled T2DM patients in Indian scenario.

Keywords: Demographics, Diabetes complication, DPP4 inhibitors, Real world data, Teneligliptin, Type 2 diabetes mellitus

INTRODUCTION

The prevalence of type 2 diabetes mellitus (T2DM) has risen consistently over the past years. It is estimated that over 425 million individuals are suffering with T2DM globally, while 50% of patients remain undiagnosed. India ranks second in the world after China for the highest number of diabetes cases. International Diabetes Federation (IDF) reported 72.9 million diabetic individuals in India, and has anticipated this number to reach 123.5 million by 2040.[1]

DPP-4 inhibitors have been considered as a cornerstone in the management of T2DM because of their robust efficacy and favorable tolerability profiles. Unlike sulfonylureas, meglitinides and insulin, DPP4 inhibitors are weight neutral and are associated with negligible risk of hypoglycemia.[2]

Teneligliptin has unique chemical structure amongst currently available DPP4 inhibitors and binds to the S1, S2 and S2 extensive subsite of the DPP-4 enzyme, leading to enhanced potency and selectivity.[3] Teneligliptin is used in the treatment of T2DM as monotherapy or in combination with metformin, glimepiride or pioglitazone and has been found to improve glycemic control even in patients with end stage renal disease.[4] Real world studies have shown that teneligliptin significantly improved glycemic control in Indian patients with T2DM when prescribed as monotherapy or as an add on to other oral anti-hyperglycemic agents (OHA).[5] However very limited real world data is available pertaining to patients profile such as demographics, duration of disease, co-morbidities, initiation of teneligliptin as monotherapy or add on therapy, starting dose of teneligliptin etc. in Indian setting.

This study was conducted to assess the demographic and clinical profile of Indian T2DM patients treated with Teneligliptin.

METHODS

Approval of independent ethics committee (IECDH/2017/074) was obtained prior to initiation of study. Study was conducted in compliance with principle of the declaration of Helsinki, International Council on Harmonization-Good Clinical Practice (ICH-GCP) and Indian regulatory guidelines (Indian Council of Medical Research and Indian GCP guidelines). Study was conducted in 154 centers across India from October 2017 to July 2018.

This was a cross-sectional, multicenter, non-interventional study of adult (>18 years of age) in Indian patients diagnosed with T2DM. Treatment naïve or T2DM patients uncontrolled on other OHA or insulin who were treated with teneligliptin as monotherapy or add on therapy were included in this study. Patients not willing to sign informed consent form or patients with incomplete health record as per protocol requirement were excluded from study.

Eligible subjects (n=5091) were enrolled in the study after obtaining informed written consent and unique allotment number was given to every subject to maintain confidentiality. Patient's demographic characteristics, disease profile, significant medical history, family history, treatment detail and concomitant medication details were recorded by investigators in case report form (CRF). Fasting plasma glucose (FPG), post-prandial plasma glucose and HbA1c were measured at the time of initiation of treatment with teneligliptin.

Statistical analysis

Demographic parameters and laboratory parameters were expressed as mean±standard deviation (SD). Patients with past medical history, complications, newly diagnosed T2DM, uncontrolled T2DM and dual or triple anti-diabetic drug therapy were presented in number and percentage.

RESULTS

Clinical data from 5091 enrolled patients were analyzed. Majority of patients were male (65.2%). Family history of T2DM was present in 43.45% of cases (n=2212), out of which paternal history was present in 50 % while maternal history was present in 45 % cases (Figure 1).

Age at onset of T2DM was 51.1±11.6 years. Among the T2DM patients, 36.2% of patients were newly diagnosed and more than half of them (54.7%) were uncontrolled with current anti-hyperglycemic drugs (Table 1, 2).
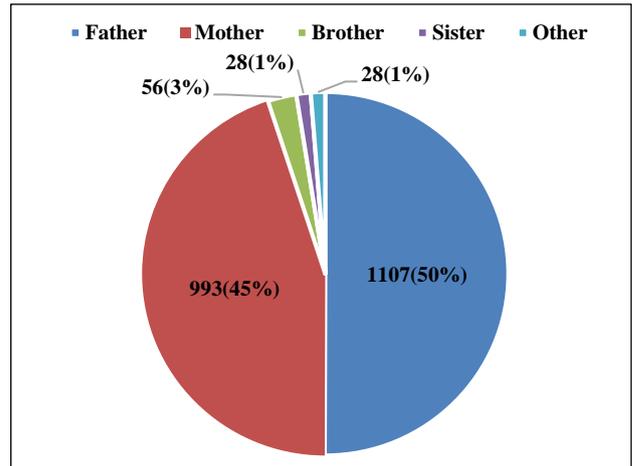
Values are expressed as number of participants (%)

Figure 1: Trend in family history of T2DM (n= 2212).

Table 1: Demographic profile of participants (n= 5091).

Variables	Mean±SD
Age	51.1±11.6 years
Height	162.2±9.3 cm
Weight	68.9±11.3 kg
Age at onset of T2DM	47.6±15.8 years

Table 2: Demographic profile of participants (n= 5091).

Variables	n (%)
Gender distribution	
Male	3274 (65.2)
Female	1817 (35.69)
Family history of T2DM	2212 (43.45)
Newly diagnosed T2DM	1843 (36.20)
Uncontrolled T2DM	2786 (54.72)

Around 569 (11.17%) participants had complications due to diabetes. Neuropathy (44.64%), hypertension (20%) and nephropathy (12%) contributed largely to the complications (Table 3). Baseline laboratory investigations were carried out before the enrollment of participant in study to assess glycemic control. At baseline, mean fasting and postprandial blood glucose levels were

170.2±46.9 mg/dl and 255.3±69.3 mg/dl respectively (Table 4).

Table 3: History of diabetic complications: n= 569 (11.17%).

Complication	No. of participants (%)
Neuropathy	254 (44.64)
Hypertension	114 (20)
Nephropathy	68 (11.95)
Retinopathy	43 (7.56)
Dyslipidemia	12 (2.11)
Ischemic heart disease	6 (1.05)
Coronary artery disease	5 (0.88)
Erectile dysfunction	5 (0.88)
Other	62 (10.90)

Table 4: Baseline laboratory investigations (n=5091).

Laboratory investigation	Mean±SD
HbA1c (%)	8.09±1.3
Fasting plasma glucose (mg/dl)	170.2±46.9
Post-prandial plasma glucose (mg/dl)	255.3±69.3

Majority of patients (69.89%) had HbA1c of more than 8%, while HbA1c of 7-8 and >7% was present in 22.61 and 7.5 percentage of patients respectively (Figure 2).
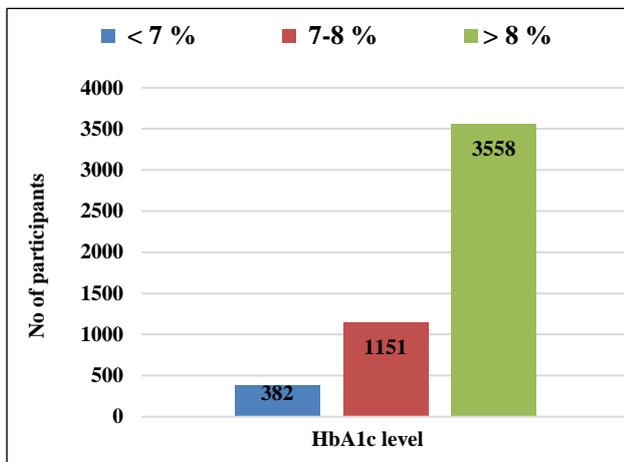

Figure 2: HbA1c distribution among participants (n=5091).

Teneligliptin was prescribed as monotherapy in 2165 (41.66%) of patients while as dual, triple and quadruple therapy in 2346 (46.08%) and 551 (10.82%) and 29 (0.56%) respectively. Fixed dose combination containing Teneligliptin was prescribed in 1244 (24.44%) of participants while it was given in free dug combination in rest of cases (Figure 3).

Among the patients on current anti-hyperglycemic treatment, most commonly prescribed drugs along with Teneligliptin were metformin (43.39%) followed by glimepiride (10.9%) and voglibose (3.42%) (Table 5).
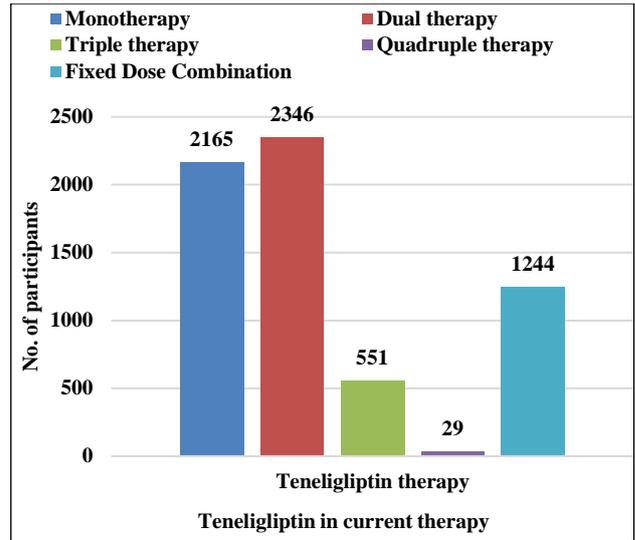

Figure 3: Teneligliptin in current anti-diabetic treatment (n= 5091).

Table 5: Current Anti-diabetic Treatment-individual drugs* (n=5091).

Anti-diabetic drug	N (%)
Teneligliptin	5091 (100)
Metformin	2209 (43.39)
Glimepiride	555 (10.90)
Voglibose	174 (3.42)
Insulin	35 (0.69)
Gliclazide	27 (0.53)
Glargine	22 (0.43)
Pioglitazone	19 (0.37)
Canagliflozine	16 (0.31)
Empagliflozine	13 (0.26)
Vildagliptin	7 (0.14)
NPH 70	7 (0.14)
NPH 30	6 (0.12)
Glibenclamide	4 (0.1)
Linagliptin	3 (0.06)
Human insulin	2 (0.04)
Insulin aspart	2 (0.04)

*values are mutually exclusive of each other.

DISCUSSION

According to International Diabetes Federation (IDF) 2017 report, India ranks second after China for number of people with diabetes. Commonly metformin and sulfonylureas (mainly glimepiride) are widely used for the treatment of T2DM in India and this use is as per guideline recommendations.[6,7] However these drugs are associated with side effects like weight gain and hypoglycemia with sulfonylureas and gastrointestinal upset with metformin, which may largely restrict the ability to intensify therapy and attain stringent glycemic target.[3] Glucagon-like peptide-1 (GLP-1) analogues and sodium-glucose cotransporter 2 (SGLT2) inhibitors, relatively new

therapies for the treatment of T2DM have advantages of weight loss, low risk of hypoglycemia and cardiovascular benefit.[8] However cost and affordability are major limiting factor for their widespread use in developing countries like India. DPP4 inhibitors have emerged as one of the suitable option having advantages of weight neutrality and low risk of hypoglycemia.[9] Teneligliptin, a DPP-4 inhibitor was added to the armamentarium for use in patients with type 2 diabetes in India. In different clinical trials conducted in Japan, Korea, and India, it has been shown to be safe and effective in T2DM patients when used either as monotherapy or in combination with other conventional OADs. In a phase 3, randomized, double-blind, non-inferiority study of subjects with T2DM (n=201), teneligliptin has shown non-inferior efficacy over sitagliptin.[10] In our study, teneligliptin was prescribed in 36% of newly diagnosed T2DM patients and in 55% of those inadequately controlled on current anti-hyperglycemic drugs. In this study, the mean age of the population was 51 years and 43.45% of participants had family history of diabetes mellitus which was in line with Indian study published by Haghighatpanah M el al, in 2018, reporting family history in 48.1% of cases of T2DM. Patients with family history were more likely to have poor glycemic control.[11] Also the risk of poor glycemic control was higher amongst the patients that were 65 years old or younger in Haghighatpanah M el al, study.[11] These subgroup of population need special attention for optimum glycemic control to avoid further complications.

Both 2018 ADA guidelines and 2018 ICMR guidelines for diabetes management recommend HbA1c target of < 7% to prevent diabetes related complication and to improve quality of life.[2,8] In present study, more than half of them (54.7%) were uncontrolled with current anti-hyperglycemic drugs and majority of (92.5%) of population had HbA1c >7% at baseline. Various previous studies reported poor glycemic control (HbA1c >7%) in the range of 67.5 to 78.2% of diabetic patients.[12,13] Poor glycemic control was found significantly associated with duration of diabetes, age of onset, family history, antidiabetic drugs, body mass index, hypertension, lipid and fasting plasma glucose levels.[12] Higher proportion of patients with poor glycemic control at baseline in our study could be because of inadequate antidiabetic medication use and associated complications. Teneligliptin may have potential role to improve glycemic control in such patients.

In this study, most common diabetes associated complications were neuropathy (44.64%), hypertension (20%) and nephropathy (12%). In TD2M patients, neuropathy is the highest reported microvascular complication in all regions, ranging from 25% in South Asia to 83% in Russia.[14] In screening India's Twin Epidemic (SITE) Study, Diabetes and hypertension were coexistent in 20.6% patients.[15] In a study conducted by Maniarasu in rural population of Tamil Nadu, 10.4% of T2DM patients had nephropathy.[16] These findings regarding complication associated with T2DM are consistent with present study.

In present study, metformin was most commonly prescribed concomitant drug with teneligliptin followed by glimepiride and voglibose. This is in line with Indian studies which have shown that metformin and glimepiride are the most commonly prescribed anti-hyperglycemic agents followed by voglibose.[6,7] However there has been trend of increasing use of teneligliptin with metformin in Korean and Japanese population as well.[17,18] Real-world evidence supplements Randomized controlled trials (RCT) data and adds to clinical evidence regarding clinical efficacy of a drug.[19,20] Real-world data suggests that teneligliptin significantly improves glycemic control in Indian patients with T2DM when prescribed either as monotherapy or as an add-on to one or more other commonly prescribed antidiabetic drugs.[5] Teneligliptin, a cost effective DPP4 inhibitor holds promising role in the treatment of Indian T2DM patients.

This study has certain limitations, because of the observational and cross-sectional design, the possibility of selection bias cannot be ruled out. Information related to diet and lifestyle modification and information regarding dosing pattern of concomitant medication was not analyzed. Long-term follow up study to address the shortcomings of the present study are warranted.

CONCLUSION

Teneligliptin is preferred as monotherapy and in combination with metformin and sulfonylureas (mostly glimepiride) in newly diagnosed and uncontrolled T2DM patients in Indian scenario. Teneligliptin certainly holds the promising role in the treatment of Indian T2DM patients.

ACKNOWLEDGEMENTS

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