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Cross-Sectional Analyzis of Antihyperglycemic Drug Prescriptions from Large Pan India Apollo Sugar Clinics Database.

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Abstract

Objectives: Our current study objective was to assess the nature of antidiabetes prescriptions across the Apollo Sugar Ecosystem, India, a healthcare organization with more than 30 centers (standalone, secondary and tertiary institutions) that provide care to patients with diabetes

Methods: An eligible 20608 prescriptions with a diagnosis of type 2 diabetes mellitus (T2DM) from 2017 to 2019 were included in this analyzis to determine the choice of therapy, frequency of usage of a different class of antidiabetes medications, types of insulin, combination and number of oral hypoglycemic agents (OHAs) with insulin. Descriptive statistics were applied to do the analyzis and report the results.

Results: The mean age of the patients was 53.2 years, 63% males and 37% females. The majority of the patients were on OHAs (68.2%) with 22.8% of patients on OHAs+insulin and 9.0% on insulin alone. Biguanides (55.7%) were most commonly prescribed in combination with other OHAs followed by DPP4 inhibitors (DPP4i) (35%) and 63% of patients requiring insulin were using at least one oral drug. The most common drugs used along with insulin include biguanides (50.5%) and DPP4i (46.7%). Among Insulins short-acting insulin (45.6%) was most commonly prescribed followed by insulin glargine (22.5%) and premixed insulin and analogues (13.5%).

Conclusions: Our large cross-sectional data analysis reveal a significant number of patients on monotherapies other than metformin. The data provided here give a snap shot of the changing trends in the adoption of therapeutic practices with the availability of newer medications, physician education and patient ability to afford care.

Keywords: Anti-diabetes drugs; anti-hyperglycemic agents; Diabetes, India; Insulin, Prescription; oral; Type 2 diabetes mellitus

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Introduction

Diabetes is a chronic metabolic disorder associated with high blood glucose or hyperglycaemia,occurs due to disturbance in carbohydrate, fat, and protein metabolism resulting from defects in insulin secretion, insulin action, or both.[1]Although the aetiology of diabetes is complex, it is being managed with appropriate treatment strategies in routine clinical practice globally.[1-4]Moreover, beyond clinic with systematic protocols on lifestyle modifications, diet, exercise, patient education and counselling are very important to successfully combat the harmful effects of diabetes.[5]

Traditionally, the treatment approach for diabetes patients was always been with lifestyle modifications, single oral drug and after increasing to maximal recommended dose a combination treatment with two or more different class of drugs.[2]According to American Diabetes Association (ADA) the standard of medical care to improve diabetes outcomes should include cost-effective screening, diagnostic and therapeutic strategies to prevent, delay, or effectively manage diabetes and its life-threatening complications. Besides, ADA does not favour specific medication but endorse physicians to choose one based on their efficacy,

hypoglycemic risk, weight effects, side-effects, and cost.6 In the current scenario, where there is an increasing market for anti-diabetes drugs and digital management of diabetes health, proactive comprehensive treatment approach should be the recommended choice of treatment.

In spite of the availability of efficacious anti-diabetes drugs (ADD)with a different mechanism of an action either single or in fixed dose combination, many people on ADD have poor glycemic control. ADDs include orals and injectables. The major classes of anti-diabetes treatment include biguanides, sulfonylureas, thiazolidinedione (TZD), dipeptidyl peptidase 4 (DPP-4) inhibitors, sodium-glucose co-transporter (SGLT2) inhibitors, meglitinide, α-glucosidase inhibitors, glucagon-like peptide-1 receptor agonists (GLP1 RA), and insulin. However, these drugs are prescribed considering both global and local treatment guidelines to achieve glycaemic goals.

According to ADA recommendations a standard of diabetes care should include cost-effective screening, diagnosis and treatment strategies to prevent, delay, or effectively manage diabetes and its life-threatening complications to achieve and maintain the glycemic control. Literature shows geographically the prescription pattern varies not only at the country level but also at regional level.[2-4, 7] In India along with national guidelines, the most commonly preferred guidelines for diabetes treatment is ADA which helps the health care providers to choose right intervention for their T2DM patients.

The current study aimed to ascertain the nature of anti-diabetes drugs prescription pattern across the Apollo Sugar Clinics Ecosystem in India, a healthcare organization with more than 35 clinics that provide health care service to patients with diabetes.

Methods:

Patients: Type 2 Diabetes mellitus (T2DM) patients who had come for a consultation at outpatient department of Apollo Sugar Clinics. the Patients included in the analysis were age ≥ 18years either known diabetes or newly diagnosed T2DM patients from Jan 2016 to June 2017. As a routine clinical practice patients demographic, past medical history, chief complaints, previous medication, lab investigations, and information on patient lifestyle was routinely recorded against date in our electronic medical records (EMR) data bank for future reference and to keep regular and continuous follow up with the patients.

Apollo Sugar Clinics is a large center of excellence for diabetes and endocrine disorders spread over pan India with more than 35 clinics (as standalones, secondary and tertiary institutions) and >90 health care provider and more than 75000 EMR penetrance.

Study Design: A cross-sectional, observational retrospective data analysis of T2DM patients' from Hyderabad, Bangalore, Chennai, Mumbai, Kolkata and Delhi cities of India. For this retrospective observational study T2DM patients data records captured in Apollo Sugar Electronic medical records database of above cities with prescriptions were selected.

Statistical Analysis: Descriptive statistics were applied to report the results and appropriate statistical tests were used to compare the results between groups. Data are reported as the number and percentage for qualitative variables and mean and standard deviation for quantitative variables. SPSS software version 21 was used to analyze the data.

Results: A total of 20608 diabetes patients'prescriptions were screened. Mean age of the patients was 53.2 years, 63% males and 37% females. Among these majority of the prescriptions,i.e., 68.2% were oral hypoglycemic agents (OHAs) alone, 22.8% were OHAs and insulin and 9.0%insulin alone. The average number of drugs prescribed per prescription was 1.7/day. Of the total prescriptions one drug, two drugs, three –drug and four drug prescriptions were 45.3%, 38.1%, 13.4%, and 3.2%, respectively. Biguanides (55.7%) are highly prescribed followed by DPP4i (35%), insulin (31.7%), sulphonylurea (30.7%) and SGLT2 (3.8%).

In combination treatment with two drugs, DPP4i (46.0%) replaced SUs (38.8%) after biguanides (56.7%). Further, combination treatment with 3 or more drugs the use of SGLT2i and insulin have also continuously increased (Table 1). The most commonly prescribed insulins were short–acting (human soluble [21.2%], regular insulin [24.5%]) and long–acting (22.5%) insulins compared to premix insulins (13.5%), while intermediate and fasting acting insulin was low in prescriptions (Table 2). Similar to the order of prescription, insulins are highly prescribed in combination with biguanides and DPP4i compared to other OHAs.

At follow up of 3±1 month, only 7798 prescriptions were available. The analysis of these patients revealed that nearly 30% of patients initiated on

insulin had moved to oral+insulin or orals alone, while only 4% of patients on orals or orals+insulin at baseline had switched to other combination of anti-diabetes drugs.

Discussion:

Early diagnosis, the right combination of treatment with comprehensive approach plays a key role in better glycaemic outcomes. The current results on anti-hyperglycemic drug prescriptions were from large database representing the recent trends in prescription patterns in the Indian subcontinent, which are comparable to previous cross-sectional and single centre studies.

Table 1: Anti-diabetes drugs prescription as monotherapy and in combination.

No. of Drugs	N	Biguanides	Sulphonylurea	DPP4	SGLt2	Insulin
Total	20608	11479 (55.7)	6336 (30.7)	7218 (35.0)	774 (3.8)	6537 (31.7)
One drug	9341 (45.3)	4863 (52.1)	1525 (16.3)	1368 (14.6)	47 (0.5)	1472 (15.8)
Two drugs	7845 (38.1)	4452 (56.7)	3043 (38.8)	3606 (46.0)	313 (4.0)	2846 (36.3)
Three drugs	2764 (13.4)	1704 (61.6)	1910 (69.1)	1755 (63.5)	289 (10.5)	1721 (63.3)
Four drugs	658 (3.2)	460 (69.9)	536 (81.5)	489 (74.3)	125 (19.0)	498 (75.7)

Table 2: Insulin prescriptions.

Insulin Types	Prescriptions (N=6537), %	
Short Acting	Human Soluble	1388 (21.2)
	Regular insulin	1602 (24.5)
Long acting	Glargine	1476 (22.5)
	Degludec	290 (4.4)
	Detemir	37 (0.6)
Short+long acting	Premix analogues	882 (13.5)
Intermediate	NPH	560 (8.5)
Fast acting	Aspart, lispro	452 (6.9)

The typical prescription pattern in India starts with oral(s), followed by oral+insulin, and only insulin prescriptions. Our current results follow similar trends and supported by previous prospective and retrospective single centre and cross–sectional studies.[5,8-9] The low use of insulin (9%)reported in our current patient population and from other population studies could be due to phobia, inability to take insulin subcutaneously, and daily expenditure that will be spent. However, there are some studies where insulin prescriptions are high (43%) as they are intensive and aid in fast achieving the glycemic outcomes.

Our results show an average number of drugs per prescription 1.7/day and this result is consistent with previous studies conducted in Indian population.8-9 However, there are some studies where the number of drugs per prescription is more or equal to 5/day.10 The difference in the number of drugs prescribed could be attributed to the long duration of disease with uncontrolled blood glucose.

The most commonly prescribed drug was metformin alone or in combination with other drugs and its use remained the same in any combination. Similar results were observed in an Indian population-based studies and also in Asian and European countries population-based studies.[2-4,10] However, contrary to our result a population-based study in Sub-Himalayan Region of India and a hospital-based study reported that anti-diabetes drug SUs as the most frequently used drugs followed by metformin.[8,11]

Dual combination treatment observed in our analysis was metformin+DPP4i, this is in contrary to many previous studies where SU+metformin is the most common dual combination.[2]But gradually over a period of time, SUscombination faded as the new drugs with high efficacy individually or in combination, its availability and cost effectiveness.12 SU-metformin was the first dual combination, inexpensive and widely available, with better patient acceptability in comparison with other combinations.

As the duration of disease increases the number of anti-diabetes drug combinations increases to achieve glycemic goals. In our studies the prescription of SGLT2i and insulins were obvious when three or more combinations of drugs were used. SGLT2i though highly efficaciousits prescriptions are low because of their side events profile.

We found low percentage of insulin prescriptions in our analyzis and of all insulins, short–acting insulin was the most common insulin prescriptions compared to other insulins such as premix insulins.11-12Contrary to our result, a prospective cross-sectional analysis has reported high insulin prescription (46.5%). The low prescription of insulin in our study could be due to the fear of hypoglycemia, daily injections, and cost spent. But insulins provide intensive and near physiological delivery of insulin can aid in achieving glycaemic targets in a short period of time.

Limitations: The current retrospective analyzis included a large number of prescriptions to assess the prescription patterns, but the data is limited to provide more comprehensive data on the cost effectiveness, treatment satisfaction, and clinical outcomes.

Conclusions: Our large cross-sectional analysis reveals several observations. With the increasing market for diabetes drugs compared to biguanides, a significant number of patients were also another new monotherapies. In–two drug combination whether fixed dose or individual, the use of DPP4i has become the most common drug after biguanides which reflects a significant shift from a sulphonylurea (SU) dominated clinical practice system in India. SGLT2i and insulin find progressive inclusion when three or more drugs are required. Greater adoption of basal and short acting insulin as opposed to premix insulin in a country that was traditionally considered a premix market. The data provided here give a snapshot of the changing trends in the adoption of therapeutic practices with the availability of newer medications, physician education and patient ability to afford care. Further, a systematic prospective studies are recommended to evaluate the overall clinical outcomes, treatment satisfaction, and safety aspects of anti-diabetes drugs. However, the clinical practitioner should focus on prescription pattern that is individualized and compliant with current real–world evidence and local treatment guidelines for diabetes management.

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