

# An Assessment of Anti-hyperglycemic Drug Utilization Patterns and Adherence to AACE/ACE 2015 Guidelines in South Indian Tertiary Care Teaching Hospital

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## ABSTRACT

**Aim:** To compare adherence to American Association of Clinical Endocrinologists/American College of Endocrinology (AACE/ACE) 2015 guidelines for diabetes care in a tertiary care teaching hospital in India. **Method:** In this prospective observational study, 415 prescriptions of type 2 diabetes mellitus (T2DM) patients were collected in Dr. Pinnamaneni Siddhartha Institute of Medical Sciences (PSIMS) hospital from January 2015 and June 2015. Medication adherence to AACE/ACE guidelines was assessed based on glycated haemoglobin (HbA1C) values. **Results:** A total of 201 (48.4%) male and 214 (51.6%) female patients were identified. The mean age was  $53.57 \pm 10.77$  years (male) and  $53.69 \pm 10.71$  years (females). Patients with HbA1C < 7.5% (37.3%, male; 45.3%, female) were predominant followed by HbA1C 7.5% - 9% (32.3%, male; 35.3%, female) and HbA1C > 9.0% (30.4%, male; 19.2%, female). Hypertension (HTN) (39.8%, male; 39.7%, female) is the most predominant co-morbidity, followed by patients with both HTN and cardio vascular diseases (CVDs) (9.4%, male; 9.8%, female). Insulin was prescribed to control hyperglycaemia in most of the cases (40.0%) followed by dual therapy (26.9%) and triple therapy (17.8%). The overall adherence rate was 88.3% for patients with HbA1C < 7.5% ( $P < 0.0001$ ); 98.7% for patients with HbA1C 7.5%-9% ( $P < 0.0001$ ) and 100% for patients with HbA1C > 9% ( $P < 0.0001$ ). **Conclusion:** Optimal medication adherence is the ultimate goal to control the hyperglycemia in DM. The present study results revealed that the anti-diabetic medication adherence to AACE/ACE 2015 guidelines were optimal by the prescribers.

**Key words:** Type 2 Diabetes Mellitus, Medication adherence, HbA1C, AACE/ACE guidelines, Anti-hyperglycemic drugs, Physician prescribing pattern.

## INTRODUCTION

Diabetes mellitus (DM) is a most common metabolic disorder characterised by hyperglycemic.<sup>1</sup> Worldwide prevalence of DM is estimated to rise from 382 million in 2013 to 592 million in 2035.<sup>2</sup> The prevalence of Type 1 diabetes (T1DM) is about 5% to 10% and type 2 diabetes mellitus (T2DM) is about 90% to 95%.<sup>3</sup> There is no specific cause for DM, but both etiologic factors and risk factors are associated with it. The risk factors are heredity, obesity, increasing age, emotional stress, autoimmune -cell damage, endocrine diseases (e.g., Cushing

disease).<sup>4</sup> DM is one of the widely known risk factor for Peripheral vascular disease, CVD and Stroke. It also causes chronic complications like retinopathy, neuropathy and nephropathy.<sup>5</sup> Until 1990s, the biguanide (metformin), the sulphonylureas and insulin were only the few drugs of choices available for the treatment of T2DM. Since then various other classes of drugs have been accepted.<sup>6</sup> Now, hyperglycemic can be controlled through existing oral hypoglycaemic drugs and insulin by following some guidelines. The American Association of Clinical Endocrinologists/American College of

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Endocrinology (AACE/ACE-2015) is considered the “gold standard” consensus guidelines for the management of DM. The other guidelines are 2015 American Diabetes Association (ADA) and 2015 National Institute for Health and Care Excellence (NICE).<sup>7-9</sup> The most familiar principles of all these guidelines are to follow life style modification along with pharmacotherapy to manage hyperglycemic in patients with DM. In order to prevent severe complications with DM on long term, optimal adherence to drug therapy is necessary. Therefore, the objective of the study was to evaluate the antihyperglycemic drug prescribing pattern and their adherence to AACE/ACE 2015 guidelines in a south Indian tertiary care teaching hospital.

## METHODS

### Experimental Design and Data collection procedure

A prospective observational study was conducted at Dr. Pinnamaneni Siddhartha Institute of Medical Sciences (Dr.PSIMS), Andhra Pradesh and the protocol was approved by the Institutional ethics committee of the KVSRR Siddhartha College of Pharmaceutical Sciences. A total of 415 prescriptions were collected from diabetic patients. Each prescription contained the drug, quantity, duration and date of dispensing. Each anti-diabetic medication was classified into one of the following classes: Metformin, Dipeptidyl peptidase-4 (DPP-4) Inhibitors, Glucagon-like peptide (GLP-1) receptor antagonists, Sodium-glucose co-transporter 2 (SGLT-2) inhibitors, Alpha-glucosidase inhibitors (AGIs), Thiazolidinediones (TZD), Sulfonylureas (SUs) and Insulin. Medication adherence was assessed by comparing with AACE/ACE 2015 treatment guidelines shown in Figure 1.

### Statistical Analysis

Statistical analysis was determined by using Graph pad (version 5.0, Chicago, USA) and SPSS 20 version. Patient characteristics and prescription details were compared using analysis of variance and  $\chi^2$  test for continuous and categorical variables, respectively. P-values <0.05 were considered statistically significant.

## RESULTS

### Studied population characteristics

A total of four hundred and fifteen prescriptions were collected in a period of six months to assess medication adherence. The demographic and clinical characteristics were shown in Table 1. A total of 201 (48.4%) male and 214 (51.6%) female patients were identified. T2DM was

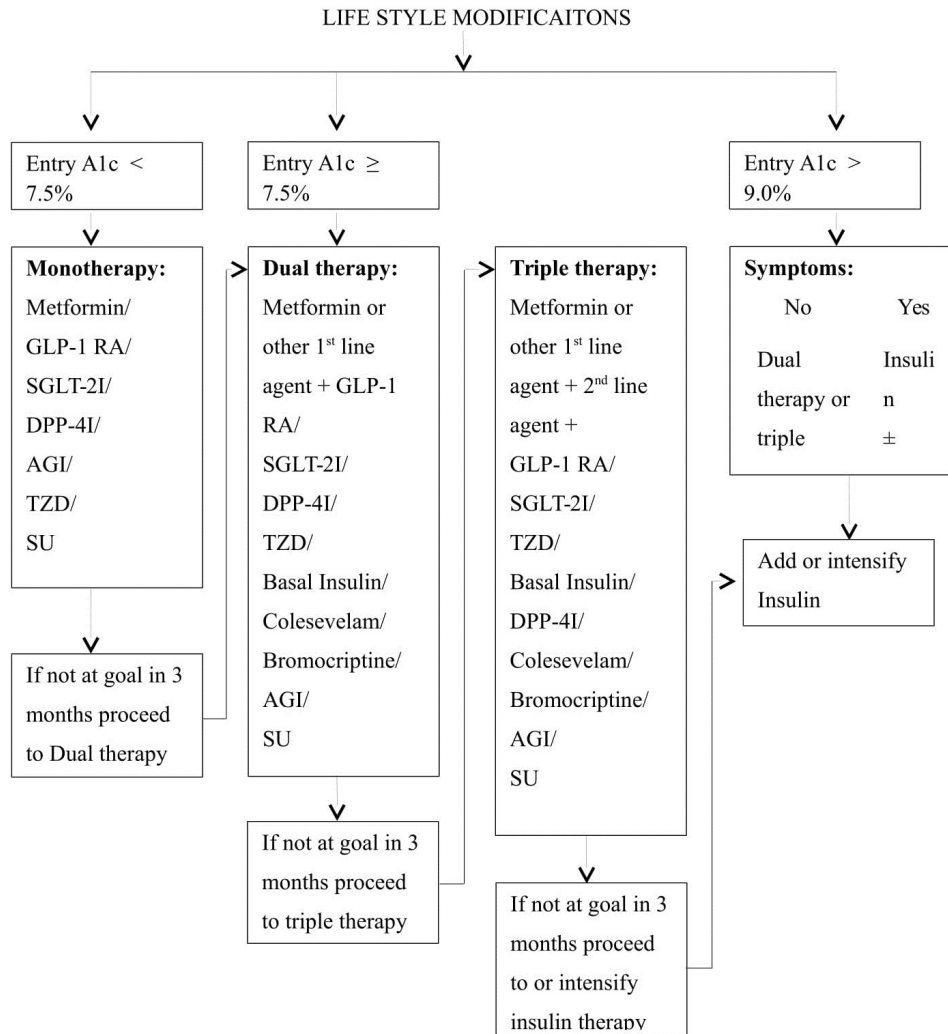
found to be almost equivalent in both male and female patients (Table 1). The mean age was  $53.57 \pm 10.77$  years and  $53.69 \pm 10.71$  years respectively. Patients with history of T2DM less than 5 years were dominant in both male (49.8%) and female (44.9%) gender followed by six to fifteen years and above 15 years of history. According to AACE/ACE guidelines T2DM was classified based on HbA1C levels and found to be 41% (HbA1C<7.5%), 34% (HbA1C 7.5%-9%) and 25% (HbA1C>9.0%). The mean HbA1C was  $8.11 \pm 1.78$  (male) and  $7.89 \pm 1.61$  (female). HbA1C<7.5% (37.3%, male; 45.3%, female) was predominant followed by HbA1C 7.5%-9% (32.3%, male; 35.3%, female) and HbA1C>9.0% (30.4%, male; 19.2%, female). HTN (39.8%, male; 39.7%, female) is the most predominant co-morbidity, followed by patients with both HTN and CVDs (9.4%, male; 9.8%, female). The average number of drug prescribed in each patient was 4-6 (66.7%).

### Adherence to guidelines

Table 2 shows the mono and combination therapies followed for the treatment of T2DM. The present study revealed that most of the physicians prescribed insulin therapy (40.0%) to control hyperglycemic followed by dual therapy (26.9%) and triple therapy (17.8%). Metformin (5.5%) is the most prescribed drug followed by DPP-4I (1.0%) in monotherapy. Metformin+Sulfonyl Ureas (SU) and Metformin+SUs+Thiazolidinediones (TZD) combination is most predominantly used in dual therapy and triple therapy respectively. The overall rate of adherence was 88.3% (HbA1C < 7.5%); 98.7% (HbA1C 7.5%-9%) and 100% (HbA1C >9%) as shown in Table 3.

## DISCUSSION

hyperglycemic is a very common metabolic disorder worldwide and is the leading cause of adult blindness and kidney failure in United States. The risk for myocardial infarction and cardiovascular death is increased by threefold to fourfold in diabetes patients respectively. Chronic microvascular complications like retinopathy, neuropathy and nephropathy can be prevented or delayed by effective management of chronic hyperglycemia.<sup>1,5</sup> Benefits of successful management of glycaemic levels were witnessed over total range of A1C values. United Kingdom Prospective Diabetes Study (UKPDS) reported that for every percentage point reduction in A1C there was 35% reduction in risk for microvascular complications.<sup>1</sup> The primary goal of DM management is to reduce diabetes associated mortality and to improve quality of life.



**Figure 1:** Algorithm for treatment of Diabetes mellitus according to AACE/ACE guidelines, 2015. GLP-1 RA, Glucagon-like peptide receptor antagonists; SGLT-2I, Sodium-glucose co-transporter 2 inhibitors; DPP-4I, Dipeptidyl peptidase 4 Inhibitors; AGI, Alpha-glucosidase inhibitors; TZD, Thiazolidinediones; SUs, Sulfonylureas.

Choice of an antihyperglycemic drug should be guided by anticipated benefits in an individual patient, taking into consideration the genetic, physiological and environmental factors that caused the disease, concurrent medical condition like hypertension, CVD, renal impairment, adverse effects of drugs and cost. AACE/ACE 2015 recommendations for management of T2DM is the most prominent evidence based clinical guideline based on A1C levels. It is supplemented by National Institute for Health and Care Excellence (NICE) 2015. As per 2015 NICE guidelines, only Metformin, Pioglitazone, DPP-4i and SU are used in monotherapy. In contrary to that 2015 AACE/ACE recommends GLP-1 RA, SGLT-2I and AGI in monotherapy along with the above drugs shown in Figure 1.<sup>7</sup> The results of the present study disclose the overall rate of adherence was 88.32% (Monotherapy-HbA1C<7.5%); 98.76% (dual therapy-HbA1C 7.5%-9%); 100% (Triple therapy and Insulin therapy HbA1C >9.0%). Some studies reported

suboptimal adherence to standard guidelines. A study conducted in UK published those prescribers who followed NICE Diabetes prevention guidelines were able to achieve higher knowledge, awareness of diabetes in high risk patients when compared to their counterparts.<sup>10</sup> Two studies reported that inadequate control of blood glucose levels are due to minimal adherence of prescribers to standard guidelines.<sup>11,12</sup> However, many studies revealed that after publishing AACE/ACE guidelines there was significant difference in drug therapy based on A1c levels prescribed by physicians in United States of america.<sup>13</sup> Another study published that there was optimal adherence to guidelines in Sweden in home health care settings than residents at nursing homes.<sup>14,15</sup> This study found there was optimal adherence to AACE/ACE guidelines in our institution resulting in better patient care. In dual therapy, triple and Insulin therapy there was unprecedented adherence.

**Table 1. Baseline demographic and clinical characteristics of diabetes patients with associated co-morbidities (n=415)**

| Patient characteristics                  | Males<br>201 (48.4%) | Females<br>214 (51.6%) | Test           | P-Value |
|--|----------------------|------------------------|----------------|---------|
| <b>Age (Mean ± SD)</b>                   | 53.57 ± 10.77        | 53.69 ± 10.71          | t-test         | 0.909   |
| Below 40 years, n(%)                     | 27 (13.4)            | 29 (13.55)             | χ <sup>2</sup> | -       |
| 41-60 years, n(%)                        | 126 (62.7)           | 130 (60.74)            | χ <sup>2</sup> | 0.891   |
| Above 60 years, n(%)                     | 48 (23.9)            | 55 (25.7)              | χ <sup>2</sup> | 0.845   |
| History of DM<br>(Mean ± SD)             | 7.63 ± 6.72          | 8.26 ± 7.65            | t-test         | 0.204   |
| 0-5 years, n(%)                          | 100 (49.8)           | 96 (44.9)              | χ <sup>2</sup> | -       |
| 6-15 years, n(%)                         | 76 (37.8)            | 91 (42.5)              | χ <sup>2</sup> | 0.295   |
| Above 15 years, n(%)                     | 25 (12.4)            | 27 (12.6)              | χ <sup>2</sup> | 0.705   |
| HbA1C<br>(Mean ± SD)                     | 8.11 ± 1.78          | 7.89 ± 1.61            | t-test         | 0.187   |
| A1C < 7.5%, n(%)                         | 75 (37.3)            | 97 (45.3)              | χ <sup>2</sup> | -       |
| A1C 7.5%-9%, n(%)                        | 65 (32.3)            | 76 (35.5)              | χ <sup>2</sup> | 0.658   |
| A1C > 9.0%, n(%)                         | 61 (30.4)            | 41 (19.2)              | χ <sup>2</sup> | 0.009   |
| <b>Co-morbid states</b>                  |                      |                        |                |         |
| No (%)                                   | 81 (40.3)            |                        | 68 (31.8)      |         |
| HTN (%)                                  | 80 (39.8)            |                        | 85 (39.7)      |         |
| History of CVDs (%)                      | 7 (3.5)              |                        | 12 (5.6)       |         |
| HTN and CVDs (%)                         | 19 (9.4)             |                        | 21 (9.8)       |         |
| HTN and Thyroid (%)                      | 9 (4.5)              |                        | 12 (5.6)       |         |
| Thyroid disorders (%)                    | 5 (2.5)              |                        | 16 (7.5)       |         |
| Number of drugs in a prescription, n (%) |                      |                        |                |         |
| 1-3                                      |                      | 36 (8.7)               |                |         |
| 4-6                                      |                      | 277 (66.74)            |                |         |
| 7-9                                      |                      | 101 (24.33)            |                |         |
| >10                                      |                      | 1 (0.24)               |                |         |

This study also revealed that Insulin therapy was mostly used in our hospital followed by two drug combination. Monotherapy was the least advised, the combination of metformin and SUs and Metformin, SUs and TZD were predominantly prescribed in Dual therapy and triple therapy respectively. This result was in accordance with the previous studies published demonstrating the order of mostly prescribed drug to be metformin, SUs and TZD.<sup>16-18</sup> Increased use of insulin was observed in most of the patients due to presence of co-morbid conditions or resistance to oral hypoglycemic drugs. Increased insulin use was also observed in many other studies.<sup>19</sup> Additionally, the use of DPP-4i was found to have significant importance in therapy. There were studies published that use of DPP-4i in both dual and triple therapy is safe and efficacious option.<sup>20-22</sup>

## CONCLUSION

The dual therapy, triple therapy and insulin therapy was the corner stone for the better patient care. In the present study, there was an optimal adherence to AACE/ACE 2015 guidelines by the physicians in our hospital.

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## CONFLICT OF INTEREST

The authors declare that this research does not have any conflict of interest with anyone or any Institute.

**Table 2: Anti-diabetic drugs used by the patients with diabetes mellitus**

| Treatment   | n (%)     |
|---|-----------|
| <b>Monotherapy</b>  |           |
| Metformin   | 23 (5.5)  |
| DPP-4I  | 4 (1.0)   |
| GLP-1 RA  | 0 (0)     |
| SGLT-2I   | 0 (0)     |
| AGI   | 0 (0)     |
| TZD   | 0 (0)     |
| SU/GLN  | 0 (0)     |
| <b>Dual therapy</b>   |           |
| Metformin or other 1 <sup>st</sup> line agent + any other drug.                       |           |
| Metformin + DPP-4I  | 2 (0.5)   |
| Metformin + SUs   | 96 (23.0) |
| Metformin + AGI   | 4 (1.0)   |
| Metformin + TZD   | 10 (2.4)  |
| <b>Triple therapy</b>   |           |
| Metformin or other 1 <sup>st</sup> line agent and second line agent + any other drug. |           |
| Metformin + DPP-4I + SUs  | 9 (2.3)   |
| Metformin + SUs + TZD   | 62 (15.0) |
| Metformin + SUs + AGI   | 2 (0.5)   |
| <b>Four drug combination</b>  |           |
| Metformin + AGI + SUs +TZD  | 9 (2.3)   |
| Metformin + DPP-4I + SUs + TZD  | 27 (6.5)  |
| <b>Insulin therapy</b>  |           |
| Insulin ± Other agents  | (40.0)    |

**Table 3. Adherence of anti-diabetic medication to AACE guidelines**

| AACE Comprehensive Diabetes Management Guidelines | Recommendations   | Adherence rate (%) | Non-adherence rate (%) | P Value |
|---|---|--------------------|------------------------|---------|
| HbA1C < 7.5%                                      | <b>Mono therapy</b>   | <b>88.32</b>       | <b>11.68</b>           | <0.0001 |
|   | 1. Metformin  | 84.41              | 11.68                  |         |
|   | 2. DPP-4I   | 3.89               |                        |         |
|   | 3. GLP-1 RA   | 0                  |                        |         |
|   | 4. SGLT-2I  | 0                  |                        |         |
|   | 5. AGI  | 0                  |                        |         |
|   | 6. TZD  | 0                  |                        |         |
|   | 7. SU/GLN   | 0                  |                        |         |
| HbA1C 7.5%-9%                                     | <b>Dual therapy</b>   | <b>98.76</b>       | <b>1.24</b>            | <0.0001 |
|   | 1. Metformin + DPP-4I   | 13.63              | 1.24                   |         |
|   | 2. Metformin + SUs  | 44.63              |                        |         |
|   | 3. Metformin + AGI  | 1.24               |                        |         |
|   | 4. Metformin + TZD  | 4.96               |                        |         |
|   | 5. Metformin + Basal insulin  | 34.30              |                        |         |
| HbA1C > 9%  | <b>Triple therapy and insulin</b>   | <b>100</b>         | <b>0</b>               | <0.0001 |
|   | Metformin or other 1 <sup>st</sup> line agent and second line agent + Insulin | 100                | 0                      |         |

**ABBREVIATION USED**

**AACE/ACE:** American Association of Clinical Endocrinologists/American College of Endocrinology; **ADA:** American Diabetes Association; **CVD:** Cardio Vascular Diseases; **DM:** Diabetes Mellitus; **HbA1c:** Glycated hemoglobin; **HTN:** Hypertension; **NICE:** National

Institute of Health Care and Excellence; **T1DM:** Type 1 Diabetes Mellitus; **T2DM:** Type 2 Diabetes Mellitus.

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