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STUDY ON PRESCRIPTION PATTERN OF ANTI-DIABETIC MEDICATION AMONG TYPE 2 DIABETES MELLITUS PATIENTS

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ABSTRACT: Background: Diabetes mellitus (T2DM) is a disorder in which the amount of sugar in the blood is elevated. Doctors often use the full name that is Diabetes Mellitus rather than Diabetes alone to differentiate from Diabetes Insipidus. Diabetes Insipidus is a relatively rare disorder that does not affect the blood glucose levels but just like Diabetes Mellitus, causing increased urination. **Method:** A prospective observational study was carried out among T2DM patients. Patient demographics, medication details, and blood glucose levels were recorded, examined, and the prescription pattern of the doctors was analyzed. **Result and Discussion:** The study included 209 T2DM patients. Metformin was more frequently prescribed single drug in 7.60% of participants. Dual drug combinations were Metformin and Glimepiride (49.04%), Metformin and Dapagliflozin (4.56%), Metformin and Vildagliptin (6.84%). About 61.84% were prescribed with short-acting insulin, 26.31% with intermediate-acting insulin, 10.52% with long-acting insulin, and only 1.31% of participants were prescribed with rapid-acting insulin. Dual drug fixed dose combination, Metformin is commonly combined with Glimepiride. A unique combination encountered was Remogliflozin and Vildagliptin. In the triple drug fixed dose combination, Metformin and Glimepiride were combined either with Voglibose or Pioglitazone. Regular insulin is more commonly used as add-on therapy (48.21%). Insulin Glargine, Insulin Aspart, and Insulin with NPH were used. **Conclusion:** This study provides a novel insight into the prescribing pattern taken up by physicians to strategize the drug regimen and improve the health of the population.

INTRODUCTION: Diabetes mellitus is a disorder of carbohydrate metabolism characterized by the impaired ability of the body to produce or respond to insulin and thereby maintain the proper levels of sugar (glucose) in the blood. The major cause of morbidity and mortality through these outcomes is not due to the immediate effects of the disorder.

They are instead related to the diseases that develop as a result of chronic diabetes mellitus. The chronic complications of diabetes make it necessary to prescribe drugs for these patients life-long [1].

Long-term complications of diabetes include retinopathy with potential loss of vision, nephropathy leading to renal failure, peripheral neuropathy with risk of foot ulcers, amputation, and many more [1]. Prescription pattern explains the extent and profile of drug use, trends, quality of drugs, and compliance with regional, state, or national guidelines like standard treatment guidelines, sometimes usage of drugs from essential medicine lists, also use of generic drugs.

Some of the patients were treated with the use of a fixed dose combination of medication while few were treated with different medication in different tablets. The prescribing percentage of different classes of OHA is of Biguanides, Sulfonylureas, Alpha Glucosidase inhibitors, DPP-4 inhibitors, SGLT-2 Inhibitors, and Thiazolidinediones. The distribution of different OHA and insulin among the different age groups of the participants is also analyzed. Rational use of drugs in the population can be effectively evaluated with drug utilization studies. This type of analysis helps us to understand the usage of drugs in a society considering its medical, social, and economic consequences [3]. Drug utilization study of OHA and insulin is therefore of paramount importance to promote rational drug use in diabetics and make available valuable information for the healthcare team.

METHODS: An observational study was carried out using a data collection form which contained information about the drugs that are given to the patient during their stay in the hospital. This information gave an understanding of the different medications given by the physicians. Glucose levels within the normal range and preventing the effects of hyperglycemia are the crucial results to be gained. This can be achieved by using a combination of 2 or 3 OHA or combining OHA with insulin. Some of the patients were treated with the use of a fixed-dose combination of medication while few were treated with different medication in

different tablets. Participants were prescribed with single drug, dual drug, and triple drug, some were also prescribed with insulin. Data is analyzed using statistical software R version 4.2.1 and Microsoft Excel. Categorical variables are given in the form of frequency tables. Continuous variables are given in Mean ± SD / Median (Min, Max) form. The chi-squaretest is used to check the association between categorical variables. Kruskal Wallis test is used to compare the distribution of variables over groups.

Study Participants:
Inclusion Criteria: Patients with type 2 diabetes mellitus, Patients with diabetes mellitus for more than 2 years, Patients with dual or triple OHA therapy, and Patients with dual or triple OHA therapy were included in the study.

Exclusion Criteria: Patients with type 1 diabetes mellitus and non-diabetic, Patients on monotherapy, and Patients not interested in being part of the study were excluded.

RESULTS: Based on the inclusion and exclusion criteria, 209 T2DM patients were enrolled in the study. The participants included in the study were in the age range of 20 - 90 years, with a mean age of 58.66 ± 10.54 years. Among the included participants 73.68% (154) were treated with OHA combination, 25.36% (53) were treated with OHA and insulin combination, and 0.96% (2) with insulin combination.

TABLE 1: COMPARISON OF DIFFERENT VARIABLES OVER GROUPS

Variables	Sub-Category	Group			Total	p-value
		OHA and Insulin	**OHA only**	**Insulin only**		
Age (years)	Mean±SD Median (Min, Max)	59.3 ± 11.71 60(20, 78)	58.31± 10.12 58(34, 90)	68 ± 8.49 68(62, 74)	58.66 ± 10.54 59(20, 90)	0.2174[K]
Gender	Female	15(28.3%)	68(44.16%)	0	83(39.71%)	0.0405[MC] *
	Male	38(71.7%)	86(55.84%)	2(100%)	126(60.29%)	

K – Kruskal Wallis test, MC – Chi-square test with Monte Carlo simulation, *indicates statistical significance.

From the Kruskal-Wallis test, it is observed that there is no significant difference in the distribution of age groups. From the Chi-Square test, it is observed that there is a significant difference in the distribution of gender over groups. A fixed-dose combination of medication was also prescribed, in varying proportions. In this study, 73.2% (153), 24.88% (52), and 0.95% (2) of subjects were prescribed one tablet, two tablets, and three tablets respectively. Various OHA are available, with

different mechanism of action, which in combination provides a synergistic effect. Some medications improve insulin secretion while others increase insulin sensitivity. Different combinations of anti-diabetic medications are used in the management of T2DM. Below is a graph showcasing different Oral hypoglycaemic agents in the X-Axis and GRBS level in the Y-Axis in the **Fig. 1.**
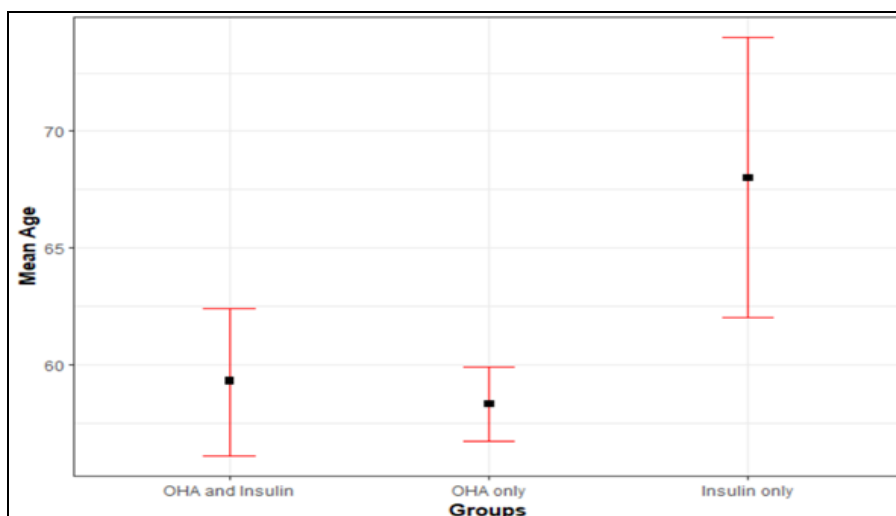
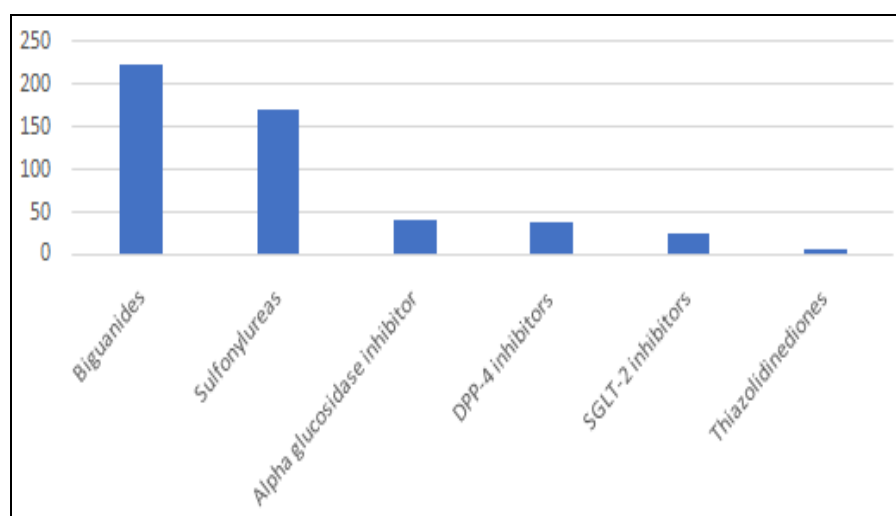**FIG. 1: DISTRIBUTION OF PARTICIPANTS BASED ON MEDICATION COMBINATION AND AGE**

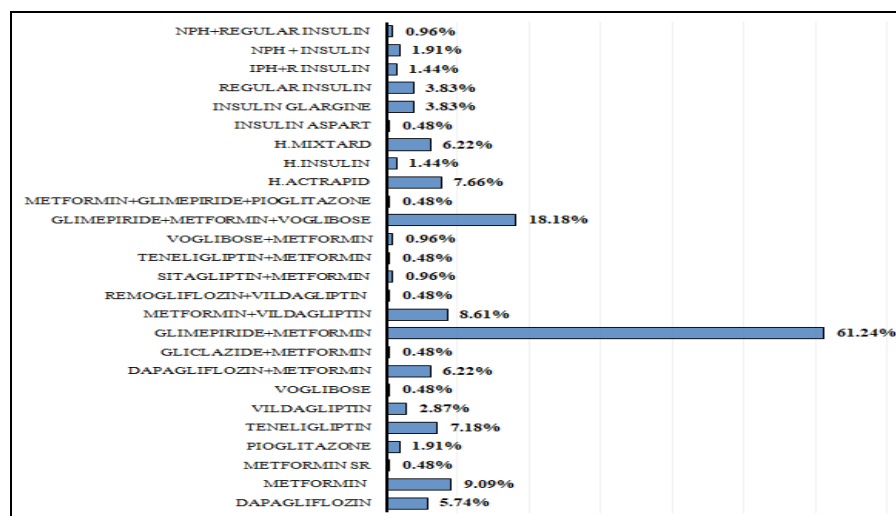**FIG. 2: PRESCRIBING PATTERN BASED ON THE CLASS OF OHA**

FIG. 3: DISTRIBUTION OF SUBJECTS ACCORDING TO PRESCRIBED MEDICATION

In some T2DM patients, insulin can be employed directly to supplement the depleted insulin. Different types of insulin are available based on duration and onset of action. In the below graph, there is a depiction of Insulin types along the X-axis and Age onthe Y-Axis.
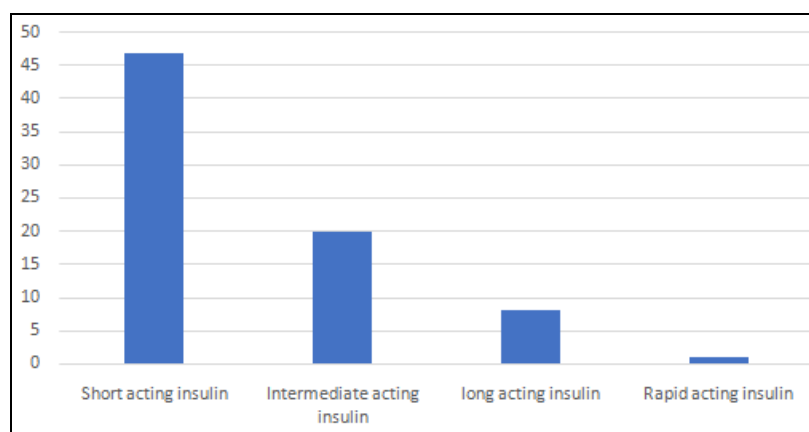
FIG. 4: FIG PRESCRIBING PATTERN OF INSULIN

DISCUSSION: With the earlier start of the disease, type 2 DM affects a large portion of the population in the world. It is a well-known fact that people experience this lifestyle disease at least 10 years sooner than other people. Even more alarming is the finding from recent studies that new-onset diabetes peaks at 30-35 years of age. The combination therapy has several potential advantages, including increased duration of the glycemic effect, simultaneous targeting of the multiple pathophysiological processes and complementary clinical benefits [2]. T2DM is marked by the body's ineffectiveness in utilizing insulin and is alternatively referred to as noninsulin-dependent or adult-onset diabetes [22].

All current recommendations state that metformin should be the oral anti-diabetic medicine of choice when diabetes first develops. However, a survey of literature from throughout the globe finds that metformin is used in various ways in the early stages of diabetes [15]. As the duration of diabetes increases, variation in prescriptions also increases, presumably due to consideration of individual factors. The availability of new medications and therapeutic classes has also led to an increase in the complexity of diabetes medical treatments.

Four new classes of oral anti-diabetic drugs (OAD) have entered the market since the introduction of metformin and sulfonylureas more than a decade ago. These include Alpha-Glucosidase Inhibitors, Thiazolidinediones, the non-sulfonylurea insulin Secretagogues glinides, and Dipeptidyl Peptidase-4 Inhibitors. Lifestyle interventions, including dietary modifications, play a pivotal role in managing and preventing complications associated with T2DM like nephropathy, retinopathy, neuropathy, and foot ulcers [27-28]. Meanwhile, because of their enhanced pharmacokinetic and pharmacodynamic features, rapid-acting and long-acting insulin analogues have also found widespread use. Clinical research indicates that these anti-diabetic medications have comparable efficacy in terms of their total glucose-lowering effect, even though they act on various pharmacological processes and have entirely different safety profiles [18]. For a balanced correction of the underlying metabolic abnormalities associated with type 2 diabetes and to prevent the adverse reactions associated with high-dose anti-diabetic agent treatment, doctors tend to prescribe a combination therapy of anti-diabetic medicines [19].

The enteroendocrine system plays a fundamental role in postprandial physiology and is central in the regulation of glucose homeostasis and satiety [24]. Although metformin is generally recommended as the first line of treatment for type 2 diabetes, there is no unambiguous recommendation for the second-line or subsequent use of these newer medicines. Uncertainty exists on how the entry of these newer drugs into the market will affect the treatment habits of the rapidly growing diabetic population.

The aforementioned prescription trends have a direct and significant impact on healthcare expenses, for both patients and third-party payers, as increasingly complex and expensive therapies are being applied to a rising diabetic population [16].Diabetes self-management involves facilitating the knowledge, skills, and abilities necessary for a patient to manage their condition effectively [22]. The study concentrated on how T2DM patients were prescribed anti-diabetic drugs. ADA offers patients a variety of anti-diabetic drugs based on their

comorbidities and glycemic control. Patients should frequently undergo reassessment and treatment modification every 3-6 months for optimal care. Among the 209 included subjects, most of the participants were prescribed 2 or 3 combinations of OHA (74%), and few were prescribed a combination of OHA and insulin (25%). This reflects the prescriber's preference for OHA more than insulin. In treating patients with a combination of OHA, choices are available either to use multiple tablets each with a single OHA, or use the fixed-dose combination. Several fixed dose combinations are available in the market, which might improve patients' convenience. Of the study participants, 73.2% were prescribed with the fixed-dose combination in a single tablet, followed by 24.8% with two tablets, and only 0.95% were treated with the triple tablet.

Although there was a belief that using metformin and sulfonylurea as the first line of treatment offered payers and policymakers a chance to reduce prescription expenditures, this approach may not always result in better clinical outcomes or higher standards of care. A tailored approach rather than the so-called "one size fits all" approach may be more appropriate given that individual patients varied in terms of age, duration of diabetes, blood glucose level and risk of hypoglycemia, body weight, other cardiovascular risk profiles, lifestyle factors, and medication adherence. To assist in the development of clinical practice guidelines and a pharmacological reimbursement policy on anti-diabetic medication, we propose that additional study into the relative effectiveness of clinical and economic results is required [17]. In patients with diabetes, the balance between insulin and glucagon is disrupted, leading to hyperglycemia [23]. The analysis provides valuable insights into the factors influencing compliance, with variables such as education level, duration of diabetes, HbA1c levels, comorbidities, and knowledge of complications exhibiting statistical significance [25].

The number of patients receiving combination therapy of OAD, either with or without insulin, significantly increased. Further studies are needed to evaluate whether this treatment pattern will lead to improved clinical outcomes in terms of cost-effectiveness [19]. It is important that clinicians are aware of careful explanations and the use of concomitant medications for appropriate treatment [26]. Identifying the factors linked to effective regulation of blood glucose aids healthcare providers in mitigating the likelihood of diabetic complications [29].

CONCLUSION: In the end, we like to conclude that the medication that is being prescribed to the patient plays an important role in determining the glycemic control of the person. It also gives an insight into the different aspects of the disease such as the knowledge of the disease and its complications, ways to overcome the disease, precautions that are taken up, and also the economic strategies to be taken up by both the patient and the physician. Through this method, the patient can decide what type of medication can be taken by them which could provide a better glycemic control on one side and is also feasible for them on the other.

CONFLICT OF INTEREST: Statement of Conflict of Interest and Adherence to Ethical Standards Melvin Kurian Abraham, Kavya S, Rameshwar C. Y. and Dr. Mohammad Mustafa Gadwal do not have any Conflict of Interest

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