

# Metformin Consumption Trends and the Impact of Adherence on the Consumption of Oral Antihyperglycemic Drugs

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**Abstract:-** Diabetes mellitus is a metabolic disease characterized by hyperglycemia. Diabetes therapy includes non-medicinal and medicinal treatment. Metformin is used in the treatment of type 2 diabetes mellitus when controlled diet and exercise are not sufficient to maintain normal blood glucose levels. After 6 months, more than one third of patients, and after one year about 50% of patients with chronic diseases stop the initial treatment. Adherence to oral antidiabetic therapy is in range of 65-85%. Non-adherence in therapy represents a large economic burden. The research was carried out on the territory of the Tuzla Canton, based on collected data on the consumption of antihyperglycemic drugs in 2022 and 2023. A comparison was made of the consumption of antihyperglycemic drugs in 2022 and 2023, in order to obtain the trend of the consumption of the mentioned drugs for the examined period. In addition to the above, a comparison of the consumption of metformin was made in relation to the consumption of other types of oral antihyperglycemic drugs for the years 2022 and 2023. The obtained data show that antihyperglycemic drugs are the most prescribed drugs from the list of drugs and that the largest part of expenditures includes this group of drugs. Metformin was the most prescribed oral antihyperglycemic drug in 2022 and 2023. The above results directly indicate how widespread the use of metformin is in the treatment of diabetes, and how much health care costs can be caused by irrational prescribing and non-adherence to metformin therapy.

**Keywords:-** Metformin; Consumption; Adherence; Antihyperglycemic; Diabetes; Drugs.

## I. INTRODUCTION

Diabetes mellitus is a metabolic disease characterized by hyperglycemia due to a disorder in insulin secretion, a disorder in its action, or due to the presence of both of these disorders [1]. Diabetes mellitus type 1 occurs most often in

children and young people, while diabetes mellitus type 2 is characteristic of adults, with more frequent diagnoses in children as well, due to the increase in the obesity rate.

According to estimates by the International Diabetes Federation (IDF), 415 million (8.8%) adults (age 20-79) globally have diabetes, and 75% of them live in low- and middle-income countries. 1 in 11 adults has diabetes. According to IDF data, 542,000 children (age 0-14) have type 1 diabetes [2].

Diabetes therapy includes non-medicinal and medicinal treatment of glycoregulation disorders, as well as complications caused by diabetes. Medical therapy includes therapy with oral antihyperglycemic agents (OAD), combined therapy (OAD + insulin) and insulin therapy. Oral hypoglycemics include: sulfonylurea derivatives (I generation - chlorpropamide, II generation - glibenclamide, gliclazide and gliclazide, III generation - glimepiride), meglitinides, biguanides (metformin), glucosidase inhibitors, thiazolidinediones or glitazones. Metformin is used in the treatment of type 2 diabetes mellitus when controlled diet and exercise are not sufficient to maintain normal blood glucose levels, especially in obese patients. The mechanism of action of metformin is based on: reducing glucose production in the liver by inhibiting gluconeogenesis and glycogenolysis, increasing muscle sensitivity to insulin and improving the entry and utilization of glucose in peripheral cells, delaying glucose absorption in the intestine. Adult patients usually start therapy with 500 mg or 850 mg of metformin two or three times a day, with meals. The maximum daily dose is 3000 mg divided into three separate doses.

After 6 months, more than one third of patients, and after one year about 50% of patients with chronic diseases stop the initial treatment [3]. Lack of patient adherence to treatment of chronic diseases, such as diabetes, has become a global public health and economic problem. Conclusions from numerous studies have shown that only 50% to 60% of patients use medications for chronic diseases as prescribed [4]. This

problem is particularly present in the countries of the European Union, where the availability of health services as well as their utilization is very high [5]. However, more recent studies show adherence values to oral antidiabetic therapy of 65-85% [6,7]. Adherence is usually considered optimal when patients take at least 80% of their prescribed medication.

Studies that followed the trend in the use of antidiabetic drugs showed that the use of these drugs is increasing, which is in line with the increase in the prevalence of this disease all over the world [8]. Pharmacoepidemiological monitoring of the use of oral antidiabetic drugs and insulin allows comparisons of the use of these drugs in different geographical areas. Thus, the use of sulfonylurea derivatives doubled in Spain, England and Denmark, while their use decreased in Germany and Sweden [9].

Poor adherence undermines efforts to improve health in poor populations and results in waste and underutilization of already limited therapeutic resources. In addition, nonadherence results in numerous, very different, poor health outcomes, including a large number of hospitalizations, disease complications, disease progression, and disability. 125,000 people die each year because they do not take their medicines as they should [10]. Non-adherence in therapy represents a large economic burden: annual costs related to the consequences of non-adherence in the United States of America amount to 100-300 billion dollars, which represents 3-10% of total health care costs [11].

## II. MATERIALS AND METHODS

The type of research is a retrospective analysis of the consumption of 6 types of oral antihyperglycemic drugs and the consumption of metformin in relation to other antihyperglycemic drugs. The sample for the research are antihyperglycemic drugs that are included in the essential list of drugs in the Tuzla Canton: metformin, glimepiride, glibenclamide, sitagliptin, vildagliptin, empagliflozin. The research was carried out on the territory of the Tuzla Canton for the period from 01.01.2022. until 31.12.2023. based on collected data on the consumption of antihyperglycemic drugs in 2022 and 2023. Data on drug consumption were obtained from the Health Insurance Institute of Tuzla Canton. A comparison was made of the consumption of antihyperglycemic drugs in 2022 and 2023, in order to obtain the trend of the consumption of the mentioned drugs for the examined period. In addition to the above, a comparison of the consumption of metformin was made in relation to the consumption of other types of oral antihyperglycemic drugs for the years 2022 and 2023. The data were obtained from the database of the Health Insurance Institute of the Tuzla Canton and statistically processed with the help of a suitable computer program, and the results are presented in tabular form.

## III. RESULTS AND DISCUSSION

The essential list of drugs in the Tuzla Canton for the period 2022 and 2023 included the following oral antihyperglycemic drugs: metformin, glimepiride, glibenclamide, sitagliptin, vildagliptin, empagliflozin. According to the report on the consumption of medicines from the List of medicines according to ATC classification for the year 2022 of the Health Insurance Institute of Tuzla Canton, expenditures in the amount of 42,252,043 BAM were realized for medicines from the List of medicines. Antihyperglycemics (medicines for the treatment of diabetes) participated with 27.61% in the amount of 11,665,675 BAM, which is 676,092 BAM (6.15%) more than in 2021. This group of drugs was realized with 417,556 prescriptions, which is 28,317 prescriptions (7.27%) more than in 2021 and they include 14.22% of the total realized prescriptions for medicines from the list of medicines. In 2022, 343,773 packs of metformin, worth 1,705,866 BAM, were prescribed and implemented at the expense of the Institute. Regarding the consumption of other oral antihyperglycemic agents in 2022, 8,346 packages of glibenclamide, 111,879 packages of glimepiride, 78 packages of sitagliptin, 446 packages of vildagliptin and 1,286 packages of empagliflozin were prescribed and consumed.

Expenditures for medicines from the List of Medicines in 2023 amounted to 46,970,155 BAM, which is 4,718,112 BAM (11.17%) more than in 2022 and represent 93.41% of total expenditures for medicines. In the structure of the consumption of drugs from the List of drugs according to ATC classification in 2023, antihyperglycemic drugs participated with 26.73% in the amount of 12,555,947 BAM, which is 890,272 BAM (7.63%) more than in 2022. This group of drugs was implemented with 500,247 prescriptions, which is 82,691 prescriptions (19.80%) more than in 2022 and represent 13.32% of the total implemented prescriptions for drugs from the List of Medicines. In 2023, 376,696 packs of metformin were prescribed and implemented at the expense of the Institute, in the amount of 1,853,458 BAM. Other oral antihyperglycemic drugs were prescribed and consumed to a greater extent in 2023: 7,151 packs of glibenclamide, 115,470 packs of glimepiride, 198 packs of sitagliptin, 1,788 packs of vildagliptin and 3,003 packs of empagliflozin.

In Table 1, we can compare the results of the total consumption of oral antihyperglycemics in 2022 and 2023, which shows an increase in the trend of consumption and prescription of oral antihyperglycemics in 2023 by 7.63%. Metformin consumption in 2023 increased by 32,923 packs (8.73%) compared to consumption in 2022, which represents an increase in costs by 147,592 BAM. An increase in consumption was also recorded for other oral antihyperglycemic drugs in 2023. For glimepiride we have an increase in consumption by 3.10%, for sitagliptin an increase in consumption by 60.60%, for vildagliptin an increase in consumption by 75.05% and for empagliflozin an increase in consumption by 57.17%. Only for glibenclamide, reduced consumption was recorded in 2023 compared to 2022.

The obtained data show that antihyperglycemic drugs are the most prescribed drugs from the list of drugs and that the largest part of expenditures includes this group of drugs. It is also evident from the above data that metformin was the most prescribed oral antihyperglycemic drug in 2022 and 2023 and that the number of prescribed packs of metformin exceeds the number of prescribed packs of all other oral antihyperglycemic drugs combined. The above results directly

indicate how widespread the use of metformin is in the treatment of diabetes, and how much health care costs can be caused by irrational prescribing and non-adherence to metformin therapy. The obtained results confirm the results of earlier studies that followed the trend of consumption of antihyperglycemic drugs and confirm that the use of these drugs is increasing from year to year, which is in line with the increase in the number of people suffering from diabetes.

Table 1 Consumption data for 2022 and 2023

Year	Consumption of Oral Antihyperglycemic Drugs by Number of Packages					
	<i>Metformin</i>	<i>Glibenclamide</i>	<i>Glimepiride</i>	<i>Sitagliptin</i>	<i>Vildagliptin</i>	<i>Empagliflozin</i>
2022.	343.773	8.346	111.879	78	446	1.286
2023.	376.696	7.151	115.470	198	1.788	3.003
The difference in consumption	+ 8,73%	- 8,57%	+ 3,10%	+ 60,60%	+ 75,05%	+ 57,17%

#### IV. CONCLUSION

Chronic diseases are the leading cause of death worldwide, and more than two-thirds of the global health budget is spent on their control [12]. According to data from the World Health Organization, adherence to therapy for chronic diseases in developed countries is on average around 50% [13]. Previous studies have shown insufficient adherence to diabetes therapy, and poor adherence is associated with disease progression, pharmacotherapeutic errors and hospitalizations, as well as increased healthcare costs. In their research from 2012, Čulig et al showed how medication adherence affects pharmacoeconomics. They showed the costs of the risks and benefits of the therapy, and measured the costs in monetary terms. The results of the pharmacoeconomic analysis depend on several factors, one of the most common of which is adherence to therapy. Poor adherence to prescribed therapy threatens the effectiveness of treatment, and increases the budget for the introduction of new drugs [14].

The National Health Service (NHS) for England estimated that in 2009 the loss to prescription drugs in primary care amounted to £300 million per year. Of this, £90 million was spent on unused prescription drugs that patients kept in their homes, and £110 million on drugs that patients returned to pharmacies [12]. Better monitoring of prescription drugs for the treatment of chronic diseases, such as diabetes, determining the reasons why patients do not take drugs regularly can result in a reduction of therapeutic problems of patients as well as a reduction of pharmaceutical waste, which leads to a reduction of unnecessary costs in the health system [12]. As we note the trend of increasing consumption of antihyperglycemic drugs, it is necessary to take measures aimed at improving patient adherence to therapy, as well as measures that would rationalize the prescription of drugs for the treatment of diabetes.

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