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A comparative study of the efficacy of different Anti-diabetic combination therapies at Al-Bayda Educational Diabetes Treatment Centre, Libya

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Abstract

Diabetes mellitus (DM) is a chronic metabolic disorder with a steadily increasing prevalence worldwide. Type II diabetes, which accounts for 90% of all diabetes, is characterised by resistance to the action of insulin and relative insulin deficiency. It usually affects people over the age of 40. Most patients with T2DM are overweight at the time of diagnosis or obese, and normal blood sugar levels can't be achieved or maintained in a near-normal range without antidiabetic drugs. This research was conducted to study 200 patients with diabetes during the period from November 2022 until April 2023. Several factors, including age, sex, duration of the disease (FBS, HBA1C), degree of diabetes duration diagnosed, hypertension, thyroid disorders, and antidiabetic medication name, Of the 200 patients, 66% (n=132) were female and 34% (n=68) were male, respectively, with an average age of 55 years (31–80) and the highest prevalence of diabetes (51-60). Later age groups (61-70) (40.5% and 23.5% of the study, respectively). About 51% of patients had been diagnosed with diabetes less than five years ago. In addition, 28% of men were diagnosed with hypertension, as were 65% of women. Antidiabetic drugs were studied, and associations between drug types, age, and diabetes duration were reported. Metformin is also considered the first choice of drug for most patients with type 2 diabetes, with approximately 30% using it as monotherapy and 24.5% in combination with Glibenclamide. During this study, there was a slight loss of weight in patients who used multiple antidiabetic drugs. Changing lifestyle advice is important even when drugs are treated to avoid further weight gain as well as a higher chance of diabetic patients.

Keywords: Type 2 diabetes, T2D, Oral antidiabetic drugs.

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1. Introduction

Diabetes mellitus [DM] is a metabolic disorder that occurs as a result of defects in insulin secretion, insulin action, or both. Insulin deficiency also leads to chronic hyperglycemia with disorders of carbohydrate, fat, and protein metabolism [1]. This type of long-term Diabetes is linked to long-term malfunction, and organ failure, particularly to the kidneys, eyes, and nervous system, heart, and blood vessels [2]. It is categorized as type 1 diabetes due to β-cell damage which often results in complete insulin deficiency and type 2 diabetes due to inadequate compensatory insulin secretory response due to resistance to insulin action [3]. Type 2 diabetes mellitus is a prevalent and increasing disease that is a major public health concern worldwide. Research suggests in America that out of 3 adults has prediabetes. About 29.1 million people in the United States have diabetes, but 8.1 million may be undiagnosed and unaware of their condition. New cases about 1.4 million of diabetes are diagnosed in United States every year [4]. Obesity is common in patients with diabetes, and obesity in general leads to insulin resistance. The risk of developing this type of diabetes probably increases with age, obesity, and inactivity; it is also more prevalent in patients associated with hypertension [5]. The World Health Organization (WHO) reports that diabetes is considered a death risk factor in 5% of the population, in addition to cardiac disease (37%), and cancer (13%). [6] [7]. Achieving good control of diabetes in the body for a long time requires a combination of lifestyle changes and pharmacotherapy. Regardless of the choice of pharmacological interventions that physicians must decide, it doesn't place a chemical emphasis on dietary modification, weight gain prevention,

or regular exercise. The pathophysiological nature of type II diabetes means it can progress over time, leading to worsening control of blood glucose levels. At some point, it is inevitable that monotherapy with any one group of drugs will become ineffective at controlling blood glucose. At this point, physicians may either increase the dose of the monotherapy drug, risking side effects, or combine it with another drug that has a different mechanism of action [8]. The most common oral forms of antidiabetic drugs include biguanides, sulfonylureas, thiazolidinediones (TZD), sodium-glucose cotransporter (SGLT2) inhibitors, and di-peptidyl peptidase 4 (DPP-4) inhibitors [9]. Biguanides are one of the main antidiabetic drugs, of which metformin is the most commonly used first-line diabetes therapy. Metformin has been shown to be effective in lowering blood glucose, inducing insulin sensitivity, reducing cardiovascular and hypoglycemic risk, and improving large artery consequences and mortality in T2DM rates. The only hypoglycemic factor to be reduced is the depressant effects of metformin, which are primarily caused by decreased hepatic glucose output such as gluconeogenesis and glycogenolysis, severe, reversible gastrointestinal side effects observed with or after metformin administration with food, and may be reduced by the use of Low incidence, gradually increasing where necessary [10–11]. Lactic AC levels are rare, with ~ 3 per 100,000 patient-years of treatment. Most cases reported as regards lactic acidosis occur in patients with anti-indications, especially impaired renal function (> 90% of the cases). In conclusion, metformin is an effective and safe treatment for type 2 diabetes [12]. Sulfonylureas act by releasing insulin from pancreatic β cells. Site-specific adenosine triphosphate (ATP)-sensitive potassium channels are caused by sulfonylureas to close potassium channels and subsequently open calcium channels. This provides extracellular insulin synthesis that is impaired. Glibenclamide (glyburide), gliclazide, glipizide, and glimepiride (Amaryl) are the main sulfonylureas for the treatment of type 2 diabetes currently in clinical use [13]. Thus, metformin's main action is to increase peripheral nerve sensitivity to insulin, which has beneficial effects on glycemic control, whereas sulfonylurea's action is to induce the secretion of insulin [14]. Therefore, this study was conducted to evaluate the efficacy of different anti-diabetic combination therapies at Al-Bayda Educational Diabetes Treatment Centre, Libya.

2. Methodology

The Diabetes Center in Albayda City is dedicated to the dedicated to the treatment and care of type 2 diabetes and achieving good health through disease reduction. Diabetes Centre staff promote self-management skills and educate patients and their families about diabetes disease. In addition, the Diabetes Centre provides day-to-day care for diabetics, including routine health education on hypoglycemia or hyperglycemia and the right administration of medications. In addition to some related body organ's function tests, this research study was conducted during the period from November 2022 until April 2023. Demographic information includes sex, age, duration of diabetes, hypertension, weight changes associated with medication use, and the name of the anti-diabetic medication. A final fasting plasma glucose (FBS) of ≤ 109 mg/dl or >110 mg/dl was recorded. HBA1C was estimated by using (Pithod 616 semi-automatic analyse for point care testing measuring HBA1c, Korean) and (Hemocue HBA1c501, Korean). Last couple assays were analysed using glucose (Photometer 4040, German, (manual beam filter photometer)) and (Jenway6051 calorimeter manual, United Kingdom. The fully automated system provides reliable results straight away for efficient diabetes care.

3. Results

Over the 200 Libyan diabetic patients that our study about them there were 66% (n=132) of them were females while there were 34% (n=68) of them were males, the most of these patients were 114 of them on combination drugs of oral antidiabetic and 86 of them were on single drug using, while that 30% (n=35) were males and 69% (n=79) were females on multiple drug using ,and there were 38% (n=33) of them males and 61% (n=53) of them females there were on single drug using (Table 1). The most of these diabetic patients age group was ranged between 51 to 60 years old with percentage 40.5% (n=81), And the least age group was 31-40 years old percentage with 6.5% (n=13), So as we mentioned there the most age group with diabetes was 51-60 years old and that were 29% (n=24) males while 70% (n=57) were females, In the other hand the least age group between 31-40 years old percentage with 30% (n=40) males and 69% (n=9) were females (Table 2). The most duration of drug intake was ranged between 1 year to 5 years ago 102 of the total number of patients while there were 69.6% (n=71) females and 30.3% (n=31) were males, in the other hand the least duration intake was between 11-15 years ago (Table 3). The most common single drug line that used as oral antidiabetic drug was metformin with percentage 30% (n=60) of the total diabetic patients followed by Amaryl with 7.5% (n=15) while there is 57% (n=114) of the patients that our study about not using single drug, and the least frequent drug was Diamicron with 0.5% (n=1) (Table 4 & Figure 1). The last FBS results of single drug using patients that were more than 110 was for Metformin medicine with percentage 68.3% (n=41) and the less than 109 results were for metformin also with 31.6% (n=19) (Table 5). And the last HBA1c results of single drug using patients that more than 7 were for Metformin with 65% (n=39) and the less **than 6.9** results was for metformin also with 35% (n=21) as shown in Table 6. In comparing with single drug using and multiple drugs using the most common line used in multiple drugs using was Glibenclamide + Metformin combination with percentage 24.5% (n=49) followed by Metformin + Amaryl with 22% (n=44), While the least percentage used multiple drugs was Ganumet + Amaryl with 1% (n=2) (Table 7 & Figure 2). And the last FBS results of multiple drugs using patients that were in less than 109 results were for Glibenclamide + Metformin with (n=29) (Table 8). The last HBA1c results of multiple drugs using patients that was in the less than 6.9 results were for Glibenclamide + Metformin combination with (n=29) (Table 9). According to the relation between the weight of the patients and the multiple drugs using line, the most combination that effect on the weight changes was Glibenclamide + Metformin with percentage 24.5% (n=49) that 17 of them shown no changes in weight and 6 of them increased in weight and 26 of them decreased in weight (Table 10).

Table1: Sex distribution in the studied patients.

	Frequency	No	%	Single drug using		Multiple drugs using	
				No	%	No	%
Valid	male	68	34	40	58.8	28	41.2
	Female	132	66	90	68.2	42	31.8
	Total	200	100				

Table 2: Diabetic distribution according to age group in the studied patients.

	Frequency	Percent	Valid Percent
Valid	31-40	13	6.5%
	41-50	39	19.5%
	51-60	81	40.5%
	61-70	47	23.5%
	71-80	20	10.0%
	Total	200	100.0%

Table 3: Duration of drug intake distribution in the studied patients.

		1-5 yrs.	6-10 yrs.	11-15 yrs.	↑16 yrs.	Total
Sex of patients	Male	31	15	7	15	68
	Female	71	26	17	18	132
Total with percentage		102(51%)	41(20.5%)	24(7%)	33(16.5%)	200

Table 4: The most common single drug line that used as oral antidiabetic drug distribution in the studied patients.

Name of drug	Frequency	Percent
Gliburide	7	3.5%
Metformin	60	30%
Amaryl	15	7.5%
Diamicron	1	0.5%
Janumet	3	1.5%
Not using single drug	114	57%
Total	200	100%

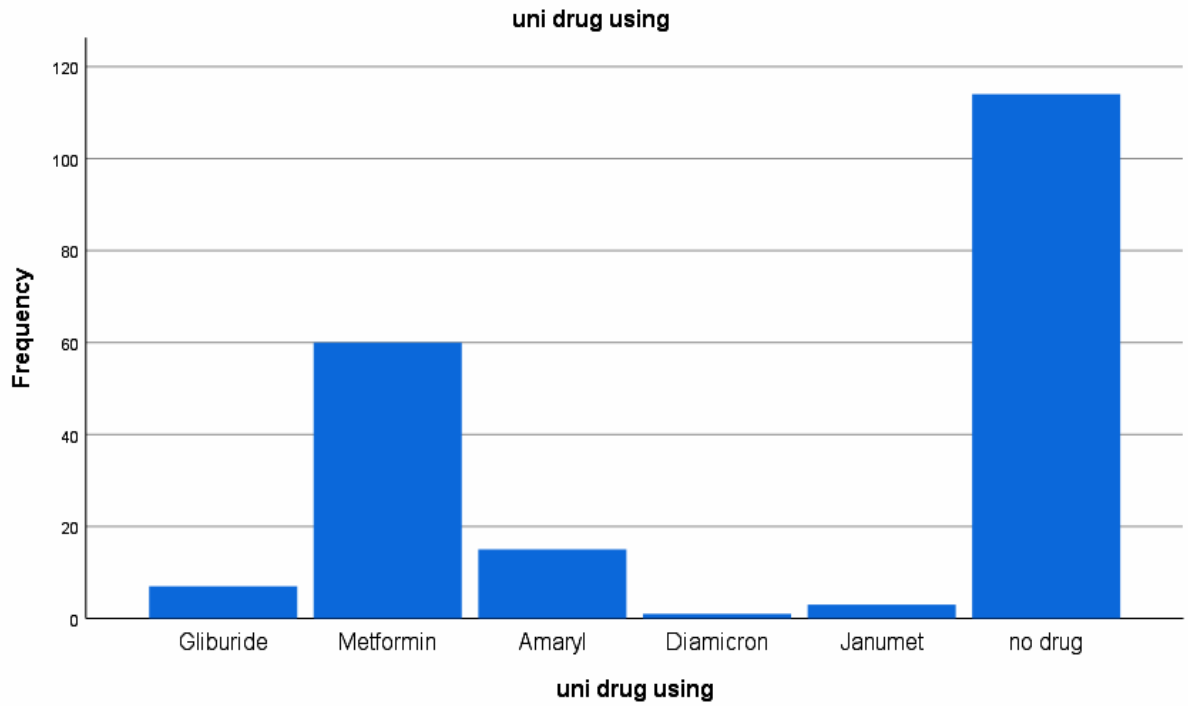

Figure 1: The most common single drug line that used as oral antidiabetic drug distribution in the studied patients.

Table 5: Distribution of the single drug used among studied patients.

		Gliburide	Metformin	Amaryl	Diamicron	Janumet	Total
Last FBS	**less than 109**	0	19	3	0	1	23
	more than 110	7	41	12	1	2	63
Total		7	60	15	1	3	86

Table 6: The last HBA1c results of single drug used among studied patients.

		Gliburide	Metformin	Amaryl	Diamicron	Janumet	total
last HbA1c	less than 6.9	0	21	3	0	1	25
	more than 7	7	39	12	1	2	61
Total		7	60	15	1	3	86

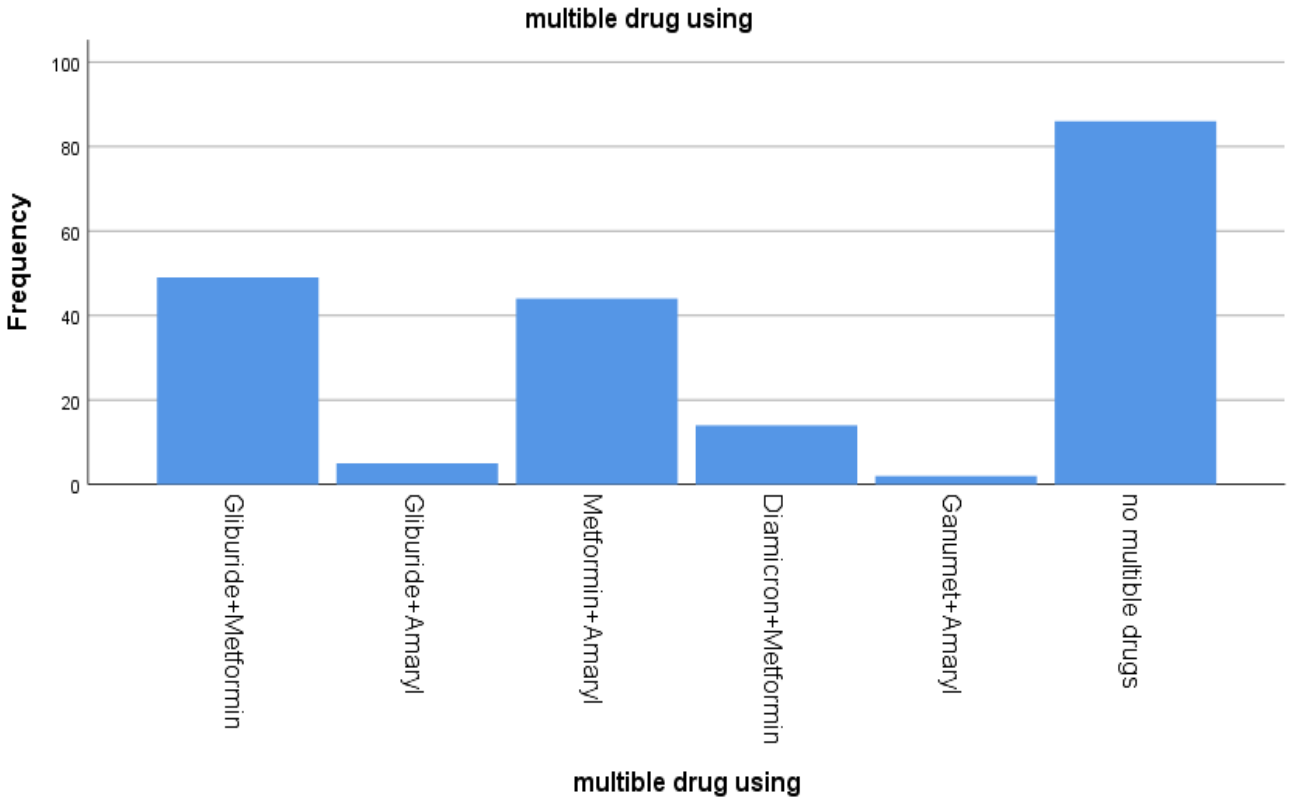

Figure 2: Distribution of the multiple drugs used among studied patients.

Table 7: Distribution of the multiple drugs used among studied patients.

Drugs	Frequency	percent
Gliburide + Metformin	49	24.5%
Gliburide + Amaryl	5	2.5%
Metformin + Amaryl	44	22%
Diamicron + Metformin	14	7%
Ganumet + Amaryl	2	1%
Not using multiple drugs	86	43%
Total	200	100%

Table 8: Last FBS results among studied patients.

	Gliburide + metformin	Gliburide + Amaryl	Metformin + Amaryl	Diamicron + metformin	Ganumet+ Amaryl	Total
Last FBS less than 109	29	2	23	5	1	60
Last FBS more than 110	20	3	21	9	1	54
Total	49	5	44	14	2	114

Table 9: Last HBA1c results among studied patients.

		Gliburide+ Metformin	Gliburide+ Amaryl	Metformin+ Amaryl	Diamicron+ Metformin	Ganumet+Amaryl	Total
Last HBA1c	less than 6.9	29	2	23	5	1	60
	more than 7	20	3	21	9	1	54
Total		49	5	44	14	2	114

Table 10: Relation between the weight and the multiple drugs among studied patients.

		wt. change			Total
		no change	increase	decrease	
multiple drug using	Gliburide+Metformin	17	6	26	49
	Gliburide+Amaryl	2	1	2	5
	Metformin+Amaryl	20	5	19	44
	Diamicron+Metformin	7	2	5	14
	Ganumet+Amaryl	2	0	0	2
	no multible drugs	35	11	40	86
Total		83	25	92	200

Table 11: Relation between gender of patients and Hypertension among studied patients.

		with HTN		Total
		yes	no	
Sex	Male	28	40	68
	female	65	67	132
Total		93	107	200

Table 12: Relation between age of patients and Hypertension among studied patients.

		with HTN		Total
		Yes	No	
age in between	31-40	2	11	13
	41-50	12	27	39
	51-60	43	38	81
	61-70	27	20	47
	71-80	9	11	20
Total		93	107	200

The cross tabulation of gender of patients with Hypertension we found there were 132 of these patients were females and that were 65 of had Hypertension with Diabetes Mellitus and 67 of them hadn`t, while there were 68 of were males of them 28 of them had Hypertension with Diabetes and 40 of them hadn`t Hypertension (Table 11). While the age between with Hypertension that was the age between 51-60 with the highest number of patients that had Hypertension or not with Diabetes Mellitus with total number 81, There were 43 of them had Hypertension in this age range and 38 of them hadn`t regardless the gender of the patients (Table 12).

4. Discussion

Currently, type II diabetes, which accounts for 90% of all diabetes, is an increasing global health problem and is closely connected to the obesity epidemic. Individuals with type II diabetes are at increased risk for multi-health disorders, microvascular complications (including neuropathy, retinopathy, and nephropathy), and macrovascular complications (for example, cardiovascular comorbidities), because individual components of hyperglycemia and insulin resistance (metabolic) syndrome are environmental factors (e.g., obesity, being unhealthy). Dietary and activity factors, in addition to genetic factors, also contribute to the recurrent pathogenicity of impaired glucose homeostasis in T2DM [15]. In this review, for the first time, a combination of ADA (American Diabetes Association) and EASD (European Association for the Study of Diabetes) guidelines for managing hyperglycemia in type 2 diabetes clearly states that metformin should be used as first-line therapy in addition to lifestyle interventions [3, 5]. The UK Prospective Diabetes Study (UKPDS) demonstrated significant benefits of metformin treatment on cardiovascular disease (CVD) outcomes, including a 36% risk reduction in all-cause mortality and a 39% risk reduction in myocardial infarction [16, 21]. Our study was carried out on 200 patients, 68 (34%) male and 132 (66%) female. Their ages range from 31-80 years old, with a mean of 3.11. All patients were coming for follow-up at the diabetic clinic centre as cases of diabetes mellitus type 2, and the patients received a lot of types of oral antidiabetic drugs for different durations, from one year to more than ten years. 114 patients (57%) were in combination drug therapy, while 86 patients (43%) were in single therapy with an antidiabetic drug. In the present study, patients with type II who received metformin only had inadequate glycemic control. Similar results were seen in studies by Brown et al. (2010), although metformin fails to control blood sugar but still has a role in preventing diabetes complications, so the usage of Janumet (metformin/sitagliptin) as a combination therapy was efficacious. because it will be controlling blood glucose with decreasing complications [17–18]. Studies showed that about 42% of diabetic patients who were undergoing combination therapy were treated with Glibenclamide or Metformin because they provide tight glycemic control to patients in a short period of time, have few side effects, and have hypoglycemic few episodes. The same results are presented in the study by Amin et al., (2015) [19]. About 38.5% of the study group (in combination therapy) were taking Amaryl/metformin, as they can be administered to each other, synergistically for therapeutic effects, causing metabolic defects caused by type 2 diabetes mellitus and bleeding decreased glucose. Park et al., (2014) obtained the same results [20].

5. Conclusions

The current study revealed that nearly half of diabetics have high blood pressure, a point that is consistent with a previous study in UK that said the incidence of diabetes mellitus type 2 is higher than the expected in the most population, particularly in a group of middle-aged patients. Approximately 40% of diabetic patients by age 55 with type 2 have hypertension, and by age 65 the rate decreases to 23.5% [21]. Combination therapy has become increasingly popular, a consensus statement was published by the American Diabetes Association recognizing its importance [22]. It is therefore useful to consider the efficacy of different combination therapies.

6. Recommendation

Regarding on our study about oral anti diabetic drugs therapy we found out that single drug therapies often fail in treatment of Diabetes Mellitus, While the multiple drug line therapies shown good effect in treatment of diabetic patients. We recommend to our patients to know the whole side effects of the drugs that they were on whatever the drug single or combined to take care, And we recommend too that they must include in their daily diet to be effective with treatment and control of the disease include fruits and vegetables, choose foods with less added sugars and avoid starchy foods, keep working out and make the exercise strategies adapted for them based on comorbidities and contraindications and realistic their personal goals.

7. Abbreviations

- DM: Diabetes mellitus.
- T2DM: Type 2 diabetes mellitus.
- FBS: Fasting blood sugar.
- HBA1C: Hemoglobin A1C.
- TZD: Thiazolidinedione.
- DPP4: Dipeptidyl peptidase 4 inhibitor.
- SGLT2: Sodium glucose cotransporter 2 inhibitor.
- ATP: Adenosine Triphosphate.
- HTN Hypertension.
- ADA: American diabetes association.
- EASD: European association for study diabetes.
- UKPDS: UK prospective diabetes study.
- CVD: Cardiovascular disease.
- HRCT: High resolution computed tomography.

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