

## CLINICAL AND THERAPEUTIC CHARACTERISTICS OF PATIENTS WITH TYPE 2 DIABETES MELLITUS IN ROMANIA – MENTOR STUDY

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### Abstract

**Background and aims:** PREDATORR Study estimated diabetes mellitus (DM) prevalence in Romania at 11.7%. MENTOR is the first national major study trying to determine the quality of the metabolic control in patients with type 2 diabetes (T2DM), the therapeutic options used, and the microvascular and macrovascular complications prevalence in order to achieve a better management for Romanian patients with T2DM. **Material and methods:** The study was designed as an observational analytical, multicenter, prospective study. Study population was selected from T2DM patients stratified by: age, diabetes duration and gender. Data was collected in an eCRF: demographics, physical examination, cardiovascular evaluation, blood tests, known pathology, treatment. **Results:** There were 54.80% women, mean age was 60.53±7.39 years. The average BMI is over 30 kg/m<sup>2</sup> with a decreasing trend over the age. 60% had their HbA1c over the threshold of 7%. Average blood pressure was less than 140/80 mmHg. 76.66% of T2DM subjects have at least one chronic complication. On oral therapy we have 55.44% of patients, on insulin only therapy 12.99% and on a combination of oral and insulin therapy 22.51%. **Conclusions:** This study showed a high prevalence of diabetes complications and metabolic alterations (obesity, hypertension, dyslipidemia, etc.). Age, male gender and diabetes duration were associated with a higher risk for poor metabolic control and complications. Further data will be collected over a 3 years period to obtain a better image over T2DM evolution in Romanian population.

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## **Background and Aims**

Type 2 diabetes (T2DM) has an increasing prevalence over the last decades, despite efforts and strategies to reduce disease burden, and it is estimated to affect about 629 million people worldwide by 2045 [1]. Increased life expectancy, along with decreased birth rates, are important factors that converge towards a high percentage of population over 45 years old and a higher T2DM prevalence.

Romania, a developing country located in a region with major changes in political and economic environment, has undergone a rapid change in the socioeconomic state over the past few years. This evolution has resulted in major changes in nutritional behavior and lifestyle, fast food consumption and sedentary lifestyle - now common features in the Romanian population. This can explain why a nation-wide study on Romanian general population revealed a high prevalence of overweight (31.1%) and obesity (21.3%) among the participants enrolled [2].

The PREDATORR Study (2013) showed a high rate of impaired glucose metabolism in the adult Romanian population with an estimated diabetes mellitus (DM) prevalence of 11.7 % [3]. Reports on clinical and therapeutic characteristics in diabetes care in developing countries are widely available, but in Romania there are significant knowledge gaps.

The main concern globally is the increasing cost of diabetes management. This could be caused by the increased survival of patients with diabetes and a higher complications prevalence. Romanian National Health Insurance House has reported a yearly increasing budget for the Diabetes National Program, but we still lack information from other sources (Clinical trials, Independent trials etc.).

“MENTOR” is the first national major study trying to cover the most important aspects of T2DM: complications, evolution, and treatment options. The aim is to quantify part of this issues in order to achieve a better management for Romanian patients with T2DM. Study primary endpoints are: death by any cause, major acute cardiovascular events and microvascular events. Secondary endpoints comprise hyperglycemic complications, hypoglycemia, chronic complications incidence, anxiety-depression prevalence, glycemic control (HbA1c in target, % of glycemia in target), lipids control (LDL cholesterol, triglycerides), renal function (eGFR > 60ml/min/1.73m<sup>2</sup>), blood pressure control.

## **Material and methods**

### *Study design*

The study was designed as an observational, analytical, multicenter, prospective study that aims to evaluate the metabolic control of patients with T2DM, the therapeutic options used for these patients, as well as the cardiovascular, microvascular and macrovascular complications prevalence.

Study population was selected from T2DM patients attending diabetologists from all over Romania (all the 41 districts and Bucharest) between Oct 2016 – Apr 2018. The sample was estimated to be representative for T2DM population of Romania, taking into consideration the estimate of Romanian population from 2011 Census and diabetes prevalence reported by the PREDATORR Study [2]. Confidence interval was set between 95-97% with an error of 2%.

Inclusion criteria were: subjects that meet the criteria for T2DM diagnosis, age between 45 and 75 years old, given informed consent to participate to the study. Main exclusion criteria are presence of type 1 diabetes mellitus, neoplasia, diseases that can affect life

expectancy in the next 3 years or patients that didn't give their informed consent.

Subjects were randomly screened from the patients that came to the periodical evaluation in each investigator practice, using the criteria of "first arrived" that matched the requirements. Due to the distribution of population from the Romanian 2011 Census and diabetes prevalence reports in Romania, the subjects enrolled were stratified by: 2 age groups (45-60 y.o. and 60 – 75y.o.), 3 diabetes duration groups (<5 years, 5-15 years, > 15years) and gender. Investigators were advised to include the first patients that come to their office, match each group combination and give their informed consent, in order to exclude physician bias of selection.

1300 subjects were enrolled in this study, with the intention of obtaining valid data for a sample of at least 1050 subjects.

#### *Data collection*

Data from 67 sites from all around Romania was collected in an electronic CRF where all the investigators could enter their patients' characteristics.

Data on patients' age, gender, medical history, concomitant medication, living conditions, education were collected.

Physical examination included measurement of weight, height, waist circumference, mid arm circumference, blood pressure and heart rate. Weight and height were measured on a calibrated standard scale with patients wearing light clothing. Body mass index (BMI) was calculated as weight (kg) divided by the square of height (m<sup>2</sup>).

After resting for at least 5 min, three blood pressure measurements, were taken using a calibrated sphygmomanometer with an appropriate sized cuff covering at least 80% of the dominant arm. We recorded the media of the three measurements. Heart rate was evaluated

over 60 seconds count with the patient resting for at least 5 minutes.

Blood samples were collected after the patients fasted for over 8 hours, with standard evaluation methods in local labs. The following parameters were determined: Fasting Blood Glucose (mg/dl), Complete Blood Count (CBC) – Hb (g/dl), CBC – Hematocrit (HCT) (%), CBC – White Blood Cells (WBC) (/μL), CBC – PLT (x10<sup>3</sup>/ μL), HbA1c (%), Urea (mg/dl), Seric creatinine (mg/dl), Uric acid (mg/dl), TGO (U/l), TGP (U/l), GGT (U/l), Total Bilirubin (mg/dl), Direct bilirubin (mg/dl), Total cholesterol (mg/dl), Triglycerides (mg/dl), HDLc (mg/dl), calculated non HDLc (mg/dl), Albumin-to-creatinine ratio.

Retinopathy presence was determined according to the fundoscopy examination performed by an ophthalmologist and was classified in non-proliferative and proliferative based on the presence of new vessels formation. Neuropathy was diagnosed after neurological exam or sensibility and autonomic testing and was classified as somatic and/or autonomic. Chronic kidney disease was defined according to the KDIGO 2012 criteria as an estimated glomerular filtration rate <60 mL/min/1.73m<sup>2</sup> and/or urinary albumin-to-creatinine ratio (ACR) ACR 30 – 300 mg/g for more than 3 months [4].

The study was conducted in accordance with ICH/GCP regulations. It was approved by the National Committee of Bioethics and it respects the Declaration of Helsinki principles. Detailed information regarding the study duration and procedures was provided to all eligible individuals, those who signed the informed consent form prior to any trial procedure were included in the study.

The study is registered with EudraCT number 2015-005578-39.

### Statistical analysis

The results from patients' evaluation were collected in an online database and data was exported in an EXCEL worksheet where primary analysis was performed.

Every sample was analyzed using descriptive statistics, every quantitative variable being calculated: the minimum and maximum values, means and the standard deviation. Along with the means (M), on the basis of the standard deviations and the volumes of each sample, standard errors were calculated (random sampling of simple means, SE). We verified the empirical distribution concordances using normal distributions (Gaussian). All statistical processing was performed in MS EXCEL, using incorporated functions.

## Results

### Population characteristics

This preliminary analysis of the MENTOR study analyzed a sample of 1093 patients from the total of 1300 patients enrolled, considered representative for the T2DM population from Romania, with most of the patients in the 50-70 years age group. Age distribution was consistent with the normal age distribution for patients with

T2DM: under 50 years old – 9.42%, between 51-60 – 37.52%, between 61-70 – 47.12%, over 70 – 5.94%. Most of the patients included live in urban areas 72.18%. Looking at their education, we observed that 19.85% have university degree, 59.74% high school degree and only 20,41% primary school.

The mean duration of diabetes was 9.90 years with the following distribution: newly diagnosed 1.28%, with 1-4 years since diagnosis 19.94%, 5-9 years 32.29%, 10-14 years 20.22%, 15-19 years 19.85%, over 20 years of evolution 6.42%. As expected, diabetes duration increases with patients' age group (Table 1) and this confirms that nowadays survival with diabetes is much increased due to improved management.

Anthropometric measurement of study population can be followed in Table 2.

Both females and males had an average BMI over 30 kg/m<sup>2</sup> with a decreasing trend over the age probably due to a decrease in muscle mass. This will be further evaluated by hand grip strength measurement. A total of 187 (37.85%) of males were overweight and 266 (53.84%) are obese. Compared to males, female population consisted of 167 (27.87%) overweight and 389 (64.94%) obese subjects.

**Table 1.** General characteristics of study population.

Gender	Age group	No	No. %	Diabetes Duration (yrs)	Heart rate (bpm)	BPC (mmHg)	BPO (mmHg)
Women	45-50	53	8.85%	8 ± 6.34	75 ± 9.94	131/78	128/76
	51-60	208	34.72%	9 ± 6.35	77 ± 9.93	138/80	136/80
	61-70	302	50.42%	10 ± 6.34	75 ± 9.91	140/80	136/79
	71-75	36	6.01%	14 ± 6.31	75 ± 9.89	135/74	133/75
	Total	599	100.00%	10 ± 6.33	75 ± 9.92	138/80	135/79
Men	45-50	50	10.12%	7 ± 6.30	80 ± 10.68	137/81	135/80
	51-60	202	40.89%	9 ± 6.36	77 ± 9.95	140/80	138/80
	61-70	213	43.12%	11 ± 6.34	74 ± 9.92	140/80	136/78
	71-75	29	5.87%	10 ± 6.33	75 ± 9.91	142/79	140/77
	Total	494	100.00%	10 ± 6.34	76 ± 10.68	140/80	138/79

Table legend (result = average ± standard deviation, BPC Blood Pressure Supine, BPO Blood Pressure Standing)

**Table 2.** Anthropometric characteristics of study population.

Gender	Age group	BMI (kg/m <sup>2</sup> )	Waist circ. (cm)	MAC (cm)	Weight (kg)	Height (cm)
Women	45-50	33.59 ± 7.09	105 ± 13.01	34 ± 8.41	89 ± 16.66	163 ± 21.16
	51-60	33.61 ± 7.61	107 ± 12.99	35 ± 8.26	86 ± 16.64	160 ± 18.75
	61-70	32.13 ± 5.29	107 ± 12.98	34 ± 7.78	82 ± 16.72	160 ± 14.32
	71-75	31.11 ± 4.77	104 ± 12.83	33 ± 7.66	79 ± 16.48	159 ± 14.35
	Total	32.72 ± 6.36	107 ± 12.99	33 ± 7.72	84 ± 16.72	160 ± 14.32
Men	45-50	36.6 ± 6.63	113 ± 12.86	35 ± 7.38	100 ± 16.41	174 ± 13.47
	51-60	31.63 ± 4.83	110 ± 13.01	34 ± 6.97	96 ± 16.59	174 ± 9.51
	61-70	30.36 ± 4.48	108 ± 13.01	33 ± 6.74	91 ± 16.70	173 ± 9.32
	71-75	29.85 ± 3.49	110 ± 12.97	34 ± 6.71	88 ± 16.57	172 ± 9.47
	Total	31.09 ± 4.90	109 ± 12.99	34 ± 6.70	94 ± 16.72	173 ± 9.51

Table legend (result = average ± standard deviation, BMI body mass index, Waist Circ. Waist Circumference, MAC Mid Arm Circumference)

**Table 3.** Glycemic control of study population according to gender and diabetes duration.

Gender	Diabetes Duration (years)	No.%	FPG (mg/dl)	HbA1c (%)	Hb (g/dl)
Women	0 -- 9	53.42%	162 ± 64.12	7.72 ± 1.67	13.24 ± 1.48
	10 -- 19	38.90%	177 ± 64.21	8.13 ± 1.67	13.17 ± 1.49
	≥20	7.68%	196 ± 64.57	8.49 ± 1.67	13.09 ± 1.49
	Total	100%	171 ± 64.21	7.95 ± 1.67	13.2 ± 1.48
Men	0 -- 9	53.64%	165 ± 64.32	7.67 ± 1.66	14.46 ± 1.49
	10 -- 19	41.50%	170 ± 64.25	7.77 ± 1.67	14.23 ± 1.49
	≥20	4.86%	192 ± 65.61	7.73 ± 1.70	13.13 ± 1.5
	Total	100%	169 ± 64.25	7.72 ± 1.67	14.3 ± 1.49

Table legend (FPG fasting plasma glucose, HbA1c glycated hemoglobin, Hb hemoglobin)

**Table 4.** Biological characteristics of study population according to gender and diabetes duration.

Gender	Diabetes Duration (years)	Urea (mg/dl)	Creatinine (mg/dl)	Uric Acid (mg/dl)	Total chol (mg/dl)	TG (mg/dl)	HDLc (mg/dl)
Women	0 -- 9	35 ± 19.46	0.79 ± 0.46	5.10 ± 1.51	194 ± 47.94	167 ± 86.22	48 ± 13.34
	10 -- 19	41 ± 19.45	0.85 ± 0.46	5.10 ± 1.51	191 ± 47.90	162 ± 72.5	50 ± 13.33
	≥20	43 ± 19.57	0.87 ± 0.46	5.40 ± 1.52	184 ± 47.75	177 ± 74.67	41 ± 13.38
	Total	38 ± 19.43	0.82 ± 0.45	5.10 ± 1.51	192 ± 47.90	166 ± 80.81	49 ± 13.31
Men	0 -- 9	38 ± 19.53	1.00 ± 0.45	5.60 ± 1.49	182 ± 47.76	194 ± 182.34	43 ± 13.35
	10 -- 19	41 ± 19.43	1.08 ± 0.45	5.60 ± 1.48	185 ± 47.91	196 ± 181.25	44 ± 13.33
	≥20	60 ± 20.14	1.45 ± 0.47	6.00 ± 1.49	159 ± 47.62	156 ± 176.49	44 ± 13.42
	Total	40 ± 19.43	1.05 ± 0.45	5.60 ± 1.48	182 ± 47.91	193 ± 168.92	44 ± 13.33

Table legend (Total chol Total cholesterol, TG triglycerides, HDLc high density lipoprotein)

A total of 756 (69%) patients have been under treatment for high blood pressure, most of already diagnosed with hypertension. Being our patients are well controlled so the average

blood pressure in supine position is less than 140/80 mmHg.

A total of 660 patients (60%) had their HbA1c over the threshold of 7%. Metabolic control is better when the diabetes evolution is of short duration, with females in the 0-9 years diabetes duration group having a mean HbA1c of 7.72%, while those with a diabetes duration for more than 20 years having a mean HbA1c of 8.49% as seen in [Table 3](#). For males, there are minor differences in HbA1c according to diabetes duration. Still, fasting glycemia is over target value in all patients' groups, and with an increasing value in parallel with diabetes duration.

Lipids are still outside of target with high LDLc and non HDLc values both in men and women and low HDLc levels, lower than recommended in women ([Table 4](#)).

### Diabetes complications

255 of the 1093 T2DM subjects enrolled had no diabetes complication while 838 (76,66%) had at least one diagnosed chronic complication. A total of 26.16% of subjects have diabetic eye diseases, with the most frequent condition being non-proliferative retinopathy (22.32%). From the patients that have proliferative retinopathy, 56% had undergone at least one session of laser therapy. Diabetic neuropathy affects 62.85% of all T2DM patients, with 35.71% of newly diagnosed already having sensitive neuropathy and the percentage increases to 85.71% in patients with more than 20 years of disease evolution. Diabetic kidney disease was encountered in about 25.89% of the patients ([Table 5](#)). After adjusting for age, the overall prevalence of complications significantly increased with disease duration. Details are provided in [Table 5](#).

**Table 5.** Diabetes microvascular complications according to diabetes duration.

Duration of Diabetes (years)	No.	No. %	Diabetic Retinopathy			Glaucoma	Cataract	Diabetic Neuropathy			Diabetic Kidney Diseases eRFG<60 and/or ACR > 30 mg/g
			NDR	PDR	Laser			SN	AN	MN	
0 --9	585	53.52%	15.90%	2.91%	1.20%	2.39%	9.06%	52.31%	6.50%	1.20%	23.25%
10 -- 19	438	40.07%	27.85%	6.85%	3.65%	3.20%	15.98%	71.00%	6.16%	2.28%	26.48%
>20	70	6.41%	41.43%	15.71%	14.29%	8.57%	22.86%	88.57%	12.86%	1.43%	44.29%
Total	1,093	100.00%	22.32%	5.31%	3.02%	3.11%	12.72%	62.12%	6.77%	4.91%	25.89%

*Table legend (NDR non-proliferative retinopathy, PDR proliferative retinopathy, SN sensitive neuropathy, AN autonomic neuropathy, MN mononeuropathy, eGFR estimated glomerular filtration rate, ACR albumin to creatinine ratio)*

### Treatment

Evaluating treatment of T2DM subjects included in our study, we have observed that most of the patients are treated with an association of 2 antidiabetic drugs (44,37%), followed as frequency by monotherapy 28.36%.

Overall the proportion of patients on diet and lifestyle intervention is 2.84%, on oral therapy we have 55.44% of patients, on insulin

only therapy 12.99% and on a combination of oral and insulin therapy 22.51% ([Table 6](#)).

Considering patients treated with metformin (760 persons 69,53%), from all study population, 27.50% are only on metformin monotherapy, 13.76% on metformin and sulfonylureas, 8.4% on metformin and Dipeptidyl Peptidase 4 (DPP-4) inhibitors, 5.5% on metformin and GLP-1 Receptor Agonists, 20% on metformin and another 2 antidiabetics, 12.24% on metformin

and basal insulin and 6.88% on metformin and multiple insulin injection therapy.

From the patients treated with insulin alone or in combination with oral antidiabetics, 52.83% are on basal insulin analogs (detemir or glargine), 28.33% on basal-bolus regimen,

2.31% on basal plus therapy, 2.83% on basal plus-plus therapy and 12.62% on premixed insulin or on a combination of rapid and premixed insulin and 1.08% on NPH. Details regarding distribution of insulin treated patients are provided in [Table 7](#).

**Table 6.** Treatment options in T2DM patients divided by gender and diabetes duration

Duration of Diabetes	No.	No.%	Diet	NA	OAD (% from each population group)					OAD+Insulin (% from each population group)			
					1 Drug	2 Drugs	3 Drugs	4 Drugs	Total	2 Drugs	3 Drugs	4 Drugs	Total
0 --9 years	585	53.52%	2.73%	6.83%	34.02%	28.89%	5.30%	0.00%	68.21%	8.55%	5.98%	0.34%	14.87%
10 -- 19 years	438	40.07%	2.74%	5.25%	12.10%	23.29%	8.45%	0.00%	43.84%	12.56%	15.75%	0.91%	29.22%
>20 years	70	6.40%	4.28%	7.14%	5.71%	12.86%	2.86%	0.00%	21.43%	17.14%	24.29%	2.86%	44.29%
Total	1,093	100.00%	2.84%	6.22%	23.42%	25.62%	6.40%	0.00%	55.44%	10.70%	11.07%	0.73%	22.51%

Table legend (No number, NA no available data, OAD oral antidiabetic treatment)

**Table 7.** Insulin regimens in T2DM patients divided by gender and diabetes duration

Duration of Diabetes	No.	No.%	Insulin (% from each population group)							Total
			Basal	Basal +	Basal ++	Basal bolus	Premix	NPH		
0 --9 years	585	53.52%	14.52%	0.51%	0.34%	4.10%	2.39%	0.17%	22.03%	
10 -- 19 years	438	40.07%	23.05%	0.68%	2.05%	15.06%	7.07%	0.22%	48.13%	
>20 years	70	6.40%	27.14%	4.28%	0.00%	28.57%	5.71%	1.42%	67.12%	
Total	1,093	100.00%	18.75%	0.82%	1.01%	10.06%	4.48%	0.27%	35.39%	

Table legend (Basal – Basal insulin analog, Basal + - Basal insulin analog plus on shot of prandial insulin, Basal++ - Basal insulin analog plus two shots of prandial insulin)

## Discussions

The population included in this study has an age and gender distribution and a diabetes duration in accordance with the structure of the population from the latest national census reports [5] and results of the PREDATORR trial [3]. Based on that, we can consider our data relevant for the Romanian T2DM population.

The prevalence of obesity among Romanian adult population was 32% and there were 34.7% overweight subjects in the PREDATORR study [6]. Obesity and overweight are currently on a rising trend. The prevalence of obesity in our study was higher among women than men, with a significant decrease in BMI with age increase. Body composition has a trend of change over the

age by decreasing lean tissue mass and increasing body fat with a slight decrease in BMI but no/minor change in waist circumference and mid arm circumference, reason why we intend to perform also bioimpedance measurements in our selected patients.

Mean blood pressure in our group was in the recommended target area for both men and women. The hypertension incidence is high as diagnosis but apparently the surveillance of both general practitioners (GP) and diabetologist results in a good control of blood pressure values. By comparison, 72% of US patients with diabetes achieved the targets of blood pressure control [7] and 78% in an Iranian population of T2DM patients [8] A further analysis should be performed involving the association of high

blood pressure with other cardiovascular complications and to identify the patients that are at risk for poor BP control.

Cardiovascular risk remains high in DM patients and a modified lipid profile as we have encountered also in our group with high LDL and non-HDL and low HDL cholesterol can increase the incidence of cardiovascular events. Hyperlipidemia treatment should be intensified to achieve targets recommended by present guidelines [9], as the main reason for high lipids remains low treatment adherence [10].

Tight glycemic control in T2DM reduces the risk of microvascular complications and, to a lesser extent, of cardiovascular complications also [11]. In our study, as well as in other observational studies, mean HbA1c varied between 7% and 8%. We observed a higher HbA1c in patients with a longer duration of diabetes and/or older, this being a possible indicator of compliance with guidelines recommendations that suggest looser HbA1c targets in the elderly population. Still, the mean HbA1c for all analyzed groups was above the recommended target. A recent meta-analysis demonstrated that HbA1c target achievement is low, with a pooled average of 43% worldwide [12]. If we take into account fasting plasma glucose, we identify some trend, with a low percentage of patients reaching targets. A further analysis will be performed in order to determine what were the main factors that play a role in low target achievement.

All patients included in our study were screened for diabetes complications, so we have a real estimate of complications in this patient population.

Chronic kidney disease prevalence was 25.89% similar to that reported in European countries [1] but lower than what US reports from CDC's Chronic Kidney Disease Surveillance System reveal [13].

From the IDF estimates, one in three people living with diabetes have some degree of diabetic retinopathy (DR) and one in ten will develop a vision threatening form of the disease. Diabetic Eye Disease (DED) was affecting around 30.65% of our T2D patients with 27.64% having various degrees of retinopathy. An intensive treatment of both hyperglycemia and hypertension such as that achieved in the UKPDS trial indicated that a 1% decrement in HbA1c equated to a 31% reduction in retinopathy and a 10-mmHg decrement in systolic blood pressure equated to an 11% reduction in photocoagulation or vitreous hemorrhage [14]. It is important to implement these strategies to limit an already increased DED prevalence.

In terms of neuropathy, a divergence in the reported prevalence between studies was observed. In our study, as expected, neuropathic complications' prevalence increased with diabetes duration with no gender differences from 35% in the first years after diagnosis to almost 90% in people with more than 20 years of T2DM evolution.

Although international guidelines such as the American Diabetes Association (ADA) Standards of Care [15], ADA/ European Association for the Study of Diabetes (EASD) Consensus on the Management of Hyperglycemia [16], American Association of Clinical Endocrinologists (AACE)/American College of Endocrinology (ACE) Algorithm 2018 [17] recommend metformin as first line of therapy even from diagnosis, 2.84% of our patients are only on diet with no glucose-lowering drug.

In Romanian population, 35.39% of T2DM patients are insulin treated, proportion that is largely consistent with national diabetes reports from other countries that show a prevalence of 15% for insulin monotherapy and 19% for the

combination of insulin therapy with oral therapy among people with T2DM in the United Kingdom [18] and a total insulin treated T2D population of 28% in the USA [19]. Access to the latest insulin molecules substantially diminished human insulin and premixed insulin use. Nowadays in Romania only 12.6% of T2DM patients use premixed insulin. A possible explanation for the high percentage of insulin treated patients in Romania is the fact that insulin treatment is free of charge, so all patients can afford it. In addition, modern therapies such as GLP-1 Receptor Agonists and Sodium Glucose Co-transporter Type 2 (SGLT2) inhibitors were only recently reimbursed.

#### *Limitations*

Our study has some limitations. Thus, there might intervene a selection bias since the patients were enrolled for a period of 2 years and we suspect that some of the patients with severe comorbidities might have not been enrolled. This study was performed having diabetologists as investigators, there might be patients diagnosed with T2DM that choose not to be consulted by a diabetes specialist, and they might increase the percentage of those with no treatment or on oral therapy.

#### **Conclusions**

This cross-sectional analysis of a Romanian representative T2DM population sample enrolled in MENTOR Study showed a high prevalence of diabetes complications and metabolic alterations (obesity, hypertension, dyslipidemia, etc.). Age, male gender and diabetes duration were associated with a higher risk for poor metabolic

control and diabetes complications. Diabetes treatment was comprised of oral medication in over a half of the patients and insulin regimens in over a third.

Further data will be collected over a 3 years periods in order to have a better image on micro and macro vascular complications evolution, as well as on treatment dynamics in T2DM patients.

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