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EVALUATION OF DEMOGRAPHIC, CLINICAL AND METABOLIC CHARACTERISTICS, AND THERAPEUTIC CORRELATIONS IN INDIVIDUALS WITH DIABETES MELLITUS FROM BRĂILA COUNTY- SUMMARY

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TABLE OF CONTENTS

LIST OF PUBLISHED SCIENTIFIC PAPERS

"Prevalence of Diabetes and Diabetes Complications in a South-Eastern County from Romania". Cristiana, Voineag, Barbu Raisa-Eloise, Bogdan-Goroftei Elena, Iuliana Moraru, Bogdan Mircea, Elkan Maria, Stefan Simona, Popescu Nicolae, and Radulian Gabriela. 2021. *Romanian Journal of Diabetes Nutrition and Metabolic Diseases* 28 (2), 178-84. https://www.rjdnmd.org/index.php/RJDNMD/article/view/992.

"Evaluation of metabolic control and chronic complications in a cohort of patients admitted to the County Emergency Hospital Braila" Cristiana Voineag, Gabriela Radulian, Bianca Demetra Postolache, Nicolae Popescu, Romanian Medical Journal – Volume 70, No. 1, 2023, Ref: Ro Med J. 2023;70(1) Two: 10.37897/RMJ.2023.1.2
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INTRODUCTION

Data available from many countries indicate that diabetes mellitus has become a major public health concern. Studies have shown that, in some countries, diabetes affects up to 10% of the population aged 20 years and older. This rate can be doubled if people with impaired glucose tolerance (IGT) are included.

The manifestations of diabetes cause considerable human suffering and enormous economic costs. Both acute and late diabetes complications are frequently encountered.

GENERAL PART

CHAPTER 1

DIABETES MELLITUS AND THERAPEUTIC MANAGEMENT

1.1. Introduction

Diabetes mellitus comes from the Greek word diabetes, which means *siphon - to pass through*, and the Latin word mellitus, which means *sweet*. A historical review shows that the term "diabetes" was first used by Apollonius of Memphis around 250 to 300 BC. The ancient Greek, Indian and Egyptian civilizations discovered the sweet nature of urine in this state and, hence, the propagation of the word Diabetes Mellitus was born.

1.2. Definition

Diabetes mellitus is a chronic, metabolic disease characterized by elevated blood glucose levels, which over time leads to serious damage to the heart, blood vessels, eyes, kidneys and nerves.

1.3. Etiology, epidemiology and physiopathology of diabetes mellitus

Inside the islets of Langerhans in the pancreas, there are two main subtypes of endocrine cells: insulin-producing beta cells and glucagon-secreting alpha cells. Beta and alpha cells continuously change their levels of hormone secretions depending on the glucose environment. Without the balance between insulin and glucagon, glucose levels become improperly skewed. In DM, insulin is either absent and/or there is an insulin resistance, thus leading to hyperglycemia.

1.3.1. Epidemiology

Worldwide, 1 in 11 adults has DM (90% have T2DM). The onset of T1DM increases gradually from birth and peaks at 4 to 6 years of age and then again from 10 to 14 years of age.[6] Approximately 45% of children are present before the age of ten.[1] The prevalence in individuals under the age of 20 is about 2.3 per 1000.

1.3.2. Physiopathology

Insulin resistance is attributed to excess fatty acids and pro-inflammatory cytokines, leading to impaired glucose transport and increased fat breakdown. Because there is an inadequate response to insulin or an inadequate production of insulin, the body responds by inappropriately increasing glucagon, thus further contributing to hyperglycemia. While insulin resistance is one component of T2DM, the full extent of the disease results from the patient having inadequate insulin production to compensate for the insulin resistance.

1.4. Classification of diabetes mellitus

1.4.1. Classification and diagnosis of diabetes mellitus: standards of medical care in diabetes-2022

The American Diabetes Association's "Standards of Medical Care in Diabetes" [2] include the current ADA recommendations, which provide important relevant data on diabetes **mellitus** management, general treatment goals and guidelines, and tools for evaluating the quality of care. Members of the ADA Professional Practice Committee, a multidisciplinary committee of experts, are responsible for updating the Standards of Care annually, or reevaluating them more frequently as warranted. [3, 4, 5]

1.4.1. Type 1 Diabetes mellitus

The rate of progression depends on the age of the onset of the autoantibody, the number, specificity and titer of the autoantibodies.

Glucose and HbA1c levels rise long before the clinical onset of the diabetes, making the diagnosis feasible long before the onset of the diabetic ketoacidosis (DKA). Three distinct stages of type 1 diabetes mellitus can be identified (and serve as a framework for future research and regulatory decision-making). [6, 7]

1.4.2. Type 2 Diabetes mellitus

Type 2 diabetes mellitus, previously called "non-insulin-dependent diabetes" or "adult-onset diabetes", accounts for 90-95% of all diabetes. This type includes individuals who have relative (rather than absolute) insulin deficiency and have peripheral insulin resistance. Initially

at least, and often throughout their entire lives, these individuals may not need insulin treatment to survive.

1.4.3. MODY type diabetes

Regardless of current age, all individuals diagnosed with diabetes in the first 6 months of life should immediately undergo genetic testing for neonatal diabetes.

Children and young adults who do not have typical features of type 1 or type 2 diabetes mellitus, and who often have a family history of diabetes throughout successive generations (suggestive for an autosomal dominant pattern of inheritance) should undergo genetic testing for maturity onset diabetes of the young.

1.4.4. LADA type diabetes

GAD autoantibodies are sensitive markers in Type 1 DM in Europeans [8], however they can also be present in people with Type 2 DM and LADA. In the UKPDS studies 10% of the individuals with Type 2 DM had GAD antibodies, and the majority progressed to being insulin dependent. [9, 10]

1.4.5. Gestational diabetes

1.4.5.1. Recommendations

Women who are planning to become pregnant, as well as those in the first 15 weeks of gestation, should be tested to diagnose diabetes mellitus according to standard criteria by screening with the glucose tolerance test and glycated haemoglobin.

1.4.5.2. Definition

For many years, GDM has been defined as any degree of glucose intolerance first acknowledged during pregnancy [11], regardless of the degree of hyperglycemia.

1.4.6. The notion of Prediabetes

"Prediabetes" is the term used for individuals whose glucose levels do not meet the criteria for diabetes, but who have an abnormal carbohydrate metabolism. Individuals with prediabetes are defined by the presence of IFG and/or IGT and/or A1C 5.7–6.4% (39–47 mmol/mol).

1.4.7. Diagnosis

IFG is defined as FPG levels of 100 to 125 mg/dL (5.6 to 6.9 mmol/l) [12, 13] and IGT as 2-hour PG levels during the 75 g OGTT of 140 to 199 mg/dL (7.8 to 11.0 mmol /L) [14]. It should be noted that the World Health Organization and numerous other diabetes organizations define the lower limit of IFG at 110 mg/dL (6.1 mmol/L).

1.5. Diagnosis criteria

1.5.1. Evaluation

T1DM is diagnosed by glycemic determinations (fasting blood glucose greater than 126 mg/dL, random blood glucose greater than 200 mg/dL) or haemoglobin A1C (HbA1c exceeding 6.5%) with or without antibodies against glutamic acid decarboxylase (GAD) and insulin.

1.5.2. Diagnostic tests for diabetes

Diabetes can be diagnosed based on glycemic criteria, either fasting glucose (FPG) or 2-hour plasma glucose (2-hour PG) during an oral glucose tolerance test (OGTT) with 75 g anhydrous glucose or HbA1C criteria [15].

1.5.3. Diet/fasting (fasting blood glucose) and 2-hour plasma glucose

2-hour FPG and PG can be used to diagnose diabetes. The concordance between the 2-hour FPG and PG tests is imperfect, as is the concordance between A1C and any of the glucose-based tests. Compared to FPG and A1C, the 2-hour PG value diagnoses more individuals with prediabetes and diabetes.[16] In individuals in whom there is discordance between HbA1C and glucose values, 2-hour FPG and PG are more accurate.[17]

1.5.4. HbA1C recommendations

To avoid misdiagnosis or missed diagnosis, the HbA1C test should be performed using a method that is certified by the NGSP and standardized for the DCCT (Diabetes Control and Complications Trial) test.

1.5.5. Diagnosis

In a patient with classic symptoms, measurement of blood glucose is sufficient to diagnose diabetes (symptoms of hyperglycemia or hyperglycemic crisis or a random blood glucose ≥200 mg/dL [11.1 mmol/L]). In these cases, knowing the plasma glucose level is essential because, in addition to confirming the fact that the symptoms are typical of diabetes, it will also give us information about the therapeutic management.

1.5.6. Recommendations for Type 1 Diabetes

Screening for presymptomatic type 1 diabetes mellitus using screening tests that detect autoantibodies against insulin, glutamic acid decarboxylase (GAD), islet antigen 2, or zinc transporter 8 is currently recommended in a research study or may be considered as an option for first-degree relatives or family members of a patient with type 1 diabetes mellitus.

1.5.7. Screening for the risk of type 1 diabetes

The incidence and prevalence of type 1 diabetes mellitus are increasing [18]. Patients with type 1 diabetes mellitus often present with acute symptoms of diabetes and significantly elevated blood glucose levels, and 40–60% of them are diagnosed with incipient DKA. [19, 20].

1.5.8. Recommendations for Prediabetes and Type 2 Diabetes

Testing for prediabetes and/or type 2 diabetes mellitus in asymptomatic individuals should be considered in adults of any age who are overweight or obese (BMI ≥25 kg/m^2 or ≥23 kg/m^2 in Asian Americans) who have one or more risk factors.

1.5.9. Screening and testing for prediabetes and type 2 diabetes mellitus in asymptomatic adults

Screening for prediabetes and type 2 diabetes mellitus is done through an assessment of risk factors, such as the ADA risk test, and is recommended by the guidelines.

1.6. Treatment

1.6.1.1. Management / Treatment

Because T1DM is a disease caused mainly by the absence of insulin, the administration of insulin by multiple daily injections (basal bolus) or continuous infusion of insulin via an insulin pump is the main treatment. In T2DM, lifestyle optimization (diet and physical activity) can be appropriate treatments, especially in the beginning. Other therapies may target insulin sensitivity or increase the secretion of insulin by the pancreas.

1.6.1.2. Prognosis

Diabetes mellitus was the seventh leading cause of death in the United States in 2015.[21] The prognosis of diabetes mellitus and reducing the risk of complications are significantly influenced by the type of metabolic management and the management of the cardiovascular risk factors.

1.6.1. Treatment of T1DM

The management of type 1 diabetes mellitus (T1DM) is a complex task that integrates several factors, but is ultimately centered on the dietary approach. Metabolic control is obtained through customized nutritional therapy as well as the adjustment of insulin doses according to the blood sugar levels, carbohydrates and physical activity to reduce hypoglycemia, glycemic variability and weight gain.

1.6.2. Medical Nutrition Therapy

General principles of medical nutrition therapy (MNT) in type 1 diabetes:

The MNT is an integral part of the diabetes management and diabetes self-management education. Nutritional advice should be customized to individuals with T1DM depending on age, health status, lifestyle and taking into account the complications associated with diabetes mellitus and other concurrent conditions for each individual. Consideration should also be given to an individual's culture and beliefs, eating patterns and food availability [22].

1.6.3. Treatment of T2DM

The rapidly increasing worldwide prevalence of type 2 diabetes mellitus, hypertension and hyperlipidemia, as a result of the population adopting an unhealthy eating pattern and a sedentary lifestyle, has led to a significant proportion of mortality and morbidity. Considering the increased prevalence of type 2 diabetes mellitus, a global strategy for optimizing lifestyle was established worldwide by the WHO in 2004 [23] to promote the primary prevention of chronic diseases through screening and nutritional information of the population.

CHAPTER 2

PREVALENCE OF DIABETES MELLITUS

2.1. Worldwide prevalence

Worlwide prevalence of diabetes mellitus in 2021 [24]

537 million adults (aged 20-79) live with diabetes mellitus, one out of 10 individuals. This number is expected to increase to 643 million by 2030 and 783 million by 2045.

More than 3 out of 4 adults with diabetes live in low- and middle-income countries.

Diabetes mellitus is responsible for 6.7 million deaths in 2021, one person every 5 seconds.

2.2. Regional-European prevalence

Europe

- 1 out of 11 adults (61 million) is living with diabetes.

- The number of adults with diabetes mellitus is expected to reach 67 million by 2030 and 69 million by 2045.
- More than 1 out of 3 (36%) adults living with diabetes are undiagnosed.
- $189 billion spent on diabetes in 2021.
- 1.1 million deaths from diabetes mellitus in 2021. [24]

2.3. Nationwide prevalence-The Predatorr Study, The Mentor Study

2.3.1. The PREDATORR study

The PREDATORR study (Prevalence of diabetes mellitus, prediabetes, overweight, obesity, dyslipidemia, hyperuricemia and chronic kidney disease in Romania) is the first national study that analyzes the prevalence of diabetes mellitus (DM) and prediabetes, as well as their association with cardiometabolic diseases, sociodemographics, and lifestyle risk factors in the Romanian population aged 20-79.

The PREDATORR study estimated the prevalence of diabetes mellitus (DM) to be 11.7%. MENTOR is the first major national study that attempts to determine the metabolic control of patients with type 2 diabetes mellitus (T2DM), the therapeutic options used and the prevalence of microvascular and macrovascular complications in order to achieve a better management of Romanian patients with T2DM.

2.3.2. Clinical and therapeutic characteristics of patients with type 2 diabetes in Romania – the MENTOR study

Type 2 diabetes mellitus (T2DM) has an increasing prevalence in recent decades, despite the efforts and strategies to decrease the rate of the disease, and it is estimated to affect approximately 629 million people worldwide by 2045 [25]. Increasing life expectancy, together with declining birth rates, are important factors converging towards a high percentage of the population over 45 years of age and a higher prevalence of T2DM.

Romania, a developing country located in a region with major changes in the political and economic environment, has undergone a rapid change in its socioeconomic status in recent years. This evolution has resulted in major changes in nutritional behavior and lifestyle, fast food consumption and sedentary lifestyle – traits now common in the Romanian population. This may explain why a nationwide study on the general population of Romania revealed a high prevalence of overweight (31.1%) and obesity (21.3%) among the enrolled participants [26].

SPECIFIC PART II

CHAPTER 3

RESEARCH METHODOLOGY

3.1. Introduction

Working hypothesis:

The research approach, which was the basis of this paper, started from the hypothesis that a better knowledge of the individual characteristics of the people with prediabetes, as well as those with diabetes mellitus, will determine the formulation of effective strategic and action guidelines. These factors are considered important both for prevention, and for ensuring optimal management of diabetes mellitus.

3.2. The design of the study

The present study represents a retrospective analysis, which includes patients diagnosed with diabetes mellitus, found in the records of the Brăila County Emergency Hospital, but also of a Roma population existing within the radius of the same county (patients who are part of a group distinct from the main group, in which we analyzed the individual characteristics, to create a specific DM management profile). Each of these two main groups will be presented in the following, in detail, with a reminder of the component elements of interest for the statistical research, but also the justification of the way in which this subdivision was thought.

Main objective:

- ✓ *To develop prognostic elements, to evaluate, but also to monitor patients diagnosed with diabetes mellitus, to facilitate the establishment and application of an optimal treatment and, of course, to improve the quality of life of the patients and to decrease the incidence of acute and chronic complications of diabetes mellitus.*

Secondary objectives:

- Cross-sectional description of a group of patients diagnosed with type 2 diabetes mellitus, patients who showed signs of impairment not only from a clinical point of view, but also from a metabolic point of view, accentuated by the presence of complications.

- The clinical, metabolic and therapeutic evaluation of these patients, admitted with previously known or newly diagnosed diabetes mellitus, was observed.
- Determination of the anthropometric measurements in a Roma population from Brăila County, as well as the evaluation of their nutritional status.

✓ Assessment of the main socio-demographic characteristics with potential favorable or unfavorable impact on the population diagnosed with diabetes mellitus.

✓ Assessment of the influence of the body mass index, metabolic imbalance, dyslipidemia, renal and liver function impairment on the evolution of diabetes mellitus.

✓ Evaluation of the incidence of acute and chronic complications of the patients in the study lot.

✓ Evaluation of the diabetes mellitus-specific parameters, such as blood glucose or glycated haemoglobin.

✓ Evaluating the prognostic role of the risk factors, as well as detecting their frequency and the influence they have on all-cause mortality of, or from cardiovascular causes.

✓ Comparative evaluation of the clinical and paraclinical characteristics of the two subgroups of patients known to have diabetes mellitus, respectively newly diagnosed diabetes mellitus (enrolled in the A.I group) and previously detected diabetes mellitus (enrolled in the A.II group).

✓ Evaluating and establishing a profile of the cases of adult patients diagnosed with diabetes mellitus based on the average values detected among the monitored variables: average age, background, paraclinical data, evolution, treatment.

✓ Establishing general recommendations regarding the prevention and management of diabetes mellitus and its complications at the local level.

3.3. Materials and methods

The present study is an analytical one, carried out on a group composed of a total number of 2587 patients divided as following:

- Group A: consisting of a number of 2493 adult patients aged between a minimum of 18 years old and a maximum of 97 years old, associating a standard deviation of +/- 12.67 years. All these patients were monitored over a period of three years, between January 2017 and December 2019, being subdivided as following:
    a. 371 patients newly diagnosed with diabetes mellitus, admitted in the Brăila County Emergency Hospital, representing subgroup I;
    b. 2,122 patients with a previously confirmed diagnosis and admitted for more than 24 hours in the Diabetes, Nutrition and Metabolic Diseases Department of the Brăila County Emergency Hospital between January 2017 and December 2019, representing subgroup II
- Group B consisting of a total number of 94 individuals, living in a socio-economic disadvantaged community on the outskirts of the city of Brăila.

- *Inclusion criteria:*
    - Adult patients, young and elderly, who have been diagnosed with type 1 and type 2 diabetes mellitus;
    - Patients who accepted to participate in the study, by signing an informed consent.
- *Exclusion criteria:*
    - Patients who did not want to sign the informed consent in order to be included in the study;
    - Patients in whose case the diagnosis of diabetes mellitus was refuted;
    - Patients with residence outside Brăila County.

3.4. Working tools

The following working tools were used: databases with complete characteristics, individual questionnaires applied to patients, final sampling lists, centralizing tables.

The individual questionnaire (appendix 1) was completed by all patients enrolled in this study group (or by their legal representatives), drawn up taking into account the current legislation enforced by the World Health Organization and the European Union regarding the research on human subjects in the medical field. The standard duration of the application of the questionnaires was approximately 15 minutes.

3.5. Statistical methods used in the analysis of data obtained from patients

Data processing was carried out with the help of ***Microsoft EXCEL 2010 (Analysis ToolPak)*** and ***SPSS V.24 software (IBM Statistical Packard for the Social Science, Chicago, Illinois)***, statistical methods of quantitative analysis.

CHAPTER 4
CLINICAL, METABOLIC AND THERAPEUTIC EVALUATION OF THE GROUP A PATIENTS WITH DIABETES MELLITUS ADMITTED TO THE BRĂILA COUNTY HOSPITAL BETWEEN 2017 AND 2019

4.1. Purpose and objectives of the study

The present study started from the hypothesis that a detailed knowledge of the characteristics of patients with diabetes mellitus treated in recent years in the Department of Diabetes, Nutrition and Metabolic Diseases of the Brăila County Emergency Hospital will allow developing realistic recommendations regarding the prevention and management of diabetes mellitus and its associated complications. Therefore, the purpose of the research approach was to carry out the clinical, metabolic and therapeutic evaluation of the patients with diabetes mellitus admitted between January 2017 and December 2019.

4.2. Materials and methods

In order to carry out the clinical and statistical study, with the approval of the Ethics Council of the Brăila County Emergency Hospital, the data from the general clinical observation sheets were collected and processed for patients admitted both via the emergency system by direct admission through the emergency rooms, and for those admitted with a referral issued by the general practitioner between January 2017 and December 2019.

4.3. Results

4.3.1. Demographic profile

The evolution of admissions demonstrates a general trend of growth in the analyzed interval, however, it was observed a decrease in their number in 2018 by 3.51% compared to the previous year. (Fig.2.1)

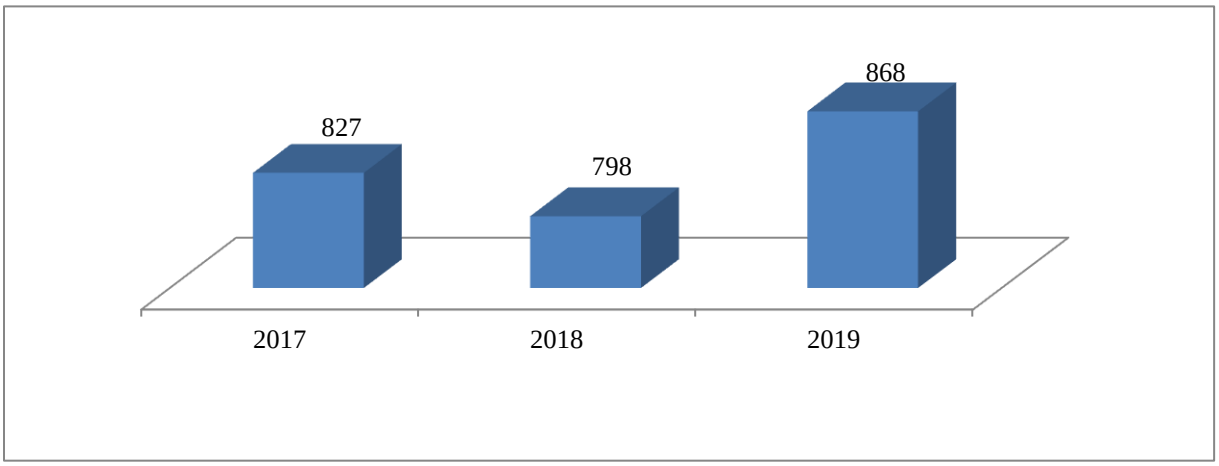

Fig.2.1. Progression of the number of admissions between 2017 and 2019

4.3.2. Anthropometric profile

The average value of the body mass index (BMI) at the level of the entire group of patients was 29.29±4.55 kg/m², with the highest proportion of values between 25-29.99 kg/m² (36.14% of all cases, overweight patients) and those between 30-34.99 kg/m² (27.52% patients with class 1 obesity).

4.3.3. Type and duration of diabetes mellitus

90.21% of patients were diagnosed with type 2 diabetes mellitus (Fig. 2.10) and a significantly higher proportion of type 2 DM was observed in the female patients population (94.22% vs 84.11% in male patients). Depending on the area of residence, the prevalence of type 2 DM is found in both categories (88.83% in rural patients and 91.46% in urban patients, respectively).

4.3.4. Metabolic profile

Of the total number of patients included in the study, 83.71% had an HbA1c level higher than 7% (Fig. 2.14), similar percentages being recorded both in female patients (83.19% with HbA1c >7%) and in male patients (84.51%).

4.3.5. Lipid profile

The processing of the data on the HDL-C values at admission shows that the percentage of cases with hypo-HDL-cholesterolemia is significantly higher in female patients (49.10% vs 21.85% in the male patients group). It was also observed the high proportion (62.96%) of male patients whose HDL-C levels were within normal range.

4.3.6. Renal profile

Regarding both the entire group of patients, and the gender distribution, serum uric acid levels ≤6 mg/dL at admission were predominantly recorded, with the relatively higher percentage of patients with hyperuricemia being observed in women (37.15% vs. 30.76% in men). The percentage ratio of patients with hyperuricemia is progressing in positive correlation with the age of the patients (from 8.33% in the age group ≤ 20 years old, to 55.28% in the age group ≥ 81 years old).

4.3.7. Hepatic profile

In order to evaluate the liver function, the AST and ALT levels, and the AST/ALT ratio (De Ritis) were analyzed. In both male and female patients, AST and ALT levels were within normal limits for the vast majority of cases, however, a higher percentage of values > 34 IU/L was observed in women (32.36%). Regarding the AST/ALT ratio, in both categories of patients the highest proportions were found in cases with values <1 (64.98% in male patients and 63.19% in female patients).

4.3.8. Complications and comorbidities

At the level of group A, it can be observed that 90.21% of the patients were diagnosed with type 2 diabetes mellitus.

A significantly higher proportion of type 2 DM patients was observed in female patients (94.22% vs 84.11% in male patients). Depending on the area of residence, the proportion of type 2 DM is found in both categories (88.83% in rural patients and 91.46% in urban patients, respectively).

4.3.8.1. Chronic complications

Evaluating the presence of Proliferative Diabetic Retinopathy (PDR) we found that the highest proportion is found in patients with a duration of diabetes mellitus of more than 20 years, 38.18% in the case of patients with T1DM and 9.76% in the case of patients with T2DM, respectively. These results are consistent with the medical literature, as it is known that a long evolution of the disease is a risk factor for the occurrence of PDR. However, the small percentage of PDR in patients with T2DM is surprising, only 3.91% of all patients have proliferative diabetic retinopathy, while in the case of T1DM 20.90% of patients presented this chronic complication of diabetes mellitus at the time of admission.

4.3.8.2. Acute complications

From the point of view of the analysis of acute complications, as they were found at the group level, we analyzed the occurrence of DKA and of hypoglycemia, respectively. The following were found:

- DKA is present in the main group in a proportion of 4.21% (n = 2493), out of which, referring directly to patients with type 1 DM, the rate is 4.74% and 4.16% in patients with type 2 DM, respectively.

4.3.8.3. Comorbidities

4.3.8.3.1. HBP and Dyslipidemia

The numbers of cases of high blood pressure detected by reference to the years of follow-up, were approximately equal in value. However, the predominance of female patients was noted, in a proportion of 65.5%, and of patients from the urban background, with a percentage of 53.4%, respectively. Thus, we can issue a first preliminary conclusion according to which the proportion of complications governed by high blood pressure in the case of patients with diabetes mellitus, enrolled in the study group, is predominant in the case of patients from urban background (conclusion strengthened by the existence of statistically significant differences, demonstrated by chi-square tests with values lower than the reference ones: 0.05 for the distribution by years, and 0.000 for the one dependent on the gender of the patients, respectively).

4.3.9. Treatment

4.3.9.1. Treatment before admission

4.3.9.1.1. The therapeutic attitude of patients with type 1 DM prior to admission

We will begin the descriptive statistical analysis, by initially presenting the percentage situation of the distribution of the therapeutic options of the patients, prior to presentation for admission. It will be noted that, of the 285 subjects diagnosed with type 1 DM, 44 of them have insufficient information regarding previous therapy, which is why they will be excluded from the statistical analysis. From the remaining subgroup (n = 241, 84.5% of patients with type 1 DM) it is observed.

4.3.9.1.2. The therapeutic attitude of patients with type 2 DM prior to admission

In the case of patients known with type 2 DM (n = 2208, a percentage of 88.6%), it was observed that the therapeutic attitude before admission depended, as in the previous case, on the adherence of the patients, but also on the rigor with which they follow the indications of the attending physician. The medical literature confirms that one of the first steps for rebalancing subjects with type 2 DM is represented by lifestyle changes through medical nutrition therapy and daily physical exercise.

4.3.9.2. Therapeutic recommendations upon discharge

4.3.9.2.1. The therapeutic attitude of patients with type 1 DM upon discharge

The patients who at discharge received the recommendation of exclusive treatment with a rapid insulin analogue were young patients with type 1 DM who had recommendations for treatment with continuous subcutaneous insulin infusion by insulin pump, they were referred to other treatment centers that are specialized in the installation and monitoring of these modern treatments of diabetes mellitus, because at that time Brăila County Emergency Hospital was not running the National Program for the installation and monitoring of glucose sensors and insulin pumps, thus explaining the low number of such patients due to the low addressability.

4.3.9.2.2. The therapeutic attitude of patients with type 2 DM upon discharge

The proportion of each drug in the treatment categories of type 2 diabetes mellitus, both in the case of oral antidiabetics (OAD), as well as in the case of insulin and GLP-1 analogues. We note that in the case of OAD agents, the highest proportion of patients were treated with biguanides and sulfonylurea, 7.16%, followed by biguanides and DPP-4 inhibitor, 3.18%. A high proportion was also found in patients treated with biguanides and basal insulin analogue, 8.18%, and with biguanides in combination with sulphonylurea and basal insulin analogue, 4.25%. Another frequently encountered treatment category was for patients treated with biguanides + GLP-1 analogue + basal insulin analogue, 6.06%.

CHAPTER 5 - COMPARATIVE CLINICAL, METABOLIC AND THERAPEUTIC EVALUATION OF PATIENTS FROM SUBGROUPS I AND II

5.1. Introduction

Corresponding to the previous chapter, in which a descriptive statistical analysis was presented, focused on all the factors that have an impact from a socio-economic, clinical, paraclinical and therapeutic point of view, on the evolution but also the prognosis of these patients, in this sub-chapter, in particular, all these conclusions will be brought to light. I will perform a comparative statistical analysis which will expose the links (statistically significant or not) between the two subgroups of patients (as presented in Chapter 5). In the end, the corroboration of these conclusions will materialize in finding an algorithm of risk stratification and therapeutic behavior applicable to patients, dependent on the existing possibilities at the county level, but also influenced by the existing outcome in the case of the current group.

5.2. The design of the study

The study carried out at this moment is an analytical one, which is based on a group of patients diagnosed with diabetes mellitus (the main group, A), consisting of a total number of 2493 subjects, distributed as following:

- patients with newly diagnosed diabetes mellitus – made up of a total number of 371 patients, subgroup I,
- patients already in the hospital's databases - subgroup II, respectively, made up of a total number of 2122 subjects)

5.3. Results and discussions

As I stated before, the results obtained through descriptive statistical analysis of the analyzed variables will be presented in a comparative manner, this time by highlighting the statistically significant or non-significant differences between the two subgroups. From the very beginning, one can observe the predominance of patients who are included in the subgroup known to have diabetes mellitus, subgroup II, (the percentage difference between them being 70 23 %).

We will continue with the systematization of the information obtained from the observation sheets, the start of the statistical analysis and interpretation of all these data, a fact that will allow the evaluation of the health of the patients from a clinical, paraclinical, and therapeutic point of view. I will try to expose the particular characteristics of each subgroup by highlighting the cardiovascular risk factors (HBP, predominantly), several characteristics determined by the presence of dyslipidemia, hyperuricemia, but also non-alcoholic hepatic steatosis. Finally, the main determining characteristics of complications associated with DM will be presented.

5.3.1. Presentation of the socio-demographic characteristics in a comparative manner at the level of the two subgroups

According to the model created in the previous chapters, displaying the comparative analysis will begin with describing the socio-demographic characteristics. As it can be seen from the table below, following the application of the chi-square test, a number of statistically significant differences are noted, demonstrated by the sig. index (whose value does not exceed the 0.05 reference threshold). In this situation, by supporting the conclusions through statistical tests, we are allowed to develop some initial working hypotheses as they will be presented next.

From the point of view of the distribution of patients depending on the years in which the presentations took place, it will be noted that the maximum incidence of presentations of patients with newly diagnosed diabetes mellitus was in the year 2019, n equal to 177. Compared to these values, in the case of patients who were known to have diabetes mellitus at the time of being taken into account in this clinical research, the existence of a descending curve of presentations will be observed, a fact that allows us to conclude that in subgroup II there is a decrease in the need for patient admissions from 2017 (from n = 757) to 2019 (when the value n = 691, with a percentage difference of 3.11%). The value of the sig index = .000*, signifies the existence of statistically significant differences between the two analyzed groups, for which reason it will be possible to conclude that (depending on the analyzed group), there is a decrease in the number of admissions for patients known to have DM, partly justified by the existence of favorable developments for them, but also an increase in the number of newly diagnosed DM cases.

5.3.2. Clinical, metabolic and therapeutic evaluation of patients with newly diagnosed DM (subgroup I)

The descriptive statistics of the three scalar variables can be seen, which define the changes in terms of carbohydrate metabolism in patients with newly diagnosed diabetes mellitus. The body mass index, the value of glycosylated haemoglobin and, not in the least, the glycemic values, may present elements that, if not optimally controlled from a medical point of view, may generate unfavorable developments.

5.3.3. Clinical, metabolic and therapeutic evaluation of patients known with DM (subgroup II)

In this sub-chapter, the descriptive statistical analysis will be carried out, by exposing the main variables of carbohydrate and lipid metabolism, indicators of renal function or the treatment chosen in the case of patients known to have DM and admitted during the course of the clinical research (n = 2122, representing 85.11% of the total of group A).

5.3.4. Comparative study of the characteristics of the two subgroups

In thefollowing part, we analyzed the existing differences between the two subgroups, from the point of view of clinical, paraclinical, therapeutic, but also socio-demographic characteristics. All of this will be exposed as following.

a) The years of presentation

The existence of distinct distributions of DM cases, dependent on belonging to one of the two groups, can be noted. In the case of subgroup I, the curve is upward, with the predominance of diagnosed cases (47.7%), while, comparatively, there is a decrease of approximately 3.1% in the frequency of admissions of patients known to have DM. The differences between the formed subgroups are statistically significant (confirmed by the sig value of 0.000*).

b) Patient gender

It shows similar distributions in the case of the gender of the subjects, with the predominance of females, in both subgroups, 55.3%, and 61.3%, respectively. This time also the differences are statistically relevant (sig. = 0.029*).

c) Glycemic control

The control of the glycemic status was analyzed by exposing the levels of HbA1c (sig = 0.000*), serum glucose and, last but not least, the BMI (sig = 0.745). This will highlight the existence of approximately similar distributions of the BMI, which is why the existence of significant differences from a statistical point of view is not noted. On the contrary, HbA1c levels above the 9% threshold are predominant in the case of subgroup I (75.4% of its total), while in subgroup II a proportion of elevated glycated haemoglobin levels can be noted in 48.4% of the patients.

CHAPTER 6 - DETERMINATION OF ANTHROPOMETRIC MEASUREMENTS IN A ROMA POPULATION FROM BRĂILA COUNTY AND EVALUATION OF THE NUTRITIONAL STATUS

6.1. Introduction

We analyzed a group of 94 people of Roma ethnicity from a socio-economic disadvantaged area, on the outskirts of Brăila municipality, as part of a volunteer campaign carried out in August 2019, through which we aimed to test blood glucose, determine anthropometric indices, measure blood pressure, correlated with anamnestic data, important in increasing the cardiovascular risk (family medical history, personal medical history, smoking status, increased ethanol consumption and changes in sleep duration, psycho-social stress, pro-risk diet, level of physical activity).

6.2. Purpose and objectives of the study

The purpose of the present study is the statistical analysis of the individual characteristics of a group of patients of Roma ethnicity. The distributions of the anthropometric indices were brought to light and at the same time the evaluation of the nutritional status was carried out. Thus, these distributions were exposed in a population of Roma ethnicity (n = 94) from a socio-economic disadvantaged community within Brăila County.

6.3. Materials and methods

The present clinical research includes a final group consisting of a number of 94 Roma individuals from a socio-economic disadvantaged area. The patients live on the outskirts of Brăila Municipality.

6.4. Results

Of the 94 subjects included in the study group, 73.40% (n=69) were female. The simultaneous application of the chi-square test χ^2[$\chi^2 = (69- 55.5)^2 / 55.5 + (25 – 55.5)^2 / 55.5 = 20.04$], had a final value higher than the reference value in the Fisher table, which is why we will continue with the rejection of the null hypothesis that there are no statistically significant differences in the case of the Roma group, in terms of gender distribution.

CHAPTER 7- DISCUSSIONS

In the Mentor study, better metabolic control was observed in patients with type 2 DM of less than 9 years duration in the sample aged 45-75 years old (the Mentor study was done for T2DM and patients aged between 45-75 years old). In our study, in the category of patients with a duration of less than 9 years, we found the highest values for HbA1c both in men 10.19%±1.49 and in women 10.40%±2.00, in patients with type 1 DM.

In our study, we found the lowest HbA1c average values as following:

- in type 1 DM in men, in the age group 51-60 years old, 9.01%±1.35 and in women, in the age group ≥81 years old, 8.90%±1.29;

- in type 2 DM in men, in the age group 71-80 years old, 9.85±1.98 and in women, in the age group ≥81 years old, 8.90%±2.12.

We can thus state by correlating the results of these studies, that in our study the lowest average values were also found in the female gender, only in older age categories, both in type 1 DM and type 2 DM.

DM - both type 1 and type 2 can be associated with specific complications of the retina and the kidneys and with multiple forms of macrovascular disease of the heart, brain, and lower extremities, as well as peripheral and vegetative neuropathy. Macrovascular events are 10 times more frequent than severe microvascular complications and occur with excessive frequency in patients with changes in carbohydrate metabolism, even before the onset of type 2 diabetes. [27]

In the case of diabetic polyneuropathy, a slightly increased proportion is observed in patients with type 1 diabetes mellitus for less than 9 years, 81.18%, compared to patients with type 2 diabetes mellitus with 79.72%, in which context, however, as seen in the medical literature, there is an increased prevalence of polyneuropathy from prediabetes and at the onset of type 2 diabetes mellitus.

A statistically significant correlation is observed in the case of nephropathy and chronic kidney disease in patients with type 1 diabetes mellitus compared to patients with type 2 diabetes mellitus. In patients with type 1 DM, nephropathy was found in 22.54% of the cases, while in those with type 2 DM, it was found in 8.80% of the cases. CKD was present in 14.34% of the type 1 diabetes patients and in 13.83% of those with type 2 diabetes mellitus.

Analyzing the results of our study related to the renal profile of the patients, in comparison with other studies in the medical literature, we can state that our results show a higher rate of diabetic kidney disease. In the study conducted by Gheith et al., it was described that more than 40% of the diabetic patients develop CKD. In our study, in group A, we had 26.4% patients with stage IIIa CKD, 26.7% stage IIIb CKD, 7.8% with stage IV CKD and 1.3% with stage V CKD, a total amount of 62.2% of the patients had renal impairment. Again, we can think that our patients are part of a population that required intervention in the context of metabolic imbalance, and for this reason, the renal function either suffered a faster decline, or was accelerated by other nephrotoxic factors. [28]

In the study by Tomasso et al. it was shown that 27.9% of the diabetic patients with poor diabetes control, with HbA1c level higher than 6.5%, showed signs of diabetic retinopathy. In these patients, glycemic control was poor with a basal glucose value higher than 120 mg/dL. In the previously mentioned study, the duration of diabetes mellitus was correlated with a higher prevalence of diabetic retinopathy, thus almost 40% of the patients with long duration of DM had diabetic retinopathy. [29]

In our study, within group A, the general group of patients, we also found a positive correlation between the increased value of HbA1c with the presence of diabetic retinopathy, in case of the proliferative retinopathy the positive correlation occurred at a value of HbA1c of 9.53%±1.69, while for the non-proliferative variant, the correlation occurred at a value of HbA1c of 9.48%±1.67.

Considering the above, we can state that the results of our study are consistent with the results obtained in the study conducted by Tomasso et al.

In a study conducted by Bramante et al., which aimed to treat obesity in patients with DM, rates of over 90% of patients with a BMI ≥25 kg/m² were described. The proportion of overweight and obese patients in group A in our study was 79.38%, with an average BMI of 29.23 kg/m². In our study, a higher trend of obesity was observed in women in the age group of 51-60 years old. [30]

Comparing the results of our study with those of the study conducted by Bramante et al., we can state that the rate of obesity was lower in the group analyzed from the Brăila County Emergency Hospital. We could argue that the patients who arrived at the hospital are, as the data obtained by us show, patients with chronic metabolic imbalance; we know that the state of glycemic imbalance is characterized by a hypercatabolic state produced by chronic hyperglycemia and glycosuria, so the patient can lose weight due to increased blood glucose levels.

If we are referring to the connection between poor control of DM and a lower BMI value, as we thought would be the case in our study, we have another evidence stated by Stone et al. In the study he conducted, he found results that attest to our previously formulated hypothesis, namely that patients with higher HbA1c values had a lower BMI. Thus, we can conclude that our data is in agreement with the medical literature. [31]

Also, in the aforementioned study, a European population-based study, it was found that only 53.6% of the analyzed patients reached glycemic targets of <7%. In our study, the proportion of glycemic imbalance was much higher, our results show 83.71% patients with HbA1c >7%. We can also argue here that the patients studied by us are patients who required hospitalization in the Diabetes Mellitus Clinical Department, precisely for specialized clinic and metabolic rebalancing, thus explaining the small proportion of patients who were in the therapeutic targets.

Also, in the study conducted by Stone et al., higher glycemic imbalances were described in patients with shorter duration of the diabetes. These results are in agreement with some of our results, we found the highest value of HbA1c in female patients, with a disease evolution ≤9 years, in T1DM 10.40±2.00%, and in T2DM 9.52±2.14%.

We also found similar results in the study led by Masood et al., they evaluated the proportion of patients reaching glycemic targets in a defined population from a geographically delimited

area, South Asia, which we also did, we evaluated the population only from Brăila County. In the study by Masood et al., only a percentage of 16.3%; in our study, the percentage of patients with HbA1c <7% was 16.29%. We can thus state that our results are similar to those stated in the above-mentioned study. [32]

Naseri et al. conducted a study related to the prevalence of HBP in patients with type 2 DM and found data that showed that 70.5% of the type 2 diabetes patients studied also had HBP. In our study, when we evaluated the patients with type 2 DM in group A, we found that 69.4% of them also had HBP. In conclusion, the results of the study conducted by us agree with the results of the study conducted by Naseri et al.; [33] as well as in the PREDATORR study where the prevalence of HBP was 61.7%.

Regarding the incidence of HBP in the population with type 1 DM, the results obtained in group A of our study were 21.8%. In a study conducted by Nørgaard et al., the incidence of HBP in patients with T1DM was lower, 14.7%. We could argue that the age of patients with type 1 DM in our study was higher, at the level of the entire group the average age was 61.86±12.77 years; thus, an older age predisposes to more frequent occurrence of HBP. [34]

Another aspect that we investigated in our study was the incidence of diabetes mellitus in the disadvantaged population of Brăila County, within an ethnic Roma community. The results of our study showed that the Roma population had a higher rate of risk factors involved in the occurrence of type 2 DM, with a higher rate of obesity, family history of type 2 DM, HBP and smoking. Thus, a conclusion of our study was that the population of Roma ethnicity in Brăila County has a higher risk of developing DM and chronic complications of DM compared to the general population of the county.

In a study conducted by Weissa et al., carried out on the Roma population in Hungary, it was concluded that they also have an increased risk of developing DM, also through the lens of their occupational, cultural and environmental particularities. [35]

Corroborating the results of our study with those of the study led by Weissa et al., we can state that the results regarding the risk of developing T2DM are similar for both communities of Roma patients studied.

In a review of the medical literature on diabetes, conducted by Nunes et al., a higher level of prevalence of T2DM in the Roma population, compared to the Caucasian population, was

stated as a conclusion. The results of our study are also in agreement with those stated in this review conducted by Nunes et al. [36]

CHAPTER 8- CONCLUSIONS

The analysis carried out captures the profile of metabolic patients whose medical status led to the need for hospitalization due to causes related to diabetes mellitus and/or other metabolic diseases. The even distribution of cases analyzed in the three years of the study generates the prerequisites of heterogeneity necessary for the reproducibility of the results at the population level, allowing the epidemiological inference of the data resulting from the study. The superposition of the characteristics of the studied group, from the point of view of the demographic, anthropometric, social and economic characteristics of the patients analyzed, with the characteristics of the general population of patients with diabetes mellitus in our country, demonstrates the representativeness of the sample for the population of interest to which the study is addressed.

Among the patients with metabolic pathology in Brăila County, a right-shifted distribution of the body mass index values was observed, the average value of the body mass index being 29.23 kg/m^2. Among the patients admitted for metabolic pathology, only 20.62% were of normal weight or underweight, 79.38% being overweight or obese. The proportion of overweight and obesity in patients with diabetes from Brăila County was significantly higher from a clinical point of view compared to the prevalence of overweight and obesity in the general population, thus demonstrating that even among these patients, overweight and obesity represent a main pathogenic substrate of the metabolic imbalance. Female patients consistently had a higher body mass index than matched cohorts of male patients. From the age point of view, a symmetrical distribution of the body mass index was observed, it reaching a peak value within the age group of 51-60 years old, with a symmetrical decrease in the value towards the beginning and the end of the age interval. Alongside, except for the groups under 30 years of age, the average abdominal circumference exceeded the recommended threshold value for the Caucasian population. For all groups of patients, the waist/hip ratio was subunit, thus characterizing the presence of android-type obesity.

The HbA1c value had a Gaussian distribution, with a frequency maximum near the 9%-10% range and with an average of 9.4% in conditions of a median of 9.15%, values arguing for the causality between the metabolic imbalance and hospitalization, 83.71% of the patients presenting a glycemic control considered inadequate in terms of a HbA1c value of over 7%. Regarding the distribution of HbA1c values, an important discrepancy was noticed between the genders: male patients had a Gaussian-type distribution of values, while among female patients a bimodal distribution was observed, the two modes being positioned at the extremes, towards the ends of the range. This different aspect suggests that, if among male patients glycemic imbalance was the predominant cause of hospitalization, among female patients there is also another significant group of entities that require hospitalization, apart from the glycemic imbalance.

From the point of view of glycemic control, no significant differences were observed between men and women, neither among patients with type 1 DM, nor among those with type 2 DM. From the point of view of the post-hoc analysis, stratified according to factors that could influence glycemic control, the following observations emerged:

1. Among male patients with type 1 DM there is a bimodal evolution of the average HbA1c level, the most precarious glycemic control occurring among patients aged 31-40 years old, with values of 10.34% ±1.26, and the best glycemic control among patients in the age group of 51-60 years old, with values of 9.01% ± 1.35, respectively.
2. In contrast, among female patients with type 1 DM, the most important metabolic imbalance was found among the age group of 21-30 years old (11.27% ±1.79), and the best control in the age group of 71-80 years old (8.48% ±0.28), respectively.
3. In all patients with type 1 DM, the tendency to improve glycemic control was observed as the duration of the evolution of type 1 DM increased, an aspect that can be explained by the incremental acquisition of management skills for type 1 DM throughout life.
4. Among patients with type 2 DM, both male and female, an improvement in glycemic control was observed as the age group advanced. At the same time, a surprising tendency to improve the quality of glycemic control was noted as the duration of type 2 DM evolution increased.

The lipid profile of the patients described a predominantly unsatisfactory distribution of the values of the lipid parameters. There were significant differences between the types of diabetes, with patients with type 1 DM having on average a lower LDL-C value alongside with a higher value of HDL-C compared to patients with type 2 DM. A particular evolutionary feature was observed regarding the association between hypo-HDL-C and the duration of diabetes between the two genders: male patients had an increase in the incidence of hypo-HDL-C alongside the duration of diabetes, in contrast to female patients in whom a decrease in the incidence of hypo-HDL-C was observed alongside the duration of diabetes.

High blood pressure was present in approximately 2/3 of the patients analyzed in the study, with minimal differences between the years in which the evaluation was performed. A direct association was observed between the duration of diabetes mellitus and the prevalence of high blood pressure, denoting the mechanistic and etiological interrelation of the two entities. The presence of high blood pressure was more frequent among female patients and much more frequent among patients with type 2 DM compared to type 1 DM (69.4% vs. 21.8%).

The average value of the uric acid in the studied group was positively associated with the age of the patient, as well as with the duration of the evolution of diabetes, a fact that can also be explained by the decline of the renal function, a phenomenon dependent on the duration of the evolution of the disease, marked by the renal injuries inflicted by diabetes. Confidence in this observation is strengthened by the strong parallel with serum creatinine levels, where the same time-dependent evolutionary trend is also observed. Renal damage, evaluate by calculating the estimated glomerular filtration rate, was more important among patients with type 1 DM compared to patients with type 2 DM.

In the studied group, a constant evolutionary trend was observed, reproducible regardless of the stratification factors, regarding the increase of the AST/ALT ratio in relation to the duration of diabetes mellitus, which indicates the time-dependent augmentation of the process of developing hepatic steatosis associated with diabetes mellitus.

The prevalence of chronic complications of diabetes mellitus increased consistently with the duration of diabetes mellitus. Regarding the incidence of complications, a higher rate of retinopathy, neuropathy and nephropathy was observed among patients with type 1 diabetes mellitus, while heart failure, coronary artery disease, peripheral artery disease and strokes were more common among patients with type 2 diabetes mellitus in cohorts matched in terms of

duration of diabetes evolution. The cross-sectionally measured value of HbA1c in relation to the presence or absence of diabetes complications was higher in patients with complications vs. patients without complications of diabetes mellitus.

With regard to acute complications, patients who required hospital admission due to the onset of ketosis or diabetic ketoacidosis had an increased HbA1c value, around 11%, with variations depending on stratification criteria. Regarding hospital admission due to hypoglycemic episodes, an important difference in HbA1c values was noted between patients with type 1 DM and patients with type 2 DM. If patients with type 2 DM who required hospital admission due to hypoglycemia had an average HbA1c value below 7%, patients with type 1 DM admitted due to hypoglycemia had an average HbA1c value of around 9%. This observation denotes that hypoglycemic episodes of clinical importance in patients with type 1 DM occur in the context of a phenomenon of increased glycemic variability, with glycemic zeniths and nadirs spaced, in which the nadirs are positioned in intervals characteristic of severe hypoglycemia. This phenomenon is more pronounced among patients with significant glycemic imbalance. By contrast, among patients with type 2 DM, the hypoglycemic events that required hospital admission occurred in the context of higher glycemic stability, generating, from the perspective of identification of evolutionary patterns, the premise of more effective intervention aimed at preventing subsequent events.

The group of underprivileged patients, of Roma ethnicity, included in the study, had a more pronounced risk profile due to the more frequent and more pronounced presence of the risk factors analyzed. Among these patients, a higher rate of obesity, of family history, of high blood pressure and of smoking was noted. It is worth noting that the upward curve of the prevalence of blood pressure according to the age of the patient was more pronounced among the Roma population compared to the general population studied.

Considering that in the group of vulnerable patients the enrollment was a consecutive-population one, including both patients with diabetes mellitus and patients without diabetes mellitus, respecting the proportionality of the studied population, considering the higher rate of risk biomarkers for the development of diabetes mellitus and its complications, inferentially, it can be concluded that the Roma population is at a higher risk of developing diabetes mellitus and complications of diabetes compared to the general population of Brăila County.

CHAPTER 9- ELEMENT OF ORIGINALITY

The present study is the first of its kind, at the level of Brăila County, aiming to evaluate the demographic and clinical and metabolic characteristics of patients with both type 1, and type 2 diabetes mellitus in the studied region.

The strong point of this study is the large number of included patients, a total of 2587 subjects, divided into group A, consisting of a number of 2493 patients admitted to the Brăila County Emergency Hospital, and group B, consisting of a number of 94 patients from a disadvantaged community within the county, an ethnic minority community of Roma subjects. Also, the patients from Group A were stratified into subgroup I, which included 371 patients newly diagnosed with DM, and subgroup II, with 2122 patients who had been diagnosed with diabetes mellitus prior to hospital admission.

Another element that lends authenticity to this study is the acquisition of a multitude of data related to both patient demographics and anthropometric characteristics, to the type and duration of the disease evolution, to the clinical and metabolic characteristics of the patients, which included from the evaluation of the metabolic, renal, hepatic profile to the prevalence and incidence of chronic and acute complications of diabetes mellitus.

The present study also monitored the treatment of patients before admission, in order to draw new directions in the management of the patient with diabetes mellitus, based on the results of the evaluations of laboratory and clinical parameters, directions aimed at improving their metabolic profile and quality of life, by preventing the occurrence of chronic and/or acute complications, and by appropriately addressing the complications already installed.

Such a study is extremely useful for a better understanding of the situation in Brăila County, and by knowing better the demographic and clinical and metabolic characteristics of the population in the county, as well as the knowing the characteristics of the Roma population, we can build targeted therapeutic strategies for our patients.

The objective of this study generates recommendations related to increasing the quality of medical services through monitoring more carefully the patients with diabetes mellitus, which

will ultimately lead to a decrease in the chronic complications of diabetes mellitus and an increase in the quality of life of the patients with diabetes mellitus and, therefore, an increase in their life expectancy.

SELECTIVE BIBLIOGRAPHY:

1. Writing Group for the SEARCH for Diabetes in Youth Study Group. Dabelea D, Bell RA, D'Agostino RB, Imperatore G, Johansen JM, Linder B, Liu LL, Loots B, Marcovina S, Mayer-Davis EJ, Pettitt DJ, Waitzfelder B. Incidence of diabetes in youth in the United States. JAMA. 2007 Jun 27;297(24):2716-24. [PubMed]
2. American Diabetes Association. Diagnosis and classification of diabetes mellitus. Diabetes Care 2014;37(Suppl. 1):S81–S90.
3. Rewers A, Dong F, Slover RH, Klingensmith GJ, Rewers M. Incidence of diabetic ketoacidosis at diagnosis of type 1 diabetes in Colorado youth, 1998-2012. JAMA 2015;313:1570–1572.
4. Alonso GT, Coakley A, Pyle L, Manseau K, Thomas S, Rewers A. Diabetic ketoacidosis at diagnosis of type 1 diabetes in Colorado children, 2010–2017. Diabetes Care 2020;43:117–121.
5. Jensen ET, Stafford JM, Saydah S, et al. Increase in prevalence of diabetic ketoacidosis at diagnosis among youth with type 1 diabetes: the SEARCH for Diabetes in Youth Study. Diabetes Care 2021;44:1573–1578.
6. Skyler JS, Bakris GL, Bonifacio E, et al. Differentiation of diabetes by pathophysiology, natural history, and prognosis. Diabetes 2017;66:241–255.
7. Insel RA, Dunne JL, Atkinson MA, et al. Staging presymptomatic type 1 diabetes: a scientific statement of JDRF, the Endocrine Society, and the American Diabetes Association. Diabetes Care 2015;38:1964–1974.
8. Chan JC, Yeung VT, Chow CC, et al. *Diabetes Res Clin Pract* 1996;32(1-2):27-34.
9. Turner RC, Stratton I, Horton V, et al. for the UK Prospective Diabetes *Study Group. Lancet* 1997; 350:1288-1293.
10. Owen KR, Stride A, Ellard S, et al.*Diabetes Care* 2003;26(7):2088-2093.
11. Zhang X, Gregg EW, Williamson DF, et al. A1C level and future risk of diabetes: a systematic review. Diabetes Care 2010;33:1665–1673.

12. Gambelunghe G, Forini F, Laureti S, et al. *Ann N Y Acad Sci* 2002;958:117-130.
13. American Diabetes Association, *Diabetes Care* 2009; 32(Suppl 1): S62-S67.
14. Expert Committee on the Diagnosis and Classification of Diabetes Mellitus. Report of the Expert Committee on the Diagnosis and Classification of Diabetes Mellitus. Diabetes Care 1997;20:1183–1197.
15. International Expert Committee. International Expert Committee report on the role of the A1C assay in the diagnosis of diabetes. Diabetes Care 2009;32:1327–1334.
16. Meijnikman AS, De Block CEM, Dirinck E, et al. Not performing an OGTT results in significant underdiagnosis of (pre)diabetes in a high risk adult Caucasian population. Int J Obes 2017;41:1615–1620.
17. Gonzalez A, Deng Y, Lane AN, et al. Impact of mismatches in HbA1c vs glucose values on the diagnostic classification of diabetes and prediabetes. Diabet Med 2020;37:689–696
18. Dabelea D, Mayer-Davis EJ, Saydah S, et al.; SEARCH for Diabetes in Youth Study. Prevalence of type 1 and type 2 diabetes among children and adolescents from 2001 to 2009. JAMA 2014;311:1778–1786.
19. Rewers A, Dong F, Slover RH, Klingensmith GJ, Rewers M. Incidence of diabetic ketoacidosis at diagnosis of type 1 diabetes in Colorado youth, 1998-2012. JAMA 2015;313:1570–1572.
20. Jensen ET, Stafford JM, Saydah S, et al. Increase in prevalence of diabetic ketoacidosis at diagnosis among youth with type 1 diabetes: the SEARCH for Diabetes in Youth Study. Diabetes Care 2021;44:1573–1578.
21. Heron M. Deaths: Leading Causes for 2015. Natl Vital Stat Rep. 2017 Nov;66(5):1-76.
22. Franz MJ, Bantle JP, Beebe CA, et al. Evidence-based nutrition principles and recommendations for the treatment and prevention of diabetes and related complications. Diabetes Care 2002; 25:148.
23. World Health Assembly Resolution (2007) WHA Global strategy on diet, physical activity and health. Geneva, World Health Organization 57: 17.
24. International Diabetes Federation. IDF Diabetes Atlas, 10th edn. Brussels, Belgium: 2021. Available at: https://www.diabetesatlas.org

25. International Diabetes Federation. The Global Picture in IDF Diabetes Atlas Eight Edition 2017; 40:65, 2017.
26. Roman G, Bala C, Creteanu G et al. Obesity and health-related lifestyle factors in the general population in Romania: a cross sectional study. Acta Endocrinologica, Bucharest 11(1): 64-71, 2015.
27. A Vathsala, HK Yap (2005) Annals Academy of Medicine 34(1).
28. Gheith O., Farouk N., Nampoory N., Halim M.A., Al-Otaibi T. Diabetic kidney disease: World wide difference of prevalence and risk factors. *J. Nephropharmacol.* 2016;5:49–56. doi: 10.4103/1110-9165.197379.
29. Observational Study Acta Diabetol. 2020 Jun;57(6):645-650. doi: 10.1007/s00592-019-01466-8. Epub 2020 Jan 7.Diabetes and diabetic retinopathy in patients undergoing cataract surgery: a prevalence study-DiCat study report #2Tommaso Rossi 1, Giacomo Panozzo 2, Giulia Della Mura 2, Diana Giannarelli 3, Daniele Ferrari 4, Giovanni Alessio 5, Carmela Palmisano 5, Serena Telani 4, Guido Ripandelli 6
30. Bramante CT, Lee CJ, Gudzune KA. Treatment of Obesity in Patients With Diabetes. Diabetes Spectr. 2017 Nov;30(4):237-243. doi: 10.2337/ds17-0030. PMID: 29151713; PMCID: PMC5687113.
31. Stone MA, Charpentier G, Doggen K, Kuss O, Lindblad U, Kellner C, Nolan J, Pazderska A, Rutten G, Trento M, Khunti K; GUIDANCE Study Group. Quality of care of people with type 2 diabetes in eight European countries: findings from the Guideline Adherence to Enhance Care (GUIDANCE) study. Diabetes Care. 2013 Sep;36(9):2628-38. doi: 10.2337/dc12-1759. Epub 2013 Apr 29. PMID: 23628621; PMCID: PMC3747883
32. Masood MQ, Singh K, Kondal D, Ali MK, Mawani M, Devarajan R, Menon U, Varthakavi P, Viswanathan V, Dharmalingam M, Bantwal G, Sahay R, Khadgawat R, Desai A, Prabhakaran D, Narayan KMV, Tandon N; CARRS Trial Group. Factors affecting achievement of glycemic targets among type 2 diabetes patients in South Asia: Analysis of the CARRS trial. Diabetes Res Clin Pract. 2021 Jan;171:108555. doi: 10.1016/j.diabres.2020.108555. Epub 2020 Nov 24. PMID: 33242515; PMCID: PMC7854496.

33. Mohammad Wali Naseri, Habib Ahmad Esmat, Mohammad Daud Bahee,Prevalence of hypertension in Type-2 diabetes mellitus,Annals of Medicine and Surgery,Volume 78,2022,103758,ISSN 2049-0801,https://doi.org/10.1016/j.amsu.2022.103758
34. Nørgaard K, Feldt-Rasmussen B, Borch-Johnsen K, Saelan H, Deckert T. Prevalence of hypertension in type 1 (insulin-dependent) diabetes mellitus. Diabetologia. 1990 Jul;33(7):407-10. doi: 10.1007/BF00404089. PMID: 2401396.
35. Werissa NA, Piko P, Fiatal S, Kosa Z, Sandor J, Adany R. SNP-Based Genetic Risk Score Modeling Suggests No Increased Genetic Susceptibility of the Roma Population to Type 2 Diabetes Mellitus. Genes (Basel). 2019 Nov 19;10(11):942. doi: 10.3390/genes10110942. PMID: 31752367; PMCID: PMC6896051.
36. Nunes MA, Kučerová K, Lukáč O, Kvapil M, Brož J. Prevalence of Diabetes Mellitus among Roma Populations-A Systematic Review. Int J Environ Res Public Health. 2018 Nov 21;15(11):2607. doi: 10.3390/ijerph15112607. PMID: 30469436; PMCID: PMC6265881