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GRADUATION THESIS

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Thesis Mentor: Assoc. Prof. Sanja Klobučar, MD, PhD

The graduation thesis was graded on …… in …….., before the Committee composed of the following members:

1. Assist. Prof. Tomislav Jakljević, MD, PhD (Committee Head)
2. Prof. Ivan Bubić, MD, PhD
3. Assoc. Prof. Dijana Detel, MD, PhD

The graduation thesis contains 20 pages, 1 figure, 8 tables, 20 references.

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List of abbreviations and acronyms

DM	diabetes mellitus
T2DM	type 2 diabetes mellitus
WHO	World Health Organization
CHC Rijeka	Clinical Hospital Centre Rijeka
IFG	impaired fasting glucose
FPG	fasting plasma glucose
HbA1c	hemoglobin A1c
OGTT	oral glucose tolerance test
CVD	cardiovascular disease
LDL	low-density lipoprotein
HDL	high-density lipoprotein
TG	triglycerides
VLDL	very low-density lipoprotein
ADA	American Diabetes Association
BMI	body mass index
IQR	interquartile range

1. INTRODUCTION

Diabetes Mellitus (DM) describes a group of diseases that are primarily associated with an increased glucose blood level, known as hyperglycemia, due to insulin resistance or a lack in pancreatic insulin secretion. Type 2 Diabetes Mellitus (T2DM) is one type of DM that is responsible for about 90% of all DM cases and thus plays a major clinical role. (1)

According to the World Health Organization (WHO) Diabetes Mellitus was the 6th most common cause of death in Croatia in 2019 among both sexes and all age groups. The precise number is 47.52 deaths per 100.000 population. In contrast, the USA shows higher absolute numbers of deaths associated with DM, but comparing the deaths per 100.000 citizens, the USA shows much better mortality rates with a Number of 18.67/100.000, than Croatia. (2)

This large number highlights the significance to investigate benefits of well controlled patients with T2DM to reduce morbidity and mortality rates in the future.

The aim of this research is to analyze how well the patients of the Clinical Hospital Centre in Rijeka (CHC Rijeka) are adjusted to their glycemic and metabolic control of T2DM.

T2DM can have different causes leading to the disease, but it is always associated with some kind of failure in glucose metabolism, which can be due to insulin resistance, impaired insulin secretion and increased hepatic glucose production. Insulin resistance is shown to be prior to defects in insulin secretion and it is described as a state where secreted insulin is unable to act on specific tissues, such the liver, muscles or fat tissue and fails to provide them with sufficient glucose from the blood. This condition consequently leads to a constant rise in blood glucose levels and can secondarily result in inadequate insulin secretion or increased hepatic glucose production. (3)

1.1 Diagnostic criteria for prediabetes and diabetes

If the glucose homeostasis worsens constantly, it will ultimately lead to a point where the blood glucose level exceeds the value for definitive clinical diagnosis of the disease. This intermediate stage is defined as prediabetes. (3)

Prediabetes can be defined by three different parameters. These are fasting plasma glucose (FPG) of 5.6-6.9 mmol/L, two-hour plasma glucose after a glucose challenge of 7.8-11.0 mmol/L or a hemoglobin A1c (HbA1c) of 5.7-6.4%. Either one of these values can be used to determine whether a patient has an impaired fasting glucose (IFG) or glucose intolerance and therefore is in a state of prediabetes. (4)

If prediabetes fails to be controlled in patients, it can consequently proceed to T2DM. (5) A definitive diagnosis of T2DM can be made if diagnostic parameters exceed the threshold for diagnosis. The thresholds are defined as FPG ≥ 7mmol/l or 2-hour plasma glucose ≥ 11.1 during oral glucose tolerance test (OGTT) or HbA1c ≥ 6.5%. (4)

1.2 Complications of diabetes mellitus

Long standing T2DM with not well controlled blood glucose levels can lead to life-threatening complications that significantly increase the mortality rate in patients with T2DM. Such chronic complications can be divided in macrovascular and microvascular complications, according to the vessel size they affect. Microvascular changes can for example lead to diseases of the eye, kidney or nerves like diabetic retinopathy, nephropathy, or neuropathy. On the other hand, it has been shown that macrovascular changes provide a base for the development of cardiovascular diseases (CVD) and lead to an even higher risk if hypertension occurs simultaneously with T2DM. (6)

Such CVD are mainly a consequence of atherosclerosis and include diseases as coronary artery disease, cerebrovascular disease, and peripheral artery disease. Until recently, it was found out that CVD were responsible for about 52% of deaths in patients with T2DM. (7)

1.3 Lipid control in diabetes mellitus

This number shows the significant impact on mortality rates of CVD on T2DM patients, which underlines the importance of a good metabolic control in patients with T2DM. To reduce mortality rates of T2DM and its complications, it's not only beneficial to keep blood-glucose levels with antihyperglycemic therapy in in the normal range, but its highly important to control other metabolic parameters such as lipid levels like low-density lipoprotein (LDL), high-density lipoprotein (HDL), and triglycerides (TG).

Other studies have shown that the blood glucose level positively correlates with LDL and triglyceride values, meaning that higher LDL and triglyceride values are found in patients with higher glucose levels. Consequentially, it can be said that stabilizing blood glucose levels in patients with T2DM has a beneficial effect on lowering lipid levels and vice versa. (8)

1.4 Atherogenic dyslipidemia

Diabetic patients, especially patients with T2DM follow certain lipoprotein patterns, also known as diabetic dyslipidemia or atherogenic dyslipidemia.

Atherogenic dyslipidemia is defined with increased levels on triglycerides, a great number of small-dense LDL particles and low HDL values. (9)

Atherogenic dyslipidemia is commonly associated with a state of insulin resistance which in turn leads to a significant increased risk of atherosclerosis and cardiovascular disease. This mechanism is due to insulin resistance causing hyperinsulinemia which stimulates hepatic gluconeogenesis and the general glucose output. Furthermore, high concentration of insulin in the blood also reduces the suppression of lipolysis in adipose tissue which leads to a high flux of free fatty acids as well as higher secretion of hepatic very low-density lipoprotein (VLDL). This leads to hypertriglyceridemia and at the same time reduces the plasma levels of HDL. (10)

LDL levels of patients with T2DM may be equal or similar as in non-diabetic patients, but the parameter that makes a marked difference between diabetic and non-diabetic population is the amount of small dense LDL particles. Small dense LDL is much more pathogenic and prone to cause atherosclerosis compared to large LDL. (11)

Therefore, it is of the utmost importance for patients with T2DM to be aware of the state of their lipidogram to reduce the risks of cardiovascular diseases. The American Diabetes Association (ADA) has introduced reference values for lipid levels in patients T2DM to lower risk and complications of CVD. Profitable values include LDL < 70 mg/dl (1.8 mmol/L), HDL > 40 mg/dl (1 mmol/L) in men and > 50 mg/dl (1.3 mmol/L) in women, and triglycerides < 150 mg/dl (1.7 mmol/L). (9)

1.5 Lowering lipid levels

Methods for reducing lipid levels in T2DM patients are primarily lifestyle changes such as expanding the amount of physical activity, nutritional changes and losing weight, since it has been found out that a reduction in body mass index (BMI) of patients influences their lipid levels accordingly. (12)

Today there are several pharmacological possibilities of lowering dyslipidemia in T2DM patient. First line therapy includes statins, a group of drugs that block the coenzyme HMG-CoA reductase and thus inhibit the synthesis of cholesterol, being one the most effective drugs to lower high cholesterol levels. (9) Another type of drugs against dyslipidemia are fibrates, drugs that activate the peroxisome proliferator-activated receptor alpha (PPAR–α) which reduces

LDL and TG levels by increasing their degradation hence increase HDL levels. (9) Newer and promising drugs in the management of metabolic control in diabetic patients include ezetimibe and PCSK9 inhibitors, which are frequently used in a combination therapy with statins to lower lipid levels in T2DM patients. (13)

2. AIMS AND OBJECTIVES

The objective of this study is to assess the level and quality of metabolic control in patients diagnosed with Type 2 Diabetes Mellitus in the CHC Rijeka. This is assessed by investigating the relationship between demographic variables (such as sex, age and duration of the disease) and clinical variables (e.g., HbA1c, FPG, BMI, total cholesterol, LDL, HDL, and non-high-density lipoprotein cholesterol).

Overall, the aim of this study is to better understand which variables have a significant impact on the metabolic control of patients suffering from Type 2 Diabetes Mellitus and to be able to improve management of the disease. The study is directed towards the prevention of long-term macrovascular and microvascular complications leading to an increased mortality rate due to cardiovascular diseases mainly caused by atherosclerosis.

3. PARTICIPANTS AND STUDY DESIGN

A cross-sectional study was conducted retrospectively by collecting the relevant data from patients receiving care for T2DM in the period from the 16th of March 2022 until the 29th of March 2023. The group of patients was selected as being participants that were admitted to the Daily hospital for endocrinology, diabetes and metabolic diseases in the CHC Rijeka for counseling. This counseling program consists of groups of 4-12 individuals that have either been newly diagnosed or have a long-term diagnosis of a form of DM and have shown to have a badly regulated blood sugar over time despite receiving adequate treatment. The criteria for including participants were the diagnosis of T2DM. This comprised newly diagnosed patients as well as patients that knew about their disease over a longer period of time.
Patients excluded from the study were those diagnosed with Type 1 Diabetes Mellitus and Gestational Diabetes Mellitus.

The data was collected from a mandatory screening test that participants had to undergo in order to attend the counseling in the Daily clinic. This included blood work assessing the patient's lipids and blood sugar as well as an interview about the prior course of the disease with the physician in charge of overseeing the program.

To assess the patient's level of glycemic control the guidelines of the ADA were used.
An inadequate glycemic control was defined as a HbA1c: ≥ 7.0%.
To categorize a participant as having "poor metabolic control" the following values were used: (9)

LDL	HDL	Triglycerides
≥ 1.8 mmol/L	≤ 1.5 mmol/L	≥ 1.7 mmol/L

The statistical analyses were performed in the R statistical environment version 4.2.2. Functions and expansions of the ggplot R-package were used to visualise the data. Either the function stat_compare_means() or t.test() was used to perform Student's t-tests. Correlations were calculated using the base R function cor() and significance was tested using the function lm().

4. RESULTS

For this cross-sectional study patient data of 104 individuals was collected. From this group, 58 out of 104 participants or more than half were female (55.77%). The mean age at the time of examination was 61.6 years, the median was 62 years, and the interquartile range (IQR) was 55-69.25 years while the minimum was 37 years and the maximum 81 years.

The mean value for HbA1c was 8.2% (standard deviation 1.8%) and the median was 7.8% (see Figure 1).

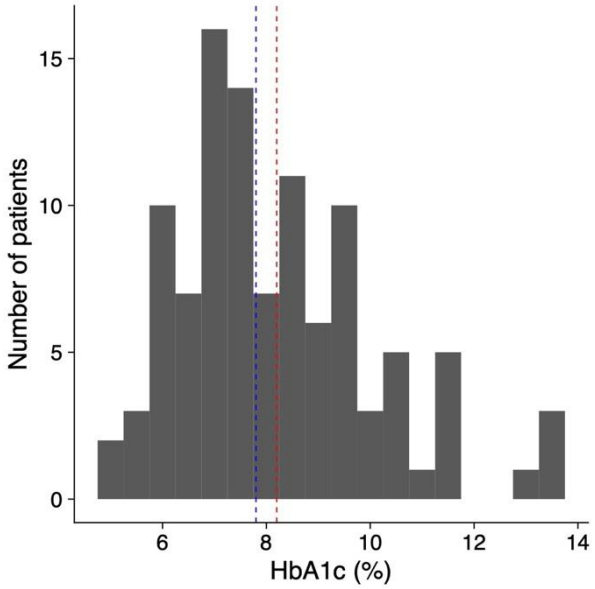

Figure 1: Histogram showing distribution of HbA1c values across patients.The blue line indicates the median; the red line indcates the mean across the cohort.

In accordance with the ADA guidelines 28 patients (or 26.92%) had a well-regulated HbA1c of < 7% meaning they had a well-regulated blood glucose in the last three months. The prevalence of elevated HbA1c was seen particularly in patients that were diagnosed a longer time ago than in patients that had received a diagnosis recently (R=0.21, p=0.031). (Figure 2).

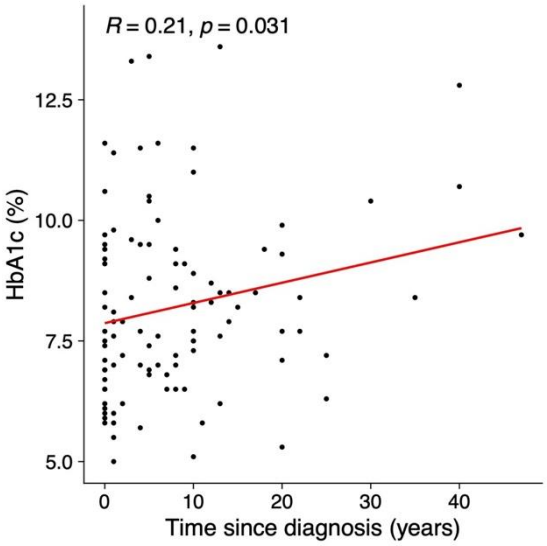

Figure 2: Scatterplot showing relationship between time since diagnosis and HbA1c values. Red line indicates the line of best fit from a linear regression. Pearson's correlation R = 0.21, p = 0.031

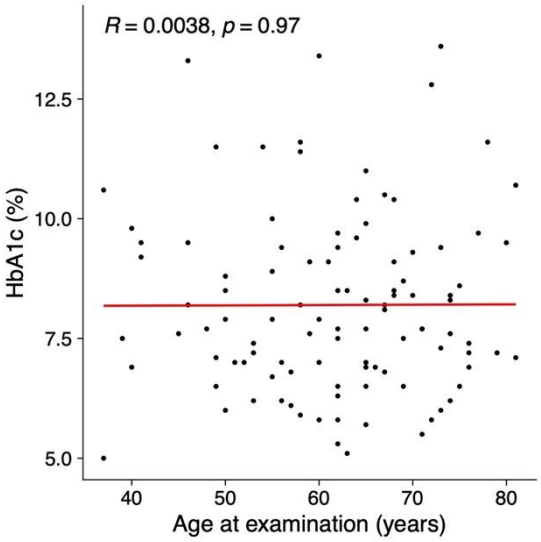

Figure 3: Scatterplot showing the relationship between age of examination and HbA1c values. Red line indicates the line of best fit from a linear regression. Pearson's correlation R= 0.0038, p= 0.97

There was no correlation (R=0.0038) between the age at the time of examination and the value of HbA1c. (Figure 3)

The mean value for FPG was 8.7 mmol/L (standard deviation 3.32 mmol/L) and the median was 7.85 mmol/L with an IQR of 6.6-9.7 mmol/L. In the study 30 patients out of 104 (28.85%) had a FPG that was below the threshold of 7.0 mmol/L.

Of those 30 individuals 11 (10.58% of the entire cohort) had a value of 5.5 mmol/L or lower. In total 6 participants (5.77%) have HbA1c values below 6.5% and a FPG of 5.5 mmol/L or lower, which indicates excellent glycemic control. Contrarily, the other 74 participants (71.15 %) did not reach the FPG threshold under 7.0 mmol/L and thus were shown to have a bad

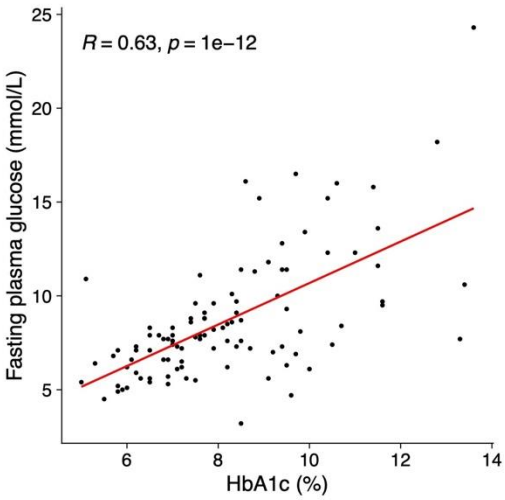

Figure 4: Scatterplot showing the relationship between HbA1c and FPG values. Red line indicates the line of best fit from a linear regression. Pearson's correlation R= 0.63, p= 1e-12

adjusted glucose control. Participants with a high FPG consistently had an elevated value of HbA1c (p=1e-12). (Figure 4)

The mean value for total cholesterol was 4.88 mmol/L (standard deviation 1.39 mmol/L) and the median was 4.5 mmol/L with an IQR of 3.98-5.53. There was an almost perfect correlation (R=0.98) between total cholesterol and non-HDL which also showed high significance (p<2.2e-16).

The mean value of HDL was 1.25 mmol/l (standard deviation 0.3 mmol/L) and the median was 1.2 with an IQR of 1.0-1.5 mmol/L.

The mean value of LDL was 2.74 mmol/L (standard deviation of 1.19 mmol/L) and the median was 2.5 mmol/L with an IQR of 1.88-3.4 mmol/L.

The mean value of triglycerides was 2.07 mmol/L (standard deviation 1.55 mmol/L) and the median was 1.65 mmol/L (IQR 1.2-2.2 mmol/L). Patients that were older at the time of examination had generally lower values of triglycerides than the patients that were younger (R=-0.26, p=0.0067). (Figure 5)

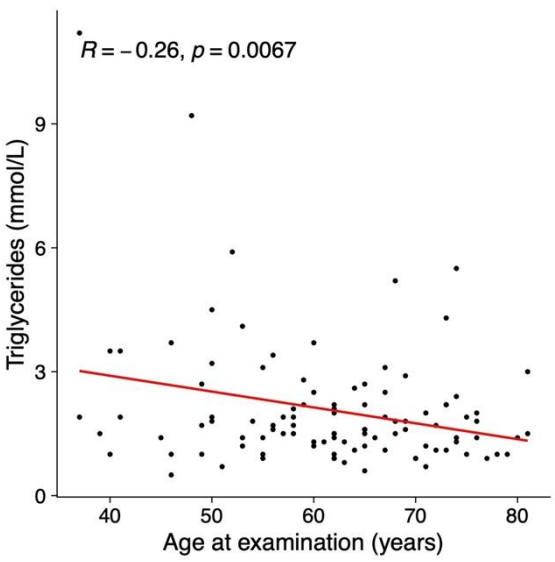

Figure 5: Scatterplot showing the relationship between age of examination and triglyceride values. Red line indicates the line of best fit from a linear regression. Pearson's correlation R= -0.26, p= 0.0067

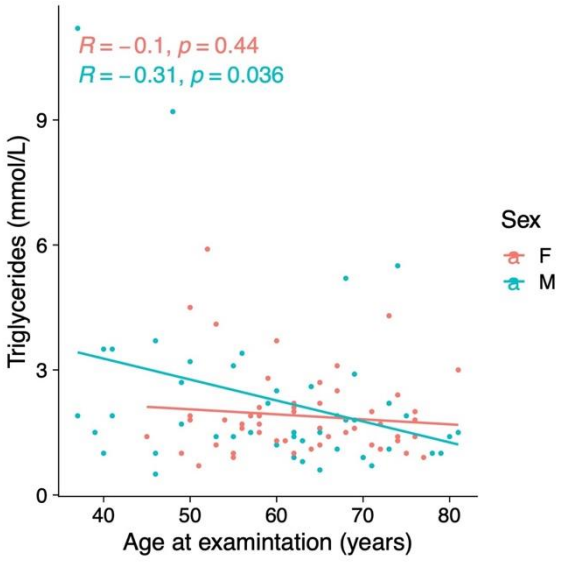

Figure 6: Scatterplot showing the relationship between age of examination and HbA1c values. Points in red indicate female and blue male participants respectively with the lines of best fit indicated in the same color for each group

If divided by sex, it can be seen that the negative correlation as well as the significance is higher in men than in women for triglycerides at the age of examination. (Figure 6)

In total, 21 out of 104 participants have reached values below the threshold for LDL which lies at <1.8 mmol/L and accounts for 20.2 % of participants.

Considering triglycerides levels, 52 patients (50%) were below the reference value of ≤1.7 mmol/L.

The threshold levels for HDL can be divided according to sex, female reference value lies at ≥ 1 mmol/L and male at ≥ 1.3 mmol/L. From 58 female participants in this study, 51 have reached the reference values, that accounts for 87.9%. In contrast, only 13 male participants from 46 in total have reached the reference values and are with 28.3% significantly lower than the female fraction. Overall, 64 of 104 participants reached profitable HDL values and are making up 61.5 % in total.

From 104 participants 12 (11.54%) have reached the desired values in LDL and TG values. Five of those even gained beneficial metabolic control considering LDL, TG and HDL values, meaning only 4.81% of patients are adjusted excellently according to all 3 parameters.

Table 1: Most important parameters in metabolic control of T2DM and their values

	Mean	Median	Min	Max	Reference value	Adequate control in %
FPG (mmol/L)	8.7	7.85	3.2	24.3	≤ 7.0	28.8%
HbA1c (%)	8.2	7.8	5.0	13.6	< 7	26.9%
LDL (mmol/L)	2.74	2.5	0.5	6.8	≤ 1.8	20.2%
HDL (mmol/L)	1.25	1.2	0.6	2.0	≥ 1.3 ♂ ≥ 1.0 ♀	61.5%
TG (mmol/L)	2.07	1.65	0.5	9.2	≤ 1.7	50%

The mean body mass index (BMI) was 30.19 kg/m2 (standard deviation 6.17 kg/m2) and the median was 28.75 kg/m2 (IQR 26.1-34.4) while the minimum was 19.5 kg/m2 and the maximum was 53.2 kg/m2. If we differentiate by sex the figure shows that females have a tendency for a lower BMI when they are older at the time of examination. (Figure 7)

There was no correlation seen between BMI and non-HDL values. (Figure 8)

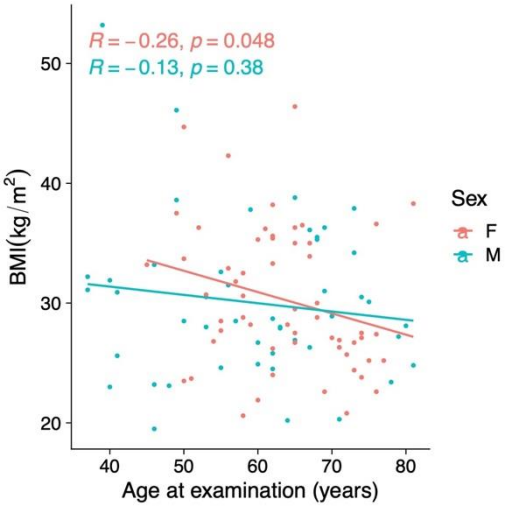

Figure 7: Scatterplot showing the relationship between age of examination and BMI values. Points in red indicate female and blue male participants respectively with the lines of best fit indicated in the same color for each group

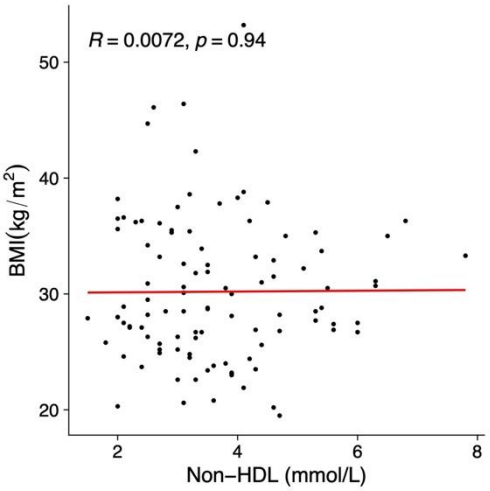

Figure 8: Scatterplot showing the relationship between non-HDL and BMI values. Red line indicates the line of best fit from a linear regression. Pearson's correlation R= 0.0072, p= 0.94

5. DISCUSSION

In this study 55.77% of the participants were female although it is described that among patients with T2DM men are more commonly affected than women. In the PANORAMA study that included 5817 patients with T2DM across all over Europe 53.7% were male. (14) This difference is most likely due to the sample size of this study (n=104) as well as the patients only being from a very limited region of Croatia, namely in and around the city of Rijeka. Since participation at the program at Rijeka is voluntary, participation of women may be more likely, and this difference must be taken into account when analyzing our results.

The prevalence of patients with inadequate glycemic control considering only HbA1c ≥ 7% was 73.08% which was somewhat expected since the group that was admitted to the study were patients admitted for counseling to either improve regulation of either a badly managed long-term diagnosis or after a newly discovered T2DM. Therefore, the statement that can be made with this study isn't about how well the average patients with T2DM that are being treated but is restricted to the patient population seen in the outpatient clinics of CHC Rijeka. Our data is a representation of how patients' glycemic control is at the time they are firstly diagnosed with T2DM as well as how a patient's glycemic control is after a long-term diagnosis in case they were not able or willing to properly regulate their blood sugar.

If we compare this study's inadequate glycemic control of 73.08% to that of the PANORAMA study (37.4% of patients with HbA1c ≥ 7%) (14) it might seem that patients in the CHC Rijeka have especially badly regulated blood glucose in comparison to the rest of Europe. But as mentioned before the nature of this selection of patients warrants the results that were obtained.

It might be surprising that there is a constant rise of T2DM in the population of Croatia and that patients are poorly adjusted despite supposedly adhering to the Mediterranean diet that, if correctly followed over a long period, has been proven to be beneficial for patients with metabolic syndrome as well as T2DM. This includes consumption of whole grains, seafood like fish and, olive oil, garlic, fruits, and vegetables as well as moderate amounts of red wine. In contrast the modern western diet that consists of highly processed food and contains low fiber, high amounts of salt, sugar and lipids has shown to propel obesity, insulin resistance and hyperglycemia which in turn leads to T2DM and metabolic syndrome. (15)

Despite Croatia being associated with the Mediterranean diet the prevalence of diabetes is rising in the country as well as in the nearby countries. After Serbia and Bosnia and Herzegovina,

Croatia has the third highest prevalence in this region with 11.1%. This can be associated to the generally increased caloric intake over the past two decades, but it must also be mentioned that many countries of the South-East Europe were or are currently still in social transition and belong to the group of middle-income and some even to low-income countries. The high caloric intake comes from cheap and readily available meals such as white bread, inexpensive animal products (such as pork and fatty cheese) and overconsumption of sunflower oil. (16)

We could see that there were high HbA1c values particularly in patients diagnosed a longer time ago than in patients recently diagnosed (see Figure 2) confirms that the reason for glycemic control is how the blood sugar was managed over the course of the disease. If patients were admitted to counseling with a long history of T2DM they were more likely to be insufficiently regulated over an extended period and therefore generally had worse HbA1c values than patients with a new onset of T2DM.
This shows that proper education on how to correctly manage T2DM in newly diagnosed patients, gives better long-term HbA1c value results for those patients. (17)

The fact that no correlation exists between the age at the time of examination and the HbA1c (see figure 3) tells us that the age of patients doesn't affect the glycemic control in and of itself. Difference in glycemic control management among different age groups can be attributed to different times passed from the diagnosis, rather than the age itself.

Among the 104 participants of this study, 30 reached a fasting plasma glucose FPG level below the threshold under 7 mmol/L, which makes about 28.85% of all participants. 6 out of those 30 even show an excellent glycemic control with FPG of 5.5 mmol/L and an HBA1c below 6.5%. Unfortunately, the majority consisting of 74 participants or 71.15% did not reach threshold levels and as seen in figure 4 this great number ultimately also positively correlates with the HBA1c value, which is increased in patients with high FPG levels. Those high numbers can most likely be credited to the fact that a majority of participants in this study are already under suspicion of having inadequate glycemic control.

LDL threshold values are reached by slightly more than a fifth of the participants (20.2%), which is not a satisfying result but considering the patients, that were chosen for the study belong to a cohort of persons with doubtful glycemic and metabolic control it is adequate and has great potential for improvement through medical intervention and lifestyle changes. The

values for TG values were even more promising. It turned out that already 50% of participants had favorable values with the median (1.65 mmol/L) only being slightly above the reference value of ≤ 1.7 mmol/L. As seen in Fig. 5 and Fig. 6 the TG values are consistently decreasing with age, in males even more than in females. Studies found out that plasma-clearance of TG in elderly patients > 60 years old is similar to young patients < 30 years old, explaining a rise in TG until about 60 years of age with a consistent decline after a certain peak. (18)

Surprisingly, most of the female patients (87.9%) reached desirable HDL values, comparing to the male fraction, where only 28.3% reached beneficial HDL levels. One explanation for that contrast in HDL values, could be the difference in the reference values for HDL, which are slightly higher in males (≥ 1.3 mmol/L) than in females (≥ 1 mmol/L). Another answer for the variety of value between male and female sex could be the possible beneficial role of estrogen on HDL, especially in premenopausal women, compared to man. (19)
Newer metanalysis also found out that the HDL values of postmenopausal women don't significantly decrease compared to premenopausal women. (20)
Overall excellent metabolic control, considering LDL, HDL and TG values were only reached by 16.3 % of all participants, which is a poor result and leaves room for improvement.
BMI examinations showed that BMI values are consistently declining with age, with higher significant changes in women. We can assume that males don't adhere properly to a healthy diet and prefer the consumption of processed foods and are less physically active compared to women. On the other hand, BMI values showed no correlation with non-HDL values.

6. CONCLUSION

The quality of metabolic control in the participants from this study wasn't particularly high however, this was to be expected since the participants were admitted to the group counseling in order to educate them on how to manage their diabetes (administration of medication, dietary intake, physical activity, etc.). It was found that HbA1c values correlate with the time since the first diagnosis. The longer ago the diagnosis the higher the HbA1c. Contrarily there was no correlation between the age at the time of the examination and the value of HbA1c.

Limitations of this study were the number of participants which was 104 and therefore fairly small in comparison to other cross-sectional studies. The city of Rijeka, however, is not very large and patient data from over one year of group counseling was used which in turn is adequate for the size of the overall population.

A follow-up study would be of great interest to see whether the patients metabolic control sees any improvement after the group counseling which would help to understand how big of an impact the program has on patients and how willing they are to follow the guidelines they are being given.

7. SUMMARY

Diabetes mellitus is a disease that is defined as impaired glycemic control due to insulin resistance or impaired pancreatic insulin production. The prevalence is rising worldwide with Croatia not being an exception. It effects patient's lipid metabolism which is one of the main causes of morbidity and mortality.

The aim of this study was to investigate the state of metabolic control in patients being treated for T2DM in the CHC Rijeka. The data of 104 patients was used that were admitted for a counseling program of the daily hospital in the period from the 16th of March 2022 until the 29th of March 2023. Parameters included the age at the time of examination, age at the time of diagnosis, hemoglobin A1c, fasting plasma glucose, body mass index, total cholesterol, low-density lipoprotein, high-density lipoprotein, and triglycerides.

The median age of participants at the time of examination was 62 years and the mean BMI was 30.19 kg/m^2. The mean value of HbA1c was 8.2% and the mean of LDL was 2.74 mmol/L, respectively. HbA1c values were higher in patients with a long-term diagnosis compared to those that have been recently diagnosed with T2DM. Target value of HbA1c < 7% was reached by only 26.9% of participants. LDL threshold values were reached by slightly more than a fifth of the participants (20.2%). Overall excellent metabolic control, considering LDL, HDL and TG values were only reached by 16.3 % of all participants.

The study showed the metabolic control off the participants wasn't satisfactory however, it was to be expected since they were all referred to the daily hospital to be educated on how to manage their disease. Reasons for referral were either evidence of long-term neglect of glycemic control or a recent diagnosis of T2DM.

Key words: type 2 diabetes mellitus, glycemic control, cholesterol, triglycerides

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9. CURRICULUM VITAE

Daniel Fabian Hübner was born on the 12th of July 1997 in Boston, Massachusetts, USA. In 2004 his family moved to Freiburg im Breisgau in Germany after he had attended pre-school and 1st grade in Brookline, MA. Daniel's mother was born and raised in Croatia and his father in Germany, therefore Daniel grew up speaking Croatian, English and German fluently. In Freiburg he spent eight years. During that time Daniel was very active musically (taking violin lessons and playing in an orchestra, playing electrical bass, and singing in a band), in sports (playing tennis and basketball) as well as acting in an English theater program. In 2012 he moved with his parents to Munich, Bavaria where he finished his Abitur in 2015. After that he spent almost half a year in Colombia, learning Spanish and working in a laboratory.

In the fall of 2017 Daniel started studying medicine in Rijeka where he was active as a student representative and sang in the choir for the entirety of his studies. Furthermore, he learned Italian and reached an A2 level during that time. He is set to receive his medical degree in the summer of 2023.