Correlating the Cholesterol Levels to Glucose for Men and Women

Ilija Vishinov, Marjan Gusev
Ss. Cyril and Methodius University,
Faculty of Computer Sciences and Engineering,
Skopje, North Macedonia

Lidija Poposka, Marija Vavlukis
Ss. Cyril and Methodius University,
University Clinic of Cardiology
Skopje, North Macedonia

***Abstract*—Objectives: This paper explores the correlation between multiple cholesterol levels of the lipid profiles of patients and their diabetes regulation abilities in men and women.**

***Methodology*: The methodology includes the following techniques: i) Pearson correlation ii) Spearman rank correlation and iii) setting thresholds for certainty of class assumption.**

***Data*: The methods were applied on data from 161 patients of which 110 male and 41 female, analyzing the variables about patients' age, height, weight, BMI, lipid profile (total cholesterol, HDL cholesterol, LDL cholesterol, triglycerides), glycated hemoglobin levels with respective glucose regulation and diabetes classes, history of heart, diabetes and other chronic illnesses, habitual behaviors (smoking, alcohol consumption, physical activity), and medications intake (calcium channel blockers, BETA blockers, anti-arrhythmics, AKE/ARB inhibitors, diuretics, statins anti-aggregation medication and anticoagulants).**

***Conclusion*: Analyzing the correlations between the lipid profile and glucose regulation in patients led to different results when the analysis was done separately on men and women. Thus, better predictions and insights can be made dependent on gender. The research found no strong stand-alone correlation when analyzing all data, but when the data was segmented in male and female records, a strong negative linear (r=-0.52, p=0.001) and non-linear (r=-0.55, p=0.001) correlation was found for the HDL-C and glucose levels in female patients. In men, statistically significant negative correlations with HbA1c were assessed for Chol (r=-0.27, p=0.009), LDL-C (r=-0.33, p=0.002) and HDL-C (r=-0.23, p=0.026).**

***Index Terms*—cholesterol, diabetes, glucose regulation, correlation, lipid profile**

I. Introduction

This research is part of the Glyco project [1] aiming to detect blood glucose level out of an electrocardiogram (ECG) measurement. In addition to the main research goal of this project, we have noticed possible correlations between the lipid profile and glucose regulation ability of the patients. Therefore, in this paper, we present the research and findings analyzing all possible correlations between measured biochemical parameters that describe a complex health condition of a patient, and especially analyzing the gender differences in the correlations.

The dataset within the realized project contains a total of 161 patients (110 male and 41 female) and among all medical records we focused on patients' age, height, weight, BMI, lipid profile (total cholesterol, HDL cholesterol, LDL cholesterol, triglycerides), history of heart, chronic and diabetes illnesses, habitual behaviors (smoking, alcohol consumption, physical activity), medications intake (calcium channel blockers, beta blockers, anti-arrhythmics, ake/arb inhibitors, diuretics, statins, anti-aggregation medication and anticoagulants) and glycated hemoglobin levels with respective glucose regulation and diabetes classes.

Particularly, the research question in this paper focuses on determination if the measured cholesterol levels are correlated to blood glucose levels and whether these correlations are different for men and women.

II. Related work

Researchers typically have been investigating various correlations between patient's lipid profile and glucose regulation ability. We classify their findings according to the diabetes category (predabetes, type1 and type 2 diabetes).

A. Prediabetes patients

Calanna et al. [2] concluded that prediabetes patients exhibited lower HDL and higher Triglycerides levels.

B. Type 1 diabetes

Prado et al. [3] found that HbA1c levels are positive correlated to Total Cholesterol, Triglycerides and LDL cholesterol, but found that there is no significant correlation between HDL cholesterol and HbA1c. Kim et al. [4] had a similar conclusion except for the LDL cholesterol, and concluded that for LDL cholesterol there is no a statistically significant correlation.

C. Type 2 diabetes

Triglycerides are positively and HDL cholesterol is negatively correlated with HbA1c in diabetic patients according to [5] and [2].

A significant positive correlation is found for Total Cholesterol, Triglycerides and LDL cholesterol when compared to HbA1c by several studies [6], [7], [8], [9], [10], although no significant correlation of HDL cholesterol is reported for worsened diabetes condition.

Similar conclusion for positive correlation of non-HDL (Total Cholesterol, Triglycerides and LDL) cholesterol is reported by [11], [12], [13], [14], [15], [16] and a significant negative correlation with HDL cholesterol.

TABLE I
GENDER STATISTICS OF THE PROPRIETARY DATASET

Gender	Quantity	Percentage (%)
Male	110	68.3
Female	41	31.7

TABLE II
NUMERICAL FEATURES STATISTICS OF THE PROPRIETARY DATASET (INNOVATION DOOEL)

	mean ± std		
Feature	All	Male	Female
Age	60.23 ± 10.49	59.65 ±9.86	61.47 ±11.74
Weight	81.80 ± 14.31	84.38 ± 14.99	76.29 ± 10.97
Height	171.53 ± 8.44	175.02 ± 7.67	164.33 ±4.49
BMI	28.16 ± 4.43	28.04 ±4.52	28.42 ± 4.28

III. METHODS

A. Experimental setup

Data of 161 patients was analyzed within this research. Table I shows the distribution of male and female patients. Table II and Table III show the distribution of the numerical and categorical variables which consist of the patients' age, height, weight, BMI, lipid profile, glycated hemoglobin levels with respective glucose regulation and diabetes classes, history of heart, diabetes and other chronic illnesses, habitual behaviors (smoking, alcohol consumption, physical activity), medications intake (calcium channel blockers, BETA blockers, antiarrhythmics, AKE/ARB inhibitors, diuretics, statins, antiaggregation medication and anticoagulants).

Table IV presents the blood glucose i.e. glycated hemoglobin HbA1c and the lipid profile which is made up of four continuous variables: Total Cholesterol (Chol), LDL Cholesterol (LDL-C), HDL Cholesterol (HDL-C) and Triglycerides (TG). These are the main variables that will be subject to analysis for possible correlations between the lipid profile and glucose regulation.

B. Correlation methods

The research is based on the following correlation methods compliant to the research goal:

- *Pearson correlation*
  Pearson's correlation captures only linear correlations between two continuous variables.
- *Spearman rank correlation*
  In order to capture non-linear correlations as well, Spearman rank correlation was included. Spearman's coefficient captures all relationships, linear and non-linear.

IV. RESULTS

As HbA1c is the marker for glucose regulation diagnosis, we can further indirectly reevaluate the correlation between the cholesterol attributes and the glucose regulation by assessing the Pearson and Spearman coefficients. The results of conducting the Pearson and Spearman rank correlation methods are presented in Table VI.

TABLE III
CATEGORICAL STATISTICS OF THE PROPRIETARY DATASET (INNOVATION DOOEL)

	Distribution(%)		
Feature with classes	All	Male	Female
Known high blood pressure in the past			
Controlled with medication	60.6	55.0	72.5
No high blood pressure in the past	35.0	40.4	23.5
Uncontrolled	4.4	4.6	3.9
Known diabetes in the past			
No diabetes in the past	62.3	65.7	54.9
Regulated with medication	21.4	21.3	21.6
Regulated with insulin	13.2	11.1	17.6
Regulated with diet	3.1	1.9	5.9
Diabetes mellitus in the family			
No	82.9	84.3	80.0
Yes	17.1	15.7	20.0
Known heart disease in the past			
No heart disease	80.6	79.8	82.4
CAD (Coronary artery disease)	19.4	20.2	17.6
Known other chronic disease			
No chronic disease	93.8	95.5	90.0
Hyper / Hypothyreosis	2.5	0.9	6.0
Chronic lung disease	1.9	0.9	4.0
Chronic kidney disease	1.9	2.7	0.1
Alcohol consumption			
No	94.3	91.7	100.0
Recommended quantity	5.7	8.3	0.0
Smoking			
Current smoker	45.9	56.0	24.0
Nonsmoker	45.9	34.9	70.0
Former smoker	8.2	9.2	6.0
Daily physical activity			
Occasionally (about 3 hours/week)	38.4	44.0	26.0
Regularly (more than 3 hours/week)	32.7	41.3	14.0
None (less than 3 hours/week)	28.9	14.7	60.0
BETA Blockers			
No	67.7	64.5	74.5
Yes	32.3	35.5	25.5
Calcium Channel blockers			
No	98.8	99.1	98.0
Yes	1.2	0.9	2.0
Antiarrhythmics class 1-3			
No	99.4	100.0	98.0
Yes	0.6	0.0	2.0
AKE inhibitors/ARB			
Yes	83.2	83.6	82.4
No	16.8	16.4	17.6
Diuretics			
No	80.1	75.5	90.2
Yes	19.9	24.5	9.8
Antiagregation medications			
Yes	90.7	92.7	86.3
No	9.3	7.3	13.7
Anticoagulants medications			
No	98.1	97.3	100.0
Yes	1.9	2.7	0.0
Statins			
Yes	90.1	92.7	84.3
No	9.9	7.3	15.7

This solidifies our findings about the lack of strong correlation between diabetes and cholesterol without splitting the data set. After the division, one coefficient and it's p-value stand out the most and that is the HDL-C and HbA1c correlation for the female patients.

Table VII contains thresholds for the cholesterol variables for specific scenarios where we can decide if the patient has or does not have diabetes and the corresponding certainty of

TABLE IV
DISTRIBUTION OF CONTINUOUS CHOLESTEROL AND GLUCOSE VARIABLES OF THE PROPRIETARY DATASET (INNOVATION DOOEL)

			mean ± std		
Abbreviatoin	Feature	Unit of measurement	All	Men	Women
Chol	Total Cholesterol	mmol/L	5.21 ± 1.23	5.16 ± 1.30	5.33 ±1.07
TG	Triglycerides	mmol/L	1.96 ± 1.23	1.98 ±1.25	1.91 ±1.20
LDL-C	Low-Density Lipoprotein	mmol/L	3.06 ± 1.11	3.03 ± 1.16	3.12 ± 1.02
HDL-C	High-Density Lipoprotein	mmol/L	1.20 ± 0.35	1.15 ±0.34	1.33 ± 0.36
HbA1c	Glycated Hemoglobin	%	6.85 ± 1.59	6.82 ± 1.74	6.93 ± 1.18

TABLE V
DISTRIBUTION OF GLUCOSE REGULATION CLASSES OF THE PROPRIETARY DATASET (INNOVATION DOOEL)

			Distribution(%)		
ID	class	HbA1c(%)	All	Male	Female
W	Well regulation	≤ 6.4	52.8	56.4	45.1
B	Bad regulation	> 6.4	47.2	43.6	54.9

TABLE VI
PEARSON AND SPEARMAN CORRELATION COEFFICIENTS BETWEEN THE LIPID PROFILE AND HBA1C

feature1	feature2	Pearson c.	p-value	Spearman c.	p-value
All					
Chol	HbA1c	-0.264	0.002	-0.225	0.009
LDL-C	HbA1c	-0.297	<0.001	-0.271	0.002
HDL-C	HbA1c	-0.280	0.001	-0.225	0.009
TG	HbA1c	0.178	0.03	0.116	0.18
Men					
Chol	HbA1c	-0.27	0.009	-0.23	0.027
LDL-C	HbA1c	-0.33	0.002	-0.31	0.003
HDL-C	HbA1c	-0.23	0.024	-0.16	0.112
TG	HbA1c	0.19	0.07	0.08	0.458
Women					
Chol	HbA1c	-0.24	0.14	-0.21	0.206
LDL-C	HbA1c	-0.17	0.31	-0.07	0.704
HDL-C	HbA1c	-0.52	0.001	-0.55	0.001
TG	HbA1c	0.16	0.328	0.2	0.226

TABLE VII
THRESHOLDS FOR SIGNIFICANT CORRELATIONS BETWEEN LIPID PROFILE AND GLUCOSE REGULATION IN DIFFERENT SCENARIOS

Feature	Class	Condition	Outcome	Certainty(%)
Men				
All	All	LDL-C $\geq$ 4.1	No Diabetes	89
High blood pressure	No	LDL-C $\geq$ 4	No Diabetes	99
BETA Blockers	Yes	LDL-C $\geq$ 3.8	No Diabetes	99
BETA Blockers	Yes	Chol $\geq$ 5.5	No Diabetes	85
High blood pressure	No	Chol $\geq$ 5.5	No Diabetes	90
Women				
All	All	HDL-C $\geq$ 1.6	No Diabetes	88
AKE /ARB inhibitors	Yes	HDL-C $\geq$ 1.5	No Diabetes	90
Diabetes in family	No	LDL-C $\geq$ 3.3	No Diabetes	82
Diabetes in family	No	Chol $\geq$ 5.5	No Diabetes	76

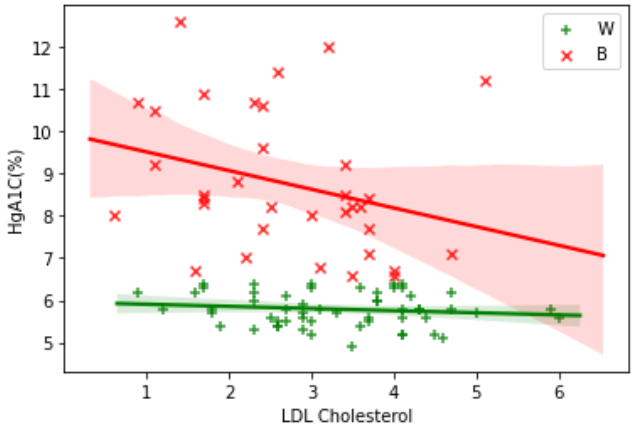

Fig. 1. Scatter Plot for LDL-C and HbA1c for male patients

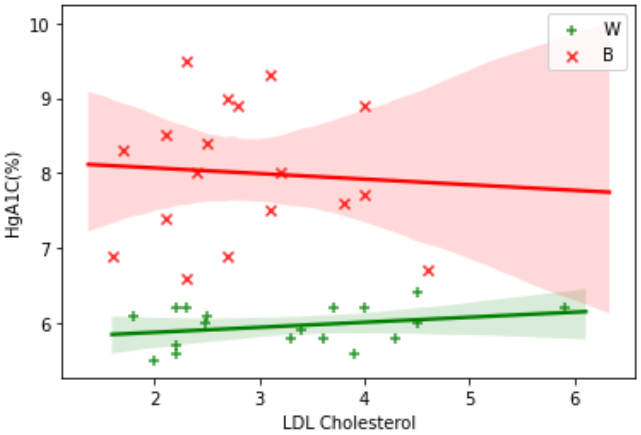

Fig. 2. Scatter Plot for LDL-C and HbA1c for female patients

the conclusion based on our data.

V. DISCUSSION

A. Pearson and Spearman rank coefficient

The Pearson and Spearman rank coefficients separated the HDL cholesterol in women as a strong stand-alone correlation with high statistical significance.

B. Thresholds for inferring

Since many factors could influence the glucose regulation classes alongside the lipid profile, we analyzed the correlations and possibilities for inference of positive or negative outcome for the glucose regulation classes (Well or Bad).

Table VII presents the outcomes of setting this threshold. The results (thresholds) were calculated from the percentage of the Well regulation and Bad regulation classes correspondingly and the scatter plots of HbA1c and the cholesterol variables were used to initially place the threshold and then move it around to find the best one.

Figure 1 and Figure 2 present the plots and express the differences in correlation between the male and female patients pointing the different gender behavior of lipid profile and glucose regulation.

C. Comparison to other research

Our findings overlapped in the correlation results regarding the Triglycerides which were positively correlated and HDL-C levels which were negatively correlated with glucose regulation and worse cases of diabetes.

There was a clash in the results when correlating Total Cholesterol and LDL-C levels, which we found to get lower with worse diabetes and glucose regulation classes, instead of elevated as the other papers revealed. This could be the result of some confounding factors in the data that we worked with.

VI. Conclusion

We have conducted a clinical research study on 161 patients in order to analyze if the glucose regulation is correlated to the lipid profile of the patient, knowing that the same autonomous nervous system is responsible for them.

Analyzing the correlations between the lipid profile and glucose regulation in patients led to different results when the analysis was done separately on men and women. Thus, better predictions and insights can be made dependent on gender.

The research results show that there are no strong stand-alone correlation when analyzing all data, but when the data was segmented in male and female records.

However, a strong negative linear (r=-0.52, p=0.001) and non-linear (r=-0.55, p=0.001) correlation was found for the HDL-C and glucose levels in female patients, while in men, statistically significant negative correlations with HbA1c were assessed for Chol (r=-0.27, p=0.009) and LDL-C (r=-0.33, p=0.002).

These findings motivate us to continue the research towards a deeper explanation about different correlations between lipid profile and glucose regulation level for men and women.

References

[1] Innovation Dooel, "Glyco project - measure ECG and glucose levels with a small, non-invasive, wearable monitor," 2019, project partially funded by Fund of Innovations and Technical Development, North Macedonia. [Online]. Available: http://glyco.innovation.com.mk/

[2] S. Calanna, R. Scicali, A. Di Pino, F. Knop, S. Piro, A. Rabuazzo, and F. Purrello, "Lipid and liver abnormalities in haemoglobin a1c-defined prediabetes and type 2 diabetes," *Nutrition, Metabolism and Cardiovascular Diseases*, vol. 24, no. 6, pp. 670–676, 2014.

[3] M. M. Prado, T. Carrizo, A. V. Abregú, and T. Meroño, "Non-hdl-cholesterol and c-reactive protein in children and adolescents with type 1 diabetes," *Journal of Pediatric Endocrinology and Metabolism*, vol. 30, no. 3, pp. 285–288, 2017.

[4] S.-H. Kim, I.-A. Jung, Y. J. Jeon, W. K. Cho, K. S. Cho, S. H. Park, M. H. Jung, and B. K. Suh, "Serum lipid profiles and glycemic control in adolescents and young adults with type 1 diabetes mellitus," *Annals of pediatric endocrinology & metabolism*, vol. 19, no. 4, p. 191, 2014.

[5] H. Drexel, S. Aczel, T. Marte, W. Benzer, P. Langer, W. Moll, and C. H. Saely, "Is atherosclerosis in diabetes and impaired fasting glucose driven by elevated ldl cholesterol or by decreased hdl cholesterol?" *Diabetes care*, vol. 28, no. 1, pp. 101–107, 2005.

[6] S. REDDY, S. Meera, E. WILLIAM, and J. Kumar, "Correlation between glycemic control and lipid profile in type 2 diabetic patients: Hba1c as an indirect indicator of dyslipidemia," *Age*, vol. 53, pp. 10–50, 2014.

[7] J.-B. Chang, N.-F. Chu, J.-T. Syu, A.-T. Hsieh, and Y.-R. Hung, "Advanced glycation end products (ages) in relation to atherosclerotic lipid profiles in middle-aged and elderly diabetic patients," *Lipids in health and disease*, vol. 10, no. 1, p. 228, 2011.

[8] A. Hussain, I. Ali, M. Ijaz, and A. Rahim, "Correlation between hemoglobin a1c and serum lipid profile in afghani patients with type 2 diabetes: hemoglobin a1c prognosticates dyslipidemia," *Therapeutic advances in endocrinology and metabolism*, vol. 8, no. 4, pp. 51–57, 2017.

[9] A. Ghari Arab, M. Zahedi, V. Kazemi Nejad, A. Sanagoo, and M. Azimi, "Correlation between hemoglobin a1c and serum lipid profile in type 2 diabetic patients referred to the diabetes clinic in gorgan, iran," *Journal of Clinical and Basic Research*, vol. 2, no. 1, pp. 26–31, 2018.

[10] M. M. Eftekharian, J. Karimi, M. Safe, A. Sadeghian, S. Borzooei, and E. Siahpoushi, "Investigation of the correlation between some immune system and biochemical indicators in patients with type 2 diabetes," *Human antibodies*, vol. 24, no. 1-2, pp. 25–31, 2016.

[11] Y.-C. Hwang, H.-Y. Ahn, S.-W. Park, and C.-Y. Park, "Apolipoprotein b and non-hdl cholesterol are more powerful predictors for incident type 2 diabetes than fasting glucose or glycated hemoglobin in subjects with normal glucose tolerance: a 3.3-year retrospective longitudinal study," *Acta diabetologica*, vol. 51, no. 6, pp. 941–946, 2014.

[12] H. Khan, S. Sobki, and S. Khan, "Association between glycaemic control and serum lipids profile in type 2 diabetic patients: Hba 1c predicts dyslipidaemia," *Clinical and experimental medicine*, vol. 7, no. 1, pp. 24–29, 2007.

[13] H. A. Khan, "Clinical significance of hba 1c as a marker of circulating lipids in male and female type 2 diabetic patients," *Acta diabetologica*, vol. 44, no. 4, pp. 193–200, 2007.

[14] T. Grant, Y. Soriano, P. R. Marantz, I. Nelson, E. Williams, D. Ramirez, J. Burg, and C. Nordin, "Community-based screening for cardiovascular disease and diabetes using hba1c," *American journal of preventive medicine*, vol. 26, no. 4, pp. 271–275, 2004.

[15] M. F. Lopes-Virella, H. J. Wohltmann, R. K. Mayfield, C. Loadholt, and J. A. Colwell, "Effect of metabolic control on lipid, lipoprotein, and apolipoprotein levels in 55 insulin-dependent diabetic patients: a longitudinal study," *Diabetes*, vol. 32, no. 1, pp. 20–25, 1983.

[16] Y. Hu, W. Liu, R. Huang, and X. Zhang, "Postchallenge plasma glucose excursions, carotid intima-media thickness, and risk factors for atherosclerosis in chinese population with type 2 diabetes," *Atherosclerosis*, vol. 210, no. 1, pp. 302–306, 2010.