

Prevalence of Type 2 Diabetes and Cardiometabolic Risk Parameters in Evros

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ABSTRACT

Introduction: The aim of this study was to estimate the prevalence of Type 2 Diabetes and related metabolic disorders in the Evros region.

Material-Methods: A random sample of 541 people was studied using the Finnish Type 2 Diabetes Risk Score, and measurement of weight, height, waist and hip circumference, blood pressure, as well as Fasting Glucose and Postprandial Glucose with a reflectometer. The participants with a score of 15-20, score ≥ 20 , FG ≥ 100 mg/dl and / or PG 140 mg/dl (n = 206) were subjected to a oral glucose tolerance test, according to WHO. Lipid profile, metabolic syndrome and cardiovascular risk were also assessed.

Results: Prevalence of DM T2 in the study population was: 29.6%, and that of prediabetes was 10.9%. Obese (Body Mass Index ≥ 30 kg/m²) were: 52.5%, overweight (BMI 25-30kg/m²) were 33.2% and normal/low weight (BMI <25 kg/m²) were 14.1% of the population. Central obesity with a waist circumference of ≥ 102 cm had 58,6% of men and ≥ 88 cm 86,8% of women. Hypertension was 66.9% of the sample and 58.8% were on antihypertensive treatment. In 206 subjects, CHOL 200-239 mg/dl had 32.5% and CHOL ≥ 240 mg/dl 13.6%. 10.2% of women had HDL - CHOL <45 and <35:3,4 % of men. 5,9 % of subjects had LDL - CHOL ≥ 160 mg/dl. 18% of subjects had TG: 200 - 499 mg/dl and TG ≥ 500 mg/dl:1.5%. High index Apo-B / Apo-A1 had 19.4% and Lp (a) 33% of individuals. 92.2% of these people had metabolic syndrome.

Conclusions: The upward trend of DM T2 and cardiometabolic risk parameters raises the need for targeted prevention and treatment policies.

KEY WORDS: Prevalence, DM Type 2, metabolic disorders, cardiometabolic risk

INTRODUCTION

The increase in the prevalence of Type 2 Diabetes (DM T2) and related metabolic disorders is a major public health

problem. Although epidemiological studies in Greece differ with regard to methodology self-reporting of known DM T2 or data recording from medical notes vs blood glucose measurements and Oral Glucose Tolerance Test (OGTT), there is an increase in the prevalence of DM T2 in the Greek population as well as globally, with a parallel increase in the prevalence of obesity and the Metabolic Syndrome (MetS), due to the current lifestyle¹⁻⁴.

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The aim of the present study was to estimate the prevalence of DM T2 and cardiometabolic risk parameters in the rural population of Evros, using combined methodology. The reason for choosing the area of Evros was because there were available data from previous studies in the region⁵.

MATERIAL – METHODS

Population study: A random sample of 541 people, 239 men and 302 women, aged ≥ 18 years, mean age $64,1 \pm 8,0$ years) from the villages (Loutra, Antheia, Areistino, Doriko and Nipsa) of the Evros area was studied, in the year 2015-2016.

Methodology: The participants completed a questionnaire (Finnish Type 2 Diabetes Risk Score, FINDRISK) with questions related to the diagnosis of DM T2 and disease expression factors giving the participants points and overall score⁶. Weight, height, waist-hip circumference, blood pressure, Fasting Glucose (FG) and Postprandial Glucose (PG) with reflectometer were recorded. The self-report of the disease with DM T2 was considered known DM T2. These individuals were not subjected to laboratory examination. The individuals, according to the total score, were classified into 5 DM T2 risk levels (Low: score < 7 , Fairly low: score 7 - 11, Medium: score 12 - 14, High: score 15-20, Very high level: score ≥ 20).

Study criteria: The individuals with a score of 15-20 and score ≥ 20 and in individuals with FG $\geq 100 - 125$ mg/dl and / or PG > 140 mg/dl underwent further investigation with an OGTT after overnight fasting between 8.0-9.0 a.m. according to WHO criteria⁷, for the diagnosis of unknown DM T2 and Prediabetes (Impaired Glucose Tolerance - IGT and Impaired Fasting Glucose - IFG).

Of the total sample, 139 people (25.7%) stated that they had DM T2. Of the remaining 402, 214 met the study criteria, of which 206 people (90 men and 116 women) came for laboratory testing (OGTT). Also, in these individuals a test was performed for the lipid profile (Cholesterol - CHOL, HDL-CHOL, LDL - CHOL and Triglycerides, TG), measurement of apolipoproteins Apo-B and Apo-A1 and Lp (a). The prevalence of MetS and cardiovascular risk were also calculated based on the atherosclerotic index Apo-B / Apo - A1 and Lp (a)⁸⁻⁹. The laboratory test was performed using their social security number at the University General Hospital of Alexandroupolis.

Bioethics: The study protocol was approved by the University of Ioannina as part of the thesis of S. Ventouri, under the supervision of Prof. A. Tsatsoulis, and all the participants in the study gave their written consent.

Statistical analysis: The analysis of the data was performed with Superior Performance Software System (SPSS) version 21, using descriptive statistics.

RESULTS

Demographic Data: The demographic data of the population study, as well as of the selective sample of the study are shown in Table 1 and Table 2.

Prevalence of DM: The prevalence of DM T2 in the study population (n = 541) was 29.6% (known DM T2: 25.7% + unknown DM T2: 3.9%) and that of Prediabetes was 10.9 % (Table 1). The prevalence of DM T2 was 13.3% in men and 16.3% among women.

Cardiometabolic risk parameters: The analysis of the cardio-metabolic risk parameters (Table 1) showed;

a) Obesity: 52.5% of people were obese with Body Mass Index (BMI) ≥ 30 kg/m², 33.2% were overweight

TABLE 1. Demographic data and prevalence of DM 2 and cardiometabolic parameters in the study population

Sex	Number	%
Male	239	44,2
Female	302	55,8
Total	541	100
Age	541	64,1 \pm 8,0 years
Type 2 Diabetes	160	29,6
Known DM T2	139	25,7
Unknown DM T2	21	3,9
Prediabetes	59	10,9
IGT +IFG	(31+28)	
Obesity	284	52,5
BMI ≥ 30 kg/m ²	(130+154)	M: 54,4 F:51
Overweight	180	33,3
BMI 25-30 kg/m ²	(78+102)	M:32,6 F:33,8
Normal / underweight	77	14,2
BMI < 25 kg/m ²	(31+46)	M:13 F:15,2
Waist circumference		
Male ≥ 102 cm	140	58,6
Female ≥ 88 cm	262	86,8
Waist -to- Hip Ratio		
Male WHR $\geq 1,0$	121	50,6
Female WHR $\geq 0,90$	220	72,8
Hypertension	362	66,9
SBP ≥ 140 mm Hg		
DBP ≥ 90 mm Hg		
Known Hypertension	318	58,8
(on antihypertensive treatment)		
Unknown Hypertension	44	8,1

DM T2: Type 2 Diabetes; IGT: Impaired Glucose Tolerance; IFG: Impaired Fasting Glucose; BMI: Body Mass Index; WHR: Waist -to- Hip Ratio; M: Male; F: Female; SBP: Systolic Blood Pressure; DBP: Diastolic Blood Pressure.

TABLE 2. Population with laboratory examination for Lipid profile and cardiometabolic risk indicators

	n=206	Values N (%) or mean ± SD
Sex		
Male	88	42,7
Female	118	57,3
Total	206	100
Age		
	206	62,5 ± 10,5
Lipid profile		
CHOL ≥ 240 mg/dl	28	13,6
CHOL 200-239 mg/dl	67	32,5
CHOL < 200 mg/dl	111	53,9
HDL-CHOL < 40 mg/dl	23	11,2
HDL-CHOL 40-59 mg/dl	119	57,8
HDL-CHOL ≥ 60 mg/dl	64	31
Male HDL-CHOL < 35 mg/dl	3	3,4
Male HDL-CHOL ≥ 35 mg/dl	85	96,6
Female HDL-CHOL < 45 mg/dl	12	10,2
Female HDL-CHOL ≥ 45 mg/dl	106	89,8
LDL-CHOL ≥ 190 mg/dl	3	1,5
LDL-CHOL 160-189 mg/dl	9	4,4
LDL-CHOL 130-159 mg/dl	48	23,4
LDL-CHOL 100-129 mg/dl	74	36,1
LDL-CHOL < 100 mg/dl	71	34,6
TG ≥ 500 mg/dl	3	1,5
TG 200-499 mg/dl	37	18
TG 150-199 mg/dl	34	16,5
TG < 150 mg/dl	132	64,1
Cardiovascular markers		
Lp (a) > 30 mg/dl	68	33
Lp (a) 0-30 mg/dl	138	67
Apo- B/ Apo – A1 ratio Total	40	19,4
Apo- B/ Apo – A1 ratio Male > 1,0	19	21,6 of male
Apo- B/ Apo – A1 ratio Female > 0,90	21	17,8 of female

CHOL: Total Cholesterol; HDL-CHOL: high density lipoprotein-cholesterol; LDL-CHOL: low density lipoprotein-cholesterol; TG: Triglycerides; Apo-A: Apolipoprotein A1; Apo-B: Apolipoprotein B; and Lp (a): Apolipoprotein Lp (a).

with BMI 25-30 kg/m², while normal/underweight with BMI <25kg/m² were 14.1%.

b) Central Obesity: 86.8% of women and 58.6% of men had central obesity with waist circumference values ≥ 88

cm and 102 cm respectively. For WHR (Waist / Hip Ratio) values ≥ 1.0: 50.6% of men and for WHR ≥0.90: 72.8% of women had a central distribution of fat tissue.

c) Hypertension: 66.9% of the sample had hypertension with 58.8% on antihypertensive treatment.

d) Lipid profile: In the selected sample of 206 individuals, with CHOL values 200 - 239 mg/dl were 32.5% of individuals and 13.6% with CHOL values ≥ 240 mg/dl. 42.7% of men with HDL - CHOL values <35 and 10.2% of women with HDL - CHOL values <45. At LDL-CHOL levels 130-159 mg/dl were 23.7% of women and 1.5% at LDL-CHOL levels ≥190mg/dl. A total of 19.5% of individuals were found to have hypertriglyceridemia (18% with TG values: 200 - 499 mg/dl and 1.5% with severe hypertriglyceridemia: TG ≥ 500 mg / dl) (Table 2).

e) Metabolic Syndrome: The highest prevalence of MetS (92.2%) was found using the criteria of A. A.C.E 2002, and there was 100% correlation between the diagnosis of MetS and the diagnosis of unknown DM T2 and 90.3% with a diagnosis of IGT Table 3-4, and

z) Cardiovascular risk: 52.43% were found to be at a high risk level, based on the atherosclerotic index Apo-B / Apo -A1: 19.43% and based on the values of Lp (a):33 % (Table.2).

DISCUSSION

The present study is the most recent attempt to record the prevalence of DM T2 and the cardiometabolic risk parameters in the Greek population. The results confirm the raising trend in the prevalence of DM T2 as well as of obesity and the related metabolic disturbances that characterize the MetS and, also, are in agreement with the predictions of IDF for the rapid increase in the incidence of DM T2 worldwide¹⁻⁴.

The studies for the prevalence of DM T2 in Greece, belong to two different categories: a) self - reporting, in which an individual answers the question whether he/she is suffering from DM, or medical record reviewing, and b) blood glucose measurement and the performance of OGTT. It is obvious that the studies of the second category are more sensitive, revealing cases of undiagnosed DM and Prediabetes, and the estimated prevalence is expected to be higher¹.

The so far studies show the increasing trend in the prevalence of DM in the Greek population. Thus, in the region of Attica, the prevalence increased from 2.4% in the year 1974 to 9.5% (studies of self reporting) or to 11.6% (massments of blood glucose and OGTT) in the year 2006¹⁰⁻¹¹. Regarding the rural population, where prevalence was low (1.5%) during 1988-1993 there was a dramatic increase to 11.7% during 2003-2005, so it became similar to urban population¹²⁻¹³. This change is similar to

TABLE 3. Population with MetS according to AACE 2002 criteria

Criteria MetS AACE 2002	n= 206		Values N (%)
	Male	Female	
BMI \geq 25 Kgr/m ²	81	114	94,7
And of these people who meet \geq 2 factors from the following:	78	112	92,2
Waist circumference	\geq 102cm	\geq 88 cm	
SBP	\geq 130 mm Hg	\geq 130 mm Hg	
DBP	\geq 85 mm Hg	\geq 85 mm Hg	
	Antihypertensive treatment	Antihypertensive treatment	
TG	\geq 150 mg/dl	\geq 150 mg/dl	
HDL-CHOL	\leq 40mg/dl	\leq 50 mg/dl	
IFG	\geq 100 mg/dl	\geq 100 mg/dl	

BMI: Body Mass Index; TG: Triglycerides; SBP: Systolic Blood Pressure; DBP: Diastolic Blood Pressure; HDL-CHOL: high density lipoprotein-cholesterol; IFG: Impaired Fasting Glucose.

TABLE 4. Recognition of DMT2 and IGT cases based on MetS criteria

Criteria	n= 19*		n=31	
	MD T2	Values N (%)	IGT	Values N (%)
MetS WHO 1999	17	89,5	22	71
MetS NCEP III 2001	13	68,4	15	48,4
MetS NCEP-R 2004	14	73,7	17	54,8
MetS AACE 2002	19	100	28	90,3
MetS IDF 2006	14	73,7	18	58

*plus 2 people with random IFG \geq 200mg/dl measurement with typical symptoms of hyperglycemia.

DM T2: Type 2 Diabetes; IGT: Impaired Glucose Tolerance; mets: Metabolic Syndrome; WHO: World Health Organization; NCEP III: National Cholesterol Education Program 2001; NCEP-R: American Heart Association National Heart, Lung, and Blood Institute 2004; AACE: American Association of Clinical Endocrinologists 2002; IDF: International Diabetes Federation 2006.

the rising trend worldwide, and the cause of this increase is the change in the lifestyle, with a consequent decrease in physical activity, junk food and obesity³.

The present study followed combined methodology: self-reporting of DM in the study population and measurement of blood glucose and OGTT in the selected sample of people after the use of the FINDRISK questionnaire⁶. The FINDRISK has been evaluated and used as a tool for the detection of people with an increased risk of developing DM and MetS¹⁴.

The data of the present study revealed that during the years 2015-2016, the prevalence of DM T2 in the rural population in the region of Evros has increased considerably at the level of 29.6%. A similar increase has been noted in all the cardio metabolic risk parameters, as in obesity and especially

in central obesity, in hypertension and in dyslipidemia.

In compassion with the data provided by papazoglou et al⁵ in the year 1993, when the prevalence of DM T2 in the prefecture of Evros was 1.6 % (study of reviewing data from medical notes and records of local pharmacies) a rapid increase in the incidence of DM has been observed within two decades. Although the two studies differ regarding the methodology, it is obvious that the increase should be attributed to the changes in the socio economic conditions over the last decades in Greece with the consequent dramatic changes in the lifestyle of the inhabitants of rural Greek villages. Another parameter that should be considered is the changes in the population synthesis in the Greek rural areas with the greater proportion belonging to the aging population.

A limitation of the present study, that should be considered, is the relatively small number of the initial population study, and consequently the small number of the selective sample of people in response to FINDRISK questionnaire, who underwent the laboratory investigation for the detection of undiagnosed DM and Prediabetes, as well as for the measurement of the lipid profile and detection of the prevalence of the MetS.

Obviously the selective sample is, by definition, sample with increased risk for developing metabolic disorders. This also explains the rather high prevalence of the MetS in the present study.

In conclusion, the present study represents the most recent attempt for the detection of the prevalence of DM T2 in the rural population of Evros, and shows the rapid increase of the disease and the related cardiometabolic risk parameters to epidemic laves. As a consequence, measures should be taken to prevent this epidemic that should be aiming in changing the lifestyle of the Greek population.

ΠΕΡΙΛΗΨΗ

Επιπολασμός Σακχαρώδη Διαβήτη Τύπου 2 και παραμέτρων Καρδιομεταβολικού Κινδύνου στον Έβρο

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Εισαγωγή: Σκοπός της παρούσης μελέτης ήταν η εκτίμηση του επιπολασμού του Σακχαρώδη Διαβήτη Τύπου 2 (Σ.Δ. Τ2) και των συναφών μεταβολικών διαταραχών σε αγροτικό πληθυσμό της περιοχής του Έβρου.

Υλικό-Μέθοδοι: Σε τυχαίο δείγμα 541 ατόμων μελετήθηκε με τη χρήση του ερωτηματολογίου Finnish Type 2 Diabetes Risk Score, την μέτρηση του βάρους σώματος, ύψους, περιμέτρου μέσης - ισχίων, αρτηριακής πίεσης καθώς και Γλυκόζης Νηστείας (Γ.Ν) και Μεταγευματικής Γλυκόζης (Μ.Γ) με ανακλασίμετρο. Οι συμμετέχοντες με score 15-20, score ≥ 20, Γ.Ν ≥ 100 mg/dl ή/και Μ.Γ ≥ 140 mg/dl (n=206) υποβλήθηκαν σε δοκιμασία καμπύλης σακχάρου, σύμφωνα με τον Π.Ο.Υ. Εκτιμήθηκαν λιπιδαιμικό προφίλ, μεταβολικό σύνδρομο και καρδιαγγειακός κίνδυνος.

Αποτελέσματα: Στον πληθυσμό της μελέτης 29,6% των ατόμων είχαν ΣΔ Τ2 και 10,9% είχαν Προδιαβήτη. Παχυσαρκία: Δείκτη Μάζας Σώματος (Δ.Μ.Σ) ≥ 30kg/m² είχε το 52,5%, υπέρβαρο: Δ.Μ.Σ 25-30kg/m² ήταν 3,3% και φυσιολογικά/λιποβαρή: Δ.Μ.Σ < 25kg/m² ήταν 14,2% των ατόμων. Κεντρική παχυσαρκία: περιφέρεια μέσης ≥ 102cm είχε το 58,6% των ανδρών και 88cm το 86,8% των γυναικών. Υπέρταση 66,9% του δείγματος και 58,8% ήταν υπό αντι-υπερτασική αγωγή. Στο επιλεγμένο δείγμα 206 ατόμων, CHOL 200 – 239 mg/dl είχε το 32,5% και CHOL ≥ 240 mg/dl το 13,6%. Το 10,2 % των γυναικών είχε HDL – CHOL < 45 και < 35 το 3,4% των ανδρών. Το 5,9 % είχε LDL – CHOL ≥ 160 mg/dl. Το 18% είχε TG: 200 - 499 mg/dl και TG ≥ 500 mg/dl: 1,5%. Υψηλό δείκτη Apo-B/Apo – A1 είχε 19,4% και Lp (a) 33%. Μεταβολικό σύνδρομο είχε το 92,2%.

Συμπεράσματα: Η αυξητική τάση του Σ.Δ. Τ2 και των παραμέτρων καρδιομεταβολικού κινδύνου θέτει την ανάγκη στοχευμένων πολιτικών πρόληψης και θεραπείας για την ελληνική επικράτεια.

ΛΕΞΕΙΣ ΚΛΕΙΔΙΑ: Επιπολασμός, Σακχαρώδης Διαβήτη Τύπου 2, Μεταβολικές διαταραχές, καρδιομεταβολικός κίνδυνος

REFERENCES

1. Loupa C, Kalantzi S, Maris A. Trends in epidemiology of Diabetes Mellitus in Greece. Review of epidemiological studies. Clin Case Rep Rev. 2017;3(10):1-4. Doi: 10.15761/CCRR.1000371.
2. Touloumi G, Karakosta A, Kalpourtzis N, Gavana M, Vantarakis A, Kantzanou M, et al. High prevalence of Cardiovascular risk factors in adults living in Greece: The EMENO National Health Examination Survey. BMC Public Health [Internet]. 2020 Nov [2021 Aug 27];1665. Available from: <https://bmcpubhealth.biomedcentral.com/articles/10.1186/s12889-020-09757-4>.
3. Anagnostis P. Metabolic syndrome in the Mediterranean region: Current status. Indian J Endocrinol Metab. 2012 Jan-Feb;16(1):72-80.
4. International Diabetes Federation. Global Burden: Prevalence and Projections 2011 and 2030. 2011 [2015 Apr 27]. Available from: <http://www.diabetesatlas.org/content/diabetes-and-impaired-glucose-tolerance>.
5. Papazoglou N, Manes C, Soulis G, Kirtzis I, Christakidis D, Nikolaidis I, et al. Epidemiology of Diabetes in Greece. II Evros County, (9 article in Greek). Hellenic Dialectological Chronicle. 1993;6:134-140.
6. Lindstrom J, Tuomilehto J. The diabetes risk score: A practice tool to predict type 2 diabetes risk. Diabetes Care. 2003 Mar;26(3):725-31.
7. Report of World Health Organization and International Diabetes Federation meeting. Screening for Type 2 Diabetes. 2003. [2015 Apr 27]. Available from: <https://apps.who.int/iris/handle/10665/68614>.
8. Marcovina S, Packard CJ. Measurement and meaning of apolipoprotein AI and apolipoprotein B plasma levels. J

- Intern Med. 2006 May;259(5):437-46.
9. Walldius G, Jungner I. The apoB/Apo A-I ratio: A strong, new risk factor for cardiovascular disease and a target for lipid-lowering therapy - a review of the evidence. *J Intern Med.* 2006 May;259(5):493-519.
 10. Katsilampros N, Aliferis K, Darviris C, Tsapogas P, Alexiou Z, Tritos N, et al. Evidence for an increase in the prevalence of known Diabetes in a sample of an urban population in Greece. *Diabetic Medicine [Internet].* 1993 Jan-Feb [2014 Apr 27];10:87-90. Available from: <https://doi.org/10.1111/j.1464-5491.1993.tb02002.x>
 11. Panagiotakos DB, Pitsavos C, Chrysohoou C, Skoumas I, Stefanadis C. Prevalence and five-year incidence (2001-2006) of cardiovascular disease risk factors in a Greek Sample: the ATTICA study. *Hellenic J Cardiol.* Sep-Oct 2009;50(5):388-95.
 12. Gikas A, Sotiropoulos A, Panagiotakos DB, Pastromas V, Paraskeyopoulou E, Skliros E, et al. Rising prevalence of diabetes among Greek adults: findings from two consecutive surveys in the same target population. *Diabetes Res Clin Pract.* 2008 Feb;79(2):325-9.
 13. Melidomis A, Tournis S, Kompoti MG, Lentzas I, Roussou VR, Iraklianos SL, et al. Increased prevalence of Diabetes mellitus in a rural Greek population. *Rural Remote Health.* 2006 Jan-Mar;6(1):534.
 14. Makrilakis S, Liatis S, Grammatikou S, Perrea D, Stathi C, Tsiligros P, et al. Validation of the Finish Diabetes Risk Score (FINDRISK) questionnaire for screening for undiagnosed type 2 Diabetes, dysglycaemia and the Metabolic Syndrome in Greece. *Diabetes Metab.* 2011 Apr;37(2):144-51.