

## INCREASED PREVALENCE OF *IMPAIRED GLUCOSE TOLERANCE* IN A REPRESENTATIVE RURAL POPULATION FROM DELENI, ROMANIA

DANA STEFANA POPESCU<sup>1,2</sup>, ALIN CIOBICA<sup>3,4</sup>, LIDIA IULIANA ARHIRE<sup>1</sup>, LAURA MIHALACHE<sup>1</sup>, OTILIA NITA<sup>1</sup>, IONELA LACRAMIOARA SERBAN<sup>1\*</sup>, ROMEO DOBRIN<sup>1</sup>, DIDONA UNGUREANU<sup>1</sup> and MARIANA GRAUR<sup>1</sup>

<sup>1</sup>"Grigore T. Popa" University of Medicine and Pharmacy, 700115, Iași, Romania

<sup>2</sup>Medical Center Deleni, Romania

<sup>3</sup>"Alexandru Ioan Cuza" University, Iași, 700506, Romania

<sup>4</sup>Center of Biomedical Research of the Romanian Academy, Iași Branch, Iași, 700506 Romania

**Abstract** - The aim of this study was to determine the frequency of impaired glucose tolerance (IGT) in a cross-section of the adult rural population of the village Deleni in northeast Romania. We observed a IGT in 25.9% and diabetes in 14.55% of the general population, and only 60% of randomly selected subjects with a normal glucose tolerance. With regards to gender, we observed slightly higher values in female patients (28.3% with IGT, 17.3% with diabetes), as compared to 10.47% with diabetes and 20.95% with IGT in males. Our report reveals a high prevalence of diabetes and IGT among the rural population of Deleni, Romania. Therefore, there is an urgent need for an increased awareness of diabetes and for an energetic intervention against diabetes and similar lifestyle-related diseases in the rural areas of Romania.

**Key words:** impaired glucose tolerance; rural population; diabetes; 75-g oral glucose load.

### INTRODUCTION

The so-called "westernization" of lifestyle, which implies a high-fat, high-caloric diet and decreased physical activity, often promotes metabolic dysfunction, such as obesity and diabetes in the general population (Vienberg et al., 2012; Brøns et al., 2009; Westerbäck et al., 2005; O'Dea et al., 1988). Although it is generally believed that rural populations tend to have a lower prevalence of type 2 diabetes (Raghupathy et al., 2007; Ramachandran et al., 1997), it is estimated that by 2030, more than 75% of the world's 366 million adults with diabetes will live in developing areas (Wild et al., 2004; Raghupathy et al., 2010). Recent evidence points to an increase in diabetes is even

in rural areas, and that the pre-diabetic condition which is characterized by IGT, occurs as frequently as in urban populations. This presents a worrying scenario in rural and small-town populations, which will probably result in an even higher burden of the disease in the future (Raghupathy et al., 2007; Jørgensen et al., 2012).

IGT can be studied using a 75 g oral glucose tolerance test. In healthy individuals, after the administration of a high concentration of glucose, the insulin response appears rapidly and reaches a minimum after 30-60 min. Thus, when there is a sufficient amount of insulin to metabolize the administered glucose at the beginning of the test, normalized concentration of

glucose appears in about 3 h (Barth et al., 2001). However, the release of an insufficient quantity of insulin and peripheral insulin resistance will result in a significant increase in glycemia (Fischbach et al., 2009).

Considering that there are very few reports published regarding the prevalence of diabetes, and especially IGT, in rural populations, the aim of this study was to determine the frequency of these metabolic dysfunctions in a cross-section of the adult population from the village of Deleni, an area that was previously defined as stable and representative for our region in terms of the number of inhabitants, education, religion and ethnicity (Mihalache et al., 2010, 2012) from the northeast of Romania.

## PATIENTS AND METHODS

The subjects in this study came from the rural area of Deleni, situated in the northwest Iasi region of north-eastern Romania. A cross-section of the adult population was surveyed. In a random sample of the adult population, a total of 105 men and 156 women were included in the study. The selection was not made by the researchers and was not based on anthropometry or any other known risk factor for type 2 diabetes. The sole criterion was to sample a representative age distribution above 18 years.

### *Preparation of the patients*

Intake of food was accepted at least 8 h and no more than 16 h before testing. Small quantities of water ingestion were allowed and a normal diet was required in the last 72 h before the test. Use of alcohol was not allowed (Fischbach et al., 2009), and neither were smoking or physical exertion during the test (Barth et al., 2001).

A fasting blood sample was taken, after which the subjects drank 75 g of glucose dissolved in 300 ml of water. Subsequent blood samples were collected 1 and 2 h afterwards.

Impaired glucose tolerance (IGT) was defined as glycemia between 140-200 mg/dL (7.8-11.1 mmol/L)

after 2 h during the 75 g oral glucose load test. Diabetes was established when two values for fasting glucose concentration were  $\geq 126$  mg/dL (7.0 mmol/L) or when the concentration was  $\geq 200$  mg/dL ( $\geq 11.1$  mmol/L) after 120 min. Normal glucose tolerance was considered when fasting glycemia was  $< 100$  mg/dL ( $< 5.6$  mmol/L) and  $< 140$  mg/dL (7.8 mmol/L) 2 h after the 75 g oral glucose load. Additionally, a fasting glycemia of 100-125 mg/dL (5.6-6.9 mmol/L) was considered as impaired fasting glucose (IFG) (American Diabetes Association, 2010).

In addition, weight was measured in the morning before breakfast with subjects wearing light clothes. Height was measured with the subjects standing without shoes.

The study was conducted according to the provisions of the Helsinki Declaration and the local ethics committee's approval was obtained before the start of the study. All the patients signed a consent form for their participation in this study.

### *Data analysis*

The statistical analysis was performed using one-way analysis of variance (ANOVA). All results are expressed as mean  $\pm$  SEM.

## RESULTS

As mentioned, 105 men and 156 women were tested. Their age distribution and their anthropometric data relative to that of the total population tested are presented in Table 1.

We did not observe any significant differences regarding age, height, weight and BMI between the two genders analyzed, as studied through the analysis of covariance (Table 1).

We observed a prevalence of 25.9% for IGT and 14.55% for diabetes, with only 60% of our randomly selected subjects having a normal glucose tolerance in the general population (Table 2). With regards to gender, we observed slightly higher values in our

**Table 1.** Age and anthropometric data on the studied population.

	Men <sup>a</sup>	Women <sup>a</sup>	Total <sup>a</sup>	F <sup>*</sup>	P <sup>*</sup>
Population tested (n)	105	156	261	-	-
Age (years)	53.4 ± 1.06	54.2 ± 1.2	53.8 ± 1.12	0.132	0.79
Height (m)	1.613 ± 0.01	1.625 ± 0.006	1.619 ± 0.0087	0.009	0.922
Weight (kg)	74.25 ± 1.56	72.51 ± 1.32	73.6 ± 1.4	0.713	0.399
Body mass index (kg/m <sup>2</sup> )	28.59 ± 0.56	27.8 ± 0.44	28.2 ± 0.51	0.014	0.82

<sup>a</sup>- Each value represents mean and standard deviation.

\*- Analysis of covariance for men and women groups for age, height, weight and body mass index.

**Table 2.** Frequency of diabetes and impaired glucose tolerance (IGT) in a cross section of rural patients.

	Normal glucose tolerance			Impaired glucose tolerance (IGT)		Diabetes	
	N	n	%	N	%	n	%
Men	105	72	68.57	22	20.95	11	10.48
Women	156	85	54.48	44	28.2	27	17.32
Total (men +women)	261	157	60.1	66	25.9	38	14

**Table 3.** Glycemia before (fasting), and 1 and 2 h after intake of a 75 g oral glucose.

	Glycemia (mg/dL)
Men	
Fasting	103.7 ± 1.28
1 h	183.51 ± 4.55
2 h	126.59 ± 3.88
Women	
Fasting	103.54 ± 1.02
1 h	181.46 ± 3.78
2 h	125.57 ± 3.01
Total	
Fasting	103.6 ± 1.1
1 h	182.4 ± 4.1
2 h	125.1 ± 3.44

female patients (28.3% with IGT and 17.3% with diabetes), as compared to 10.47% with diabetes and 20.95% with IGT in the males (Table 2).

In Table 3 we present the mean values of glycemia for the fasting and 1 h/2 h after a 75 g oral glucose load, with a worrying level of 103.6 mg/dL in the general rural population and 182.4 mg/dL after 1 h and 125.1 mg/dL after 2 h. We did not observe

any significant differences between sexes for fasting ( $F(1,259) = 0.03$ ,  $p = 0.85$ ), as well as between 1 h ( $F(1,259) = 0.003$ ,  $p = 0.9$ ) and 2 h ( $F(1,259) = 0.001$ ,  $p = 0.8$ ) after the glucose load (Table 3).

## DISCUSSION

This cross-sectional study included 261 randomly selected adults from the village of Deleni in Ro-

mania. IGT and diabetes were diagnosed using the oral glucose tolerance test. The premises that led us to this study were the fact that people with IGT, as well as those with IFG, comprise a group of patients that present abnormal glycemic profiles, although these levels are not high enough to be considered a diagnostic criterion for diabetes. As we initially mentioned, the literature considered these patients as “pre-diabetics” (Nathan et al., 2007). However, new recommendations of the American Diabetes Association state that IGT and IFG are not separate clinical entities, but mostly risk categories for diabetes and cardiovascular diseases, considering that they are strongly associated with abdominal obesity, arterial hypertension and dyslipidemia (American Diabetes Association, 2010).

It is generally believed that increased physical activity, weight loss, as well as the administration of some pharmacological agents could prevent the developing of diabetes in IGT patients (American Diabetes Association, 2010). These aspects are extremely important to the population that we studied, considering their exposure to western influences is relatively recent. Results from previous research on a larger scale in the same population were recently published (Mihalache et al., 2013). Based only on fasting glycemia, the prevalence of diabetes was 5.2% and for 3% for IFG. Since our results were obtained using the oral glucose tolerance test, they suggest that urbanization could directly result in an increased prevalence of IGT and diabetes. Similar aspects were also reported in isolated populations that were subjected to rapid changes in their general life-style, such as the Greenland population (Jørgensen et al., 2002, 2012), Australian Aborigines from the desert (O’Dea et al., 1988), Pima Indians (Aronoff et al., 1977) and Nauruans (Balkau et al., 1985; O’Dea et al., 1988).

Our results indicate a prevalence of 25.9% for IGT and 14.55% for diabetes, with only 60% of our randomly selected subjects presenting a normal glucose tolerance. We also obtained higher values in our female patients, with 28.3% having IGT and 17.3% diabetes, compared to males where 10.47% were dia-

betics and 20.95% had IGT. Similar results for IGT and diabetes in the female population of Australian Aborigines was previously reported, with a 5% increase in the IGT prevalence under 35 years and approximate 6% for diabetes (O’Dea et al., 1988). In this way, the present study provides additional indirect evidence for the frequent occurrence of these metabolic dysfunctions in the current rural population.

We also present in this study new data regarding the one-hour glycemia after a 75 g oral glucose load, which was around 182 mg/dL in our population. Recent studies have identified that in normal glucose tolerance, arterial stiffness is advanced in subjects with higher 1 h post-challenge plasma glucose in spite of the normal range of BMI, systolic blood pressure, fasting plasma glucose and lipid variables. This indicates that a higher 1 h plasma glucose level is a risk factor for arterial stiffness in normal glucose tolerance patients (Niiijima et al., 2012).

Regarding the risk factors which could generate the aforementioned dysfunctions (with a special focus on risk factors for developing glucose intolerance), we should mention heredity, age, obesity, low intake of fruit and alcohol consumption (Tominaga et al., 1999). IGT is closely associated with insulin resistance, which is partly genetically determined and partly due to modifiable factors such as physical activity, obesity, body fat distribution and diet (Jørgensen et al., 2002). In addition, it is considered that besides age, positive family history, overall obesity, lack of physical activity, diet and alcohol consumption, there is also a recently demonstrated correlation between newborn size and post-natal growth to glucose intolerance, as demonstrated in south Indian adults (Raghupathy et al., 2010). Additionally, Levitt showed that the link between low birth weight and adult glucose intolerance and blood pressure elevation occurs in young adults in a high risk, disadvantaged population and that cortisol axis activation plays a fundamental role in this matter (Levitt et al., 2000).

Our results show an increased prevalence of IGT in a rural population from Deleni, Iasi, Romania.

They indicate an even greater degree of susceptibility to type 2 diabetes than initially expected in Romanian rural areas.

## CONCLUSIONS

The present study shows a high prevalence of diabetes and IGT among the rural population of Deleni, Romania, an area that was previously defined as stable and representative for our region in terms of number of inhabitants, education, religion and ethnicity. Our report also emphasizes the urgent need for an increased awareness of diabetes and for energetic intervention against diabetes and similar life-style-related diseases in the rural areas of Romania.

## REFERENCES

- American Diabetes Association* (2010). Standards of Medical Care in Diabetes. *Diabet. Care*. **33**, 11-61.
- Aronoff, S.L., Bennett, P.H., Gorden, P., Rushforth, N. and M. Miller (1977). Unexplained hyperinsulinemia in normal and "prediabetic" Pima Indians compared with normal Caucasians. *Diabetes*. **26**, 827-40.
- Balkau, B., King, H., Zimmet, P. and L.R. Raper (1985). Factors associated with the development of diabetes in the Micronesian population of Nauru. *Am J Epidemiol*. **122**, 594-605.
- Barth, J.H., Butler, G.E. and P. Hammond. (2001). Glucose Tolerance Test for Diabetes Mellitus. In *Biochemical Investigations in Laboratory Medicine*. Association of Clinical Biochemists, London, 146-147.
- Brøns, C., Jensen, C.B., Storgaard, H., Hiscock, N.J., White, A., Appel, J.S., Jacobsen, S., Nilsson, E., Larsen, C.M., Astrup, A., Quistorff, B. and A. Vaag (2009). Impact of short-term high-fat feeding on glucose and insulin metabolism in young healthy men. *J Physiol*. **587**, 2387-97.
- Fischbach, F. (2009). Chemistry studies. In *A Manual of Laboratory and Diagnostic Tests*. Lippincott Williams & Wilkins, USA, 8 Ed., 352-356.
- Jørgensen, M.E., Bjeregaard, P. and K. Borch-Johnsen (2002). Diabetes and impaired glucose tolerance among the Inuit population of Greenland. *Diabetes Care*. **25**, 1766-71.
- Jørgensen, M.E., Borch-Johnsen, K., Witte, D.R. and P. Bjerregaard (2012). Diabetes in Greenland and its relationship with urbanization. *Diabet Med*. **29**, 755-60.
- Levitt, N.S., Lambert, E.V., Woods, D., Hales, C.N., Andrew, R. and J.R. Seckl (2000). Impaired glucose tolerance and elevated blood pressure in low birth weight, nonobese, young South African adults: early programming of cortisol axis. *J Clin Endocrinol Metab*. **85**, 4611-8.
- Mihalache, L., Popescu, D. and M. Graur (2010). Prevalence of overweight and obesity in a rural population. *Rev Med Chir Soc Med Nat Iasi*. **114**, 715-20.
- Mihalache, L., Graur, L.I., Popescu, D.S., Nita, O., Popa, A., Aursulesei, V. and M. Graur (2013). Anthropometric characteristics associated with dysglycaemia in a rural population. *Journal of Diabetes*. **5**, 158.
- Mihalache, L., Graur, L.I., Popescu, D.S., Boiculescu, L., Badiu, C. and M. Graur (2012). The prevalence of the metabolic syndrome and its components in a rural community. *Acta Endocrinologica (Buc)*. **7**, 595-606.
- Nathan, D.M., Davidson, M.B., DeFronzo, R.A., Heine, R.J., Henry, R.R., Pratley, R. and B. Zinman (2007). Impaired fasting glucose and impaired glucose tolerance: implications for care. *Diabetes Care*. **30**, 753-9.
- Niiijima, K., Muranaka, Y., Ando, T., Okada, S., Niiijima, Y., Hashimoto, K., Yamada, M., Ohshima, K., Mori, M. and K. Ono (2012). Elevated 1-h plasma glucose following 75-g oral glucose load is a predictor of arterial stiffness in subjects with normal glucose tolerance. *Diabet Med*. **29**, 457-60.
- O'Dea, K., Traianedes, K., Hopper, J.L. and R.G. Larkins (1988). Impaired glucose tolerance, hyperinsulinemia, and hypertriglyceridemia in Australian aborigines from the desert. *Diabetes Care*. **11**, 23-9.
- Raghupathy, P., Antonisamy, B., Fall, C.H.D., Geethanjali, F.S., Leary, S.D., Saperia, J., Priya, G., Rajaratnam, A. and J. Richard (2007). Insulin profile and prevalence of type 2 diabetes mellitus and impaired glucose tolerance among young adults; a worrying scenario in rural and small town populations of south India. *Diab. Res. Clin. Pract*. **77**, 269-79.
- Raghupathy, P., Antonisamy, B., Geethanjali, F.S., Saperia, J., Leary, S.D., Priya, G., Richard, J., Barker, D.J. and C.H. Fall (2010). Glucose tolerance, insulin resistance and insulin secretion in young south Indian adults: Relationships to parental size, neonatal size and childhood body mass index. *Diabetes Res Clin Pract*. **87**, 283-92.
- Ramachandran, A., Snehalatha, C., Dharmaraj, D. and M. Viswanathan (1992). Prevalence of glucose intolerance in Asian Indians; urban-rural difference and significance of upper body adiposity. *Diab. Care*. **15**, 1348-55.
- Tominaga, M., Eguchi, H., Manaka, H., Igarashi, K., Kato, T. and A. Sekikawa (1999). Impaired glucose tolerance is a risk factor for cardiovascular disease, but not impaired fasting

glucose. The Funagata Diabetes Study. *Diabetes Care*. **22**, 920-4.

Vienberg, S.G., Brøns, C., Nilsson, E., Astrup, A., Vaag, A. and B. Andersen (2012). Impact of short-term high-fat feeding and insulin-stimulated FGF21 levels in subjects with low birth weight and controls. *Eur J Endocrinol*. **167**, 49-57.

Westerbacka, J., Lammi, K., Hakkinen, A.M., Rissanen, A., Salminen, I., Aro, A. and H. Yki-Jarvinen (2005). Dietary fat content modifies liver fat in overweight nondiabetic subjects. *J Clin Endocrinol Metab*. **90**, 2804-2809.

Wild, S., Roglic, G., Green, A., Sicree, R. and H. King (2004). Global prevalence of diabetes; estimates for the year 2000 and projections for 2030. *Diabetes*. **27**, 1047-53.