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ASPECTS OF ENDOCRINE DYSFUNCTION IN PATIENTS WITH CHRONIC PANCREATITIS

Abstract. *Chronic pancreatitis is considered to be a rare cause of diabetes mellitus. However, in both the developed and developing world, there is an increasing number of patients suffering from pancreatitis probably due to lifestyle changes, which is partially associated with both social factors and the poor health status of immigrants. Owing to these circumstances, chronic pancreatitis has evolved with one of the possible causes of diabetes in a selected group of patients and should be included in the differential diagnosis of diabetes. In this study we aimed to demonstrate a close link between diabetes mellitus and chronic pancreatitis, researching the family history, the clinical picture, the paraclinical and imagistic manifestations of these two pathologies.*

Keywords*: Diabetes mellitus, chronic pancreatitis*

Introduction

Chronic pancreatitis (CP) can be defined as a continuous inflammatory disease of the pancreas, characterized by irreversible morphological change and typically causing pain and/or permanent loss of function [1].

Reliable population-based estimates of the epidemiology of CP are not widely available as the diagnostic criteria for CP vary widely. However, limited evidence suggests that the incidence of CP ranges from 5 to 12/100.000 with a prevalence of approximately 50/100.000 persons [2].

Most patients with chronic pancreatitis have more than one underlying etiology. The causes of CP are commonly classified using a system termed "TIGAR-O". This refers to toxic-metabolic, idiopathic, genetic, autoimmune, recurrent and severe acute pancreatitis, and obstructive [3]

Abnormal glucose tolerance and diabetes complicate around 40 – 50% of cases of chronic pancreatitis. Unlike acute pancreatitis, the cause here is damage to the β - cells, owing to loss of trophic signals from the exocrine tissue [1, 4]. The diabetes is of insidious onset and usually occurs several years after the onset of pain. The prevalence has been assessed at 60% after 20 years. Half or more of patients require insulin for optimal glycemic control, but ketoacidosis is rare, even if insulin is withdrawn.

Possible explanations include better preservation of β - cell function (compared with type 1 diabetes; T1, reduced glucagon secretion and lower body stores of triglyceride, the major substrate for ketogenesis. On account of the lower glucagon reserve, these patients are also prone to severe and prolonged hypoglycemia, and often diabetes is difficult to control with wide fluctuations of blood glucose levels. [5]

Diabetes mellitus (DM) is the major late sequelae of CP. It is an independent risk factor for mortality in patients with CP, whether they have undergone surgery, and it affects the quality of life. Contrary to exocrine pancreatic insufficiency, endocrine pancreatic insufficiency may lead to life-threatening complications such as severe hypoglycemia or to chronic microangiopathic and macroangiopathic complications, which are as frequent in CP patients with diabetes as in other diabetic patients. [6]

The most recent data from the International Diabetes Federation indicated that an estimated 415 million adults aged 20–79 years worldwide have DM in 2015 and the number will project to 642 million in 2040, with the prevalence increasing from

8.8 to 10.4%. Despite the high prevalence of diagnosed DM, as many as 193 million people representing close to half of all people with DM are unaware of their disease. Regionally, the age-adjusted prevalence of DM is 3.8% in Africa, 7.3% in Europe, 10.7% in Middle East and North Africa, 11.5% in North America and Caribbean, 9.6% in South and Central America, 9.1% in Southeast Asia, and 8.8% in Western Pacific. China, India, and the USA remain the top three countries with the largest number of people with DM. [7]

Aim. Study of the clinical-paraclinical characteristics of DM in CP to highlight the direct link between these two pathologies, as well as their evolution.

Objectives.

– Evaluation of the prevalence by gender and age of DM and CP in the study group;

– Study of clinical - paraclinical manifestations of DM in patients with CP

– Prevalence of other pathologies associated with these patients with CP

Materials and methods

The study included group of 30 patients with CP and DM which is characterized by an evolution with virtually absent or poorly manifested pain syndrome, exocrine and/or endocrine insufficiency. Clinical-paraclinical changes, specific CP, have been identified in accordance with the recommendations of the European Society of Gastroenterology, International Association of Pancreatology and National Clinical Protocol.

The endocrine function of the pancreas was assessed according to WHO criteria, by determining fasting blood glucose and oral glucose tolerance test (TOTG). Fasting or basal normoglycemia is considered blood glucose level < 6,1 mmol /l; altered basal blood glucose - at a basal plasma blood glucose of > 6.1 to < 6.9 mmol / l.

The preventive diagnosis of diabetes can be established at a basal blood glucose level ≥ 7,0 mmol/l, but requires confirmation by repeated level determination of glycemia. TOTG is indicated more than 2 hours after glucose loading: normal tolerance - at a blood glucose level <7,8 mmol/l, decreased tolerance glucose-plasma glucose ≥ 7,8 mmol/l to 11,1 mmol /l. A presumptive diagnosis of diabetes can be

established at a blood glucose level ≥11,1 mmol / l, but requires confirmation by investigation subsequent.

Classical symptoms of hyperglycemia are considered: polyuria, polydipsia, weight loss. TOTG is indicated if basal blood glucose is normal, but risk factors are present, basal blood glucose is higher than normal, but below 7 mmol/l.

For the calculation t-test we used the values given from the literature; in the case of examining a group with a small number of patients, the data from the literature are used as standard values [8, 9].

Results.

The study lot was composed of 16 men and 14 women, aged between 18-90 years old. The average age of the patient group was 54,6 ± 2,56 years old.

During our research, it was found that the study group is largely composed of patients with compensated type II DM:14 patients and only 8 – with decompensated type II DM form; 4 - with type I compensated DM and 4 with decompensated type I DM.

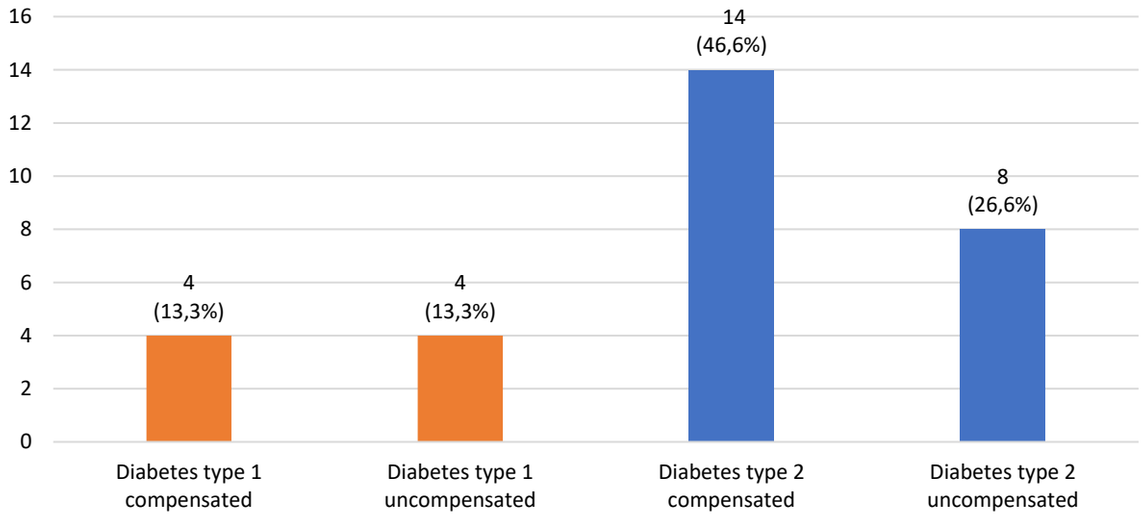

Diagram 1. **The level of diabetic compensation**

Dividing the patients in the study group by age according to the classification proposed by the WHO in 2012, it was found that the vast majority (Diagram 2)-12 patients constitute the elderly category (60-74), followed by 7 middle-aged patients (45-59 years) type II DM. Higher prevalence of patients with DM type I is observed - 4 patients are young man (18-44) and 3 patients are older (60-74).

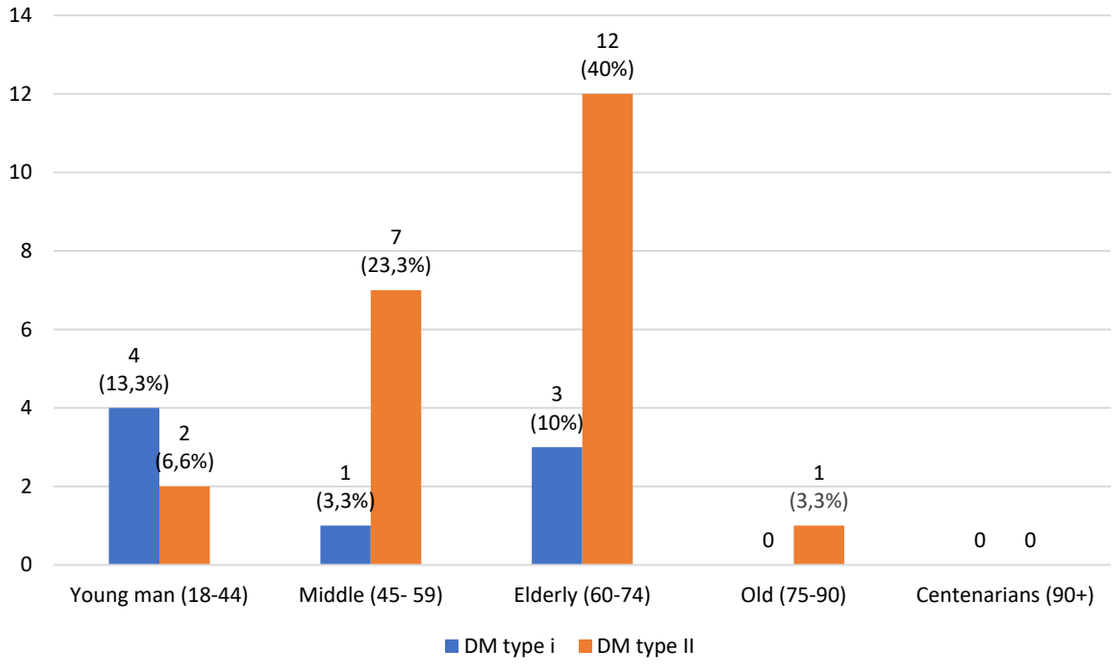

Diagram 2. **Age group classification for DM patients**

In patients in the study group, the following concomitant diseases are present: Chronic hepatitis – 7%, Chronic colitis – 12%, Chronic gastritis – 21%, Gastric ulcer – 3%, Pyelonephritis – 9%, COPD – 14%, HTA – 34% (Diagram 3.)

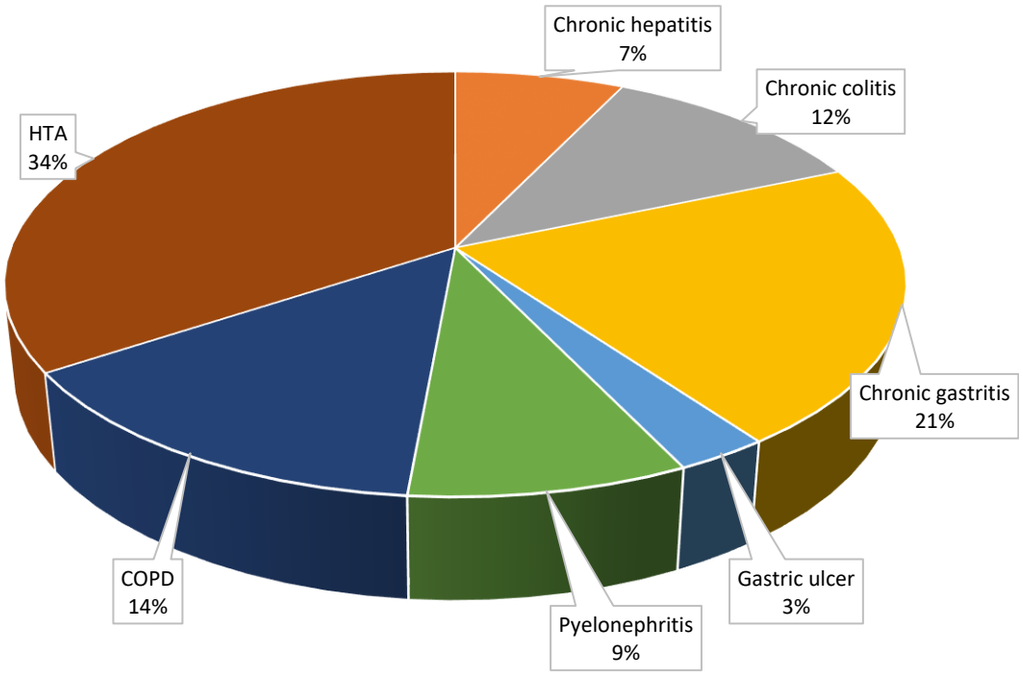

Diagram 3. **Concomitant diseases of DM and CP**

Table 1

CBC

Evaluated parameters (reference values)		**Pacienţi cu DZ/PC**	**M±ES**	**T-statistic**	**p-value**
		n.			
Hb, g/l (b.130-160 / f.120-140)	↓	11	129,9±4,73	2,09	0,04
	↑	11			
Er., $x10^{12}$/l (b.4,5-5,0/ f.3,7-4,7)	↓	6	4,39±0,16	2,43	0,02
	↑	8			
HT. % (b. 40-48 / f. 36-42)	↓	10	37,8±1,23	2,3	0,02
	↑	0			
Plateles, $x10^{9}$/l (180-320)	↓	10	224,43±14,67	2,34	0,02
	↑	3			
Leukocyte,$x10^{9/}$l (4,0-9,0)	↓	7	7,38±0,44	3,04	0,004
	↑	1			
Neutrophils, % (47-72)	↓	4	55,44±2,34	2,34	0,02
	↑	4			
Eosinophils, % (0,5-5)	↑	2	2,60±0,28	2,10	0,044
Lymphocytes, % (19-37)	↓	5	31,42±2,07	3,10	0,004
	↑	10			
Monocytes, % (3-11%)	↑	10	9,41±0,514	2,76	0,009
ESR, mm / hour (b, 2-10 f, 2-15)	↓	1	20,6±2,85	3,01	0,005
	↑	16			

Analysed the hemouleucogram (Table 1), we encountered: increased values of HT in 10 cases and it is 37,8±1,23 mmol/l, t-test=2,3 and p=0,02; increased Plateles values in 10 cases and decreased in 3 and it is 224,43±14,67 mmol/l, t-test=2,34 and p=0,02 ; increased Leukocytes values in 1 cases and decreased in 7 and it is 7,38±0,44 mmol/l, t-test=3,04 and p=0,004; increased *Neutrophils* values in 4 cases and decreased in 4 and it is 55,44±2,34 mmol/l, t-test=2,34 and p=0,0202 ; increased Eosinophils values in 2 it is 2,60±0,28 mmol/l, t-test=2,10 and p=0,044; increased Lymphocytes values in 10 and decreased in 5 and it is 31,42±2,07 mmol/l, t-test=3,10 and p=0,004; increased Monocytes values in 10 and it is 9,41±0,51 mmol/l, t-test=2,76 and p=0,009 increased ESR values in 16 and decreased in 1 and it is 20,6±2,85 mmol/l, t-test=3,01 and p=0,005.

Table 2

Lipidogram indices of the patients included in the study

Evaluated parameters (reference values)		Number of patients	M±ES	T-statistic	p-value
Cholesterol, mmol/l (3,8-6,7)	↓	2	5,41±0,34	1,20	0,24
	↑	5			
HDL, mmol/l (1,2-1,7)	↓	13	1,13±0,11	0,27	0,7
	↑	2			
LDL, mmol/l (2,33-5,77)	↓	2	3,73±0,16	2,07	0,05
		4			

There are the lipidogram parameters (Table 2), we encountered: increased values of cholesterol values in 5 cases and decreased in 2 and it is 5,41±0,34 mmol/l, t-test=1,20 and p=0,4; increased HDL values in 2 cases and decreased in 13 and it is 1,13±0,11 mmol/l, t-test=0,27 and p=0,7; increased LDL values in 4 cases and decreased in 2 and it is 3,73±0,16 mmol/l, t-test=2,07 and p=0,05.

Table 3

Biochemistry indices of the patients included in the study

Evaluated parameters (reference values)		Number of patients	M±ES	T-statistic	p-value
ALAT u/l (0-49)	↑	3	36,95±6,30	1,10	0,28
ASAT u/l (0-46)	↑	7	36,02±3,37	1,77	0,09
GGTP u/l (5-45)	↑	7	50,18±5,81	1,75	0,09
The basal glucose, mmol/l (3,8-5,8)	↑	22	14,01±1,07	7,98	1,27

Biochemical assessment (Table 3) revealed: increased values of ALT values in 3 cases (36,95±6,3 mmol/l, t-test=1,1 p=0,28); increased AST values in 7 cases (36,02±3,37 mmol/l, t-test=1,77, p=0,09); increased GGTP values in 7 cases (50,18±5,81 mmol/l, t-test=1,75 p=0,09); increased the basal glucose values in 22 cases (14,01±1,07 mmol/l, t-test=7,98, p=1,27).

Conclusion

Following the data from the family history, the clinical picture, the paraclinical and imaging data obtained from the study group, essential changes were estimated both clinically and paraclinically in the Diabetes mellitus and pancreas. The research

indicates a link between CP disease and Diabetes mellitus . A prevalence of compensated form type II diabetes was observed. Our study found a prevalence of endocrine failure in elderly patients with PC (60-74 years), a fact confirmed by data from the literature. An increased prevalence of pathologies associated with CP are hypertension - 34%, chronic gastritis - 21%, chronic colitis - 12%.

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