

ORIGINAL PAPER

**DIABETES MELLITUS IS A NEGATIVE PROGNOSTIC FACTOR
FOR ACUTE PANCREATITIS****M. Lică¹, I. Negoî^{1,2}, I. Lică^{1,2}, G. Mircescu^{1,3}, B. Stoica², M. Beuran^{1,2}**¹The University of Medicine and Pharmacy "Carol Davila", Bucharest, Romania²The Clinical Emergency Hospital of Bucharest, Romania³The Clinical Nephrology Hospital "Carol Davila", Bucharest, Romania

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Abstract

Type 2 Diabetes Mellitus (T2DM) and Acute Pancreatitis (AP) are usually perceived as two different types of pancreatic pathology. Even though, there is a growing evidence that there is a mutual influence between these two diseases. Our aim is to assess the risk of patients with T2DM to develop AP according to the three grades of severity of Atlanta 2012 Classification of AP. We consider the hypotheses that patients with T2DM have a greater risk of more severe forms of AP because they have a reduced resistance for acute illnesses. We analyzed all consecutive cases of Acute Pancreatitis admitted to Surgical Clinic during the entire year of 2014.

Keywords: *diabetes mellitus, acute pancreatitis***Introduction**

Type 2 Diabetes Mellitus (T2DM) and Acute Pancreatitis (AP) are apparently two different types of pancreatic pathology, but there is a growing evidence that there is a mutual influence between these two diseases.

The first suggestion for association between T2DM and AP emerged in 2005 during a randomized controlled trial of fenofibrate in patients with T2DM [1] and the first observational study which reported an increased risk of AP for patients with T2DM was using a US healthcare database in 2009 [2].

The epidemiological data indicate that T2DM is relatively common in patients who suffer from AP: the prevalence can range from 11% in Japan [3] to 14.9 % in Spain [4], 17.7% in California [5] and 19.3% in Taiwan [6].

Most of the recent studies showed that there is an increased risk of AP in patients with T2DM [7-12] and even diets with high glycemic load are also associated with this risk of AP [13].

A few studies also observed that T2DM has also an influence on severity of acute pancreatitis. Patients with diabetes have an increased risk of severe acute pancreatitis (SAP), AP with local complication and higher in-hospital mortality [14-15].

On the other hand, patients with AP often develop dysfunction of glucose metabolism and/or T2DM after hospital discharge, especially after severe disease with necrosis [16-19].

The progresses on pathology and evolution of AP led to new revisions and classification, Atlanta 2012 being one of them [20]. This classification first published online in October 2012, takes into consideration only local

complications and organ failure in order to stratify the severity of AP and since then its utility has been certified by several comparative studies [21-23].

Material and Methods

We analyzed all consecutive cases of Acute Pancreatitis admitted to Surgical Clinic during the entire year of 2014. We defined and categorized patients with AP according to Atlanta 2012 criteria and excluded the ones that were transferred to our hospital and didn't have the proper medical documents for analyses.

Patients were divided into the three categories of severity: mild AP (MAP), moderately-severe AP (MSAP) and severe AP (SAP). The patients were further grouped with T2DM and without T2DM. The primary outcome of the current study was: in-hospital mortality. The secondary outcomes were: in-hospital stay, Intensive Care Unit (ICU) admission and stratification according to Atlanta 2012 severity categories.

Categorical variables were compared by Chi-square test or Fisher exact test and continuous variables by the Independent Samples T-Test or Mann-Whitney U test, as appropriate. For assessing distribution of data we used Kolmogorov Smirnov test. A level of $p < 0.05$ was used to declare statistical significance. For statistical analysis we used IBM SPSS Statistics software, version 20.

237 patients with AP met the inclusion criteria. 44 patients (18.6%) had T2DM.

Grouping the cases according to Atlanta 2012 severity groups we find that in Mild AP 14.8% of patients have T2DM, in Moderately-Severe AP 20% of patients have T2DM and in Severe AP 41.2% of patients have T2DM ($p = 0.028$, $R=0.136$) (Table 1, Figure 1).

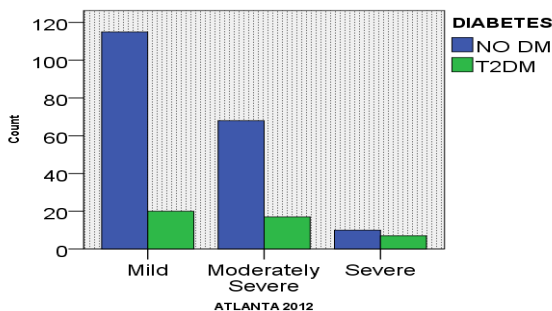


Figure 1 - Correlation of type 2 diabetes mellitus patients according to Atlanta 2012 classification

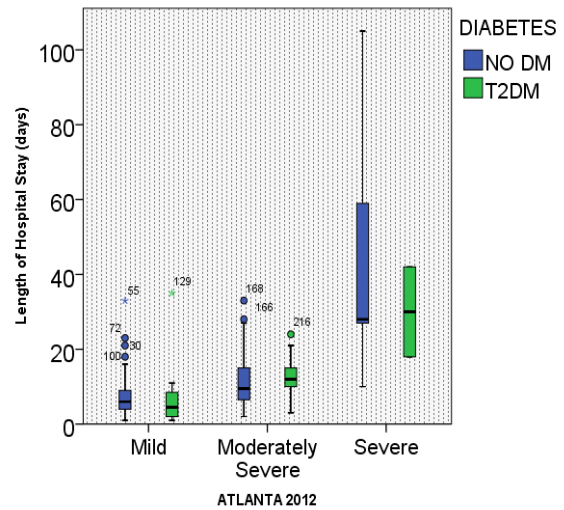


Figure 2 - Correlation of in-hospital stay with severity of acute pancreatitis in survivors

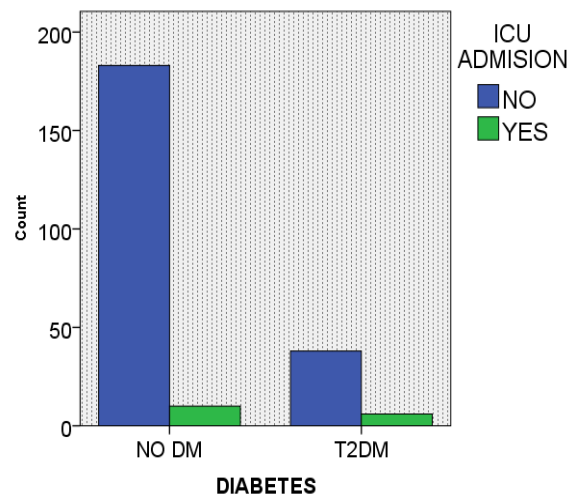


Figure 3 - Correlation of ICU admission and diabetes mellitus

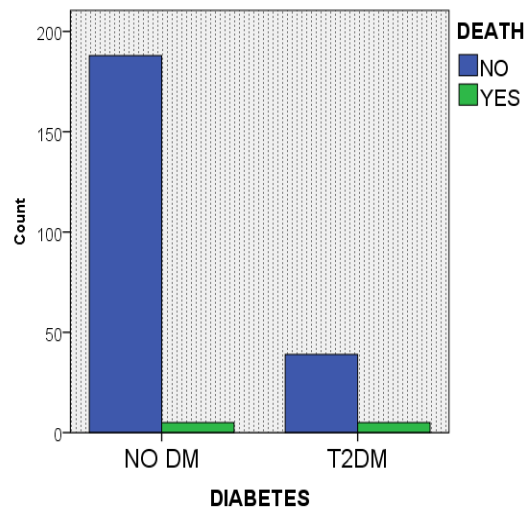


Figure 4 - Correlation between in-hospital mortality and diabetes mellitus

			DIABETES		Total
			NO_DM	T2DM	
ATLANTA 2012	Mild	Count	115 _a	20 _a	135
		% within ATLANTA_2012_C	85.2%	14.8%	100.0%
	Moderately Severe	Count	68 _a	17 _a	85
		% within ATLANTA_2012_C	80.0%	20.0%	100.0%
	Severe	Count	10 _a	7 _b	17
		% within ATLANTA_2012_C	58.8%	41.2%	100.0%
Total	Count	193	44	237	
	% within ATLANTA_2012_C	81.4%	18.6%	100.0%	

Table 1 - Correlation of type 2 diabetes mellitus patients according to Atlanta 2012 classification

ATLANTA 2012	DIABETES	N	Mean	Std. Deviation	Std. Error Mean
Mild	T2DM	20	6,55	7,430	1,661
	NO_DM	115	7,09	4,680	,436
Moderately_S	T2DM	17	12,94	5,093	1,235
	NO_DM	68	11,69	6,814	,826
Severe	T2DM	2	30,00	16,971	12,000
	NO_DM	5	45,80	37,519	16,779

Table 2 - Correlation of in-hospital stay with severity of acute pancreatitis in survivors

			ICU ADMISSION		Total
			NO	YES	
DIABETES	NO_DM	Count	183 _a	10 _b	193
		% within DIABETES	94.8%	5.2%	100.0%
	T2DM	Count	38 _a	6 _b	44
		% within DIABETES	86.4%	13.6%	100.0%
Total	Count	221	16	237	
	% within DIABETES	93.2%	6.8%	100.0%	

Table 3 - Correlation of ICU admission and diabetes mellitus

			DEATH		Total
			NO	YES	
DIABETES	NO DM	Count	188 _a	5 _b	193
		% within DIABETES	97.4%	2.6%	100.0%
	T2DM	Count	39 _a	5 _b	44
		% within DIABETES	88.6%	11.4%	100.0%
Total	Count	227	10	237	
	% within DIABETES	95.8%	4.2%	100.0%	

Table 4 - Correlation between in-hospital mortality and diabetes mellitus

Looking at the hospital stay of survivors there was no statistical significant difference between the groups ($p > 0.05$) (Table 2, Figure 2).

The ICU admission was significantly higher for patients with diabetes mellitus (5.2% versus 13.6%) ($p = 0.05$, $R = 0.13$) (Table 3, Figure 3).

Analyzing the correlation between mortality and diabetes, we observed a higher mortality for diabetic patients ($p = 0.022$, $R = 0.167$) (Table 4, Figure 4).

Discussions

We found a significant association between diabetes mellitus and morbidity and mortality in patients with acute pancreatitis.

In our study we found that almost 1 in 5 patients with AP have T2DM (18.6%) which is a percentage similar with literature, but among the highest rates (11% in Japan to 19.3% in Taiwan)[3],[6].

The relationship between AP and T2DM is a bidirectional one: patients with T2DM are more prone to AP[9] and people after an attack of AP could develop glucose metabolism impairments or even T2DM[16]; this data came only from observational studies and that is why some authors consider that more fundamental research is needed to elucidate the biological mechanism of this connection [8].

Regarding the influence of T2DM on severity of AP, the current opinions are very different: some studies showed that DM is associated with an increased risk of severe acute pancreatitis, local complication [14] and have a higher hospital mortality [15]; another author considered that the severity of AP or in-hospital mortality did not differ from non-diabetic patients [24] and Shen et al. in 2012 on a national population-based study in Taiwan found out that hospital mortality was lower in diabetic AP patients than in non-diabetic ones [25].

The severity stratification of AP was reestablished in 2012 along with new definition of AP, local and systemic complication and we know it and use it as Atlanta 2012 Classification [20]. Since then multiple studies have validated its accuracy and usefulness [22], [26].

In our study across the three severity categories of Atlanta 2012, we observed that the higher the severity, the greater percentage of T2DM. This observation also reached statistical significance ($p < 0.05$) and let us think that a diabetic patient has a greater risk to develop a more severe form of AP and that is a confirmation of our initial hypotheses.

Another observation was that the T2DM patients have a much higher admission to ICU rates and that this is an indirect proof of their severity and finally the in-hospital mortality rate is almost four-times higher in diabetic patients.

Considering the length of hospital stay we took into considerations only the survivals, because death occurred in a very variable time frame from admission. The survivors have a similar length of hospital stay across all three AP severity groups and diabetes status. In our study T2DM is not related to a longer in-hospital stay.

To summarize our statistical data we can say that a diabetic person is more likely to have a severe form of AP, to be admitted to ICU and to die than a non-diabetic one.

Conclusions

Diabetes mellitus in patients with acute pancreatitis is a negative prognostic factor, associated with significant morbidity and mortality.

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