

BLOOD PRESSURE PROFILE IN TYPE 1 DIABETES MELLITUS

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Abstract

Background: *The precise occurrence of hypertension in type 1 diabetes mellitus may be foreseen by monitoring any circadian pressure changes – it seems that an increase in the nocturnal systolic blood pressure is the first detectable manifestation. Blood pressure may be influenced by a series of factors, such as: microalbuminuria, lipid imbalance, HbA1c, history of diabetes mellitus, insulin treatment. **Material and method:** The study included 315 patients suffering from type 1 diabetes mellitus, with a history of disease older than 10 years, recorded in the Diabetes, Nutrition and Metabolic Disease Center of Iași. Their blood pressure was permanently monitored using a portable oscillometer, which is an Automatic Blood Pressure Monitoring (ABPM) – Oscar 2 device, periodically calibrated and checked. **Results:** 119 patients from the group under survey suffered from hypertension. Statistically speaking, 67.5% of the type 1 diabetes mellitus patients experienced non-dipper blood pressure and a moderate negative correlation between systolic blood pressure and HbA1c. The gathered data suggested a direct connection between type 1 diabetes mellitus blood pressure changes and nutritional status. The study revealed no significant statistical correlation between blood pressure and the overall insulin intake; however, the closest blood pressure variability connection was revealed in patients having several shots of insulin per day. Blood pressure, objectively determined by the ABPM device, was higher in type 1 diabetes mellitus patients with a long history of disease, while their nocturnal blood pressure drop was small, and the physiological dipping phenomenon diminished. **Conclusions:** Type 1 diabetes mellitus blood pressure depends on the history of the disease, on the nutritional status, on the insulin treatment and also on the metabolic control quality. An early nocturnal BP rise may play a key role in detecting disease progression towards diabetic nephropathy – useful as potential marker and it may account for the idea of treating susceptible patients before microalbuminuria inset.*

keywords: *type 1 diabetes mellitus, arterial blood pressure*

One of the unique aspects of blood pressure (BP) ambulatory monitoring is the ability of recording diurnal variations. Blood pressure should normally drop by about 10-20 % during the night, that is during sleep,

which drop is also known as dipping. This phenomenon is defined as a relative nocturnal blood pressure decrease that does not exceed 10% of the diurnal value, both as systolic and diastolic BP. About 25 % of the type 1

diabetes mellitus patients also suffering from hypertension experienced a nondipping phenomenon, which means that there was no nocturnal blood pressure drop. Some authors used a classification designed to identify the patients with an excessive BP drop (extreme dippers, whose nocturnal BP drops by more than 20 %), or even an increase (risers). Nocturnal BP reading is important. The dipping and nondipping classification is a binary classification and, although useful in treatment-related decisions, the dipper/nondipper separation limit is arbitrary. Scientifically speaking, the research intends to determine the importance of the continuous 24 hours blood pressure monitoring and of the ability of this monitoring to predict cardiovascular risks. Also, it is necessary to determine the importance of nocturnal BP monitoring as compared to diurnal monitoring.

Type 1 diabetes mellitus hypertension with clear clinical manifestations is generally diagnosed after several years of disease progression. It is usually secondary to nephropathy and it occurs in up to 30% of the cases. The moment of its occurrence may be predicted by monitoring any circadian pressure changes. It seems that an increase in the nocturnal systolic blood pressure is the first detectable manifestation of blood pressure regulation disorders in type 1 diabetes mellitus. An early nocturnal blood pressure rise may play a key role in detecting early disease progression towards diabetic nephropathy. Any blood pressure increase during sleep, only of the systolic blood pressure in the beginning, influences glomerular circulation and it determines intrarenal hemodynamic changes, whose

progression ends up in microalbuminuria and structure destruction [1].

Blood pressure variations may be influenced by a series of factors, such as: microalbuminuria, lipid imbalance, HbA1c, history of diabetes mellitus, insulin treatment (enhanced/conventional). Their correction actually prevents blood pressure changes and it slows down specific chronic complication progression.

Given these type 1 diabetes mellitus hypertension characteristics, the main purpose of this research is to analyze the blood pressure variations of patients suffering from type 1 diabetes mellitus and to identify the factors influencing the blood pressure pattern.

Material and method

The study included 315 patients suffering from type 1 diabetes mellitus, with a history of disease older than 10 years, recorded in the Diabetes, Nutrition and Metabolic Disease Center of Iasi. The patients' blood pressure was constantly evaluated. The exclusion criteria were secondary hypertension or the patient's refuse. Type 1 diabetes mellitus was defined according to the ADA criteria, acknowledged by international forums.

Their blood pressure was permanently monitored using a portable oscillometer, which is an **Automatic Blood Pressure Monitoring (ABPM) – Oscar 2**, periodically calibrated and checked. [2] Two different periods were defined: the daytime period, from 6 am to 10 pm, and the nocturnal period, which included the measurements from 10 pm to 6 am. The blood pressure was registered at 15 minutes' intervals during daytime and at 30 minutes' intervals during the nocturnal period.

The mean values of systolic blood pressure (SBP) and of diastolic blood pressure (DBP) registered throughout a day or a night were stored as SBP and DBP values for that period. A ratio of 0.9 or smaller between the nocturnal SBP value and the diurnal DBP was defined as a normal decrease during the nighttime. The phenomenon, called “non-dipper”, is defined as a relative decrease of the nocturnal blood pressure, smaller than 10% of the diurnal value, for the systolic, as well as for the diastolic blood pressure.

Results

Of the 351 patients suffering from type 1 diabetes mellitus, 193 were male and 158 female. The subjects’ mean age was of 38.3 ± 11 years, with variations between 18 and 50 years. The history of DM varied between 5 and 15 years, with an average of 9.86 ± 3.92 years (Table 1).

Table 1. Group characteristics

	N = 351
Sex (m/f)	193/158
Age	38.3 ± 11 years
BMI	24.08 ± 3.51 kg/m ²
Duration of type 1 DM	9.86 ± 3.92 years

In the studied group, 119 patients with type 1 diabetes mellitus suffered from hypertension. The statistical analysis showed the fact that 67.5% of the type 1 diabetes mellitus patients, with a history of the disease of at least 10 years, registered non-dipper blood pressure (Table 2, Figure 1).

Table 2. Dipper/non-dipper status

Dipper/non-dipper	No. of cases	%
Dipper	114	32.5%
Non-dipper	237	67.5%
Total	351	

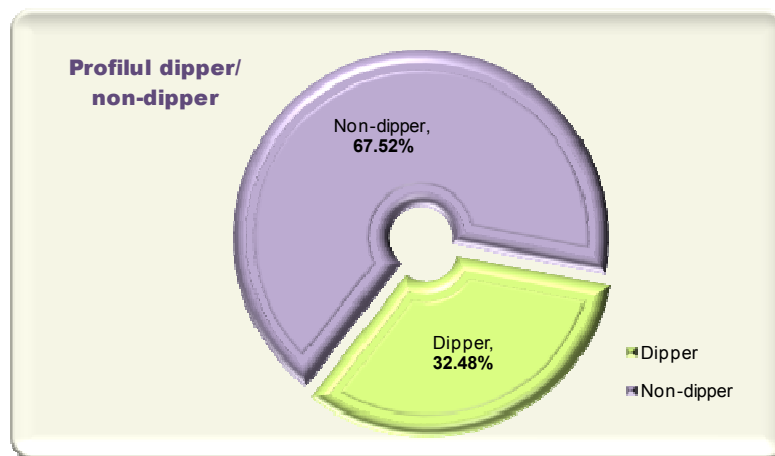


Figure 1. Dipper/non-dipper status

One of the factors that influence the blood pressure pattern is the level of metabolic control, expressed via the glycosylated hemoglobin. The statistical analysis identified a moderate reverse correlation between systolic blood pressure and HbA1c, for the Pearson correlation coefficient had a small

value ($r=-0.31$, $p=0.03$, 95%CI). The diastolic blood pressure does not correlate with HbA1c, but there is a significant direct correlation ($r=0.48$, $p=0.0141$, 95% CI) between the mean blood pressure (MAP) and HbA1c (Figures 2,3,4,5).

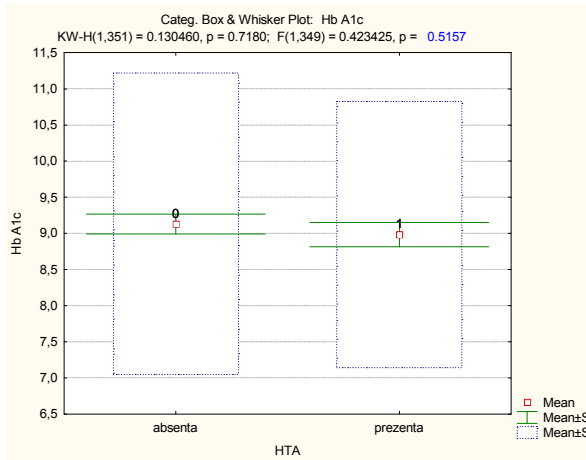


Figure 2. Mean HbA1c, depending on hypertension

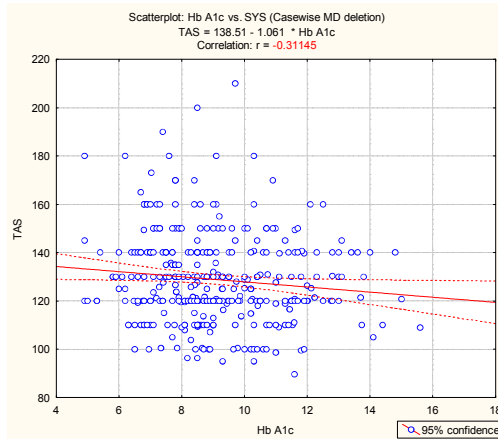


Figure 3. Regression right in the systolic BP vs. glycemia correlation

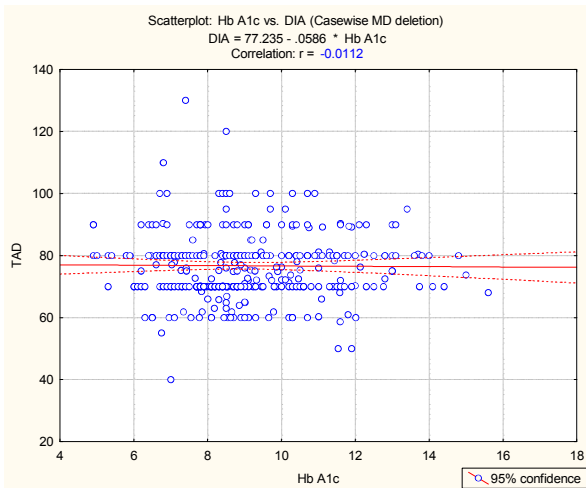


Figure 4. Regression right in the diastolic BP vs. glycemia correlation

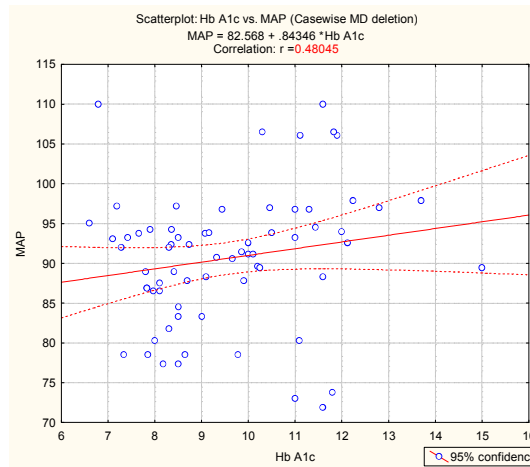


Figure 5. Regression right in the mean BP (MAP) vs. glycemia correlation

Depending on the continuous metabolic control, expressed via the glycosylated hemoglobin (HbA1c), we divided the patients into 2 groups: with values below 7% (expression of an optimum glycemic control) and with values over 7% (expression of metabolic lack of balance). Thus, the first group comprised 165 patients with a mean value of the HbA1c of $6.22 \pm 0.78\%$, and the mean HbA1c of the second group of 186 patients was $7.65 \pm 0.65\%$. The nocturnal

diastolic blood pressure was smaller in the patients belonging to the first group. The systolic blood pressure of the two groups did not have significantly different values. The nocturnal decrease of the systolic and diastolic blood pressure was bigger in the group with optimum metabolic control. The mean nocturnal BP was bigger in the second group. The diurnal systolic and diastolic BP and the diurnal heart rate were similar for the two groups. (table 3, figure 6)

Table 3. ABPM Results

Blood pressure	Group 1 (HbA1c≤7%)	Group 2 (HbA1c>7%)	p Value
Diurnal SBP	124 ± 9 mm Hg	122 ± 8 mm Hg	Insignificant
Diurnal DBP	81 ± 7 mm Hg	82 ± 9 mm Hg	Insignificant
Diurnal MBP	83 ± 4 mm Hg	86 ± 7 mm Hg	Insignificant
Nocturnal SBP	110 ± 5 mm Hg	120 ± 6 mm Hg	Insignificant
Nocturnal DBP	60 ± 8 mm Hg	69 ± 6 mm Hg	p < 0.01
Nocturnal MBP	71 ± 8 mm Hg	80 ± 9 mm Hg	p < 0.01
% nocturnal decrease of SBP	11 ± 8 mm Hg	5 ± 6 mm Hg	p < 0.01
% nocturnal decrease of DBP	21 ± 7 mm Hg	8 ± 8 mm Hg	p < 0.01

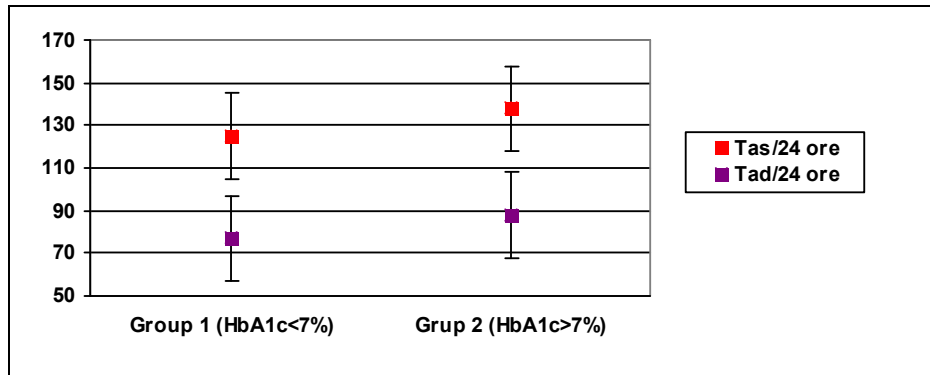


Figure 6. Blood pressure variability depending on HbA1c

By using the multi-varied statistical analysis methods, we identified the predictive factors of nocturnal blood pressure. For this purpose, we examined the multiple correlation results, taking into consideration the dipper/non-dipper profile modifications, depending on:

- microalbuminuria,
- nutritional status (BMI),
- HbA1c,
- history of the disease,
- insulin treatment (intensified/conventional).

Table 4. Factors influencing blood pressure in type 1 diabetes mellitus

Partial correlation	Correlation coefficient (Beta)	Std.Err.	t	p 95% confidence interval
Intercept			0.60137	0.87731
Microalbuminuria	0.724821	0.044100	19.1568	0.000000
BMI	0.620978	0.054794	12.2069	0.000292
HbA1c	0.54733	0.057421	16.9532	0.034240
History of the disease	0.644631	0.049877	8.56441	0.000057
Insulin treatment	0.257106	0.05498	0.54987	0.078912

The significant value of the significance level (p) calculated for the “intercept” variable shows that, apart from the factors considered in this study, there are predictive

factors which may help in the determination of the non-dipper profile (Table 4).

Statistical analysis showed that the risk of progression towards microalbuminuria

significantly differs in patients with normal nocturnal blood pressure, when compared to patients with abnormal nocturnal blood pressure. In this study, the microalbuminuria risk in the group with normal nocturnal blood pressure was 70% smaller than in the group with modified nocturnal BP. At the initial evaluation and throughout the investigations, the HbA1c values were higher in patients who eventually contracted microalbuminuria. Thus, the microalbuminuria risk, marker of renal disease in type 1 DM, is very low in patients whose blood pressure remains within normal limits. The blood pressure pattern is also influenced by the nutritional status, the history of the disease, with statistically significant correlations. As concerns the insulin treatment, we did not find a statistically significant correlation between blood pressure and the overall insulin intake; however, the closest blood pressure variability connection was revealed in patients having several shots of insulin per day.

Discussions

Results have clearly shown that the continuous monitoring of BP differed in type 1 DM patients with optimum or precarious long-term metabolic control. In patients with precarious glycemia control, the nocturnal physiological decline of the systolic and diastolic BP was diminished when compared to the patients with optimum HbA1c values. There were no differences between the diurnal measurements for the 2 groups. Precarious metabolic control accelerates the progression of renal diseases in patients suffering from type 1 DM. Several studies noticed a higher decline rate of the renal function in non-dipper patients, when compared to the control group:

7.9 ml/min/year vs. 2.9 ml/min/year. On the other hand, as microalbuminuria progresses, blood pressure increases by approximately 2-5 mmHg per year [3].

The earliest modification of ambulatory blood pressure, revealed in patients suffering from type 1 diabetes mellitus, with normal blood pressure and microalbuminuria values, is the physiologic decrease of the blood pressure values during the night, phenomenon called *non-dipper*. The *non-dipper* phenomenon in type 1 diabetes mellitus can be interpreted as follows:

- it is considered a premature manifestation of vegetative diabetic neuropathy and consists in the maintenance, during the night, of the sympathetic tonus at high levels, close to the diurnal ones, unlike the control subjects, where we may notice the nocturnal prevalence of the parasympathetic activity in the context of the physiological decrease of the sympathetic tonus.
- based on a meta-analysis study, we may assume that in persons with type 1 DM and incipient nephropathy, the rise of the nocturnal BP leads to the occurrence of microalbuminuria. On the other hand, the two diseases can occur simultaneously. [4].
- it is important to determine whether nocturnal hypertension occurs before or simultaneously with microalbuminuria in order to establish the progression risk of nephropathy, since it is known that this disease is influenced more by the blood pressure values than by the values of the glycemia. If the nocturnal blood pressure rise, expressed as nocturnal hypertension, leads to microalbuminuria, then this

remark is useful as a potential marker of diabetic nephropathy and it may account for the idea of treating susceptible patients before microalbuminuria onset.

Type 1 diabetes mellitus, in combination with blood pressure, worsens the prognosis for these patients, increases the mortality rate and leads to the shortening of the patient's life; therefore, an essential means for the improvement of the prognosis, as important as optimum glycemic control, consists in the diminution, in as many patients as possible, of the blood pressure values below 130/80 mmHg. [5].

The gathered data revealed a connection between the blood pressure changes in type 1 diabetes mellitus and nutritional status. This connection is much stronger in younger patients, a fact confirmed by specialized data [6]. The insulin intake can also influence blood pressure monitoring, via sodium retention; as shown in several studies, long-term insulin treatment leads to an increase in natriuretic activity [7].

Hyperinsulinism in essential hypertension has been repeatedly proven and the plasma concentration of insulin registered high values at the periphery, because of the subcutaneous administration mode of insulin. This study did not reveal a statistically significant correlation between blood pressure and the overall insulin intake; however, the closest blood pressure variability connection was revealed in patients having several shots of insulin per day, and the clinical significance of this discovery has yet to be elucidated in future research works.

The results of this study clearly showed that blood pressure, objectively measured with the help of the ABPM, is higher in patients suffering from type 1 diabetes, with a long

history of disease. Also, the nocturnal blood pressure decrease is low, accompanied by the diminution of physiological dipping. It is assumed that the increase of nocturnal BP in patients suffering from type 1 DM and incipient nephropathy leads to the occurrence of microalbuminuria. On the other hand, the two conditions may occur simultaneously [8].

The DCTT study revealed the role of appropriate long-term metabolic control, expressed via the values of the glycolized hemoglobin, in the prevention of specific chronic complications. In association, these two conditions (non-dipper blood pressure and precarious metabolic control) increase the cardiovascular risk in patients with type 1 diabetes mellitus.

Conclusions

The gathered data suggest that the blood pressure in type 1 diabetes mellitus depends on the history of disease, as well as on the quality of metabolic control. An early nocturnal BP rise may play a key role in detecting disease progression towards diabetic nephropathy – useful as potential marker and it may account for the idea of treating susceptible patients before microalbuminuria onset.

The prevalence of nondipper blood pressure is higher in patients with a long history of disease and with precarious long-term metabolic control. Thus, nocturnal hypertension becomes a clinical marker of the progression towards renal diseases.

It is important to monitor the blood pressure of these patients in order to determine how many of them will develop hypertension, in what time interval and how this will affect specific chronic complications.

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