Blood pressure control in diabetic subjects: a nationwide epidemiological survey among Italian pharmacies customers

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ABSTRACT

Background: Hypertension and diabetes mellitus are closely related and contribute to increase the risk of cardiovascular diseases (CVD). We analyzed data from a nationwide, cross-sectional epidemiological survey on pharmacies customers in order to have an overview of the prevalence and awareness of cardiovascular (CV) risk factors, with particular focus on hypertension and diabetes.

Design and methods: The survey was conducted in 3956 Italian pharmacies from 17 to 20 May 2018. Self-presenting participants who gave their consent to participation were asked to answer a questionnaire on their clinical and demographic characteristics and lifestyle habits. Trained pharmacists measured their blood pressure (BP) according to guidelines. Prevalence of CV risk factors and hypertension rate/control according to the latest version of the European guidelines on hypertension was examined by diabetic status. Statistical analyses were performed using software R (v3.5.1).

Results and conclusions: A total of 47217 subjects were enrolled in the project. Of them, 5695 (12%) had diabetes. Compared to non-diabetic patients, those with diabetes tended to be older, to declare a family/personal history of CVD/chronic kidney disease (CKD), to have prevalent/uncontrolled hypertension, dyslipidemia, higher mean systolic BP (135,96±18,38 mmHg vs 128,32±17,77 mmHg), and greater CV risk ($p<0.001$). No significant differences in terms of salt intake, vegetable consumption, and smoking habits were recorded between the examined groups. Diabetic subjects with uncontrolled hypertension showed a lower propensity to physical activity ($p=0.016$).

Management of hypertension and diabetes represents an ambitious challenge for the national health system. For this reason, similar awareness-rising campaigns might be a useful tool to identify new/uncontrolled patients and to promote CV health.

INTRODUCTION

The prevalence of hypertension is estimated at around 30% of the adult population in industrialized nations (1). Furthermore, high blood pressure (BP) can be found twice as frequent in patients with diabetes mellitus and it contributes significantly to the development of micro and macrovascular complications in this category of subjects (2).

Hypertension constitutes an independent risk factor for the development of cardiovascular disease (CVD) and chronic kidney disease (CKD). The simultaneous presence of diabetes further increases cardiovascular (CV) risk, which is four times higher in patients with diabetes mellitus and hypertension than in normotensive non-diabetic controls (3).

In particular, data from the Framingham study showed that the population with hypertension at the time of diagnosis of diabetes mellitus exhibited higher rates of all cause mortality (32 against 20 for 1000 people-year, $P < 0.001$) and of CV events (52 versus 31 for 1000 people-year; $P < 0.001$) compared to normotensive subjects with diabetes, thus suggesting that a large part of this "excess risk" was attributable to coexisting hypertension (4).

In this context, it is important to emphasize that the percentage of hypertensive individuals whose condition is treated and controlled is globally low (5). In Italy, approximately 60% of hypertensive patients are treated, but only 33% achieve an effective control of BP levels (6).

The reasons behind this discouraging situation may include shortcomings in the current pharmacological and non-pharmacological management strategies (7).

Lifestyle interventions, including dietary changes, weight loss, and increased physical activity, have been shown to be extremely useful in reducing BP and the incidence of diabetes mellitus in several controlled studies (8).

In a cross-sectional data analysis of the “Study to Help Improve Early evaluation and management of risk factors Leading to Diabetes (SHIELD)”, patients suffering from diabetes, hypertension and obesity showed a greater use of healthcare resources, a higher incidence of depression and a worse quality of life compared to patients suffering exclusively from diabetes mellitus (9). In support of this, in a retrospective study of Eaddy MT et al (10), the coexistence of hypertension and diabetes was associated with higher costs and greater healthcare resource utilization.

In this context, awareness-rising campaigns could be of fundamental importance to promote CV health.

STUDY PURPOSE

On the occasion of the Word Hypertension Day, the Italian Society of Hypertension (SIIA), in collaboration with the National Federation of Italian Pharmacies (Federfarma), sponsored a nationwide survey (*Abbasso la Pressione!*). This cross-sectional epidemiological survey, which involved 3956 pharmacies throughout the national territory, was conducted in order to have an overview of the prevalence and awareness of CV risk factors among Italian pharmacy customers, with particular focus on hypertension (11). We analyzed data from this project to evaluate the relationship between hypertension and diabetes, focusing on the clinical and demographic characteristics of the study population and on the variables related to BP control.

DESIGN AND METHODS

The survey was conducted among self-presenting individuals who entered the participating pharmacies from 17 to 20 May 2018. After signing the informed consent, participants were asked to answer a questionnaire. Trained pharmacists measured their BP using standardized procedures and methods. Specifically, BP was measured for each participant after 2 minutes rest, in sitting position, by automated oscillometric device, and the average of the second and third measurements was used for the analysis. BP was treated both as a numeric value (mmHg) and as a categorical variable (i.e. *BP categories*, expressed as: optimal BP, normal BP, high-normal BP, grade 1-2-3 hypertension, and isolated systolic hypertension; and *BP status*, expressed as: normotensive; untreated/undiagnosed hypertension; controlled/uncontrolled hypertension). Enrolled subjects self-reported their anthropometric data (age, height, weight) and provided information on their own clinical history and lifestyles habits. Diabetes diagnosis was also self-declared. Geographic provenance was recorded automatically. The 10-year CV risk was established according to guidelines (12).

Diabetic status was defined as being diabetic or non-diabetic. Prevalence of CV risk factors and hypertension rate/control according to the latest version of the European Society of Cardiology/European Society of Hypertension (ESC/ESH) guidelines on hypertension (13) was examined by diabetic status. Specifically, controlled hypertension was defined as BP <130/80 mmHg. Differences in participants' characteristics were evaluated with unpaired t tests for continuous variables and $\chi 2$ tests for categorical

variables. Bonferroni correction was applied as appropriate. Statistical analyses were performed using R (v3.5.1), considering statistical significance for $p < 0.05$.

RESULTS

General characteristics of the sample.

A total of 47217 participants were enrolled in the project (5695 diabetics and 41522 non-diabetics). Their clinical and demographic characteristics are summarized in **Table 1**.

Among patients with diabetes, 61.3% were older than 65 years and 47.7% came from southern Italy. Diabetic individuals showed a high prevalence of overweight (41%) and obesity (30.3%). Moreover, the diabetic group had a significantly greater prevalence of family/personal history of CVD/CKD and dyslipidemia, compared to non-diabetic participants ($p<0.001$). The totality of diabetic individuals had a 10-year CV risk from moderate-high to very high.

BP profile.

Data on BP by diabetic status are reported in **Tables 2 and 3**. Diabetic participants were less likely to have optimal or normal BP (**Table 2**). The percentage of treated hypertensive patients was 68.7% among diabetics and 42% among non-diabetics. Among diabetic individuals, the prevalence of uncontrolled hypertension was high (43.9%) (**Table 2**).

Mean systolic BP was overall higher in the diabetic group (135,96±18,38 mmHg vs 128,32±17,77 mmHg, $p<0.001$). This finding was confirmed by BP status (**Table 3**). Among normotensive individuals, no significant difference was observed in diastolic BP between diabetics and non-diabetics participants ($p=0.7039$, **Table 3**). On the other

hand, diabetic patients with newly detected or untreated hypertension, controlled hypertension and uncontrolled hypertension showed significantly lower values of diastolic BP than non-diabetics patients ($p<0.001$) (**Table 3**).

Lifestyle habits.

Lifestyle habits were examined by diabetic status alone (**Table 4**) or in combination with BP status (**Figure 1**). While diabetic participants more frequently self-reported consuming less salt, more vegetables, and being more active than non-diabetics (**Table 4**), no significant differences in terms of salt intake, vegetable consumption and smoking habits were recorded when they were stratified by BP status, except for a lower propensity to physical activity ($p=0.016$) among diabetic individuals with uncontrolled hypertension (**Figure 4**).

DISCUSSION

BP control in patients affected by diabetes is still far to be achieved. The coexistence of hypertension and diabetes significantly contributes to the development of micro and macrovascular complications, thus determining a worse prognosis and unfavorable outcomes in these patients (14).

Hypertension and diabetes mellitus share common risk factors, such as overweight, unhealthy lifestyles, and ageing. Moreover, these conditions are strictly linked from a pathophysiological point of view (15). In particular, insulin resistance is associated with sodium and fluid retention, which can elevate BP levels. Furthermore, insulin signaling involves molecules which modulate vascular tone. Other factors involved in the pathogenesis of both conditions include inflammation, oxidative stress, inappropriate activation of renin-angiotensin-aldosterone system, sympathetic system imbalance, and dysfunctional immune response (15). In addition to this, some antihypertensive drugs (e.g. thiazidic diuretics and β-blockers) can exert unfavorable effects on glyco-insulinemic profile. Conversely, the use of certain antidiabetic medications can be related to sodium and water retention, and may contribute to a rise in BP.

In line with this, a multivariate analysis from the PAMELA study determined that BP levels at baseline and the use of anti-hypertensive drugs were independent predictors of the onset of alterations in glyco-insulinemic metabolism, although with lower strength of association than basal BMI and fasting plasma glucose (16). Data from this study confirm the evidence of a close relationship between hypertension (clinical, ambulatory and home BP) and impaired glycemic and lipid profile (16).

A study by Tsimihodimos V et al. (17) showed that the development of hypertension and diabetes co-predicts each other over time. The authors suggest that diabetic individuals with BP levels near the upper limit of normality should be monitored for the development of hypertension. They also affirm that antidiabetic drugs with favorable actions on BP status might be the preferred choice for this population (17). In this context, our study reveals a high prevalence of hypertension among diabetic subjects. This may in part be due to the older age and to the higher prevalence of overweight/obesity, CKD and dyslipidemia in this group. A worth mentioning aspect emerging from our research is that, despite the finding of a higher percentage of diabetic individuals on anti-hypertensive treatment, BP control in this category was still worse compared to the non-diabetic group (uncontrolled hypertension: 43.9% vs 25.4%). This observation is consistent with previous literature and underlines the great complexity of patients with concomitant diabetes and hypertension.

In support of this, our study shows a much higher 10-year CV risk in the diabetic group than in the non-diabetic counterpart. Several studies confirm this finding: the Emergency Risk Factors Collaborations demonstrated that diagnosis of diabetes significantly increases the risk for various vascular diseases, independent of the presence of other conventional risk factors (18, 19).

In agreement with other studies, our research shows that patients with diabetes have higher values of systolic BP than those without diabetes, while diastolic BP levels are similar in the two groups. Moreover, the present analysis describes a higher prevalence of isolated systolic hypertension among diabetic subjects. This finding is in line with

current literature. In fact, diabetes is associated with vascular smooth cells proliferation and increased arterial stiffness, leading to higher systolic pressure and pulse pressure (19).

Our research also highlights the fact that hypertension rarely occurs as an isolated CV risk factor, but it is more often associated to other conditions that negatively affect CV health (20). In addition, our data confirm that diabetic status is more frequently associated to dyslipidemia and CVD/CKD, thus emphasizing the high complexity of individuals with concomitant diabetes mellitus and hypertension.

A research by Tatsumi Y. (21) reported that, in Japan as in Western countries, approximately 50% of patients with diabetes had concomitant hypertension and 20% of hypertensive patients presented with simultaneous diabetes. Subjects with either hypertension or diabetes mellitus had 1.5-2.0-fold higher risk of having both conditions.

As the prevalence of hypertension and diabetes is increasing worldwide, and being these conditions related to the development of severe CV complications, it is necessary to achieve satisfactory results in terms of prevention and treatment.

The last important finding of our study is the poor awareness/control of the various modifiable unhealthy lifestyle factors in this highly-complex population. In particular, diabetic subjects with uncontrolled hypertension showed a lower propensity to physical activity. Based on this, prevention-focused interventions are probably the best strategy to reduce the incidence of CVD and its associated risk factors. In this context, campaigns aimed at identifying patients with increased CV risk, and to improve the awareness

towards the importance of risk factors control, may be considered a powerful tool to improve global CV health and should be strongly promoted.

Some limitations of the present study need to be pointed out. First of all, being a clinical survey, it can only describe association, without identifying putative cause-effect relationships. Another limitation is related to selection bias and the use of self-reported data. Moreover, our research only considers office BP, without recognizing conditions such as white-coat hypertension and masked hypertension. A further limitation is the lack of data on medications and treatment compliance.

CONCLUSIONS

Despite the limitations identified, our results are substantially in line with the available literature, underlining that BP control is more challenging in diabetic patients, who normally present with a higher global CV risk. As lifestyle interventions (including dietary changes, weight loss, increased physical activity) appear effective both in lowering BP and reducing the incidence of diabetes, similar awareness-rising campaigns might be extremely useful to promote CV health.

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Table 1. Clinical and demographic characteristics of participants with and without diabetes. Chi-squared test, Student's t test and Bonferroni correction are applied, as appropriate.

	NON-DIABETICS	**DIABETICS**	p-value
n.	41522	5695	
Geographic Area (%)			<0.001
North (%)	17625 (42.4)	1999 (35.1)	<0.001
Center (%)	6928 (16.7)	980 (17.2)	0.331
South (%)	16969 (40.9)	2716 (47.7)	<0.001
Gender = M (%)	15820 (38.1)	2794 (49.1)	<0.001
Age category (%)			<0.001
<35	3267 (7.9)	135 (2.4)	
35-44	4819 (11.6)	249 (4.4)	
45-64	17854 (43.0)	1821 (32.0)	
≥65	15582 (37.5)	3490 (61.3)	
BMI category (%)			<0.001
Underweight	975 (2.3)	42 (0.7)	
Normal	18932 (45.6)	1591 (27.9)	
Overweight	15133 (36.4)	2335 (41.0)	
Obesity I	5075 (12.2)	1264 (22.2)	
Obesity II	1114 (2.7)	330 (5.8)	
Obesity III	293 (0.7)	133 (2.3)	
Familiar history of CVD (%)	15534 (37.4)	2394 (42.0)	<0.001
Dyslipidemia (%)	12636 (30.4)	2686 (47.2)	<0.001
CVD/CKD(%)	4613 (11.1)	1495 (26.3)	<0.001
10-years CV risk (%)			<0.001
None	1194 (2.9)	0 (0.0)	
Low	9448 (22.8)	0 (0.0)	
Low-moderate	17260 (41.6)	0 (0.0)	
Moderate	1367 (3.3)	0 (0.0)	
Moderate-high	5746 (13.8)	2656 (46.6)	
High	1894 (4.6)	1499 (26.3)	
High-very high	0 (0.0)	45 (0.8)	
Very high	4613 (11.1)	1495 (26.3)	

Table 2. BP status of participants with and without diabetes.

	NON-DIABETICS	DIABETICS	p-value
BP category (%)			<0.001
Optimal	11382 (27.4)	909 (16.0)	
Normal	8957 (21.6)	947 (16.6)	
High normal	9007 (21.7)	1277 (22.4)	
Grade 1 HTN	3494 (8.4)	498 (8.7)	
Grade 2 HTN	1367 (3.3)	271 (4.8)	
Grade 3 HTN	55 (0.1)	9 (0.2)	
ISH	7260 (17.5)	1784 (31.3)	
BP status (%)			<0.001
Uncontrolled HTN	10545 (25.4)	2500 (43.9)	
Controlled HTN	6901 (16.6)	1410 (24.8)	
Normotensive	18789 (45.3)	1139 (20.0)	
Undiagnosed/Untreated HTN	5287 (12.7)	646 (11.3)	

HTN = Hypertension; ISH = Isolated Systolic Hypertension

Table 3. Mean BP (systolic, diastolic; mmHg) by diabetes status (yes/no). Difference in BP by BP status is reported (ΔSBP, ΔDBP). Pairwise t Student's test is applied.

	NO DIABETES			WITH DIABETES			ΔSBP (mmHg)	p	ΔDBP (mmHg)	p
BP status	**n.**	**SBP, mmHg (sd)**	**DBP, mmHg (sd)**	**n.**	**SBP, mmHg (sd)**	**DBP, mmHg (sd)**				
Uncontrolled HTN	10545	142.5 (14.7)	83.4 (8.9)	2500	146.9 (15)	82.1 (10)	4.4	<0.001	-1.3	<0.001
Controlled HTN	6901	120.5 (10.9)	69.1 (7)	1410	122 (11.2)	67.4 (7.6)	1.5	<0.001	-1.7	<0.001
Normotensives	18789	118 (12.3)	72.9 (8.6)	1139	121.5 (11.8)	72.8 (9)	3.5	<0.001	-0.1	0.7039
Undiagnosed/Untreated hypertensives	5287	146.9 (12.4)	86.7 (9.7)	646	149.2 (12.4)	84.2 (10.3)	2.3	<0.001	-2.5	<0.001

Table 4. Lifestyles habits of participants with and without diabetes.

	NON-DIABETICS	DIABETICS	p-value
Salt use (%)	11124 (26.8)	1436 (25.2)	0.012
Vegetables use (%)	33665 (81.1)	4504 (79.1)	<0.001
Physical activity (%)	19254 (46.4)	2397 (42.1)	<0.001
Smoke (%)	8420 (20.3)	1122 (19.7)	0.318

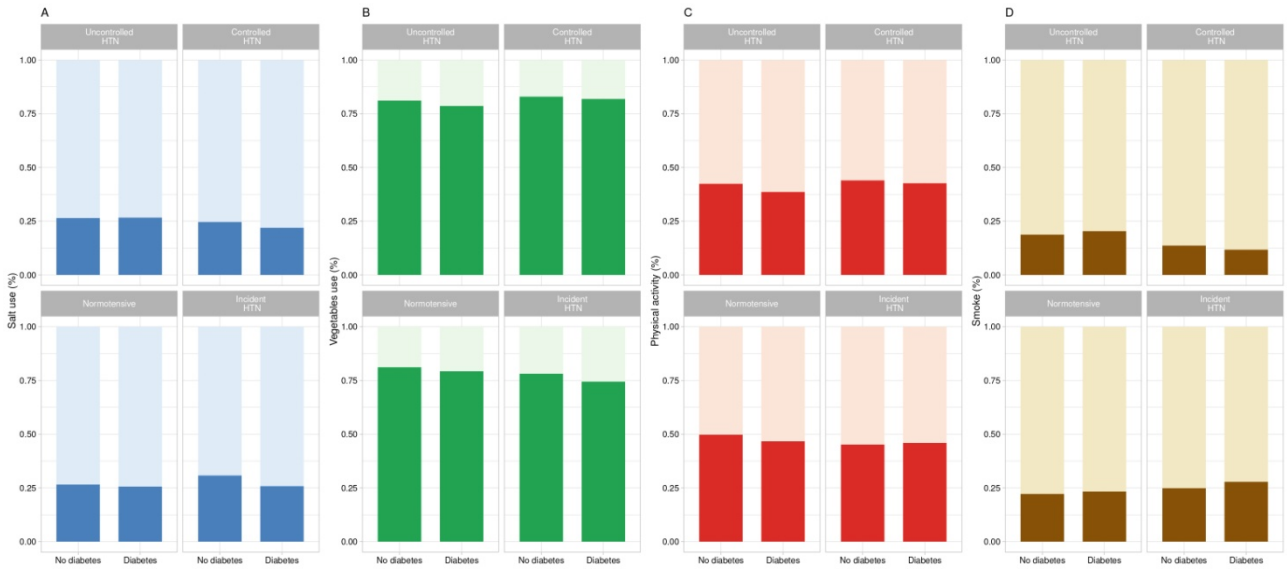

Figure 1. Distribution of salt use (%), vegetables use (%), physical activity (%), smoking habit (%) by BP status (normotensive, undiagnosed/untreated HTN, controlled HTN, uncontrolled HTN) and diabetes (yes/no). Bonferroni correction is applied. p=0.016 for the difference in physical activity by diabetes status in participants with uncontrolled HTN. Other comparisons are NS.