Global cardiometabolic risk profile in patients with hypertension: results from the Turkish arm of the pan-European GOOD survey

Hipertansiyonlu hastada genel kardiyometabolik risk profili: Pan-Avrupa GOOD çalışmasının Türkiye kolunun sonuçları

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Objectives: We evaluated the results of the Turkish arm of the GOOD survey which investigated the cardiometabolic risk profile and the control of blood pressure (BP) of adult hypertensive outpatients in 12 countries across Europe.

Study design: A total of 218 hypertensive patients (139 females, 79 males; mean age 57.2±10.9 years) from Turkey were included in this pan-European survey. Blood pressure control (defined as BP <140/90 mmHg for nondiabetics and <130/80 mmHg for diabetics) and cardiometabolic risk factors such as diabetes mellitus, metabolic syndrome, obesity, sedentary lifestyle, and atherogenic dyslipidemia were evaluated in accordance with the 2003 ESH/ESC guidelines on management of hypertension.

Results: Control of BP was achieved in only 21.6% of the patients diagnosed with hypertension for a mean duration of 7.7±5.4 years. The mean systolic and diastolic BPs were 144±21 mmHg and 88±14 mmHg, respectively. The most frequent concomitant disease was type 2 diabetes mellitus (66 patients, 30.3%). Patients with diabetes had a higher prevalence of metabolic syndrome compared to nondiabetics (78.8% *vs.* 48%, p<0.01). The absence of BP control was more pronounced among diabetics than in nondiabetics for systolic (77.3% *vs.* 63.8%) and diastolic (84.9% *vs.* 57.2%) pressures. Nearly half of the hypertensive patients had atherogenic dyslipidemia, but only 35.8% of them were treated with lipid lowering drugs.

Conclusion: Despite appropriate treatment, poor BP control in Turkish hypertensive patients was associated with metabolic syndrome, diabetes, and undertreatment of atherogenic dyslipidemia. Therefore, more effective measures must be taken in the management of cardiovascular risk factors to improve BP control.

Key words: Diabetes mellitus, type 2; dyslipidemias; hypertension/epidemiology/therapy; metabolic syndrome X; prevalence; Turkey/epidemiology.

Amaç: Avrupa'da 12 ülkede erişkin hipertansif hastalarda kardiyometabolik risk profili ve kan basıncı (KB) kontrolünü araştıran GOOD çalışması kapsamında, Türk katılımcıların sonuçları değerlendirildi.

Çalışma planı: Avrupa genelinde yürütülen bu çalışmaya Türkiye'den toplam 218 hipertansif hasta (139 kadın, 79 erkek; ort. yaş 57.2±10.9) katıldı. Kan basıncı kontrolü (diyabetik olmayanlarda KB <140/90 mmHg, diyabetiklerde <130/80 mmHg) ve diabetes mellitus, metabolik sendrom, obezite, sedanter yaşam ve aterojenik dislipidemi gibi kardiyometabolik risk faktörlerinin varlığı 2003 ESH/ESC hipertansiyon tedavi kılavuzuna göre değerlendirildi.

Bulgular: Ortalama 7.7±5.4 yıldır hipertansiyon tanısı almış olan hastaların sadece %21.6'sında KB kontrolü sağlanabilmişti. Sistolik ve diyastolik KB ortalamaları sırasıyla 144±21 mmHg ve 88±14 mmHg bulundu. Eşlik eden en sık hastalık tip 2 diabetes mellitus (66 hasta, %30.3) idi. Diyabetli hastalarda metabolik sendrom sıklığı diyabet olmayanlara göre anlamlı derecede daha fazlaydı (%78.8 ve %48, p<0.01). Kan basıncı kontrolünün sağlanamaması diyabetiklerde diyabetik olmayanlara göre daha belirgindi (sistolik KB için sırasıyla %77.3 ve %63.8; diyastolik KB için %84.9 ve %57.2). Hipertansif hastaların neredeyse yarısında aterojenik dislipidemi saptandı, fakat tüm grubun sadece %35.8'i lipit düşürücü ilaçlar ile tedavi görmekteydi.

Sonuç: Türk hipertansif hastalarda, uygun tedavilere rağmen kötü KB kontrolü, metabolik sendrom ve diyabet ile birliktelik göstermektedir ve bu hastalarda dislipidemi tedavisi ihmal edilmektedir. Bu nedenle, KB kontrolünü iyileştirmek için kardiyovasküler risk faktörlerinin tedavisinde daha etkili önlemler alınmalıdır.

Anahtar sözcükler: Diabetes mellitus, tip 2; dislipidemi; hipertansiyon/epidemiyoloji/tedavi; metabolik sendrom X; prevalans; Türkiye/epidemiyoloji.

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Hypertension is considered to be a major contributor to the development of cardiovascular disease and stroke[1,2] and a common disorder estimated to affect approximately 1.5 billion people worldwide by 2025.[3] Achievement and maintenance of blood pressure (BP) control is important given the significant cardiovascular morbidity and mortality associated with the hypertensive status. Indicating the possible influence of several cardiometabolic risk factors in the treatment success of hypertension,[4] only about 40% of treated hypertensives have been reported to have their BP controlled despite the availability of various effective therapeutic agents.[5,6]

Although few data are available on the coexistence of cardiometabolic risk factors and uncontrolled hypertension across the broad European population,[7,8] the association between high BP and metabolic risk factors has been a well-known phenomenon.[4,9]

Since the nature of the interaction between hypertension and cardiovascular risk factors is considered to be consistent, continuous and independent of other risk factors,[10-12] investigation of potential underlying concomitant factors that may influence BP control seems to be quite reasonable. The present substudy was designed to evaluate the current status of BP control with respect to associated cardiometabolic risk factors in treated hypertensive patients in Turkey.

PATIENTS AND METHODS

Study design and patient selection criteria. The Global Cardiometabolic Risk Profile in Patients with hypertension disease (GOOD) survey is a pan-European, observational, cross-sectional survey conducted at 305 sites in 12 European countries including Belgium, Germany, Hungary, Italy, the Netherlands, Norway, Portugal, Slovenia, Spain, Sweden, Turkey and the UK.[13]

Aiming to determine the cardiometabolic risk profile of hypertensive patients in Turkey, a total of 218 hypertensive patients were included in 15 different centers in Turkey, between October 6, 2006 and May 16, 2007.

Investigators were randomly selected from two lists of practitioners containing three- to ten-fold of the number of investigators needed, one list included general practitioners (70% of investigators) and the other included specialists (30% of investigators: cardiologists, internists, and hypertension specialists). Thus, 15 investigators took part in the study, including 10 general practitioners (66.7%), and five cardiologists (33.3%). Most of them (66.7%) were working in urban practices, and 33.3% were working in rural practices. Most of the investigators (60%) had more than 10 years of medical practice and 33.3% had 5-10 years of experience.

Investigators were requested to complete a questionnaire regarding their practice and specialty. Patient inclusion was systematic. The first patient of each physician's working day who fulfilled the inclusion criteria was asked to participate. If he/she declined, the next patient was asked to participate. A maximum of two patients were recruited per day per physician. There was no selective exclusion of patients. Each investigator was requested to provide information for 10 to 15 patients.

The inclusion criteria of the study encompassed the following features: men or women outpatients at least 30 years of age, who were already receiving treatment for hypertension or had newly diagnosed

Table 1. Patients' demographics and general features related to hypertensive illness based on past history and control status (n=218)

	n	%	Mean±SD
Age (years)			57.2±10.9
Sex			
Men	79	36.2	
Women	139	63.8	
Height (cm)			163.0± 9.0
Weight (kg)			78.5±13.0
Body mass index (kg/m^2)			
Overall (n=218)			29.6± 4.7
<25 kg/m^2	32	14.7	
25-30 kg/m^2	98	45.0	
≥30 kg/m^2	88	40.4	
Waist circumference (cm)			
Male			97.1±8.4
Female			97.1±13.5
Heart rate (bpm)			76.6±11.3
Blood pressure			
Controlled	47	21.6	
Uncontrolled	171	78.4	
Type of hypertension			
Currently treated	198	90.8	
Newly diagnosed	20	9.2	
Duration of hypertension (years) (n=198)			7.7±5.4
Distribution of patients based on duration of hypertension			
Newly diagnosed	20	9.2	
<5 years	61	28.0	
5-10 years	93	42.7	
>10 years	44	20.2	

hypertension defined as either systolic blood pressure (SBP) ≥140 mmHg or diastolic blood pressure (DBP) ≥90 mmHg in nondiabetic patients or both, or SBP ≥130 mmHg and/or DBP ≥80 mmHg in patients with diabetes, assessed on two previous consultations and confirmed on the day of inclusion in the survey. Exclusion criteria included known pregnancy, menstruation, hospitalization, secondary hypertension, fever, known renal disease with serum creatinine level greater than 177 mmol/l, or current drug treatment and/or concomitant conditions that could alter microalbuminuria testing.

Accordingly, among 225 patients recruited in the study, 218 patients (139 females, 79 males; mean age 57.2±10.9 years) were analyzed, since seven patients (3.1%) were excluded due to high creatinine values (>177 μmol/l; n=3) and type 1 diabetes mellitus (n=4).

Written informed consent was obtained from each subject following a detailed explanation of the objectives and protocol of the survey. The study was conducted in accordance with the ethical principles stated in the Declaration of Helsinki and after obtaining approval of the institutional ethics committee.

Data collection. Assessments were made during patient's visit including measurements of weight, height, waist circumference, seated BP (two measurements taken after at least 3 min rest), heart rate at rest, and microalbuminuria (30-300 mg urine albumin/g creatinine). The investigator also collected information on demographics and cardiometabolic risk factors including duration of hypertension, history of diabetes, cardiovascular disease or stroke; lifestyle factors including alcohol consumption, physical exercise, and smoking habit; and laboratory measurements of fasting blood glucose, fasting lipid profile, and serum creatinine levels (these data were obtained from the patient's file if they had been collected within the previous 6 months).

Metabolic syndrome was defined according to the ATP III criteria,[14] based on the presence of three or more of the following: BP >130/85 mmHg; waist circumference >102 cm (men) or >88 cm (women); triglyceride >1.69 mmol/l; HDL cholesterol <1.03 mmol/l (men) or <1.29 mmol/l (women); fasting glucose >5.55 mmol/l.

Statistical analysis. All patients with evaluable data on age, gender, BP, and antihypertensive treatment(s) were included in the analysis. Comparisons between participants with controlled BP (<140/90 mmHg for nondiabetic patients, <130/80 mmHg for diabetics) and uncontrolled BP (≥140/90 mmHg for nondiabetic patients, ≥130/80 mmHg for diabetics) were made using the chi-square test for qualitative variables, and Student's t-test or Wilcoxon test for quantitative variables. Data were expressed as mean ± standard deviation (SD) or percentage (%) where appropriate. A P value of less than 0.05 was considered statistically significant.

RESULTS

The demographic and clinical characteristics of the patients are given in Table 1.

According to the 2003 ESH/ESC guidelines, BP was controlled in 47 patients (21.6%). Hypertension was newly diagnosed in 20 patients (9.2%), while 90.8% of the study population had hypertension with a mean duration of 7.7±5.4 years and were already receiving antihypertensive medications (Table 1).

Table 2. Comparison between diabetic and nondiabetic patients in terms of blood pressure

	Overall (n=218)			Type 2 diabetic (n=66)			Nondiabetic (n=152)		
	n	%	Mean±SD	n	%	Mean±SD	n	%	Mean±SD
Systolic blood pressure									
Overall (mmHg)			144± 21			143±22			144±21
<130 mmHg	39	17.9		13	19.7		26	17.1	
130-140 mmHg	42	19.3		13	19.7		29	19.1	
140-160 mmHg	102	46.8		30	45.5		72	47.4	
160-180 mmHg	27	12.4		8	12.1		19	12.5	
>180 mmHg	8	3.7		2	3.0		6	4.0	
Diastolic blood pressure									
Overall (mmHg)			88±14			87±11			89±15
<80 mmHg	40	18.4		10	15.2		30	19.7	
80-90 mmHg[	60	27.5		25	37.9		35	23.0	
90-100 mmHg[	55	25.2		20	30.3		35	23.0	
≥100 mmHg	63	28.9		11	16.7		52	34.2	
Overall pulse pressure (mmHg)			55±16			56±17			55±15

Table 3. Cardiovascular medications

		n	%
At least one cardiovascular medication (n=205)	No	7	3.4
	Yes	198	96.6
At least one antihypertensive drug (n=205)	No	7	3.4
	Yes	198	96.6
At least one diuretic (n=205)	No	133	64.9
	Yes	72	35.1
At least one antiplatelet agent (n=218)	No	99	45.4
	Yes	119	54.6
Number of antihypertensive drugs (n=205)			
0		7	3.4
1		85	41.5
2		79	38.5
≥3		34	16.6
ARBs and/or ACE inhibitors (n=205)	No	39	19.0
	Yes	166	81.0
Thiazides (n=205)	No	135	65.9
	Yes	70	34.2
Loop diuretics (n=205)	No	201	98.1
	Yes	4	2.0
Aldosterone antagonists (n=205)	No	202	98.5
	Yes	3	1.5
Alpha-blockers (n=205)	No	200	97.6
	Yes	5	2.4
Calcium channel blockers (n=205)	No	157	76.6
	Yes	48	23.4
Beta-blockers (n=205)	No	149	72.7
	Yes	56	27.3
Nitrates (n=205)	No	198	96.6
	Yes	7	3.4
Digitalis (n=205)	No	202	98.5
	Yes	3	1.5
Aspirin (n=218)	No	103	47.3
	Yes	115	52.8

Table 4. Antidiabetic and lipid lowering treatments

		n	%
Anti-diabetic agents (66 patients)			
At least one diabetes drug therapy	No	3	4.6
	Yes	63	95.5
Number of diabetes therapies			
0		3	4.6
1		39	59.1
2		22	33.3
≥3		2	3.0
Biguanides	No	54	81.8
	Yes	12	18.2
Sulfonylureas	No	25	37.9
	Yes	41	62.1
Insulin	No	61	92.4
	Yes	5	7.6
Glinides	No	53	80.3
	Yes	13	19.7
Thiazolinediones	No	54	81.8
	Yes	12	18.2
Alpha-glucosidase inhibitors	No	61	92.4
	Yes	5	7.6
Lipid lowering agents (218 patients)			
At least one lipid lowering agent	No	140	64.2
	Yes	78	35.8
Number of lipid lowering therapies			
0		140	64.2
1		76	34.9
2		2	0.9
Statins	No	146	67.0
	Yes	72	33.0
Fibrates	No	210	96.3
	Yes	8	3.7
Statins and/or fibrates	No	140	64.2
	Yes	78	35.8

The mean SBP and DBP were 144±21 mmHg and 88±14 mmHg, respectively. Systolic blood pressure was higher than 140 mmHg in 62.8% of the patients, and DBP was higher than 90 mmHg in 54.1% of the patients (Table 2).

Despite treatments for hypertension and diabetes, BP was controlled only in 21.6% of hypertensive and diabetic patients. Metabolic syndrome was more prevalent with a higher number of components in patients with type 2 diabetes mellitus. Blood pressure was higher than the recommended systolic and diastolic values in 77.3% and 84.9% of diabetic patients, respectively, compared with lower rates of uncontrolled SBP (63.8%) and DBP (57.2%) among nondiabetic patients. The mean pulse pressures were 56±17 mmHg and 55±15 mmHg in diabetic and nondiabetic patients, respectively (Table 2).

At least one drug for cardiovascular therapy (namely antihypertensive medication) was prescribed in 96.6% of the patients. Most of the patients were on either monotherapy (41.5%) or on dual-drug therapy (38.5%). The remaining patients (16.6%) were prescribed more than two antihypertensive medications (Table 3).

Considering diabetic treatment, at least one glucose-lowering drug was used in 95.5% of the diabetics. Most of the diabetic patients were on either monotherapy (59.1%) or on dual-therapy (33.3%). Sulfonylureas (62.1%) were the most commonly prescribed antidiabetic drug (Table 4). At least one lipid-lowering medication was used in 35.8% of the patients, while statins and/or fibrates (35.8%) were the most commonly prescribed lipid-lowering drugs (Table 4).

Metabolic syndrome was diagnosed in 125 patients (57.3%) with or without diabetes. The five components of the metabolic syndrome were distributed as follows: elevated waist circumference

Table 5. The prevalences of metabolic syndrome components

Metabolic syndrome components		n	%
Waist circumference			
≤102/88 cm	Overall	94	43.1
	Male	60	63.8
	Female	34	36.2
>102/88 cm	Overall	124	56.9
	Male	19	15.3
	Female	105	84.7
Fasting triglycerides			
<150 mg/dl		115	52.8
≥150 mg/dl		103	47.3
HDL cholesterol			
≥40-50 mg/dl	Overall	136	62.4
	Male	60	44.1
	Female	76	55.9
<40-50 mg/dl	Overall	82	37.6
	Male	19	23.2
	Female	63	76.8
Blood pressure	No	34	15.6
(≥130/85 mmHg)	Yes	184	84.4
Fasting glucose			
<100 mg/dl (5.55 mmol/l)		104	47.7
≥100 mg/dl (5.55 mmol/l)		114	52.3

(>102 cm in men or >88 cm in women) in 56.9%, high levels of fasting triglycerides (≥150 mg/dl) in 47.3%, reduced HDL cholesterol (<40-50 mg/dl) in 37.6%, elevated BP (≥130/85 mmHg) in 84.4%, and high levels of fasting blood glucose (≥5.55 mmol/l) in 52.3%. The average number of components of the metabolic syndrome was 2.8±1.3. Most of the patients had either two (27.5%) or three (27.1%) of these components, only 9.6% of the patients had all of the components (Table 6).

The prevalence of metabolic syndrome was significantly higher in diabetic patients compared to nondiabetic patients (78.8% *vs*. 48.0%, p<0.01; Table 6). The number of metabolic syndrome components was also higher in diabetic patients compared with nondiabetic patients (3.5±1.1 *vs*. 2.5±1.2; p<0.05). The presence of type 2 diabetes was associated with the increased likelihood of having five metabolic syndrome components compared with nondiabetic patients (21.2% *vs*. 4.6%; p<0.05; Table 6).

DISCUSSION

According to our results, BP control, defined according to the 2003 ESH/ESC guidelines, was achieved in 47/218 (21.6%) of the patients. This percentage of BP control was consistent with both the results of the whole GOOD survey[13] stating less than 30% success for the control of BP in treated hypertensive patients across 12 European countries including Turkey and with other previous studies conducted across Europe.[8,15,16] Considering similar durations of hypertension (7.7±5.4 years) and diabetes mellitus (6.4±6.0 years) in our patients, the influence of cardiometabolic risk factors seems to be accentuated in the control of BP levels.[4,17]

Indeed physicians' attitudes and treatment strategies as well as patient-related factors[18-20] have been accused for the poor BP control. Similarly, the disparity between clinical practice and guideline recommendations was reported recently in a study conducted with 1,259 primary care physicians from 17 countries (including Europe, the USA, Asia, and Africa) in which 41% of physicians stated that they discontinued treatment before the recommended BP

Table 6. The prevalence of metabolic syndrome and the number of components based on the presence or absence of type 2 diabetes mellitus

	Overall (n=218)		Type 2 diabetic (n=66)		Nondiabetic (n=152)	
	n	%	n	%	n	%
Metabolic syndrome (MS)						
Absent	93	42.7	14	21.2	79	52.0
Present	125	57.3	52	78.8*	73	48.0
Number of MS components						
0	9	4.1	0	0.0	9	5.9
1	24	11.0	2	3.0	22	14.5
2	60	27.5	12	18.2	48	31.6
3	59	27.1	16	24.2	43	28.3
4	45	20.6	22	33.3	23	15.1
5	21	9.6	14	21.2+	7	4.6
Mean	2.8±1.3		3.5±1.1+		2.5±1.2	

ANOVA and Tukey test were used for comparison of the mean number of components and chi-square test was used for the prevalence of metabolic syndrome: *p<0.01 and +p<0.05 compared to nondiabetic patients.

goals were reached as they thought reductions to an acceptable level had been achieved.[21] Since almost all hypertensive and diabetic patients are under appropriate medical treatments with at least one antihypertensive and/or antidiabetic agent, and many also present with other cardiovascular indications, factors other than the role of physicians' attitudes may contribute to poor BP control, such as patient compliance and persistence. However, insufficient prescription of lipid lowering drugs by physicians may also account for poor BP control by overlooking the need for effective management of cardiovascular risk factors in the hypertension treatment.

In agreement with the results of the GOOD survey reporting a significant association between uncontrolled hypertension and increased prevalence of cardiometabolic risk factors including metabolic syndrome and/or diabetes,[13] metabolic syndrome was more frequent among diabetic patients and type 2 diabetes mellitus was the most frequent concomitant risk factor in this sub-study.

Moreover, the presence of other cardiovascular disorders was consistent with impaired lipid profile presenting as higher LDL cholesterol levels in males and lower HDL cholesterol levels in females, with increased total cholesterol and triglyceride levels in the entire patient population. The findings of the TEKHARF study demonstrated a significant and independent association between atherogenic dyslipidemia and BP only in women in Turkey, which was interpreted as a marker of proinflammatory state among Turkish women.[22]

Age, female sex, and waist circumference were found as major determinants while serum insulin and CRP as modest determinants of incident hypertension in middle-aged Turkish adults, and it was reported that current cigarette smoking played a modest protective role.[23] The higher prevalence of metabolic syndrome among type 2 diabetic patients seems to emphasize the crucial role of achieving target BP control among these patients. Moreover, compared to nondiabetics, both the incidence of metabolic syndrome and the number of syndrome components were found to be increased significantly among type 2 diabetics. The presence of all five components was also significantly more common in diabetic patients compared to nondiabetics (21.2% *vs*. 4.6%, $p<0.05$).

Almost all hypertensive and diabetic patients in the present sub-study were receiving at least one antihypertensive or antidiabetic drug. However, lipid lowering agents were used in only one-third of the patients despite the existence of atherogenic dyslipidemia in approximately half of the patients. In this regard, our data support the conclusion of the global GOOD survey[13] emphasizing the need to consider the overall cardiometabolic profile of a patient, rather than BP per se, while determining the optimal management strategy of hypertension. A close relationship of metabolic syndrome with hypertension and the long-term cardiovascular impact of "dyslipidemic hypertension" among Turkish patients were documented previously by the TEKHARF study.[24]

Treatment of concomitant risk factors such as dyslipidemia is often not considered in the clinical practice, as revealed by a retrospective cohort study performed in the UK,[9] indicating a bypass of cardiovascular risk factors among hypertensive patients. MacDonald et al.[9] reported that, of patients with at least three cardiovascular risk factors in addition to hypertension, only 24% were given lipid lowering drugs, a rate very similar to that determined in our study.

Despite the fact that almost all hypertensive and diabetic patients were under medical treatment with at least one antihypertensive and/or antidiabetic agent, high BP could be controlled in only 1/5 of our patients, highlighting the role of cardiometabolic risk factor management in BP control. This finding also confirms the well-known difficulty in controlling BP in patients with diabetes and metabolic syndrome, recognized as a high-added risk in the ESH/ESC guidelines.[4]

In accordance with the pan-European results of the GOOD survey,[13] poor BP control among Turkish population was also related to increased prevalence of metabolic syndrome with all components including abdominal obesity, elevated fasting blood glucose, decreased fasting HDL cholesterol, elevated fasting triglycerides, and elevated BP. The results of the GOOD survey showed the presence of uncontrolled BP in 95.3% of patients with both metabolic syndrome and type 2 diabetes.[13] Our data support the global GOOD survey[13] for the role of metabolic syndrome per se and devastating nature of accompanying diabetes. The fact that only less than one-third of treated hypertensive patients had controlled BP and that metabolic syndrome and diabetes were associated with poor BP control underline the consideration of cardiometabolic risk factors as a prerequisite in achieving target BP control especially among type 2 diabetic hypertensive patients.

In conclusion, since hypertension-related risk has been shown to be reversible and reductions in BP by antihypertensive drugs are accompanied by major decreases in cardiovascular morbidity and mortality,[25,26] consideration of the global cardiometabolic profile, rather than BP alone, may be crucial in the management of patients with hypertension especially in those presenting with a high cardiometabolic risk with or without diabetes.

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