ORIGINAL ARTICLE

National Registry of Hypertension. Epidemiological Characteristics of Hypertension in Argentina. The RENATA-2 Study

Registro Nacional de Hipertensión Arterial. Características epidemiológicas de la hipertensión arterial en la Argentina. Estudio RENATA-2

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ABSTRACT

Background: Hypertension is the main risk factor for cardiovascular disease and cardiovascular mortality. As the prevalence of hypertension is increasing, it is necessary to know the updated information in Argentina.
Objective: The aim of this study was to evaluate the prevalence, awareness, treatment and control of hypertension in Argentina.
Methods: A cross-sectional study was conducted including subjects ≥18 years from 25 cities in Argentina. The participants were surveyed and blood pressure was measured using validated automated sphygmomanometers.
Results: A total of 5,931 subjects were surveyed. Mean age was 43.5±17.1 years. The prevalence of hypertension was 36.3% (95% CI, 35.1-37.6), was higher in men (43.7% vs. 30.4%; p < 0.0001), and increased with age in both sexes. Among subjects with hypertension, 38.8% were unaware of their condition while 5.7% knew it but were not receiving treatment. In 55.5% of cases, subjects were receiving therapy, and only 24.2% were well controlled, particularly women. In treated subjects, 73.4% were receiving monotherapy and hypertension was controlled in only 43.6%. Patients who adhered to treatment had better blood pressure control than those who did not (46.9% vs. 40.1%; p=0.01).
Conclusions: The prevalence of hypertension in Argentina is 36.3%, in agreement with the reports of the World Health Organization for the region. In 38.8% of cases, participants were unaware of their condition. Half of the subjects with hypertension were receiving drug therapy and only 25% were controlled. Three out of four patients treated were receiving monotherapy. Blood pressure control was associated with better adherence to treatment.

Key words: Blood Pressure - Hypertension - Prevalence - Epidemiology

RESUMEN

Introducción: La hipertensión arterial es el principal factor de riesgo para enfermedad y muerte cardiovascular. Su prevalencia va en aumento, lo cual hace necesario conocer los datos actualizados en la Argentina.
Objetivo: Evaluar la prevalencia, el conocimiento, el tratamiento y el control de la hipertensión arterial en la Argentina.
Material y métodos: Estudio de corte transversal que incluyó individuos ≥18 años de 25 ciudades argentinas. Los participantes fueron encuestados y se midió la presión arterial con presurómetros automáticos validados.
Resultados: Se encuestaron 5.931 individuos, con una edad promedio de 43,5 ± 17,1 años. La prevalencia de hipertensión arterial fue del 36,3% (IC 95% 35,1-37,6), siendo mayor en varones (43,7% vs. 30,4%; p < 0,0001). La prevalencia aumentó con la edad en ambos sexos. El 38,8% de los hipertensos desconocían su enfermedad y el 5,7% la conocían pero no recibían tratamiento. El 55,5% estaban tratados y solo el 24,2% se encontraban controlados, observándose más control en las mujeres. El 73,4% de los hipertensos tratados recibían monoterapia y solo el 43,6% estaban controlados. Los pacientes adherentes al tratamiento tuvieron mejor control de la presión arterial que los no adherentes (46,9% vs. 40.1%; p = 0.01).
Conclusiones: La prevalencia de hipertensión arterial en la Argentina es del 36,3%, en coincidencia con los reportes de la Organización Mundial de la Salud para la región. El 38,8% de los participantes desconocían su enfermedad. La mitad de los hipertensos recibían tratamiento farmacológico y solo la cuarta parte estaban controlados. Tres de cada cuatro pacientes tratados recibían monoterapia. El control de la presión arterial se relacionó con mejor adherencia al tratamiento.

Palabras clave: Presión arterial - Hipertensión - Prevalencia - Epidemiología

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Abbreviations

CCB	Calcium channel blockers	**CI**	Confidence interval
ARB	Angiotensin II receptor blocker	**WHO**	World Health Organization
BB	Beta blockers	**BP**	Blood pressure
NIC	National identity card	**DBP**	Diastolic blood pressure
HT	Hypertension	**SBP**	Systolic blood pressure

INTRODUCTION

Hypertension (HT) is the main risk factor for cardiovascular morbidity and mortality. (1, 2) In addition, over the past 25 years, HT scaled from being the 4th leading risk factor to the first place for global disease burden and all-cause mortality. (3) On the other hand, the evidence favoring antihypertensive drug therapy to reduce cardiovascular events and mortality is conclusive. (4)

The high prevalence of hypertension and its poor control demand local governmental and non-governmental organizations to be aware of the updated prevalence of the disease. According to the World Health Organization (WHO), (5) in 2008 the prevalence of HT worldwide was about 40% in adults >25 years, with the highest prevalence in the African Region (46%), while the lowest prevalence was observed in the Region of the Americas (35%). In the United States, HT affects almost one third of the population >18 years and is not controlled in about half of them. Among uncontrolled hypertensive patients, 33% are not aware of their condition, 20% know they have HT but are not treated and approximately 47% are treated but not controlled. (6) In regional studies, as the CARMELA (Cardiovascular Risk Factor Multiple Evaluation in Latin America) (7) and the CESCAS I (Centro de Excelencia en Salud Cardiovascular para el Cono Sur) trials, (8) which surveyed cities of different South American countries, the prevalence of HT differed according to the city and country analyzed.

In Argentina, different epidemiological studies have tried to establish what the population knows about HT. (9-14) The Third National Risk Factor Survey (15) determined that, in Argentina, 17.6% of survey respondents had not had their BP measured over the past 2 years and 34.1% received the diagnosis of high blood pressure.

The RENATA study, (16) performed during the period 2008-2009, was the first registry providing information about the prevalence, awareness, treatment and control of HT in Argentina. The study was conducted in 7 cities and reported a prevalence of 33.5%.

After 7 years, and with the intention of establishing an epidemiological surveillance of HT in our country, the Argentine Society of Cardiology and the Argentine Federation of Cardiology have designed the 2nd National Registry of Hypertension (RENATA-2 study) with the primary aims of establishing: 1) the updated prevalence of HT in Argentina; 2) the percentage of patients aware of their condition, and 3) the percentage of pharmacologically treated and controlled hypertensive patients. The secondary aims were to determine adherence to antihypertensive treatment, type of antihypertensive treatment, salt intake, level of education and type of access to the health care system in the study participants.

METHODS

The RENATA-2 study was conducted between August 2015 and March 2016 in 25 cities of Argentina. This cross-sectional study included a non-probability, randomized sample of subjects of both sexes ≥18 years of age who signed an informed consent form before entering the study. The sample was obtained in 25 districts of 18 provinces of Argentina: Autonomous City of Buenos Aires, Southern Greater Buenos Aires, Mar del Plata, Bahia Blanca, Azul, Olavarria, Cordoba, Villa Maria, Santa Rosa, Rancul, La Rioja, Mendoza, Lujan de Cuyo, Trelew, San Miguel de Tucuman, Salta, San Juan, Santiago del Estero, Corrientes, Rosario, Parana, San Luis, Neuquen, Formosa, Tierra del Fuego and Rio Grande. In all cases, the surveys were conducted in subjects attending the National Registry of Persons offices to obtain their national identity card (NIC). Participants were randomized in the waiting room by a surveyor. Participants whose NIC had a final digit ending in an even number on even days and those ending with an odd number on odd days were invited to participate. The survey was administered once the informed consent form was signed (data about medications, risk factors, smoking habits, level of education and access to the health care system). The adherence to treatment was evaluated using the Morisky-Green-Levine test. (17) The questionnaire is focused on evaluating compliance to antihypertensive treatment within the past 6 months and consists of four questions: 1) Do you ever forget to take your medication?, 2) Do you take your medication at the time indicated?, 3) Do you ever skip your medication if you feel well?, and 4) Do you stop your medication if you ever feel not well after taking it? Hypertensive subjects receiving treatment who answered correctly the 4 questions, "no" to questions 1, 3 and 4 and "yes" to question 2, were considered "adherent". Blood pressure was measured following the recommendations of the Consensus on Hypertension of the Argentine Society of Cardiology (18) using validated automated sphygmomanometers (Microlife BP200 afib). Hypertension was defined as systolic blood pressure (SBP) ≥140 mmHg or diastolic blood pressure (DBP) ≥90 mmHg and/or presence of antihypertensive treatment. Controlled hypertension was considered in subjects under antihypertensive treatment with BP levels <140/90 mmHg. The survey was administered by previously trained cardiology technicians or nurses who also measured BP levels. For stratification and further analysis, the population was divided into five age groups proportionally to the general population of the last 2010 National Census (≤34, 35-44, 45-54, 55- 64 and ≥65 years).

Statistical analysis

Sample size was calculated using Pocock's formula to evaluate the primary endpoint, considering an alpha level of 0.001, with a confidence interval of 99.9% and a study power of 95%. Therefore, considering the 33.5% prevalence of HT ("primary endpoint") with confidence interval (CI) of 2% from the first RENATA study, the number of subjects needed to survey was 2,142 [(33.5 × 66.5) / (2/1.96) 2]. Considering awareness, treatment and control of the disease and its nationwide distribution as secondary endpoints, the inclusion of 6,000 persons was deemed to be sufficient to obtain a national representative sample. Categorical variables are presented as numbers and percentages. Continuous variables are expressed as mean ± standard deviation, or as median and interquartile range, respectively, according to their distribution with the Kolmogorov-Smirnov test. Categorical variables were compared with contingency tables using the chi-square test with Yates correction or Fisher's exact test, as applicable. Means of variables with normal distribution were analyzed and compared using paired t-test or ANOVA. Variables with non-parametric distribution were analyzed using the Mann-Whitney test or the Kruskall-Wallis test. The association between the prevalence of HT and other variables, as level of education and medical coverage, was analyzed with a logistic regression model adjusted for sex and age. A p value < 0.05 was considered statistically significant. All the calculations were performed using Epi-Info and StataSE™ statistical software packages.

Ethical Considerations

The protocol design and the survey were evaluated and approved by the Ethics Committee of the Argentine Society of Cardiology.

RESULTS

A total of 5,931 subjects were surveyed; 2,647 were men (44.6%) and 3,284 were women (55.4%). Mean age was 43 ± 17.1 years. Table 1 shows that SBP, DBP and pulse pressure were significantly higher in men than in women. The prevalence of HT in the general population was 36.3% (95% CI, 35.1-37.6%) and was greater in men (43.7%; 95% CI 41.8-45.6) compared with women (30.4%; IC 95% CI, 28.8-31.9%) (p <0.0001). The prevalence of HT increased with age in both sexes, from 12.2% in subjects <35 years to 77.4% in those aged ≥65 years, and was greater in men compared with women (Figure 1). Table 1 shows that 6% of the general population had diabetes mellitus with no differences between both sexes and 17.1% had high cholesterol levels, with the highest levels among women. Smoking habits were reported by 26.9% of the respondents, and the percentage of former smokers was higher in men. Regular physical activity was significantly more frequent in women compared with men.

Among hypertensive subjects, 38.8% were unaware of their condition (Figure 2); 47.1% were men and 29.3% were women, while 5.7% knew they had hypertension but were not receiving treatment (6.2% were men and 5% were women). Among overall hypertensive subjects, 55.5% were treated with different antihypertensive agents (n=1,196), but only 24.2% (95% CI 22.4-26.0%) had controlled BP with better control in women (33.0%; 95% CI 30.1-35.9%) than in men (16.6%; 95% CI 14.6-18.9%) (p <0.0001) (see Figure 2). Younger patients were less likely to be aware of their condition (Figure 3).

In a model adjusted for sex and age, the highest educational level was associated with a lower prevalence of HT (OR 0.769, 95% CI, 0.67-0.88%, p=0.0001), whereas no association was found for medical coverage (OR = 1.08, 95% CI, 0.93-1.27%, p=ns).

Among hypertensive subjects under medical treatment, 73.4% were taking one drug, 21.4% two drugs and 5.2% three drugs or more, with an average of 1.3 drugs per patient. The most commonly used agents were: angiotensin-converting enzyme inhibitors (42.5%), angiotensin II receptor blockers (ARBs; 35.6%), beta blockers (BBs; 20.1%), calcium channel blockers (CCBs; 12.7%) and diuretics (11.4%). The least used antihypertensive drugs were aldosterone antagonists (0.5%). With the exception of CCBs which were more common in men than in women (15.4 vs. 10.5%; p=0.01), there were no differences between both sexes in the drug groups (Figure 4). The most common drug combinations included an ARB (with

Table 1. Blood pressure and cardiovascular risk factors

	Total (n=5,931)		Men (n=2,647)		Women (n=3,284)		
Blood pressure	**x̄ ± SD**	**SE**	**x̄ ± SD**	**SE**	**x̄ ± SD**	**SE**	**p**
SBP	127.4 ± 19.2	0.25	133.3 ± 18.5	0.36	122.7 ± 18.4	0.32	<0.0001
DBP	79.3 ± 12.0	0.15	82.6 ± 12.1	0.24	76.7 ± 11.2	0.19	<0.0001
PP	48.1 ± 13.0	0.17	50.7 ± 12.9	0.25	46.0 ± 12.69	0.22	<0.0001
CRF	**n/total**	**%**	**n/total**	**%**	**n/total**	**%**	**p**
Smoker	1,581/5,883	26.9	718/2,632	27.3	863/3,251	26.5	0.52
Former smoker	941/5,883	16.0	493/2,632	18.7	448/3,251	13.8	<0.001
Diabetes	353/5,880	6.0	168/2,630	6.4	185/3,250	5.7	0.26
↑ cholesterol	1,004/5,880	17.1	412/2,630	15.7	592/3,250	18.2	0.01
Sedentary lifestyle	3,287/5,827	56.4	1,613/2,599	62.1	1,674/3,228	51.9	<0.0001

x̄: Mean. SD: Standard deviation. SE: Standard error. SBP: Systolic blood pressure. DBP: Diastolic blood pressure. PP: Pulse pressure. CRF: Cardiovascular risk factors.

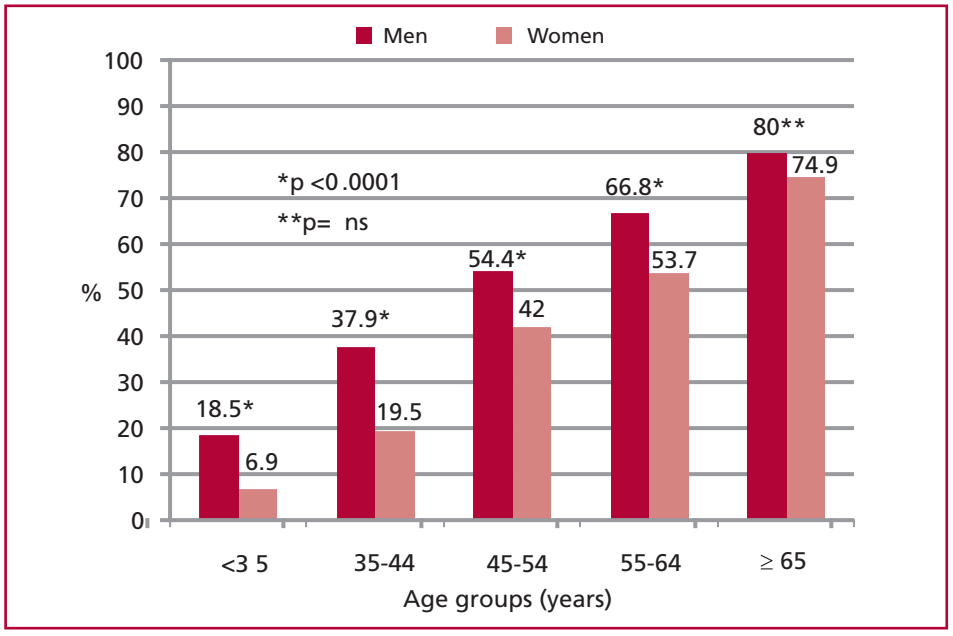

Fig. 1. Prevalence of hypertension by sex and age * p <0.0001: men vs. women. ** p=ns: men vs. women. ns: Non-significant.

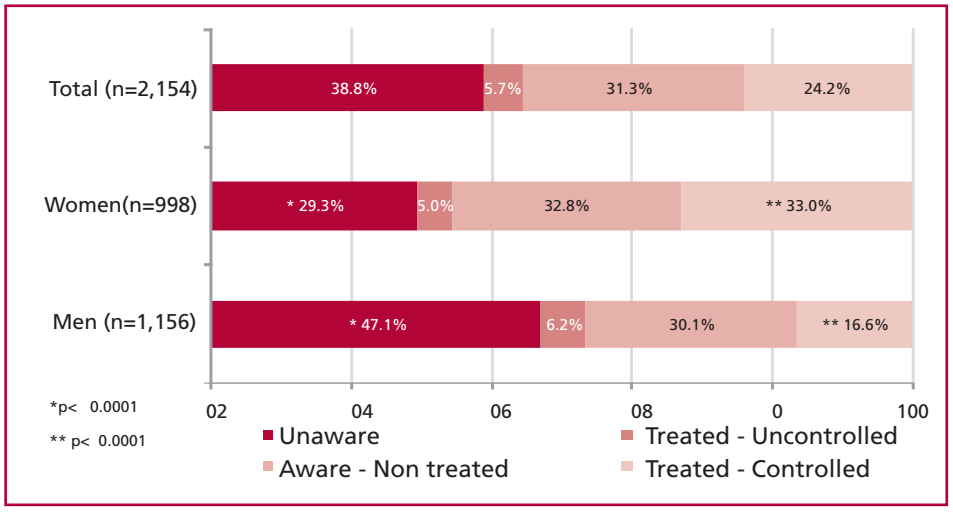

Fig. 2. Awareness, treatment and control of hypertension in the general population and by gender. * p <0.0001, among hypertensive women and men unaware of their condition. ** p <0.0001, among hypertensive women and men treated and controlled.

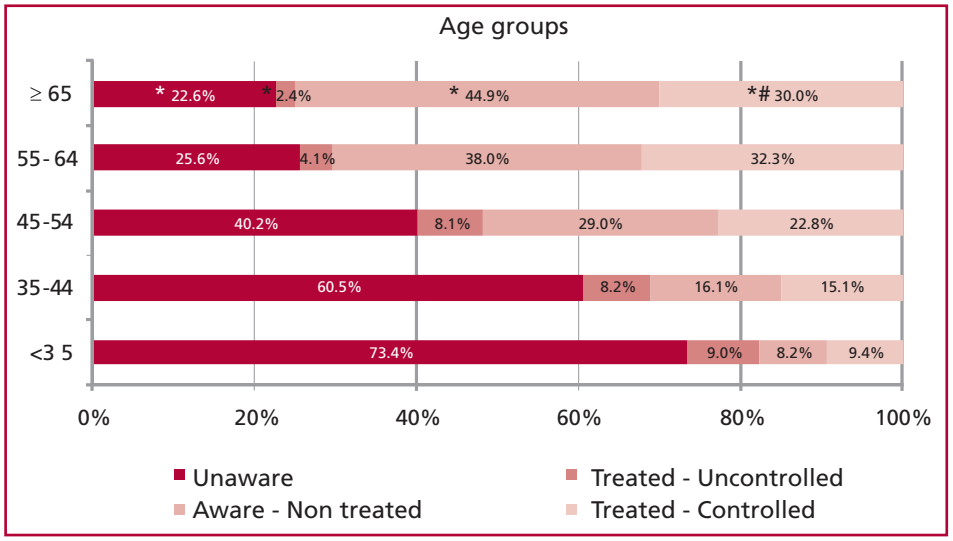

Fig. 3. Awareness, treatment and control of hypertension according to age. * p <0.0001, <35 years vs. >65 years and vs. the rest of the age groups. # p <0.05, <35 vs. the rest of the age groups.

CCB=6.4%, with diuretics 6.1% and with BB=6.0%), representing 18.5% of the total of patients treated. Among hypertensive subjects receiving antihypertensive therapy, 26.6% were taking combination therapy, and about one third of them (31.5%) included a fixed-dose combination regimen. The number of patients receiving a fixed-dose combination regimen (n=99) represented 8.2% of the total of hypertensive patients treated.

Only 43.6% of the hypertensive subjects receiving drug therapy had controlled BP. When the influence of the use of combined therapies on BP control was analyzed, subjects who included a fixed-dose combination therapy in their antihypertensive regimen had significantly higher percentage of BP control than those who were taking a combination therapy that did not include a fixed-dose regimen (52.5 vs. 39.1%; p=0.025).

About half of the patients treated were taking the medication adequately (adherence=50.4%), and BP control was significantly higher compared with non-adherent patients (46.9 vs. 40.1%; p=0.01).

DISCUSSION

The current prevalence of HT is 36.3%, in agreement with the WHO reports for the Region of the Americas. (5) The increasing prevalence of HT worldwide is attributed to population growth, aging and behavioral risk factors, such as unhealthy diet, harmful use of alcohol, lack of physical activity, excess weight and exposure to persistent stress. (5)

In the RENATA-2 study, 4 out of 10 hypertensive subjects are not aware of their condition. This observation is not different from what happens worldwide. The PURE (Prospective Urban Rural Epidemiology) study (19) examined the prevalence, awareness and control of HT in 142,042 subjects from rural and urban communities in high, middle and low-income countries. In this study, in South America, 42.9% of subjects with HT were unaware of their condition, a proportion that is similar to our results. Although in the RENATA-2 study 43.6% of the hypertensive subjects receiving treatment were controlled, when all the hypertensive subjects (aware and unaware of their condition) were considered, only 1 out of 4 was controlled with blood pressure–lowering drugs. In the PURE study, 18.8% of the subjects with HT in our region were well controlled. Similarly to the RENATA-2 study, the awareness and control of BP in the PURE study was lower in men and in young persons. (19) The latter observation reinforces the importance of the commitment physicians should assume in their daily practice, of the scientific societies in training doctors and paramedics and of governmental organizations in educating the community and schoolchildren about the risks of HT.

About 30% of hypertensive patients treated with monotherapy achieve BP targets, (20) indicating that most patients will need two or more antihypertensive drugs. The high proportion of hypertensive persons receiving monotherapy in the RENATA-2 study (> 70%) may explain the low rate of BP control.

It was also seen that subjects who included a fixed-dose combination therapy in their antihypertensive regimen were better controlled compared with those who were not taking a fixed-dose combination treat-

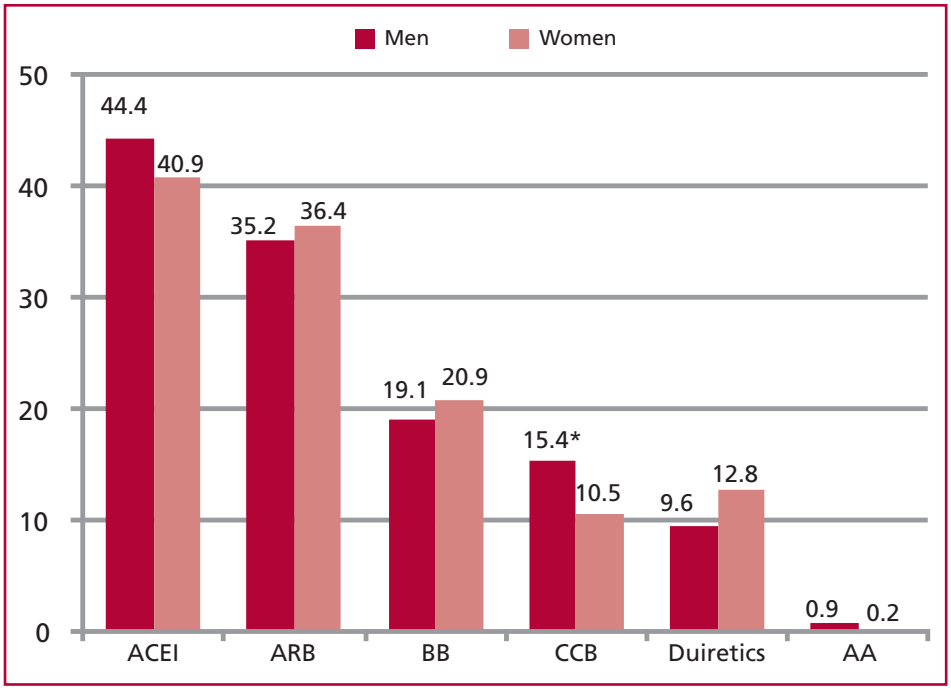

Fig. 4. Family of antihypertensive drugs used by gender. ACEI: Angiotensin-converting enzyme inhibitor. ARB: Angiotensin II receptor blocker. BB: Beta blocker CCB: Calcium channel blocker. AA: Aldosterone antagonist. * p=0.01: men vs. women.

ment. This information would strengthen the current recommendation about the use of a fixed-dose combination of two and three antihypertensive agents in a single tablet, as adherence to treatment improves and BP control is optimized by reducing the number of pills a person must take each day. (21)

Considering that around 50% of the patients comply with their antihypertensive treatment after the first year, (22, 23) it is understandable that poor adherence to treatment is considered one of the causes that explain the low rates of BP control in the community. However, in our country the evidence on the association between lack of adherence and low control is scarce. (24) In the RENATA-2 study, in which half of the hypertensive patients reported to be compliant with the treatment, it was demonstrated that adherence is associated with a higher rate of BP control.

Using educational level as a surrogate of economic status, the PURE study (19) showed lower rates of awareness, treatment and control of BP among participants with primary education or without education in low-income countries. Likewise, in our study educational level was inversely associated with the prevalence of HT. These results are similar to the social patterns of HT occurrence observed in some low-income countries. (25)

In the general population, salt intake was greater in men than in women. This finding, together with the lower rate of disease awareness observed among men would let us infer that women are more conscious of the risks attributable to HT.

Finally, we must say that the greatest power of our study lies on the fact that randomization and the site of administration of the survey allowed the inclusion of subjects with different educational levels, socioeconomic status and access to the health care system in each of the cities. Thus, we can state that the RENATA-2 study is really representative of HT in Argentina.

CONCLUSIONS

The prevalence of HT in Argentina is 36.3%, in agreement with WHO reports for the region. The percentage of patients who are not aware of their condition and the lack of control suggest the need to improve the methods to detect the disease and the way of treating HT. Our findings compel us to develop interventions and strategies focused on prevention, early detection and adequate control of patients with HT.

Participants

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Conflicts of interest

(See authors' conflicts of interest forms on the website/ Supplementary
material).

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1. Given Name (First Name): Alejandro
2. Surname (Last Name): Delucchi
3. Date: 10-December-2017

4. Are you the corresponding author? [✓] Yes [ ] No

5. Manuscript Title
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1. Given Name (First Name): Claudio
2. Surname (Last Name): Majul
3. Date: 10-December-2017

4. Are you the corresponding author? ☑ Yes ☐ No

5. Manuscript Title
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2. Surname (Last Name): Vicario
3. Date: 10-December-2017

4. Are you the corresponding author? [✓] Yes [ ] No

5. Manuscript Title
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1. Given Name (First Name): Gustavo
2. Surname (Last Name): Cerezo
3. Date: 10-December-2017

4. Are you the corresponding author? [✓] Yes [ ] No

5. Manuscript Title
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2. Surname (Last Name): Fábregues
3. Date: 10-December-2017

4. Are you the corresponding author? [✓] Yes [ ] No

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