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Hypertension as a risk factor for developing depressive symptoms among community-dwelling elders

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ABSTRACT

Objective. To determine whether hypertension (HTA) is an independent predictor of depressive symptoms (DS) in a sam ple of elderly Mexican community dwelling persons. **Material and methods.** Two year longitudinal study of 3,276 com munity dwelling persons aged 60 years and older, participa ting in the Mexican Health and Aging Study. Subjects that self reported both having or not having HTA while denying DS at baseline were included. Two year follow up data were analyzed, and multiple regression analyses were used to test whether HTA is an independent predictor of incident DS after adjusting for many potential confounders. **Results.** Mean age of participants was 68.4 ± 6.9 years. Prevalence of HTA was 36.6%. At follow up, 28.7% developed DS. After adjusting for multiple covariates (age, sex, education level, relationship status, self reported health and economic status, diabetes, ar thritis, stroke, ischemic cardiopathy, falls, pain, hearing im pairment, visual impairment, urinary incontinence, cognitive impairment, smoking, alcohol use, and baseline disability), HTA was an independent predictor of DS at two years follow up (Adjusted Odds Ratio = 1.18; 95% confidence interval = 1.01 1.40). **Conclusions.** Hypertension is an independent risk factor for the development of depressive symptoms. Pro grams to support early treatment of cardiovascular disease and hypertension should be implemented in order to prevent late onset of depressive symptoms.

Key words. Elderly. Depression. Depressive symptoms. Hy pertension.

Hipertensión como factor de riesgo para el desar- rollo de síntomas depresivos en adultos mayores de la comunidad

RESUMEN

Objetivo. *Determinar si la hipertensión arterial (HTA) es un predictor independiente de la aparición de síntomas depresivos (SD) en una muestra de adultos mayores de la comunidad en México.* ***Material y métodos.*** *Estudio longitudinal con dos años de seguimiento de 3,276 adultos de 60 años y más, todos participantes en el Estudio Nacional sobre Salud y Envejec imiento en México (ENASEM). Fueron incluidos aquéllos que auto reportaron tener o no HTA, así como aquéllos que nega ron SD a su entrada en el estudio. Se analizaron los datos a los dos años de seguimiento y modelos de regresión logística fueron utilizados para analizar si la HTA fue un predictor in dependiente de la incidencia de SD aun tras el ajuste por múl tiples variables de confusión.* ***Resultados.*** *La edad media de los participantes fue de 68.4 ± 6.9 años. La prevalencia de la HTA fue 36.6%. En el seguimiento, 28.7% desarrollaron SD. Tras el ajuste por múltiples confusores (edad, sexo, educación, estado marital, auto reporte de salud y financiero, diabetes, artritis, enfermedad vascular cerebral, cardiopatía isquémica, caídas, dolor, deterioro visual y auditivo, incontinencia urinaria, deterioro cognoscitivo, tabaquismo, uso de alcohol y dis capacidad a la entrada del estudio), la HTA fue un predictor independiente de SD a los dos años de seguimiento (Razón de Momios ajustada = 1.18; intervalo de confianza al 95% = 1.01 1.40).* ***Conclusiones.*** *La hipertensión es un factor de riesgo independiente para el desarrollo de síntomas depresivos. Deben implementarse programas que apoyen un tratamiento temprano de las enfermedades cardiovasculares, así como la HTA con lo que podría prevenirse la aparición de síntomas depresivos en la vejez.*

Palabras clave. *Adulto mayor. Depresión. Síntomas depre sivos. Hipertensión.*

INTRODUCTION

A common health problem in the elderly is hypertension (HTA), which has a prevalence rate greater than 50% among adults aged 50 years and older.[1-5] Similarly, depressive symptoms (DS) are highly prevalent among older persons, whose late-onset has been related to several vascular risk factors and cerebral white matter changes.[6-9] Depression and depressive symptoms have been associated with a decline in health status, physical performance, and disability, and their impact may be even greater than that of chronic diseases.[10-13]

Recently, the relationship between HTA and DS has been highlighted, and specific lesions on white matter have been described more frequently among hypertensive older patients with late-onset depression or depressive symptoms.[5,14-16] This concept of "vascular depression" proposes microvascular disease of the brain leading to structural and cognitive brain deficits.[7] Vascular comorbidity, including an increased prevalence of hypertension, is common in late-onset depression.[17] However, a causal relationship between HTA and DS remains unclear and controversial. If this relationship is established, programs to support early treatment of cardiovascular risk factors and hypertension could be a strategy for intervention to prevent late-onset depressive symptoms. Therefore, the purpose of this report is to determine whether hypertension is an independent predictor of depressive symptoms in a sample of elderly Mexican community-dwelling adults. The main hypothesis is that hypertensive persons have a higher risk of depressive symptoms, even after adjustment for potential confounders.

MATERIAL AND METHODS

Study population

The participants in the present study are a subset from the Mexican Health and Aging Study (MHAS), a prospective panel study of health and aging in Mexico. The aim and design of the MHAS have been published previously.[18] Briefly, the baseline survey was conducted in the summer of 2001, and a follow-up in 2003. It was derived from the fourth round of the National Employment Survey and it is regarded as a nationally representative sample of Mexicans aged 50 and older and their spouse/partners regardless of their age. It considers subjects from both urban and rural areas. Data were obtained from direct, face-to-face interviews and individual audits, and proxy interviews were conducted when poor health or temporary absence prevented a direct interview. The MHAS is only representative of community-dwelling people. In the case of Mexico, it is not an important omission because, according to the 2000 National Population Survey, less than 1% of people aged 60 years and older live in an institution. The MHAS includes data from 15,230 interviews (9,806 index cases and 5,424 spouses/partners). It contains self-reported information regarding health measures (functional status and healthy related behaviors [e.g., smoking and drinking history]), access to health services, depressive symptoms, pain, cognitive performance, and anthropometrical measurements. Additionally, it considers childhood demographic data, education, migratory history, and marital status. The MHAS was supported by a grant from the National Institutes of Health/National Institute of Aging. The study is a collaborative effort among researchers from the University of Pennsylvania, the University of Maryland, and the University of Wisconsin in the US and the Instituto Nacional de Estadistica, Geografia e Informatica (INEGI) in Mexico.

Definition of hypertension

Hypertension (HTA): Participants answering "yes" to the both following questions at baseline were categorized as being hypertensive: "*Has a doctor or medical personnel ever told you that you have hypertension or high blood pressure?* and *"Are you currently taking any medication to lower your blood pressure?"* Those who responded "no" to either of these questions were considered to be without HTA.

Outcomes

Depressive symptoms (DS): This variable was determined using a modified version of the Center for Epidemiological Studies-Depression scale (CES-D), which was previously validated in this population.[19] Briefly, the tool is a nine-item questionnaire assessed how people felt during the last week. The instrument was significantly associated with the depression clinical diagnosis (Diagnostic and Statistical Manual of Mental Disorders, DSM-IV)[20] and to the 15-item Geriatric Depression Scale (GDS) score.[21] The internal consistency was adequate (alpha coefficient: 0.74), and test-retest reliability was excellent (interclass correlation coefficient: 0.933). The cut-off ^{3} 5/9 points indicates "depressive symptoms" with a sensitivity of 80.7% and a specificity of 68.7%. Those

with a score below 5 were considered to be without depressive symptoms. This variable was treated as binary in multiple regression analyses.

Covariates

Socio-demographic variables included age (years), sex, living alone (yes or not), and educational level (years). The self-reported health and financial situation were recorded and treated as a categorical variable (good, regular or poor).

Participants were asked whether they had a physician's diagnosis of diabetes, myocardial infarction or angina pectoris, stroke, or arthritis. The presence or absence of visual impairment or hearing impairment was also self-reported, as well as presence or absence of pain, and falls in the last two years.

Smoking status "*Have you ever smoked cigarettes more than 100 cigarettes or 5 pack in your lifetime?*" and alcohol intake "*Do you ever drink any alcoholic beverages?*" were dichotomous self-reported variables.

Two measurements of disability were investigated: instrumental (IADL) and basic activities of daily living (ADL). For the IADL, participants responded whether they were able to perform four activities of daily living based on the Lawton & Brody scale (responsibility for own medication, managing money, shopping and grooming).[22] For the ADL, participants were asked about five tasks based on the Katz ADL scale (bathing, walking, transferring from bed to chair, continence and feeding).[23] For each domain of disability, participants who reported that they needed help or were unable to perform at least one of the tasks were considered as having an IADL or ADL disability. Urinary incontinence was a dichotomous variable analyzed separately from the ADL.

Cognitive impairment was estimated from the brief version of the Cross-cultural cognitive examination (CCCE).[24] The CCCE includes five items that evaluate different cognitive domains: verbal primary memory, verbal secondary memory, constructional praxis, visual memory and visual scan. Considering that the CCCE test didn't have standardized data for the Mexican population, cut-offs for the different items were set using the 10^{th} percentile by sex and educational level for respondents in the MHAS aged 50 to 59. The cognitive diagnosis was made by a group of geriatricians and neuropsychologists blind to the CCCE scores. Sensitivity and specificity was estimated for the different number of failed tests. Failing two or more tests was considered the best cut-off (sensitivity: 84.2% and specificity: 100%).

For the present research, 7,172 participants aged 60 years and older were considered. However, in order to determine incident depressive symptoms, 2,544 participants with them at baseline were excluded as well as 629 subjects because of missing mood data at the two-year follow-up. Finally, 723 were also excluded for missing clinical data. As expected, those excluded were significantly older (70.0 *vs*. 68.4 years), and more likely to be disabled for IADL (10.3% *vs*. 4.2%) and ADL (6.2% *vs*. 2.0%).

Statistical analysis

Variables are described using arithmetic mean and standard deviation (SD) or frequency and proportion where appropriate. Participants without depressive symptoms at baseline were evaluated once again two years later, and the two-year incidence of depressive symptom was established. The following statistical procedures were used where appropriate according to the characteristics of each variable: chi square test for qualitative data or Student t test for continuous variables. Binary logistic regression models were used to analyze the unadjusted effect of hypertension on the two-year incidence of depressive symptoms. In a second model, multiple logistic regression analyses were used to study the effect of hypertension adjusting for multiple covariates obtained at baseline, which were selected based on univariate analysis where those with lowest p values were kept (socio-demographic data, chronic diseases, cognitive status, lifestyle, and disability). With the main effects model thus obtained, two-by-two interaction terms were then introduced (hypertension*age and hypertension*sex) and judged for their significance, with none proving statistically significant. Residual and diagnosis analyses were performed to check for violation of the assumptions underlying regression analyses. All statistical tests were performed at the 0.05 level and 95% confidence intervals (CI) were given. Statistical tests were performed using the SPSS software for Windows® (SPSS Inc., Chicago, IL, version 13.0).

RESULTS

The study sample was comprised of 3,276 individuals. General characteristics of participants are shown in table 1. Mean age was 68.4 ± 6.9 years and 47.9% were females. The prevalence of HTA was 36.6%. Comparisons of demographic and health cha-

racteristics according to presence or absence of HTA are shown in table 2. In comparison with the non-hypertensive survey participants, those with HTA were more likely to be female ($p < 0.001$), more educated (p 0.023), and reported more chronic diseases (diabetes, myocardial infarction or angina pectoris, stroke, and arthritis; $p < 0.001$ for all). There was no difference with respect to age (p 0.423) or presence of cognitive impairment (p 0.457). In addition, subjects with HTA reported more falls ($p < 0.001$), poorer self-reported health status ($p < 0.001$), and more disability for IADL ($p < 0.001$) and ADL (p 0.034) in comparison with non-hypertensive subjects.

The two-year incidence of DS was 28.7%. Table 2 presents comparative analyses among participants who developed or did not developed DS. Subjects with DS at follow-up were older ($p < 0.001$), less educated ($p < 0.001$), and self-reported a poorer health ($p < 0.001$) and economic status ($p < 0.001$). HTA was significantly more common among those who developed DS in comparison to subjects without DS at follow-up (41.5 *vs.* 34.7%, respectively; $p < 0.001$). In comparison with participants without DS, those with DS more frequently reported hearing impairment ($p < 0.001$), and visual impairment ($p < 0.001$), as well as more falls ($p < 0.001$), pain ($p < 0.001$), urinary incontinence (p 0.029), and disability in IADL ($p < 0.001$) and ADL ($p < 0.001$).

Table 1. Demographic characteristics and health status at baseline (n = 3,276).

Variable	n (%)
Women	1,570 (47.9)
Have no partner	1,074 (32.8)
Poor self-reported health	1,875 (57.2)
Poor self reported economic situation	2,524 (77.0)
Smoking	1,532 (46.8)
Current drinker	1,018 (31.1)
Falls the last two years	1,122 (34.2)
Visual impairment	1,347 (41.1)
Hearing impairment	839 (25.6)
Pain	1,041 (31.8)
Cognitive impairment	795 (24.3)
Urinary incontinence	213 (6.5)
Hypertension	1,200 (36.6)
Diabetes mellitus	485 (14.8)
Ischemic cardiopathy	110 (3.4)
Stroke	86 (2.6)
Arthritis	661 (20.2)
Disability≥ 1 activity of daily living task	65 (2.0)
Disability ≥ 1 instrumental activity of daily living task	141 (4.3)

Table 2. Demographic characteristics and health status according to presence or absence of hypertension and depressive symptoms.

Variable	Without HTA n = 2,076 (63.4%)	With HTA n = 1,200 (36.6%)	*p*	Without DS n = 2,336 (71.3%)	With DS n = 940 (28.7%)	*p*
Age, mean (SD)	68.5 ± 6.9	68.3 ± 6.2	0.423	68.1 ± 6.5	69.3 ± 7.3	< 0.001
Women, %	42.4	57.4	< 0.001	44.7	56.0	< 0.001
Education level (years), mean (SD)	4.0 ± 4.3	4.3 ± 4.1	0.023	4.5 ± 4.4	3.1 ± 3.7	< 0.001
Have no partner, %	31.1	35.8	0.006	31.8	35.3	0.050
Poor self-reported health, %	51.5	67.1	< 0.001	52.7	68.4	< 0.001
Hypertension, %	–	–	–	34.7	41.5	< 0.001
Diabetes, %	12.0	19.7	< 0.001	14.6	15.4	0.586
Ischemic cardiopathy, %	1.9	5.9	< 0.001	3.6	2.8	0.233
Stroke, %	1.6	4.4	< 0.001	2.1	3.8	0.006
Arthritis, %	17.1	25.6	< 0.001	18 2	25.1	< 0.001
Falls the last two years, %	31.6	38 9	< 0.001	31.7	40.6	< 0.001
Visual impairment, %	40.1	42.8	0.129	37 9	49.0	< 0.001
Hearing impairment, %	25.4	25 9	0.760	23.8	30.0	< 0.001
Pain, %	28.3	37 9	< 0.001	28.5	40.1	< 0.001
Smoking, %	48.9	43.0	0.001	48.8	41.6	< 0.001
Ever use of alcohol, %	35.6	32.1	0.055	36 2	29.6	0.001
Cognitive impairment, %	24.6	25.8	0.457	22.7	31.1	< 0.001
Urinary incontinence, %	5.9	7.5	0.076	5 9	8.0	0.029
Poor self-reported economic situation, %	77.8	76.5	0.685	75.3	82.4	< 0.001
Disability ≥ 1 activity of daily living task, %	1.6	2.7	0.034	1.5	3.1	0.004
Disability ≥ 1 instrumental activity of daily living task, %	3.2	6.3	< 0.001	3.3	6.8	< 0.001

SD: Standard deviation. HTA: Hypertension. DS: Depressive symptoms.

Table 3. Multiple regression model showing an independent association of hypertension with the incidence of depressive symptoms after adding one-by-one potential confounders.

	β	β error	Odds Ratio	95% CI	*p*
Unadjusted	0.290	0.079	1.36	1.14 to 1.56	< 0.001
Adjusted by: age	0.297	0.079	1.35	1.15 to 1.57	< 0.001
+ sex	0.235	0.081	1.26	1.08 to 1.48	0.004
+ education level	0.276	0.082	1.32	1.12 to 1.54	0.001
+ self-reported economic status	0.280	0.082	1.32	1.13 to 1.55	0.001
+ self-reported health	0.200	0.083	1.22	1.04 to 1.44	0.016
+ diabetes	0.201	0.083	1.22	1.04 to 1.44	0.016
+ arthritis	0.185	0.084	1.21	1.02 to 1.41	0.027
+ stroke	0.175	0.084	1.20	1.01 to 1.40	0.038
+ ischemic cardiopathy	0.192	0.085	1.21	1.02 to 1.43	0.024
+ falls	0.182	0.085	1.20	1.02 to 1.42	0.032
+ pain	0.177	0.085	1.20	1.01 to 1.41	0.038
+ visual impairment	0.174	0.085	1.20	1.01 to 1.41	0.041
+ hearing impairment	0.175	0.085	1.20	1.01 to 1.41	0.041
+ cognitive impairment	0.181	0.085	1.20	1.02 to 1.42	0.034
+ urinary incontinence	0.176	0.086	1.19	1.01 to 1.40	0.040
+ have a partner	0.176	0.086	1.19	1.01 to 1.41	0.039
+ smoking	0.177	0.086	1.19	1.01 to 1.41	0.039
+ ever use of alcohol	0.176	0.086	1.19	1.01 to 1.41	0.040
+ disability for activities of daily living	0.173	0.086	1.19	1.01 to 1.40	0.040
+ disability of instrumental activities of daily living	0.169	0.086	1.18	1.01 to 1.40	0.048

CI: Confidence intervals.

The unadjusted regression analyses showed that HTA at baseline increased the risk of depressive symptoms at two years by a factor of 1.4 (95% CI 1.14 to 1.56; $p < 0.001$). Multiple regression analysis revealed that HTA was an independent predictor of depressive symptoms after adjusting for many covariates (age, sex, education level, relationship status, self-reported health and economic status, diabetes, arthritis, stroke, ischemic cardiopathy, falls, pain, hearing impairment, visual impairment, urinary incontinence, cognitive impairment, smoking, alcohol use, and baseline disability for IADL and ADL) (Table 3). Finally, residual and diagnostic analyses did not show violations of the assumptions underlying multiple regression analysis and indicated a good fit of the model.

DISCUSSION

This study shows that in the multivariate analysis, hypertension is an independent predictor of depressive symptoms among Mexican community-dwelling elders, even after adjusting for many potential confounders because increases their risk by 18%. To our knowledge, this is the first study to examine this association among Latin-American older adults.

Although this relationship remains controversial, previous cross-sectional studies have suggested an association between HTA and DS.[25,26] A previous Mexican study showed that HTA (self-reported) was independently associated with DS (GDS) after adjustment for cognitive impairment and disability.[25] Panagiotakos, *et al*. explored the relationship between DS (GDS) and the prevalence of cardiovascular risk factors. Their analyses showed a positive association between the number of cardiovascular risk factors (like hypertension or hypercholesterolemia) and a higher GDS score.[26] Similarly, a case-control study showed that depressed groups (DSM-IV) have significantly more risk factors and/or vascular disease.[9] The longitudinal design of our study make these results more significant, and give greater support to the hypothesis that HTA is a cause of DS in the elderly.

Biological causes of late-onset depressive symptoms, such as cerebro-vascular lesions, seem to be more common than a psychological or social etiology.[6,27-30] For example, atherosclerosis has been associated with depression in old age. However, this is not be the only mechanism involved. In comparison with other cardiovascular risk factors (such as diabetes or smoking), HTA also induces

changes in the small blood vessels in the brain consisting of replacement of mural smooth muscle by fibrohyaline material, which eventually results in a thickening of the vessel wall and sometimes a narrowing of the lumen and white matter lesions.[31-33] Thus, white matter lesions may be the neuroanatomical basis for the relationship between HTA and depressive symptoms.[29] The Cardiovascular Health Study demonstrated cross-sectionally that both diagnosis of HTA at baseline and high blood pressure measured at physical examination are independently associated with the presence and severity of white matter lesions.[34] Difference between pathological mechanisms of HTA and other cardiovascular risk factors on adverse health-related outcomes has been suggested by the study of Vinkers, *et al*. who examined the prospective associations between atherosclerosis and DS in a sample of 599 adults aged 85 years and older. Linear mixed models showed no relation between atherosclerosis and DS, either in the cross-sectional analysis or in the prospective analysis, but a relationship existed between atherosclerosis and cognitive impairment.[35] Therefore, it is possible that the development of DS among hypertensive participants could be related to direct damage by HTA on white matter or "leukoaraiosis".[30]

Interactions between cardiovascular risk factors and age-related body changes (e.g. decreased blood flow and cerebral perfusion) could lead to cerebral ischemic microangiopathy, abnormal cerebral blood flow, and reduced perfusion of watershed areas. In turn, these changes contribute to development of periventricular and subcortical white matter lesions and disruption of frontal-subcortical circuits. The damage in these areas is associated with a loss of motivation and initiation which is characteristic of "vascular depression".[29]

The advent of magnetic resonance imaging (MRI) has made it possible to examine these hypotheses, because studies have demonstrated that patients with late-onset depression have more severe and frequent patchy lesions in the frontal deep white matter and basal ganglia than do controls or patients with early-onset depression. The cross-sectional study of Greenwald, *et al*. compared the frequency of signal hyperintensities in the subcortical gray and deep white matter on MRI scans of brains of hypertensive and normotensive older depressed and nondepressed comparison subjects. Their results showed that hypertensive depression exhibited significantly more-severe hypertintensities in both subcortical gray and deep white matter than did normotensive depressives and controls ($p < .05$). In addition, hypertensive controls had significantly more-severe hyperintensities in deep white matter than normotensive subjects ($p < 0.05$). Findings support the possible and heterogeneous pathogenic contribution of cerebral lesions in late-life depression.[16]

On the other hand, common geriatric syndromes such as cognitive impairment, gait disturbance, and urinary incontinence have also been shown to be closely associated with white matter lesions.[29] In this study, participants who developed depressive symptoms reported more frequent urinary incontinence, falls, and cognitive impairment at follow-up. This remains to be further elucidated.

Several caveats deserve comment. In our study, despite the fact that HTA is an independent predictor of DS, the biological mechanism underlying remains hypothetical. The lack of MRI data to show significantly more cerebral lesions among hypertensive participants who developed depressive symptoms is the main limitation of this study. However, our findings are reinforced by consistent results, which are in keeping with previous research.[6,16,26-30] It is also necessary to emphasize that the strength of association between HTA and incident DS is almost unchangeable and remains statistically significant after adjustment for many potentially confounders. In addition, exclusion of participants with missing data (around 29% from original sample) could represents a potentially source of selection bias and affected the study findings. Nevertheless, the study has several strengths, including its prospective design and large population-based sample.

By showing that HTA leads to development of DS in the elderly many opportunities for prevention of this health problem are offered which can have serious consequences for older persons. Efforts aimed at effective treatments for hypertension must be made as recommended.[1] It is reasonable to aggressively manage cardiovascular risk factors in midlife in order to prevent many clinically important events occurring in later life, including the development of cerebro-vascular lesions in strategic areas. Given the importance of hypertension and depressive symptoms in the elderly, programs that include social and psychological components should be promoted to education the population of the additional risks of cardiovascular diseases. Despite the limitations of our study, our results have important implications for the development of evidence-based health promotion interventions among older adults.

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