This is a peer-reviewed, accepted author manuscript of the following research article: González Hernández, Alfredis et al. "Prevalence of Mild Cognitive Impairment in southern regions of Colombia". Journal of Alzheimer's Disease Reports. 2023.

Prevalence of Mild Cognitive Impairment in Southern Regions of Colombia

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Abstract

Background: Recent reports suggest that by 2050 there will be an increase of around 310% of cases affected by dementia in Latin American countries. A previous study in a Southern region reported one of the highest prevalences of dementia in Latin America. It is important to explore current prevalence rates of dementia risk conditions such as Mild Cognitive Impairment (MCI). **Methods:** a cross-sectional study recruited a community-dwelling sample of 823 adults from rural and urban areas of two Southern provinces of Colombia from 2020-2022. Participants were assessed with a neuropsychological protocol validated in Colombia. To obtain general and region-specific prevalence rates, age, sex, schooling, and socioeconomic level were considered and controlled for. **Results:** Most of the participants reported low education and socioeconomic level, the participation of women was higher. It was determined that the prevalence of MCI was 53.6%, with 56.6% in the province of Caquetá followed by 51.9% in the province of Huila. The amnestic MCI represented 42.6%, the multidomain amnestic was 16.55%, and the non-amnestic was 1.81%. Our participants reported comorbidities such as diabetes and hypertension. We also observed a relationship between exposure to pesticides and MCI. **Conclusion:** We observed one of the highest prevalences of MCI in Latin America reported to date. Variables such as age, gender, and education proved risk factors for MCI in the explored regions. Our findings are very much in line with recent studies that highlight the influence of non-canonical risk factors of dementia in underrepresented countries from Latin America.

Keywords: Mild cognitive impairment; Prevalence; Epidemiology; Pesticides; Alzheimer disease.

Introduction

Recent reports on the prevalence of dementia forecast that by 250 there will be an increase of around 310% of cases affected by this epidemic disorder in in Latin American countries. Colombia seems to be well on its the way to meet such a forecast as a previous study reported one of the highest prevalence of dementia in a Latin America. It is important to explore current prevalence rates of dementia risk conditions such as Mild Cognitive Impairment (MCI). This was the aim of this study. Although MCI has been largely associated with dementia (1), other studies have found it co-existing with other health conditions known to reduce cognitive functioning including head trauma (2), depression (3), environmental pollution by pesticides (4), chronic diseases such as hypertension (5) and diabetes (6). We also address the presence and influences of such risk factors.

It has been suggested that the classification of MCI in different subtypes (amnestic MCI single domain (aMCIs), amnestic MCI multiple domains (aMCIm), Non-amnestic MCI single domain (naMCIs) and Non-amnestic MCI multiple domains (7) can aid the identification of risk profiles and the prediction of the underlying disease i.e., type of dementia the affected person will develop. Accrued knowledge suggests that approximately 14.9% of patients with aMCI will go on to develop dementia (8). Considering the imminent growth of the older population, which is anticipated to be more dramatic in low- and middle-income countries (LMIC) than in high-income countries HIC (9,10), it becomes imperative to undertake an epidemiological characterization of this health problem in Latin America. Recently, it has been acknowledged (11,12) that the lack of such studies has precluded the contribution of data from Latin America to major global initiatives such as the 10/66 study (11–13). This is unfortunate as changes in demographic structures in Latin America (LAC) due to increase in life expectancy, better health care, and others, are leading to an

unprecedented raise in the number of older adults who develop neurodegenerative diseases such as dementia (11,14).

The available evidence indicates that the prevalence of all type of MCI in LAC ranges from 6.8% to 25.5%, approximately (15). Two prevalence studies have been conducted in Colombia. The first cross-sectional study among older adults aged 50 years old was 9.7% in aMCI (16). The other, completed between 2012 and 2014, identified a prevalence of MCI of 34% and of dementia of 23% (17). However, such studies were conducted in two main capital cities of Colombia. Therefore, these earlier results are not representative of the entire Colombian population let alone of the population living in more deprived conditions (i.e., towns with low income, rural areas). In 2015, the SABE Survey (Health, Well-being, and Aging) was carried out in Colombia using a probabilistic sample that included a large amount of data (18). The study included 27.1% of participants from the central region where the departments of Huila and Caquetá are located (19). The study determined a prevalence of MCI of 17.93% amongst older adults over 60 years old (20). It is worth noting that the presence of MCI was supported via the use of MMSE. This methodological choice might have potentially limited the strength of the evidence as the sensitivity and specificity of the MMSE for the diagnosis MCI is limited (21). The evidence shows that the MMSE is not a sensitive tool to screen for cognitive decline in individuals with a low educational level (22).

As previously mentioned, it is known that demographic factors such as years of schooling and living in rural areas modify the risk of developing MCI and dementia and, therefore, more studies are needed that involve populations exposed to such factors. A previous relevant study in a region targeted by this study (Neiva, Huila) reported a dementia prevalence of 23.6% (23). This figure was strikingly high, in fact higher than that reported by other countries. Given this earlier local

evidence and that reviewed with respect to the global picture, an updated characterization of MCI in a broader region of southern Colombia is overdue. This was the objective of the present study. Based on the findings from previous research in the region, we have formulated a hypothesis where we anticipate an equally high prevalence of MCI, particularly of the amnesic subtype that we consider may have a certain relationship with low education, rurality, and demographic characteristics typical of the southern Colombian region.

Methods

A community-based cross-sectional study was carried out between 2020 and 2022 in two municipalities in southern Colombia, Huila and Caquetá. The recruitment process involved two main strategies. First, a group of psychologists with training in neuropsychology approached older adults who regularly attended community centers for the elderly in the target municipalities. These centers run government programs where older adults participate to improve their quality of life. We provided information about the study and invited those who expressed interest to participate. The older adults who attend these centers are functionally independent. Those who agreed to be involved were transported to a neuropsychological set up to undertake the study assessments.

Second, we used open invitations on social networks and institutional pages to reach people over 50 who might be interested in participating in the study. The goal was to ensure that the sample we collected was representative of the general population. As our age limit was rather low (50), there was the possibility that individuals at risk of early onset dementia were also recruited. The participants were evaluated by an interdisciplinary team comprising neuropsychologists,

psychiatrists, and neurologists who carried out the assessments at the clinics following the study protocols.

The inclusion criteria were as follows: Participants who were aged 50 years or older, had normal or corrected-to-normal vision and hearing, and could complete the neuropsychological assessment were included. Those who had uncontrolled chronic diseases even if medicated and a history of neurological diseases or psychiatric illnesses were excluded. The study was conducted in compliance with ethical standards, specifically Bioethics and Research Committee number 002-006 of the University Hospital as well as the Declaration of Helsinki. The informed consent was signed by the participant following the information session during which the procedures involved in the research project were explained and discussed. A family member or caregiver (witness) of the participant was also invited to consent. The informed consent included the signature of the participant as well as that of a witness. In the consenting stage, the principles of confidentiality, respect for autonomy, beneficence and non-maleficence were mentioned to the participants.

Sample size

Although our sample was not selected through a probabilistic method, we have taken rigorous measures to ensure it was as representative as possible. To ascertain this, we conducted a power calculation to determine the appropriate sample size for our study by utilizing a previously reported MCI prevalence of 34% [18]. OpenEpi®, an open-source software for statistics in epidemiology, indicated that we needed a sample size of 596 adults over 50 years of age in both municipalities to achieve the desired level of statistical power, with a 99% confidence level, an absolute precision of 5% (d=0.05), and a design effect of 1.0. This approach ensures that, despite our non-probabilistic sampling method, our results would be robust and supported by sufficient power, thereby enhancing the overall representativeness of our results.

Procedures

Older adults who agreed to participate in the study were evaluated in two sessions, a psychologist with knowledge and training in neuropsychology administered an assessment protocol to every participant. This helped to detect the presence of cognitive impairment and classify participants accordingly. The assessment comprised a clinical interview, and interview with a caregiver and/or accompanying person which could be completed via a telephone call, neuropsychological and functional assessments. The criteria used to detect MCI were those described by Petersen (7). We explored such criteria in participants whose MMSE was 23 or above at the screening point and who were also independent in their activities of daily living. The decision of using 23 as a MMSE cut-off score for dementia stemmed from Colombian normative studies carried out to validate the same tools we used in our protocol (all the normative groups above 50 years of age and with 0 years of education or more had a minimum average MMSE of 28 points (24)). Furthermore, a MMSE cut-off of 23 for dementia is line with that reported by other authors in similar Latin American populations. The diagnostic criteria involved the: (1) Presence of subjective memory complaint, (2) accompanied by objective cognitive decline as informed by neuropsychological assessment (scores ≤1.5SD below the norms) (24), (3) preserved abilities to perform basic Activities of Daily Living (ADL) and relatively preserved abilities to perform instrumental ADL, and (4) absent of criteria for dementia. Cases that were difficult to classify were discussed through case studies among expert panels, which involved medics, neuropsychologists, and psychologists who are collaborators of the longitudinal study on the early detection of dementias in the south of Colombia. Figure 1 shows the algorithm followed to identify and classify patients.

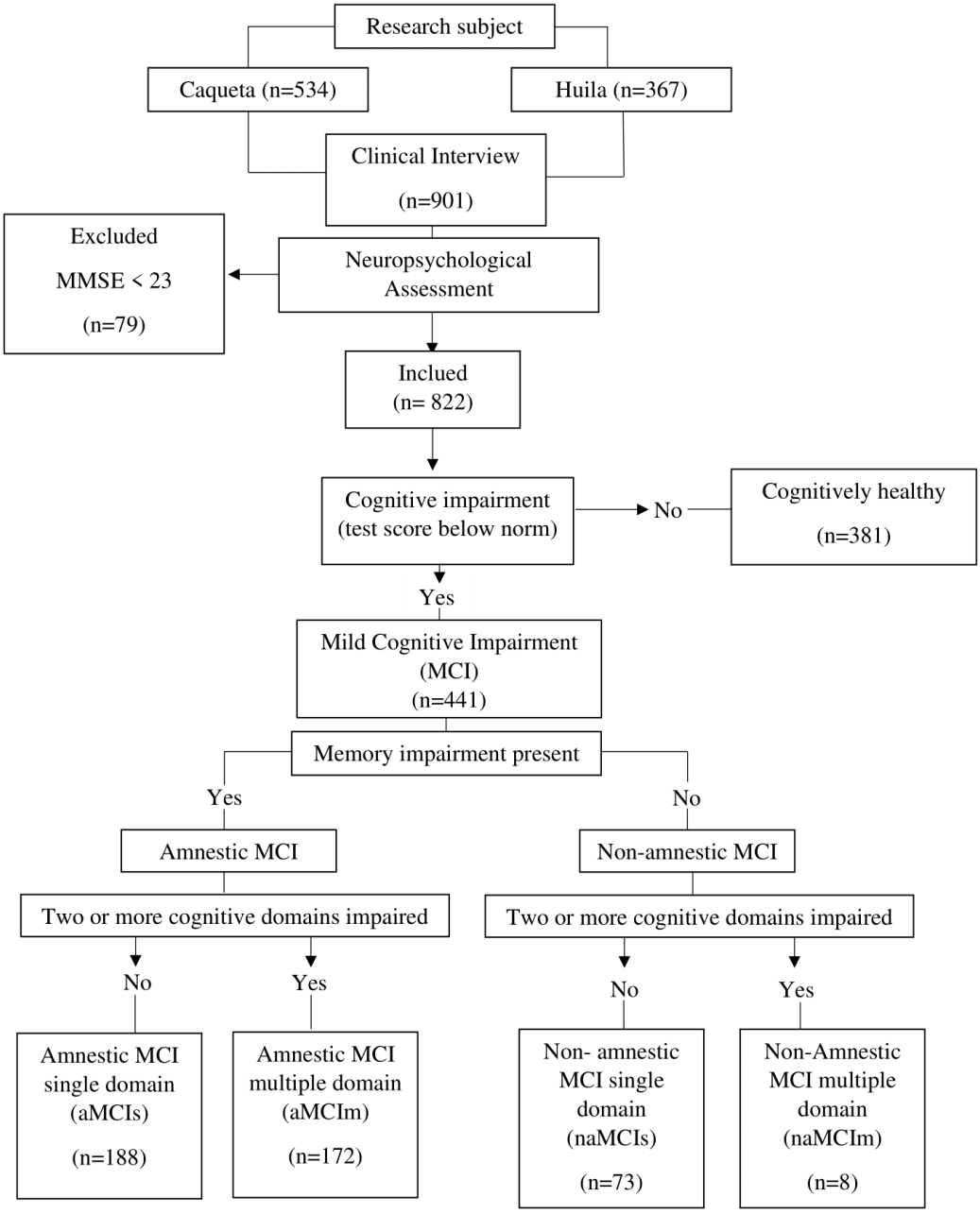

Figure 1. *Flow chart illustrating the recruitment process.*

To ensure a comfortable and effective evaluation, we divided questionnaires and tests into two sessions, making them shorter when needed. The format was engaging, tailored to participants' characteristics. Feedback and results were shared to boost satisfaction. Sessions lasted about an hour, with breaks for older adults, respecting individual needs and promoting participation.

Cognitive assessment

Addenbrooke's Cognitive Examination - Revised ACER-R Colombia: It is a brief, sensitive and specific test battery to detect early cognitive dysfunction. It evaluates five cognitive domains: attention/orientation, memory, fluency, language, and visuospatial skills (25). The version used was adapted and validated for Colombia (26) and adaptation and validation according to the ROC curve was 87 points with sensitivity of 92.72% and specificity of 90.54%.

The Consortium to Establish a Registry for Alzheimer's Disease (CERAD): is a neuropsychological screening battery originally developed in English (27), for the neurocognitive assessment we used the Colombian validation of CERAD-Col conducted by the Neuroscience Group of Antioquia (GNA) [24] and the updated normative data [20]. The CERAD tests used include. The Mental State Examination (MMSE) to assess the cognitive areas of orientation, fixation, concentration, calculation, memory, and language. The Boston Naming test (BNT-15) to assess language naming. The Word List Memory (WLM) task that assesses learning. Word List Recall (WRL) to assess free recall and the Word List Recognition (WRL) task. The Praxis Copy (PC) and Evocation (EC) task. Semantic Fluency and Phonological Fluency (FAS). Rey-Osterrieth Figure Copy and Evocation. Trail Making Test A and B (TMT A y B). For the analysis of the internal consistency of the CERAD-Col, the authors reported that the scores of each of the tests of the battery were used. The Cronbach's α was 0.83 (95% CI = 0.78-0.88) for the general population sample, and 0.87 (95% CI = 0.83-0.9) for the sample of patients with Alzheimer's disease, indicating a high level of homogeneity and equivalence high homogeneity and equivalence of responses to all tests at the same time and for all subjects. at the same time and for all subjects.

The Yesavage Scale for Geriatric Depression-GDS-15 (28): the scale quantifies depressive symptoms in older adults. In the study of consistency and factorial structure in the Colombian population, it is reported that the GDS-15 showed an acceptable internal consistency of 0.78. A systematic review showed that the 15-item version has better diagnostic accuracy and clinical utility than the 30-item version.

Data analysis

Our protocol comprised an independent variable (Group) with two levels (HOA and MCI). The allocation of participants to such groups was described above (see Figure 1). All the other variables were dependent. To describe the sociodemographic and clinical characteristics of the participants, absolute and relative frequencies were used in the case of qualitative variables, and measures of central tendency with dispersion were used in the case of quantitative variables. The overall and specific prevalence was estimated by age group, sex, education, and socioeconomic level. Chi square analyzes were performed to explore categorical variables. Multivariate logistic regression analysis was performed using as predictors Age, education, place of residence, diabetes, hypertension, cerebrovascular disease, malnutrition, exposure to pesticides and smoking and Group as the dependent variable.

Result

Before we report on the core outcomes from our study, it is worth mentioning that we subjected our design and protocol to a self-assessment focused on the ten methodological criteria recommended for prevalence studies (29). Our study successfully met such criteria (see Supplementary Material S.2). We recruited 823 older adults into the study thus exceeding our estimated sample size. Of these, 73.3% were women. After administering the above protocol, we

determined that 53.6% of those evaluated had cognitive impairment. Our sample was drawn from two cities, 503 participants were recruited in the department of Huila and 320 in Caquetá. Of the sample in Huila, 261 participants (51.9%) met the MCI criteria while in Caquetá 181 participants (56.6%) met such criteria.

Table 1 shows the distribution of the sample across Group (HOA and MCI) and socio-demographic variables. Of note, 103 (38.8%) participants with MCI were between 50-60 years of age, 250 out of 326 adults were in the lowest education band (1 and 5 years), and 86% were in low socioeconomic status. Regarding comorbidities, 60.7% (n=68) MCI patients had diabetes and 55.5% (n=176) had high blood pression. Regarding environmental risk factors, 128 (15.5%) participants (out of 823) reported exposure to agricultural pesticides of whom 73% (n=57) met MCI criteria (see Table 1).

Table 1. *Demographics variables*

Variable	Total Sample	MCI group	HOA group	p value
	823	441 (53.6)	381(46.3)	
Sex				
Male	218 (26.4)	122 (56)	96 (44)	0.424
Female	604 (73.3)	319 (52.8)	285 (47.2)	
Age				
50-59	265 (32.2)	103 (38.8)	162 (61.2)	0.000
60-69	385 (46.7)	215(55.8)	170 (44.2)	
>70	172 (20.9)	123(71.5)	49 (28.5)	

Years of Education				
1-5	326 (39.6)	250 (76.7)	75 (23.1)	0.000
6-11	267 (32.4)	121 (45.3)	145 (54.3)	
>12	227 (27.5)	67 (29.5)	160 (70.5)	
*Socioeconomic status**				
One	286 (34.7)	185 (64.6)	101 (35.4)	0.000
Two	424 (51.5)	215 (50.7)	209 (49.3)	
Three	82 (9.9)	32 (39)	50 (61)	
Four	30 (3.6)	9 (30)	21 (70)	
Place of residence				
Rural	120 (14.5)	75 (62.5)	45 (37.5)	0.932
Urban	703 (85.4)	367 (52.2)	336 (47.8)	
Department				
Huila	503 (61.1)	261 (51.9)	242 (48.1)	0.204
Caquetá	320 (38.8)	181 (56.6)	139 (43.4)	
Chronic disease				
Diabetes	112 (13.6)	68 (60.7)	44 (39.3)	0.107
Arterial hypertension	317 (38.5)	176 (55.5)	141 (44.5)	0.394
Cerebrovascular disease	17 (2)	11 (64.7)	6 (35.3)	0.356
Malnutrition	15 (1.8)	9 (60)	6 (40)	0.619
Heart disease	38 (4.6)	25 (65.8)	13 (34.2)	0.124

Tabaco	258 (31.4)	163 (63.2)	95 (36.8)	0.000
Depression				
Yes	64 (7)	42 (65.6)	22 (34.4)	0.031
No	759 (92)	399 (52.6)	360 (47.4)	
Pesticide exposure				
Yes	128 (15.5)	73 (57)	55 (43)	0.405
No	692 (84)	367 (53)	325 (47)	

* The classification of the SES is based on the classification of the Administrative Planning Departments, which classify the municipality's housing and/or land (Law 142 of 1994) in the following categories: one (low-low), two (low), three (medium-low), four (medium), five (medium-high) and six (high). This classification is based on the characteristics of the community dwellers and their urban-rural environments.

In the analysis of the association between age and the presence of MCI, significant patterns were observed. People aged 50-59 years represented 38.8% of the MCI group and 61.2% of the control group. In the 60-69 age group, 55.8% showed MCI, while 44.2% were HOA. Finally, in the age group over 70 years, 71.5% had MCI, compared to 28.5% of the HOA. The chi-square analysis revealed a highly significant association between age ($\chi2 = 46.099$, $p < 0.001$) and the presence of MCI ($\chi2= 4.649$, $p<0.005$). These findings indicate a statistically significant relationship between age and MCI, suggesting that MCI tends to increase with older age. Table 2 shows the neuropsychological characteristics of the groups. Of the evaluated sample, 188 (42.6%) met criteria for amnestic MCI, 172 (39%) for amnestic multi-domain MCI, 73 (16.55%) for non-amnestic MCI, and 8 (1.81%) for non-amnestic multi-domain.

Table 2. Frequency distribution of subtypes of MCI

MCI	Frequency (n=441)	Female	Male	Percentage (100)
Amnestic MCI	188	130	58	42.6
Multi-domain amnestic MCI	172	123	49	39
Non-amnestic MCI	73	58	15	16.55
Multi-domain amnestic MCI	8	8	0	1.81

In the logistic regression analysis, multiple variables were evaluated to determine their impact on the likelihood of individuals belonging to the MCI group. Statistically significant results were found for age ($p = 0.009$). With one year increase in age, there was approximately 3.0% increase in the probability of belonging to the MCI group (OR = 1.030 CI: 0.834 - 0.887). Years of education also proved significant ($p < 0.001$), indicating that each additional year of education was associated with a 14.0% decrease in the probability of being in the MCI group (OR = 0.860; CI= 0.834-0.887). Individuals who smoked had approximately 42.6% higher odds of developing MCI compared to non-smokers (OR = 1.426; CI= 1.015-2.003), although these results were only marginally significant. Other variables such as place of residence, chronic diseases, diabetes, hypertension, vascular disease, malnutrition, and pesticide exposure did not show statistically significant associations with the probability of MCI (see Table 3).

Table 3. Results from the logistic regression.

Variables	B	SE	Wald	Sig.	OR	95% CI	
Age	0.029	0.011	6.865	**0.009**	1.03	1.007	1.052
Years of education	-0.15	0.016	90.222	**0.000**	0.86	0.834	0.887
Place of residence	0.137	0.223	0.377	0.539	1.147	0.741	1.775
Diabetes	0.211	0.233	0.82	0.365	1.235	0.782	1.948
Hypertension	-0.142	0.167	0.725	0.394	0.868	0.625	1.203
Vascular disease	0.414	0.565	0.537	0.464	1.513	0.5	4.579
Malnutrition	-0.401	0.555	0.522	0.47	0.67	0.226	1.987
Pesticide exposure	0.217	0.224	0.938	0.333	1.242	0.801	1.927
Smoking	0.355	0.174	4.178	**0.041**	1.426	1.015	2.003

Discussion

The present study investigated the hypothesis that high prevalence of MCI would be found in Colombian regions where the prevalence of dementia had been reported to be among the highest in Latin America. We anticipated that such prevalence rates would be associated to low education, rurality, and demographic characteristics typical of the southern Colombian region. The prevalence

of MCI was 51.9% for the province of Huila and 56.6% for the province of Caquetá (average regional prevalence of 53.6%). This greatly surpasses the prevalence reported by other studies. Differences in prevalence rates of MCI may be attributed to the diagnostic criteria, study populations, methodologies and instruments used (15). The screening tools traditionally used to identify subjects with suspected MCI have proved both limited and challenging (e.g., MMSE). Such tools can explain the low prevalence reported by other studies. The fact that for the present study we relied on an assessment protocol widely used and validated in Colombia (24) grant us confidence in the reliability of our results.

Our current results are consistent with the prevalence of dementia established for this population in 2003, corresponding to 23.6% in population over 60 years (23). The prevalence of MCI here reported would match conversion rates for dementia in members of these Colombian populations. When estimating the conversion rate from MCI to dementia based on age and other healthcare factors, an annual rate between 10-15%% is expected (30); about 1 in 4 people with MCI will be at risk of dementia (31). Although the prevalence of MCI here reported might look high, other studies had also identified extremely high prevalence. For example, Mohan et al. (32) reported that the prevalence of MCI varies widely between 3% and 42% across different regions of the world. Artero et al. (33) reported a prevalence of MCI of 42% which they found to be consistently high across three recruitment sites (43%, 47% and 28%). MCI prevalence of 32.9% was reported among community-dwelling elderly Koreans aged 74.3±16.7 (34). The prevalence of MCI is a highly inconsistent epidemiological figure of a highly heterogeneous nature (32). In the case of our study, we feel confident to endorse our identified prevalence rate. Our previous characterization of the dementia prevalence in Huila (23) together with the strict methodological approach followed in the

current study indicate that the magnitude of such a problem in this region of Colombia is alarming (35).

The MCI sample found in our study showed that the amnestic type was the most common form for both genders and that the multi-domain amnestic MCI was not found in men. Regarding risk factors, we found that both age and education were significant predictors of group membership. These results are not entirely new. Recent studies have explored the social determinants of health and aging in Latin America (36) and have suggested a set of non-canonical risk factors driving aging trajectories in the region. Studies from developed countries has reported that limited access to formal education grant higher risk of anormal aging (20,37,38). Recently Santamaria-Garcia et al. (36) reported that this is also true for Latin American countries and our study confirm it does apply to Colombia; the population targeted by this study is located in regions of Colombia where the factors described by Santamaria-Garcia et al. (36) are rather abundant (See Supplementary Material S.2 for a detailed description of the targeted Colombian regions). Regarding comorbidities and environmental factors, it was found that more than 50% of our patients had other chronic diseases being diabetes (n=68, 60.7%) and cardiovascular diseases (hypertension, n=176, 55.5%) the most common comorbidities. This evidence is relevant as Livingston et al. (10) reported that diabetes is a key risk factor for dementia later in life accounting for a potential percentage reduction in dementia prevalence of 1%. Hypertension also figures among the midlife risk factors for dementia accounting for a potential percentage reduction in dementia prevalence of 2% (39). Therefore, by tackling these risk factors, we could potential reduce 3% of future dementia cases. However, in the multivariate regression analyses we did not find significant associations between chronic diseases, such as diabetes, hypertension, and vascular accidents, and the risk of MCI. This contrasts with previous studies, which have identified stroke, depression, and reduced physical

activity (less than half an hour) as independent risk factors for cognitive decline in older individuals with diabetes (40).

While a direct link between depression and MCI demonstrated a statistically significant association, multivariate logistic regression analysis, controlling for variables including age, education, chronic diseases, and pesticide exposure, failed to provide evidence supporting a connection between 'depression' and cognitive deterioration. These findings suggest that cognitive decline may be more comprehensively explained by the interplay of these other variables, which have received extensive attention in existing literature. Other studies have reported that depression is a significant risk factor for dementia in individuals with type 2 diabetes (41). Pink and colleagues found that a relationship between amyloid deposition in patients who tested positive for positron emission tomography (PET) and depression but not with clinical anxiety (42).

Finally, we observed a remarkably high number of MCI cases exposed to pesticides, although without statistically significant associations at this stage. We had 75 cases of MCI (62.5%) who reported living in the rural area in both departments and 128 participants (15.5%) had been exposed to agricultural pesticides. This is not surprising as we are aware that this population is imminently agricultural. What is surprising is that Livingston et al (9,10) did not identify environmental factors as potential sources of dementia risk. It is known that the prevalence of MCI tends to be higher in rural areas (43). Evidence is accruing suggesting the presence of learning and memory deficits following repeated occupational exposures to organophosphate (44). Therefore, it is important to inquire about these aspects, specifically in areas highly exposed to agricultural pesticides.

The study faces some limitations. For example, the type of non-probabilistic sampling in this study may limit the generalization of our results. Older adults who are experiencing cognitive decline

may be more prompted to enroll due to a desirability factor. Another limitation is the lack of dementia biomarkers to achieve a higher diagnostic accuracy.

To conclude, the prevalence of MCI found in this study was higher than that reported in Latin America, for example in Perú aMCI 17.9% (45) and Costa Rica 9% (46). Low educational level and chronic diseases are relevant factors which have been identified by others. We are the first group to report pesticide exposure as a potential factor worth investigating the Latin American populations in the future. As highlighted above, the forecast for LMIC on new dementia cases, including Latin America, is not encouraging (35). The dementia epidemic will have a more serious impact on our countries than in developed countries (11,14). It is essential to conduct further studies to explore other factors related to dementia risk among these populations. For example, given that these individuals are still in a productive stage of their lives, it is important to consider the potential impact of environmental factors such as exposure to toxic agents.

Acknowledgements

We thank the older adults for their participation and willingness to carry out the research, the community clubs of Huila and Caquetá.

Funding

This work was supported by [CONADI - Universidad Cooperativa de Colombia in agreement with Universidad Surcolombiana] under Grant [INV2384]; and [The Science, Technology, and Innovation Fund- Huila of the General System of Royalties through the Ministry of Science, Technology, and Innovation of Colombia [BPIN 2020000100011] Universidad Surcolombiana and Universidad de la Amazonia.

Conflict of interest

The authors have no conflict of interest to report.

Data availability

The data supporting the findings are available on reasonable requests via the corresponding authors.

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Prevalence of Mild Cognitive Impairment in Southern Regions of Colombia

Supplementary Material

S.1 - **Study Self-Assessment**

We have assessed the present study and its report against the ten methodological evaluation criteria for prevalence studies presented by (Munn et al., 2015). We present the outcomes from such a self-assessment below.

1.Was the sample representative of the target population? Response: Yes

When designing the prevalence study, we took into account the broadest characteristics of the population of interest. The target population for our study consists of adults over 50 years of age residing in two departments of Colombia. We carefully considered various factors, such as age range, gender, and pre-existing medical conditions, among other potentially influential factors, when selecting the study sample. As a result, we are confident that our study sample is representative of the target population, and our findings can be applied to this specific population.

2.Were study participants recruited in an appropriate way? Response: Yes

For the present study, participants were recruited using a non-probabilistic convenience sampling method. The recruitment strategy involved visiting various collection groups and activity clubs for older adults in the cities where the evaluations were carried out, as well as using open invitations on social networks and institutional pages to invite individuals over 50 years of age to participate. A sample size of 596 older adults was determined, and 823 participants were ultimately recruited and evaluated using clinical criteria and a complete neuropsychological assessment. This approach was chosen to ensure that the results are generalizable to the population of interest.

3. Was the sample size adequate? Response: Yes

The sample size for proportion studies was calculated using OpenEpi, an open source software for statistics in epidemiology. A total population of n=78372 adults over 50 years of age in both departments was taken into account, based on figures published by governmental entities. Previous prevalence studies in the country suggested an anticipated frequency of 34% (expected prevalence or proportion), and an absolute precision of 5% (d=0.05) was deemed appropriate. A design effect of 1.0 was also assumed for studies with random samples. With a confidence interval of 99%, the sample size was estimated to be 596 older adults.

4. *Were study subjects and setting described in detail?* Response: Yes

The article provides a detailed description of the subjects, highlighting their unique characteristics based on various cultural and sociodemographic conditions, such as their level of education, socioeconomic status, place of residence (urban or rural), clinical-medical history, and depression. Moreover, the study included an additional distinguishing feature of the population, namely their exposure to pesticides. This comprehensive account of the subjects enables readers to gain a deeper

understanding of the population under investigation and facilitates a more informed appraisal of the research findings.

5. Is the data analysis conducted with sufficient coverage of the condition? Response: Yes

In order to control for the impact of neuropsychological factors, the study implemented a carefully selected and adapted set of neuropsychological assessment instruments. The highly qualified personnel administering the assessments ensured that participants remained engaged throughout the study. This approach was effective in producing a comprehensive flowchart (Flowchart 1 in manuscript). The flowchart illustrates the extent of the sample assessed and categorized in accordance with Petersen's criteria (Petersen, 2004). This meticulous approach to neuropsychological assessment enabled the study to yield more reliable and informative findings about the evaluated condition.

6. *Were objective, standard criteria used for measurement of the condition?* Response: Yes

The study used internationally recognized criteria and guidelines to measure the presence of mild cognitive impairment, with a focus on early detection of Alzheimer's disease. These guidelines were carefully adhered to in order to ensure the reliability and validity of the findings. The interdisciplinary team responsible for analyzing the instruments also adhered to data standards specific to the country (Colombia) where the project was carried out, as described in the article. By adhering to these rigorous standards, the study was able to produce results that are both scientifically sound and culturally relevant. The instruments utilized in the study had been carefully adapted and validated for use in Colombia (Aguirre-Acevedo et al., 2007; Aguirre-Acevedo et al., 2016).

7. Was the condition measured reliably? Response: Yes

In order to effectively assess the large number of participants (n=823), the study's researchers employed a team of psychologists with specialized knowledge and training in neuropsychology. This team followed a protocol designed specifically for the study, based on international criteria and standardized evaluation methodologies. Any participants who were difficult to classify due to their unique characteristics were reviewed on a case-by-case basis by a panel of experts consisting of psychologists, neurologists, and psychiatrists. This multi-disciplinary approach ensured that any challenging cases were carefully evaluated and classified according to rigorous criteria, in order to ensure the accuracy and validity of the study's findings.

8.*Was there appropriate statistical analysis?* Response:Yes

In this study, a frequency and proportion analysis were carried out to determine the number of participants who presented with mild cognitive impairment, in relation to the total population evaluated. This analysis allowed the researchers to have an overview of the prevalence of this condition in the sample and to obtain an estimate of the percentage of people who might be at risk of developing a neurodegenerative disease such as Alzheimer's disease in the future. Frequency and proportion analyses are useful statistical techniques for describing and summarizing data, allowing researchers to obtain clear and concise information about the distribution of variables and the prevalence of the conditions being studied.

9. *Are all important confounding factors/ subgroups / differences identified and accounted for?* Response: Unclear

The investigators attempted to control for the most common confounding factors in the study design, such as age, education, socioeconomic status, and place of residence. However, given the heterogeneous nature of the population evaluated and the sample, it is difficult to fully guarantee that there are no confounding factors that could influence the results obtained, despite having used all the tools at your disposal to minimize their impact. Despite these limitations, the researchers made every effort to ensure the integrity and reliability of the results, including careful sample selection and the use of rigorous methods of data analysis and control. These measures help to mitigate the effects of confounding factors and to maximize the validity and usefulness of the findings obtained.

10. *Were subpopulations identified using objective criteria?* Response: Yes

In the study, objective criteria based on the international criteria for the classification of mild cognitive impairment were used to identify subpopulations within the sample. These criteria allowed researchers to classify cases of mild cognitive impairment into the four subtypes that have been defined by the scientific literature (See Flowchart 1 in manuscript).

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S.2 - Some general characteristics of the Colombian Southern Provinces of Huila and Caquetá

The departments of Huila and Caquetá are in the central and southern regions of Colombia, respectively. About 40% of the residents of the department of Huila live in rural areas (out of a total of 1,009,548 inhabitants) and 50.1% are women. The subjective poverty reported is 34.8% and the unemployment rate reaches 9.2%, which is close to the national average (figures prior to

the start of the Sars-CoV-2 pandemic). Furthermore, around 39.25% of the inhabitants live in rural areas in the department of Caquetá (out of a total of 502,410 inhabitants) and 50.4% are women. The multidimensional poverty index is 33.6%. The most representative problems in this region are associated with the high greenhouse gas emissions (third position nationwide), which is the result of deforestation and expansion of the agricultural frontier (United Nations Development Program, UNDP, 2019).

In addition to the above, this area of the country has been exposed to the effects of forced displacement, high homicide rates and the consequences of drug trafficking in urban and rural areas, which together with a cumulus of unsatisfied basic needs exert a direct impact on the access to education, which in turn represents a risk factor for the development of cognitive impairment in the medium and long term.