Knowledge of dementia and Alzheimer's disease among healthcare professionals in Peru

Conocimiento sobre demencia y enfermedad de Alzheimer entre profesionales de la salud en Perú

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Abstract

Background Primary care physicians and other healthcare providers report feeling unprepared to treat persons with dementia (PWD), especially in developing countries

Objective We aimed to assess the knowledge of dementia and Alzheimer's disease (AD) among health professionals in both primary and tertiary care in Peru.

Methods We conducted an in-person and virtual survey of healthcare professionals trained in Peru throughout the year 2020. The survey was developed based on a previously published one and reviewed by an expert panel. We compared groups using a Chi-squared test. A Bonferroni corrected *p*-value of 0.008 was used for statistical significance.

Results Out of 804 surveys, we excluded 56 due to incomplete data. A total of 41.6% of respondents were doctors and 21.8%, nurses. One fifth of participants did not recognize AD as a cause of dementia and over half considered "senile dementia" a valid clinical entity. Scores were higher among those with postgraduate training, multiple patients with dementia, or those who had practiced for over 10 years.

Conclusion There is a low level of knowledge of dementia and AD among health professionals in Peru, which worsens outside of Lima. Pernicious ideas, such as senile dementia, are still significantly present among respondents.

Keywords
- Dementia
- Peru
- Allied Health Personnel
- Alzheimer Disease

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Resumen

Antecedentes Los médicos de primer nivel de atención y otros profesionales de la salud no se consideran cómodos tratando pacientes con demencia, especialmente en países en vías de desarrollo.

Objetivo Buscamos evaluar el conocimiento sobre demencia y enfermedad de Alzheimer entre profesionales de la salud en centros de atención primaria y terciaria en Perú.

Métodos Realizamos una encuesta virtual y presencial a trabajadores de la salud entrenados en Perú en el año 2020. La encuesta fue desarrollada con base en una previamente publicada y revisada por un panel de expertos. Comparamos los grupos por medio de una prueba de Chi-cuadrado. Un valor de *p* de 0.008, obtenido por una corrección de Bonferroni, fue usado para determinar la significancia estadística.

Resultados De 804 encuestados, excluimos 56 debido a datos incompletos. En total, 41.6% de los encuestados eran médicos y 21.8%, enfermeras. Un quinto no reconocía a la enfermedad de Alzheimer como una causa de demencia, y más de la mitad consideraban a la "demencia senil" una entidad clínica válida. Los puntajes fueron mayores para aquellos con entrenamiento de posgrado, experiencia con pacientes con demencia, o más de 10 años de experiencia.

Conclusión Existe un bajo nivel de conocimiento sobre demencia y enfermedad de Alzheimer entre profesionales de la salud en Perú. Este es aún más bajo fuera de Lima. Ideas dañinas como la "demencia senil" aún están significativamente presentes entre los encuestados.

Palabras clave

- Demencia
- Perú
- Técnicos Medios en Salud
- Enfermedad de Alzheimer

INTRODUCTION

Dementia is a neurological syndrome characterized by cognitive impairment severe enough to impede independent living. There are reversible and irreversible etiologies of dementia. Although neuroimaging and other biomarkers may help ascertain specific etiology or type of dementia, the diagnosis remains clinical and is based on three core evaluation components: cognitive history, brief cognitive tests (BCTs) or complete neuropsychological evaluation, and functional assessments.[1,2]

Dementia affects 50 million people globally, over 60% of whom are from low- or middle-income countries.[3] In Latin America, the prevalence of dementia sits around 9 to 10%, with an increase of over 20 million new patients with cognitive disorders expected by 2050.[4–6] In Lima, Peru, dementia prevalence is close to 7%.

Those who take care of patients with dementia, mostly informal, female caregivers, are also affected. They report decreased working time and a self-perception of impaired health. There are financial burdens as well, with total caregiving costs exceeding 1,500 USD a month.[7,8]

However, in these countries, primary care physicians (PCPs) face significant barriers to diagnosis and treatment of persons with cognitive impairment, such as limited time for evaluation and care, difficulty accessing tertiary care for dementia, and scarce specialized testing.[9] Moreover, research suggests that PCPs may not be properly prepared to manage persons with dementia (PWD). In Peru, PCPs, psychologists, and nurses describe feeling unprepared to treat PWD, and less than a third of physicians report adequately learning about dementia during medical school.[10,11] However, these studies focused primarily on frontotemporal dementia and only tangentially assessed knowledge of dementia and Azheimer disease (AD). Likewise, their sample was limited to the country's largest city, which may not be representative of primary care in more resource-limited settings.

Thus, given the rising importance of dementia as a cause of morbidity and mortality worldwide, especially in Latin America, and the need for accessible multidisciplinary care, in this study, we aimed to determine the level of knowledge of dementia and AD—the most common irreversible etiology of dementia worldwide—among a diverse sample of Peruvian health professionals.

METHODS

Study design

We carried out a descriptive, observational, cross-sectional multicenter study. We used a survey which was handed both in-person and virtually during 2020 to healthcare professionals including doctors, nurses, nursing assistants, dentists, obstetricians, and psychologists among various centers around the country (Supplementary Material: https://www.arquivosdeneuropsiquiatria.org/wp-content/uploads/2024/06/ANP-2023.0070-Supplementary-Material.docx). We included only those professionals who had received their training in Peru and consented to participate in the study. The centers were selected by convenience sampling among

five different regions in the country: Lima, San Martin, Tacna, Piura, and Trujillo. They included both primary care centers and tertiary care hospitals; likewise, professionals working at home healthcare assistance programs at both public and private institutions were included. These were Centro Médico Naval, Clínica Centenario Peruano Japonesa, Hospital de Collique, Hospital María Auxiliadora, Hospital Nacional Cayetano Heredia, Programa de Atención Domiciliaria (PADOMI), Palliative care at OncoSalud, Red Asistencial Moyobamba, and Centro de Atención Primaria III Metropolitano de Tacna.

For the sample size, we used the study of dementia knowledge in Lima by Custodio et al.[11] For a population of around 100 thousand healthcare workers, with an expected frequency of respondents that had insufficient knowledge of dementia of 72.1%, confidence limit at 95%, design effect at 1, and drop rate of 25%, we estimated a required sample size of 387 healthcare professionals. However, we doubled this number by handling 804 surveys.

Instrument

We developed our study survey based on surveys previously used by Custodio et al. and Olavarría et al.[11,12] Our study survey was reviewed by an expert panel composed of three neurologists with expertise in dementia. The first section includes demographic data such as age, gender, training, and professional experience with dementia. The second part was composed of 19 questions covering general topics, such as types of dementia and BCTs, and AD specific questions, including risk factors, symptoms, diagnosis, and treatment.

Statistical analysis

We used the Stata 16 software (StataCorp LLC, College Station, TX, USA). We first summarized descriptive variables using frequency measures or central tendency. We dichotomized some of them according to expert consensus to facilitate analysis. That is, number of years practicing (< 10 or ≥ 10), number of patients attended per month (< 5 or ≥ 5), known types of dementia (0 or ≥ 1), known BCTs (0 or ≥ 1), and dementia symptoms (< 4 or ≥ 4). We then obtained the average number of correct answers and classified it into low (0–1.9), medium (2.0–3.9), or high (4.0–6.0) according to expert consensus.

Finally, we evaluated factors associated with a lower number of correct answers using the Chi-squared test. Values with $p < 0.008$ were considered statistically significant, after performing a Bonferroni correction to avoid multiple test bias.

Ethics

Participation in the study was voluntary and anonymous. We used an informed consent form, which was signed prior to the start of the survey. The research protocol was approved by the Ethics Committee of Universidad Científica del Sur, with certificate no. 350-CIEI-CIENTIFICA-2020. All methods were carried out in accordance with the relevant guidelines and regulations in the Declaration of Helsinki.

RESULTS

We included 748 surveys out of 804, as 56 had incomplete data. Most respondents were male (69.5%) and worked in Lima (74.6%). The average age was 41 years old, and 41.6% were doctors and 21.8%, nurses. Of all participants, 53.9% had been practicing for less than 10 years.

More than 1/3 of survey respondents (36.8%) regularly cared for patients with dementia. However, less than a third considered themselves capable of diagnosis and treating a patient with dementia. Of those who did, most reported having only undergraduate knowledge of the disease (►**Table 1**).

Knowledge about dementia and Alzheimer's disease

Less than a quarter of respondents knew more than 1 type of dementia and most (51.4%) described "senile dementia" as a valid type. A substantial proportion of respondents (19.5%) did not recognize AD as a type of dementia; among the respondents who did, 78.3% were able to recognize more than 4 of its symptoms and 71.3% more than 2 AD risk factors (►**Table 2**).

Although more than half of respondents (55.9%) correctly indicated that BCTs allow for an early diagnosis of AD, only 27.5% were able to recognize more than 1 BCT from a list of commonly used BCTs; 44% identified more than 2 auxiliary exams that contribute to diagnosis. Over 80% of respondents could not identify how to definitively diagnose AD, and over 60% could not identify the role of available AD treatments (►**Table 3**).

Factors associated with increased knowledge

Age and gender were not significantly associated with a higher number of correct responses. Respondents from Lima had a higher average of correct responses compared to those located outside the capital city ($p = 0.002$) (►**Figure 1**). Doctors and psychologists had higher average correct responses compared to other healthcare professionals.

Among physicians, those who considered themselves experienced in the diagnosis and treatment of patients with dementia had statistically significant higher scores than those who did not ($p < 0.001$). Similarly, respondents who actively cared for patients with dementia during our study obtained a statistically significant higher average of correct responses compared to those who did not ($p < 0.001$), especially if they took care of more than 5 patients per month ($p = 0.003$). Additionally, those with postgraduate studies and those who trained in specialized institutes had a statistically significant higher number of correct responses ($p < 0.001$). Additionally, doctors with more than 10 years of clinical practice obtained the highest average of correct answers ($p < 0.001$). Finally, doctors practicing in Lima had higher averages compared to those outside of Lima ($p < 0.001$) (►**Table 4**).

Table 1 Characteristics of the surveyed health professionals and level of knowledge about Alzheimer's disease

		Fr (%)	Correct answers X (SD)	*p*
Age (years)*		41.5 (11.8)	6.6 (2.3)	0.045
Sex	Male	519 (69.5)	6.5 (0.1)	0.039
	Feminine	229 (30.5)	6.9 (0.2)	
Profession	Medical doctor	311 (41.6)	7.3 (2.2)	
	Nurse	163 (21.8)	6.2 (2.4)	
	Nursing technician	211 (28.2)	6.1 (2.2)	
	Dentist	19 (1.6)	6.8 (0.9)	
	Obstetrician	14 (1.9)	6.1 (1.7)	
	Psychologist	22 (2.9)	7.3 (2.0)	
	Nutritionist	5 (0.7)	7.2 (1.1)	
	Physical therapist	3 (4.0)	4.3 (1.5)	
Number of years practicing	< 10 years	403 (53.9)	6.6 (0.1)	0.017
	> 10 years	345 (46.1)	6.7 (0.1)	
Region	Lima	558 (74.6)	6.8 (2.3)	0.002[a]
	Outside of Lima	190 (25.4)	6.2 (2.3)	
Are you capable of diagnosing and treating dementia?	Not capable	544 (72.8)	6.2 (0.1)	< 0.001[a]
	Capable	204 (27.2)	7.7 (0.2)	
How were you trained in dementia?	Does not apply	534 (71.4)	6.3 (2.1)	
	Specialized institution	42 (5.6)	7.1 (2.2)	
	Undergraduate	88 (11.8)	7.1 (2.4)	
	Postgraduate	53 (7.1)	8.9 (1.7)	
	Other	31 (4.1)	7.2 (2.6)	
Do you treat any patients with dementia?	No	473 (63.2)	6.3 (0.1)	< 0.001[a]
	Yes	275 (36.8)	7.2 (0.1)	
Number of dementia patients served per month	< 5	640 (85.6)	6.5 (0.1)	0.003[a]
	> 5	108 (14.4)	7.2 (0.3)	

Abbreviation: Fr, frequency; SD, standard deviation.
sem negrito: *Median (interquartile range); [a]$p < 0.008$ (significance level corrected with Bonferroni).

DISCUSSION

We found a surprisingly low level of knowledge of dementia, generally, and AD, specifically, among the surveyed health professionals in Peru. The surveyed population consisted mainly of physicians, followed by nurses and other health professionals in both primary and tertiary care in private and public institutions in 5 different cities of the country.

We found that only 27% of all surveyed professionals and 39% of physicians considered themselves fully capable of diagnosing and managing persons with dementia (PWDs). Another Latin American country, Chile, reported a similar frequency of 40% in a recent study.[12] Likewise, two studies in Brazil described diagnosis of dementia as the most challenging aspect for PCPs in managing PWDs.[13,14] As detection of dementia usually occurs at the PCP setting, these findings translate in low rates of appropriate referral to subspeciality care.[15,16] This, added to the lack of subspeciality care availability in low-resource settings of Peru and Latin America as a whole, constitutes an obstacle for early diagnosis, which limits the possibility to preserve and improve the quality of life of patients and caregivers.[4,17]

Additionally, we found that only 25% of the health professionals surveyed managed to list one or more types of dementia. The majority of these indicated "senile dementia" as a valid type of dementia. The concept of senile dementia is considered obsolete and non-scientific; hence, in this regard, our study findings suggest there is an urgent need to update the knowledge of dementia among healthcare professionals at the national level. Although dementia is significantly more common in old age, it is not an inevitable consequence of aging. Likewise, people younger than 65 years can also suffer from dementia. It appears, based on our study findings, that knowledge of these key concepts is lacking among a substantial proportion of health professionals in Peru.

Table 2 Answers from health professionals to questions about Alzheimer's disease

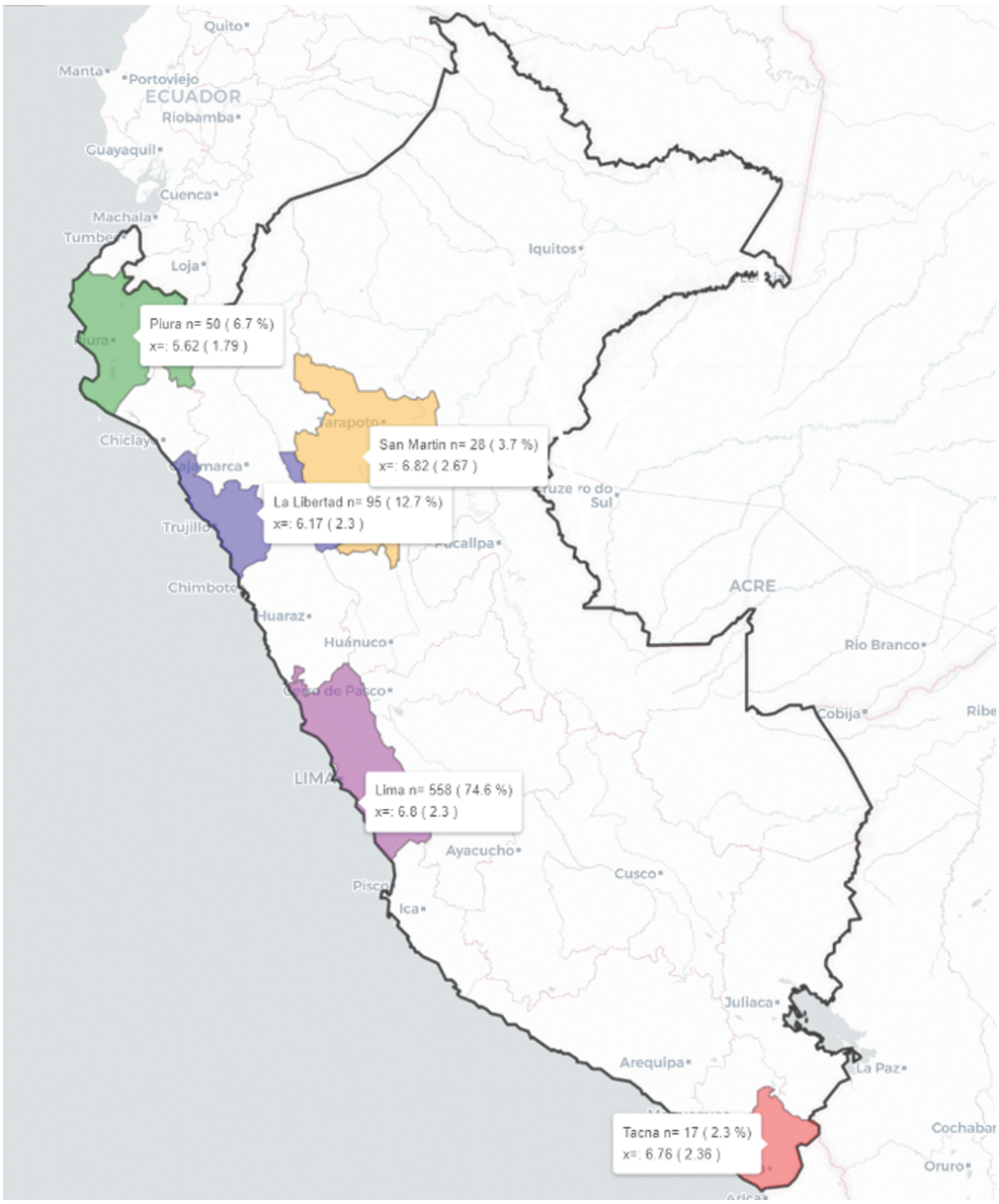
Profession	Frequency (%)	What types of dementia do you know?		Is AD a type of dementia?		What Risk Factors for AD are you aware of?		What symptoms of AD do you know?	
		None	≥ 1	No	Yes	≤ 2	> 2	≤ 4	> 4
Medical doctor	311 (41.6)	222 (71.4)	89 (28.6)	46 (14.8)	265 (85.2)	88 (28.3)	223 (71.7)	269 (13.5)	311 (86.5)
Nurse	163 (21.8)	131 (80.4)	32 (19.6)	38 (23.3)	125 (76.7)	50 (30.7)	113 (69.3)	47 (28.8)	116 (71.2)
Nursing technician	211 (28.2)	164 (77.7)	47 (22.3)	47 (22.3)	164 (77.7)	62 (29.4)	149 (70.6)	59 (28.0)	152 (72.0)
Dentist	19 (1.6)	12 (58.3)	7 (41.7)	4 (8.3)	15 (91.7)	5 (26.3)	14 (73.7)	3 (15.8)	16 (84.2)
Obstetrician	14 (1.9)	13 (92.9)	1 (7.1)	6 (42.9)	8 (57.1)	2 (14.3)	12 (85.7)	3 (21.4)	11 (78.6)
Psychologist	22 (2.9)	14 (63.6)	8 (36.4)	2 (9.1)	20 (90.9)	6 (27.3)	16 (72.7)	6 (27.3)	16 (72.7)
Nutritionist	5 (0.7)	4 (80.0)	1 (20.0)	0 (0.0)	5 (100.0)	0 (0.0)	5 (100.0)	0 (0.0)	5 (100.0)
Physical therapist	3 (0.4)	2 (66.7)	1 (33.3)	2 (66.7)	1 (33.3)	2 (66.7)	1 (33.3)	2 (66.7)	1 (33.3)
Total 748 (100)		562 (75.1)	186 (24.9)	146 (19.5)	602 (80.5)	215 (28.7)	533 (71.3)	162 (21.7)	586 (78.3)

Abbreviation: AD, Alzheimer's disease.

Table 3 Answers from health professionals to questions about Alzheimer's disease

Profession	What should the initial EA assessment include?		Do BCTs allow early dx of EA?		Which BCTs do you know?		Is a definitive diagnosis of AD possible?		How is the definitive diagnosis of AD obtained?		What is the role of AD treatment?	
	≤ 2	> 2	No	Yes	None	≥ 1	No	Yes	Incorrect	Correct	Incorrect	Correct
Medical doctor	171 (45.0)	311 (55.0)	195 (37.3)	311 (62.7)	112 (64.0)	311 (36.0)	181 (41.8)	311 (58.2)	83 (73.3)	311 (26.7)	98 (68.5)	311 (31.5)
Nurse	92 (56.4)	71 (43.6)	76 (46.6)	87 (53.4)	129 (79.1)	34 (20.9)	88 (54.0)	75 (46.0)	145 (89.0)	18 (11.0)	101 (62.0)	62 (38.0)
Nursing technician	146 (69.2)	65 (30.8)	104 (49.3)	107 (50.7)	171 (81.0)	40 (19.0)	126 (59.7)	85 (40.3)	203 (96.2)	8 (3.8)	110 (52.1)	101 (47.9)
Dentist	14 (75.0)	5 (25.0)	15 (83.3)	4 (16.7)	17 (91.7)	2 (8.3)	6 (33.3)	13 (66.7)	19 (100.0)	0 (0.0)	13 (66.7)	6 (33.3)
Obstetrician	6 (42.9)	8 (57.1)	5 (35.7)	9 (64.3)	13 (92.9)	1 (7.1)	6 (42.9)	8 (57.1)	14 (100.0)	0 (0.0)	11 (78.6)	3 (21.4)
Psychologist	13 (59.1)	9 (40.9)	9 (40.9)	13 (59.1)	5 (22.7)	17 (77.3)	10 (45.5)	12 (54.6)	20 (90.9)	2 (9.1)	13 (59.1)	9 (40.9)
Nutritionist	5 (100.0)	0 (0.0)	2 (40.0)	3 (60.0)	5 (100.0)	0 (0.0)	1 (20.0)	4 (80.0)	5 (100.0)	0 (0.0)	2 (40.0)	3 (60.0)
Physical therapist	1 (33.3)	2 (66.7)	3 (100.0)	0 (0.0)	3 (100.0)	0 (0.0)	0 (0.0)	3 (100.0)	3 (100.0)	0 (0.0)	3 (100.0)	0 (0.0)
Total	419 (56.0)	329 (44.0)	330 (44.1)	418 (55.9)	542 (72.5)	206 (27.5)	371 (49.6)	377 (50.4)	637 (85.2)	111 (14.8)	465 (62.2)	283 (37.8)

Abbreviations: AD, Alzheimer's disease; BCTs, brief cognitive tests; dx, diagnosis; EA, early Alzheimer.



Abbreviations: x, mean score; n, number of participants.
Figure 1 Map of Peru with the regions where the survey took place highlighted.

Lastly, we found higher correct responses among those with postgraduate training. Similarly, another study in Peru found that geriatricians and other specialists had increased capacity for dementia diagnosis compared with general practitioners.[11] This suggests healthcare professionals are not sufficiently exposed to dementia during their training and highlights the importance of interventions in the undergraduate curriculum. Workshops of less than a day have showed significant improvement in dementia knowledge both in Australia and Brazil; however, attitude toward dementia did not seem to improve in the Brazilian population.[18,19] Alternatively, a Canadian program of three days also found improvement in dementia knowledge.[20] Instituting a program of this kind or increasing the emphasis on mild cognitive impairment (MCI) and AD in the medical school curriculum could result in increased knowledge of the disease in healthcare professionals in the country.

Of note, a higher rate of correct responses was found among physicians and other healthcare workers based in Lima, compared to those in other regions of the country. It is important to consider that Lima's gross domestic product (GDP) is more than double the GDP of the next richest region. Further studies with a larger sample size could compare the responses of different regions to identify if there is an association between the regions GDP and the knowledge of dementia among healthcare providers.

In our study, 20% of all health professionals surveyed (including 15% of physicians) indicated that AD is not a type of dementia. This finding is astounding, as it suggests that a significant proportion of Peruvian health professionals conceptualize dementia and AD as distinct and unrelated

Table 4 Characteristics and level of knowledge about Alzheimer's disease in physicians

		Fr (%)	Correct answers X (SD)	*p*
Age (years)*		40.7 (11.8)	7.3 (2.2)	0.172
Sex	Male	133 (42.8)	7.6 (0.2)	0.015
	Female	178 (57.2)	7.1 (0.2)	
Region	Lima	221 (71.1)	7.6 (2.1)	$< 0.001^a$
	Outside of Lima	90 (28.9)	6.6 (2.3)	
Number of years practicing	$<$ 10 years	169 (54.3)	7.2 (0.2)	0.021
	$>$ 10 years	142 (45.7)	7.4 (0.2)	
Are you capable of diagnosing and treating dementia?	No	190 (61.1)	6.6 (0.1)	$< 0.001^a$
	Yes	121 (38.9)	8.3 (0.2)	
How were you trained in dementia?	Does not refer	185 (59.5)	6.6 (2.0)	
	Specialized institution	12 (3.9)	8.5 (1.6)	
	Undergraduate	65 (20.9)	7.5 (2.3)	
	Postgraduate	41 (13.1)	9.0 (1.7)	
	Others	8 (2.6)	9.4 (2.4)	
Do you treat any patients with dementia?	No	175 (56.3)	6.7 (0.2)	$< 0.001^a$
	Yes	136 (43.7)	8.0 (0.2)	
Number of dementia patients served per month	$<$ 5	245 (78.8)	6.9 (0.1)	$< 0.001^a$
	$>$ 5	66 (21.2)	8.6 (0.2)	

Abbreviation: Fr, frequency; SD, standard deviation.
Note: *Median (interquartile range); $^a p < 0.008$ (significance level corrected with Bon Ferroni).

entities. This finding alone represents a strong indicator of the lack of awareness and misunderstanding among Peruvian health care professionals regarding dementia and its causes, and the importance of launching meaningful educational efforts to address this gap.

Almost one third of the health professionals surveyed identified fewer than two risk factors for the development of AD. This is a concerning finding, as it implies that healthcare professionals in Peru are not aware that up to 40% of cases of AD and other causes of dementia may be prevented via public healthcare approaches focused on addressing key modifiable medical and lifestyle risk factors.[21]

Furthermore, although most health professionals surveyed for this study correctly identified more than four AD symptoms, they were unable to identify diagnostic procedures and tests that should be included in the clinical evaluation of persons with cognitive impairment. It is important to mention that in Peru there are nine validated BCTs, among them are: the Clock Drawing Test, Manos version (CDT-Mv), frontal assessment battery (FAB), INECO frontal screening test (IFS), Memory Alteration Test (M@T), Peruvian Money Test (PMT), Addenbrooke's cognitive examination (ACE), Verbal-Language/Orientation-Memory Ratio (VLOM), Mini-Mental State (MMSE) and Rowland Universal Dementia Assessment Scale (RUDAS).[22–24] However, most respondents were unable to identify these BCTs.

In terms of treatment of AD, 62.2% of those surveyed indicated they did not know the function of the medications currently indicated for persons with AD. Similar results have been found among other Latin American countries.[4,12] This is worrisome as PWDs may already question the benefit of seeking treatment. A recent meta-analysis showed that, contrary to evidence, the general public does not belief dementia treatment can delay functional or cognitive decline.[25] If healthcare professionals are not prepared to challenge these beliefs, it will limit the access of PWDs to appropriate care.

Finally, these findings shed light on the importance of targeted educational interventions directed at healthcare professionals, especially during their undergraduate training, to increase their exposure to dementia and, thus, their diagnostic capacity.[26]

In conclusion, the primary limitation to the present study was that participants were selected in a non-randomized fashion. However, inclusion and exclusion criteria were established that allowed us to reduce selection bias. Furthermore, we did not use the validated and widely applied Alzheimer Dementia Knowledge Scale (ADKS) as our instrument. This was because we wished to explore knowledge related to all types of dementia, not just AD. Thus, we adapted an instrument previously used by our team in the Peruvian population.

Another significant limitation is the relatively small percentage of surveyed healthcare workers outside of Lima. Although this is sufficient for larger comparisons, as we have presented above, it would be too small of a sample size to compare different regions in Peru. Further studies aimed at identifying the most vulnerable regions in the country can power their studies accordingly.

Despite these limitations, our study establishes a starting point to identify the causes of low level of knowledge of dementia among healthcare professionals in Peru, which could guide important interventions to reduce this problem here and in other Latin American countries.

In conclusion, there is a low level of knowledge of dementia and AD among health professionals in Peru. This improves among those who practice in Lima, have postgraduate studies, and frequently manage dementia patients. Pernicious ideas such as senile dementia are still significantly present among respondents. We recommend considering implanting targeted interventions at the undergraduate level to increase exposure to dementia among all healthcare professionals.

Authors' Contributions

MM: data curation, formal analysis, and writing – original draft; RJA: conceptualization, data curation, project administration, and writing – original draft; CAD: conceptualization and writing – original draft; NC: conceptualization, project administration, and writing – original draft; SL: conceptualization, project administration, and writing – review & editing; RM: project administration and writing – original draft; MPC: project administration and writing – review & editing.

Conflict of Interest

The authors have no conflict of interest to declare.

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