



The Journal of Latin American

# Geriatric Medicine

Volume 10 / Number 2 / 2024 – Published biannually  
ISSN: 2462-2958 / eISSN: 2462-4616 – [www.jgeriatricmedicine.com](http://www.jgeriatricmedicine.com)  
Indexed in: LatinRev, IMBIOMED, Latindex, MIAR, DOAJ, ERIHPLUS

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Full journal available online at: [www.jgeriatricmedicine.com](http://www.jgeriatricmedicine.com)

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ISSN: 2462-2958  
eISSN: 2462-4616  
Ref.: 10111AMEX242

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# Epidemiological, clinical, and laboratory profile of anemia in elderly population in North India

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## Abstract

**Background:** Over the past decade, anemia has emerged as a risk factor that is associated with a variety of adverse outcomes in older adults including hospitalization, disability, and mortality. Limited such literature is available in the local population. **Methods:** A single-center cross-sectional study was done after enrolling 50 elderly patients with anemia. **Results:** The study showed a male preponderance (56%) with a majority of patients in the age group 65-69 years (46%). The most common symptoms were fatigue (82%) and anorexia (64%). Normocytic normochromic anemia was the most common type (60%), followed by microcytic hypochromic anemia (36%). In patients with normocytic normochromic anemia, anemia of chronic disease (36.67%) was the most common cause followed by anemia of renal disease (33.33%). Among microcytic hypochromic anemia cases, iron-deficiency anemia was the most common cause (72.22%). Overall, the most common cause of anemia was anemia of chronic disease (32%), followed by iron-deficiency anemia (26%), and anemia of chronic kidney disease (20%). **Conclusion:** Failure to evaluate and diagnose anemia including ignorance of non-specific symptoms such as fatigue and weakness in the elderly could lead to delayed diagnosis of potentially treatable conditions. An effort should always be made to reach an etiological diagnosis before instituting specific therapy.

**Keywords:** Anemia. Elderly population. Anemia in elderly.

## Perfil epidemiológico, clínico y de laboratorio de anemia en la población de adultos mayores del norte de India

### Resumen

**Antecedentes:** En la última década, la anemia ha surgido como un factor de riesgo que se asocia con una variedad de resultados adversos en adultos mayores, incluyendo hospitalización, discapacidad y mortalidad. Se dispone de escasa bibliografía al respecto en la población local. **Métodos:** Se realizó un estudio transversal en un solo centro tras reclutar a 50 pacientes adultos mayores con anemia. **Resultados:** El estudio mostró una preponderancia masculina (56%) con la mayoría de los pacientes en el grupo de edad de 65-69 años (46%). Los síntomas más frecuentes fueron fatiga (82%) y anorexia (64%). La anemia normocítica normocrómica fue el tipo más frecuente (60%), seguida de la anemia microcítica hipocrómica (36%). En los pacientes con anemia normocítica normocrómica, la anemia por enfermedad crónica (36,67%) fue la causa más frecuente, seguida de la anemia por enfermedad renal (33,33%). Entre los casos de anemia microcítica hipocrómica, la anemia ferropénica fue la causa más frecuente (72,22%). En general, la causa más frecuente de anemia fue la anemia por enfermedad crónica (32%), seguida de la anemia ferropénica (26%) y la anemia por enfermedad renal crónica (20%). **Conclusiones:** La falta de evaluación y diagnóstico de la anemia, incluida la ignorancia de síntomas no específicos como la fatiga y la debilidad en los adultos mayores, podría conducir a un diagnóstico tardío de afecciones potencialmente tratables. Siempre debe hacerse un esfuerzo por llegar a un diagnóstico etiológico antes de instaurar una terapia específica.

**Palabras clave:** Anemia. Población anciana. Anemia en adultos mayores.

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Date of reception: 24-01-2024

Date of acceptance: 26-05-2024

DOI: 10.24875/LAGM.24000003

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## INTRODUCTION

The world population is aging with both the number and proportion of older adults increasing globally. According to the World Health Organization (WHO), the elderly is defined as a person with age  $\geq 65$  years<sup>1</sup>. At present, there are nearly 500 million adults 65 years and older in the world but by 2050, the older population will double to 1 billion. There will be 370 million older adults living in China and India alone by 2030. However, not only is the overall population aging, but the older population itself is getting older as well. In the United States, for example, the oldest-old (adults 85 years and older) is the most rapidly growing segment of the population that will quadruple to 21 million persons by 2050 at which time 1 out of every 4 older adults is projected to be 85 years and older<sup>2</sup>.

Aging population has several health-related concerns and comorbidities, with anemia emerging as an important risk factor associated with a variety of adverse outcomes in the elderly<sup>3,4</sup>. Morbidity and mortality related to anemia in the elderly can occur both from the underlying disease related to the anemia and the adverse effects of the anemia itself. Multiple epidemiologic studies show an association between anemia or even mildly low hemoglobin (Hb) above the WHO threshold for anemia and a worse outcome, including the following:

- Increased mortality<sup>5,6</sup>
- Increased hospitalization<sup>5</sup>
- Increased difficulty with mobility<sup>4,7</sup>
- Falls<sup>8,9</sup>
- Decreased activities of daily living and instrumental activities of daily living<sup>6</sup>
- The presence of other conditions (cardiovascular disease) appears to increase the negative prognostic impact on survival.

Increased incidence of anemia with age has led to speculation that lower Hb levels may be a normal consequence of aging. However, there are at least two reasons for considering anemia as a sign of disease. First, older people maintain a normal red cell count, hemoglobin, and hematocrit. Second, in most elderly patients, an underlying cause of anemia is found for Hb of  $< 12$  g/dL<sup>10</sup>.

There are very few Indian studies available on anemia in the elderly<sup>11-13</sup>. In one of the Indian studies, the prevalence of anemia among the elderly was 17.4% in males and 18% in females<sup>11</sup>. Another study conducted in south India concluded that normocytic normochromic anemia was the most common type (62%)<sup>12</sup>.

Hence, this study was planned to evaluate the profile of anemia in the elderly population.

## METHODS

A single-center cross-sectional study was done at the internal medicine unit of a tertiary care center after enrolling 50 consecutive elderly patients (age  $> 65$  years or older) presenting with anemia (Hb  $< 13$  g/dL in males and 12 g/dL in females). Patients with any of the following conditions were excluded: diagnosed patients of bone marrow disorders such as leukemia, metastatic malignancy with bone marrow involvement, and myelodysplastic syndrome; patients on any erythropoiesis-stimulating agents or received any red blood transfusion in prior 3 months; patients receiving any hematinic patients of end-stage liver disease and renal disease as defined by the need for ongoing hemo or peritoneal dialysis; and patients with substance abuse or mental health or other problems that would make compliance with the study unlikely.

All the enrolled patients underwent detailed history taking with stress on history of bleeding, non-steroidal anti-inflammatory drugs use, chronic, and prolonged illness in the past. They were subjected to thorough physical examination and underwent investigations including complete blood count with RBC indices (done by automated cell counter) with peripheral blood smear, reticulocyte count, renal function tests, hepatic function tests, C-reactive protein, serum lactate dehydrogenase, stool examination for occult blood, ova, cyst and parasite, urine routine and microscopy, thyroid function tests, serum protein electrophoresis, serum iron, total iron binding capacity, serum ferritin, serum vitamin-B12, serum folic acid assay, and bone marrow examination were done whenever indicated. Electrocardiography, X-ray chest, ultrasound abdomen, barium meal follow through, and fine needle aspiration cytology of lymph node were done depending on the clinical indication.

On the basis of MCV, patients were classified into microcytic anemia (mean corpuscular volume or MCV  $< 80$  fl), normocytic anemia (MCV 80-100 fl), and macrocytic anemia (MCV  $> 100$  fl). In cases of microcytic hypochromic anemia, anemia of chronic disease can be differentiated from iron-deficiency anemia by the following hematological parameters: serum iron, total iron binding capacity, transferrin saturation, and serum ferritin<sup>14</sup>.

Serum iron, TIBC, and serum ferritin were determined using standard biochemical methods. Patients with microcytic hypochromic anemia were also evaluated for gastrointestinal (GI) bleeding by fecal occult blood test. Serum B12 and serum folate levels were measured using Chemiluminescent Immunoassay on the Access 2 Immunoassay System (BECKMAN COULTER, Inc., USA).

If the patients could not be classified into iron-deficiency anemia, vitamin B12 deficiency, folate deficiency, anemia of kidney disease, or anemia of chronic disease, they were considered to have unexplained anemia<sup>15</sup>.

The data were entered into *Microsoft Excel*<sup>®</sup> for analysis. Descriptive statistics, i.e., mean, median, and standard deviation for the continuous variables and frequency distribution and their percentages for categorical variables were calculated. To see if there is a significant difference in outcome, appropriate statistical methods were used (ANOVA,  $\chi^2$  test, and binomial test). 'p' < 0.05 was considered significant.

## RESULTS

This study aimed to evaluate the clinical and hematological profile of anemia in elderly patients. The following observations were made. Number of male patients (56%) was slightly more than the total number of female (44%) patients (Table 1). The majority of patients were in the age group 65-69 years (46%) followed by the age group 70-74 years (42%) and age group  $\geq 75$  (12%) (Table 1). Among the study population, 44% of patients were vegetarians and 56% were non-vegetarians. However, among macrocytic anemia, all patients (4%) were vegetarians (Table 1).

The most common symptoms were fatigue (82%) and anorexia (64%) while pallor was the most common clinical finding (Figs. 1 and 2). Of the three types of anemia, normocytic normochromic anemia was the most common type (60%), followed by microcytic hypochromic anemia (36%) and macrocytic anemia (4%). The mean value of hemoglobin in normocytic normochromic blood was higher ( $9.90 \pm 1.15$ ) as compared to mean values of hemoglobin in microcytic hypochromic anemia ( $8.88 \pm 1.76$ ) and macrocytic anemia ( $8.10 \pm 1.27$ ) but this was statistically not significant ( $p = 0.07$ ) (Supplementary Table 1).

When gender was compared with types of anemia, in our study, 57.14% of male patients had normocytic normochromic anemia and 63.64% of female patients had normocytic normochromic anemia, but this was

**Table 1.** Clinical and demographic characteristics of the study population

Parameter	Total number of patients
Age group	65-69 years - 46% 70-74 years - 42% 75 years - 12%
Sex (males)	56%
Distribution of patients according to peripheral blood picture	N/N anemia - 60% M/H anemia - 36% MA - 4%
Dietary pattern	44% - Vegetarians M/H - 18%, N/N - 22%, MA - 4% 56% - Non-vegetarians M/H - 18%, N/N - 38%, MA - 0%

N/N: normocytic normochromic; M/H: microcytic hypochromic; MA: macrocytic anemia.

not statistically significant ( $p = 0.436$ ) (Supplementary Table 2). On comparing age groups with types of anemia, number of patients with normocytic normochromic anemia were more in age group 70-74 years (28%), followed by age group 65-69 years (26%) and number of patients with microcytic hypochromic anemia were more in age group 65-69 years (18%) followed by age group 70-74 years (12%), but this was not statistically significant ( $p = 0.86$ ) (Table 2).

Among microcytic hypochromic anemia cases, iron-deficiency anemia was the most common cause (72.22%) followed by anemia of chronic disease (27.28%). Among patients with iron-deficiency anemia, 46.15% of cases had GI bleed. In patients with normocytic normochromic anemia, anemia of chronic disease (36.67%) was the most common cause followed by anemia of renal disease (33.33%) and unexplained anemia (30.0%). Among anemia of chronic disease, tuberculosis (43.75%) was the most common cause of anemia of chronic disease followed by osteoarthritis (31.25%) (Supplementary Figure 1).

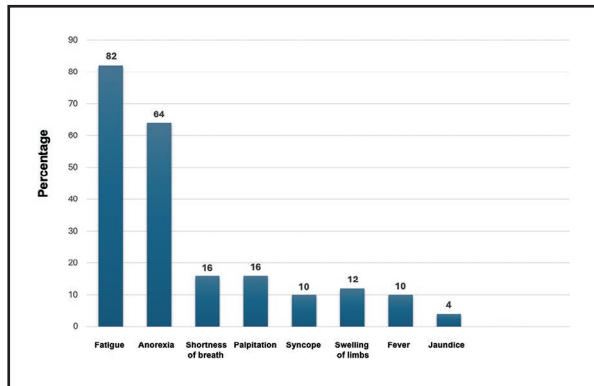
Overall, the most common cause of anemia in the elderly was anemia of chronic disease (32%), followed by iron-deficiency anemia (26%), anemia of chronic kidney disease (20%), unexplained anemia (18%), and B<sub>12</sub> deficiency anemia (4%) (Fig. 3).

## DISCUSSION

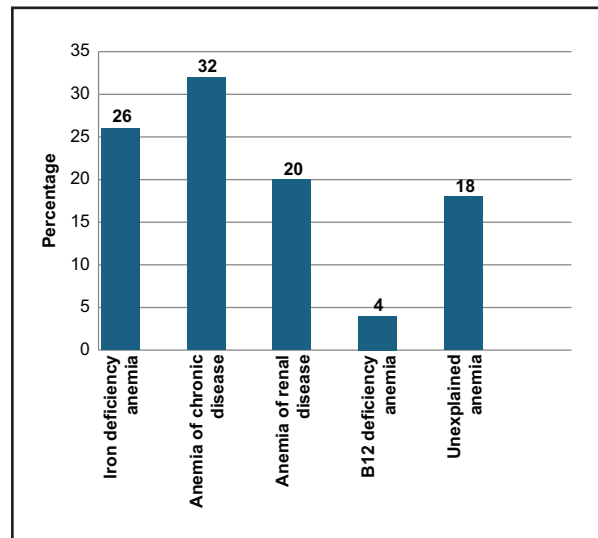
Anemia is common in the elderly and is an important sign that often points to a serious and possibly

**Table 2.** Distribution of patients of various age groups according to types of anemia

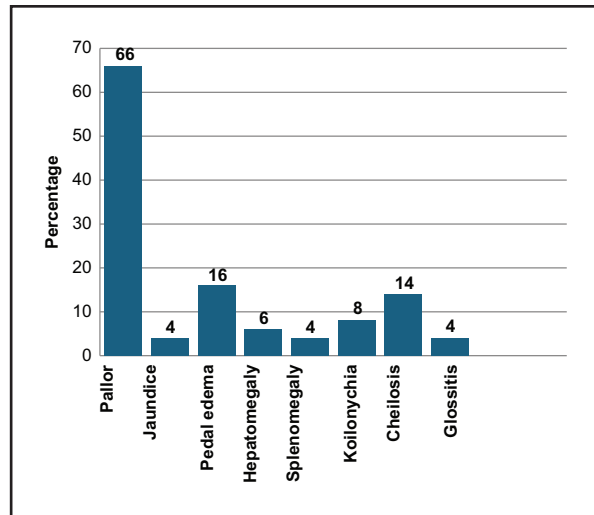
Age groups (years)	Total number of patients	Microcytic hypochromic, n (%)	Normocytic normochromic, n (%)	Macrocytic anemia, n (%)
65-69	23	9 (18.00)	13 (26.00)	1 (2.00)
70-74	21	6 (12.00)	14 (28.00)	1 (2.00)
≥ 75	6	3 (6.00)	3 (6.00)	0 (00.0)



**Figure 1.** Symptomatology in patients with anemia.



**Figure 3.** Distribution of patients according to various causes of anemia.



**Figure 2.** Physical finding in patients with anemia.

treatable medical condition. Our present knowledge about anemia in elderly is mostly based on reports from various international studies and text books.

The prevalence of anemia in elderly is high in the community as well as in nursing homes. Landi et al.<sup>16</sup> reported that 63% of older residents in a single nursing home had anemia and showed that the 2-year risk of death adjusted for age and sex was 60% higher in anemic than in non-anemic residents. Importantly, the

prevalence of anemia increased as a function of age after the 5<sup>th</sup> decade of life in both men and women; however, the age-associated increase in prevalence was more dramatic in men.

In our study, of the total 50 patients, 28 (56%) patients were males and 22 (44%) patients were females. The male predominance in our study is in concordance with the study by Skjelbakken et al.<sup>17</sup> in the Tromso study, which concluded that using the WHO criteria for anemia (Hb: < 130 and < 120 g/L, men and women, respectively), the prevalence of anemia in men increased with age from 0.6% aged 25-34 to 29.6% aged 85+. For women, the prevalence of anemia varied from 9.1%, 2.2%, and 16.5% in the age groups of 35-44, 55-64, and 85+ years, respectively. Another study by Ania et al.<sup>18</sup> concluded that, before the age of 55 years, the prevalence of anemia was lower among men than among women, but after that age, anemia became more frequent in men, reaching a 44.4% prevalence among community men 85 years of age or older. Another study by Patel<sup>19</sup> shows that the prevalence of anemia increased as a

function of age after the 5<sup>th</sup> decade of life in both men and women; however, age-associated increase in the prevalence of anemia is more dramatic in men.

The patients were divided into three age groups, patients with age between 65 and 69 years, 70 and 74 years, and 75 years and above. In our study, it was found that the number of patients were highest in the age group 65-69 years (46%) followed by the age group 70-74 years (42%) and the age group 75 years and above had least number of cases (12%).

Among the study population, 44% of patients were vegetarians and 56% were non-vegetarians. However, among macrocytic anemia, all patients (4%) were vegetarians. Patients presented with varied symptomatology. The common symptoms were fatigue (82%), anorexia (64%) followed by shortness of breath (16%), palpitation (16%), syncope (10%), swelling of lower limbs (12%), fever (10%), and jaundice (4%). Upon examination, 66% of patients had pallor, icterus was present in 4%, koilonychias in 8%, hepatomegaly in 6%, splenomegaly in 8%, cheilosis in 14%, glossitis in 4%, and pedal edema in 16% of cases.

On classifying the patients into normocytic normochromic anemia, microcytic hypochromic anemia, and macrocytic anemia, it was found that normocytic normochromic anemia was the most common type (60%), followed by microcytic hypochromic anemia (36%) and macrocytic anemia (4%). This observation in our study is similar to the observation by a hospital-based study in South India by Bhasin and Rao<sup>12</sup> which showed normocytic normochromic anemia in 62%, microcytic hypochromic anemia in 30%, and macrocytic anemia in 6% of patients. This high prevalence of normocytic normochromic in the elderly is supported by a cross-sectional study of three urban Korean population samples by Choi et al.<sup>20</sup> which observed a very high prevalence of normocytic normochromic in 93.5% followed by microcytic anemia in 3.5% and macrocytic anemia in 3%.

On comparing mean values of various hematological parameters, the mean value of hemoglobin in normocytic normochromic blood was higher ( $9.90 \pm 1.15$ ) as compared to mean values of hemoglobin in microcytic hypochromic anemia ( $8.88 \pm 1.76$ ) and in macrocytic anemia ( $8.10 \pm 1.27$ ) but this was statistically not significant ( $p = 0.07$ ). This could be because, more number of cases of unexplained anemia in a normocytic normochromic group, in which anemia is typically mild<sup>21-23</sup>.

When gender was compared with types of anemia, in our study, 57.14% of male patients had normocytic

normochromic anemia and 63.64% of female patients had normocytic normochromic anemia, but this is not statistically significant ( $p = 0.436$ ). This gender variation is less established in previous studies, but a study by Izaks<sup>22</sup> showed that anemia was mostly normocytic in 80% of all anemic women and 92% of all anemic men.

On comparing the type of anemia with various age groups, it was observed that normocytic normochromic anemia was common followed by microcytic hypochromic anemia.

Among the causes of microcytic hypochromic anemia, iron-deficiency anemia was the most common cause (72.22%) followed by anemia of chronic disease (27.28%). This high prevalence of iron-deficiency anemia is supported by a study from south India by Bhasin and Rao<sup>12</sup> in which iron-deficiency anemia constituted 83.3% among the microcytic hypochromic group. This iron deficiency in the study could be explained on the basis of decreased dietary iron intake in the Indian population.

In our study, among iron-deficiency anemia, 46.15% of cases had GI bleed. Among patients with GI bleeding, 66.67% were male patients and 33.33% were female patients. This high incidence of GI bleed was also observed in a study by Rockey and Cello<sup>23</sup> and the study concluded that 62% of cases with iron deficiency have at least one lesion potentially for blood loss. Indian study mentioned above also showed that chronic blood loss through the GI tract accounts for 68% of cases among iron-deficiency anemia.

Among the patients with normocytic normochromic anemia, anemia of chronic disease (36.67%) was the most common cause followed by anemia of renal disease (33.33%) and unexplained anemia (30.0%). This is supported by the evidence from a study by Joosten<sup>10</sup> which concluded that, of 732 consecutive patients admitted, an appropriate cause responsible for anemia was identified in 83% and anemia of chronic disease in 35% was the most common cause, as was also seen in the study by Alsaed et al.<sup>24</sup>.

Among anemia of chronic disease, tuberculosis (43.75%) was the most common cause of anemia of chronic disease followed by osteoarthritis (31.25%), this could be because of the high prevalence of tuberculosis in our country. Bhasin and Rao<sup>12</sup> which included anemia of renal failure under anemia of chronic disease showed that diseases such as tuberculosis, osteoarthritis, rheumatoid arthritis, and liver disease were also important causes of anemia of chronic disease.



Among all the causes of anemia, in our study, most cases are anemia of chronic disease (most common 32%), followed by iron-deficiency anemia (26%), anemia of chronic kidney disease (20%), unexplained anemia (18%), and megaloblastic anemia (4%). These figures from our study corroborate with the study by Joosten<sup>10</sup> which shows anemia of chronic disease in 35% of cases, iron-deficiency anemia in 15%, and unexplained anemia in 17% of cases.

One of the limitations of the study was that the sample size was small, hence the need for a study on a large population in our society for further evaluation. Another limitation of the study was that it was a hospital-based study and the results could not be applied to the general population, hence the need for community-based studies. Cases of GI bleed need further evaluation by upper GI endoscopy and colonoscopy.

## CONCLUSIONS

Anemia is a common concern in the geriatric population, and it is an important sign that often points to a serious underlying medical condition. In this population, it can have significantly more severe complications than in younger adults and greatly hamper the quality of life<sup>25</sup>. This preliminary study provides us with some baseline data on the clinical and hematological profile of anemia in elderly in our society, very few of which were available till now. Hence, this study can form the baseline for future Indian studies.

## FUNDING

The authors declare that they have not received funding.

## CONFLICTS OF INTEREST

The authors declare no conflicts of interest.

## ETHICAL DISCLOSURES

**Protection of human and animal subjects.** The authors declare that no experiments were performed on humans or animals for this study.

**Confidentiality of data.** The authors declare that no patient data appear in this article. Furthermore, they have acknowledged and followed the recommendations as per the SAGER guidelines depending on the type and nature of the study.

**Right to privacy and informed consent.** The authors declare that no patient data appear in this article.

**Use of artificial intelligence for generating text.** The authors declare that they have not used any type of generative artificial intelligence for the writing of this manuscript nor for the creation of images, graphics, tables, or their corresponding captions.

## SUPPLEMENTARY DATA

Supplementary data are available in *The Journal of Latin American Geriatric Medicine* online (DOI: 10.24875/LAGM.24000003). These data are provided by the corresponding author and published online for the benefit of the reader. The contents of supplementary data are the sole responsibility of the authors.

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## Daytime fatigue and sleep duration in Mexican elders: a study on sleep habits

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### Abstract

**Background:** Sleep disturbances significantly impact older adults, affecting daytime energy and overall health. This study investigates sleep habits' (SH) effect on daytime fatigue (DF) among the elderly in Guadalajara, Mexico. **Objective:** The objective of the study was to assess SH' prevalence and their link to DF in people over 60 at a Guadalajara geriatric care unit. **Methods:** In early 2020, 162 participants were surveyed using medical records and sleep questionnaires, analyzing SH and DF correlations through logistic regression. **Results:** The average participant age was 80, with women constituting 72.2% of the sample. Half reported DF, and 35% had insomnia. Notably, over 7 h of sleep reduced DF odds (odds ratio = 0.50). **Conclusion:** DF is prevalent among Mexican elders, more so than in similar populations. Over 7 h of sleep markedly decreases fatigue risk, underscoring the importance of sufficient sleep for elderly health and functionality. These findings highlight the need for sleep quality improvement interventions among the elderly to enhance their well-being.

**Keywords:** Sleep habits. Sleep disorders. Daytime fatigue. Older persons. Mexico.

### Fatiga diurna y duración del sueño en ancianos mexicanos: un estudio sobre los hábitos de sueño

#### Resumen

**Antecedentes:** Las perturbaciones del sueño impactan significativamente en los adultos mayores, afectando la energía diurna y la salud general. Este estudio investiga el efecto de los hábitos de sueño en la fatiga diurna entre los ancianos en Guadalajara, México. **Objetivo:** Evaluar la prevalencia de los hábitos de sueño y su relación con la fatiga diurna en personas mayores de 60 años en una unidad geriátrica de Guadalajara. **Métodos:** A principios de 2020, se encuestó a 162 participantes utilizando registros médicos y cuestionarios de sueño, analizando las correlaciones entre los hábitos de sueño y la fatiga diurna mediante regresión logística. **Resultados:** La edad promedio de los participantes fue de 80 años, con mujeres constituyendo el 72.2% de la muestra. La mitad reportó fatiga diurna, y el 35% tenía insomnio. Notablemente, más de siete horas de sueño redujeron las probabilidades de fatiga diurna (OR = 0.50). **Conclusión:** La fatiga diurna es prevalente entre los adultos mayores mexicanos, más aún que en poblaciones similares. Más de siete horas de sueño disminuyen notablemente el riesgo de fatiga, subrayando la importancia de un sueño suficiente para la salud y funcionalidad de personas mayores. Estos hallazgos destacan la necesidad de intervenciones para mejorar la calidad del sueño entre los ancianos para realzar su bienestar.

**Palabras clave:** Hábitos de sueño. Trastornos del sueño. Fatiga diurna. Personas mayores. México.

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Date of reception: 06-02-2024

Date of acceptance: 26-05-2024

DOI: 10.24875/LAGM.24000004

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## INTRODUCTION

Commonly, we allocate up to a third of our lifespan to sleep, still the daytime impact of sleep disturbances in older persons (OP) is not fully appreciated. Sleep is vital to both physical and mental health, as it involves the synthesis of optimal sleep habits (SH) and daytime functioning<sup>1,2</sup>.

By 2025, the number of OP (aged 60 and over) is projected to exceed 1200 million, highlighting the need to address the sleep quality that profoundly affects their life quality. In Mexico, significant percentages of the OP population, 58% of men and 76% of women over 65, experience symptoms of sleep disorders<sup>3</sup>.

Multiple factors can interfere with SH in OP, leading to sleep disorders characterized by difficulties in sleep initiation, maintenance, and the sensation of insufficient rest<sup>4-10</sup>. These disturbances typically lead to reduced sleep duration, despite the adult requirement of 7-8 h of sleep per night, which remains critical into older age<sup>11-16</sup>.

Fatigue is a significant issue for 70% of older adults in communities, often manifesting as physical or mental tiredness, with 43% feeling persistently tired and linking it to poorer health and functionality. It is generally described as a sensation of weakness and lack of energy. Contributing factors range from biological (like inflammation and comorbidities) to behavioral (such as exercise and sleep patterns), psychological (including depression and stress), and social aspects (like social support). Notably, both the quantity and quality of sleep are closely tied to fatigue<sup>17,18</sup>.

The ripple effects of sleep disorders extend to various adverse outcomes, with daytime fatigue (DF) being a significant one, impairing everyday functional abilities<sup>11,14,19</sup>.

As it has become evident, research on sleep in OP around the globe has consistently highlighted a range of prevalent issues. These include difficulties with sleep initiation and maintenance, increased nighttime awakenings, and alterations in sleep architecture. Such sleep-related challenges are not isolated incidents but are frequently exacerbated by a complex interplay of factors including aging, health deterioration, and environmental conditions. Moreover, the impact of compromised sleep extends beyond individual health concerns to broader socio-economic implications. Inadequate sleep and resultant DF significantly contribute to increased health-care expenditures, decreased productivity, and a heightened reliance on social and medical services.

These consequences underline the pressing public health implications, demonstrating the critical need for comprehensive approaches to address sleep disorders and improve overall quality of life in this population. These global trends create a significant backdrop to our findings within the Mexican context, indicating that the sleep-related challenges encountered by Mexican OP mirror broader international issues. Recognizing these patterns is crucial as it not only emphasizes the relevance of our study but also underscores the urgent need for targeted interventions tailored to improve sleep quality and alleviate fatigue among older adults. This research highlights the critical role of healthy SH in countering DF and enhancing overall quality of life in OP<sup>1</sup>.

## METHODS

### Participants

In this cross-sectional study, we included 162 individuals aged 60 or above from a geriatric care unit in a university hospital in Guadalajara, Mexico. Recruitment occurred from January to February 2020, utilizing a convenience sampling method. Potential participants were briefed and provided written informed consent at their geriatric consultation appointments. The research protocol received approval from the institutional Ethics Committee.

### Measures

#### *Dependent variable*

DF was the primary dependent variable, measured by responses to the inquiry: 'How often in the past 2 weeks have you experienced fatigue due to lack of rest and motivation during the day?'. Options ranged from 'none' to 'almost every day', with dichotomization applied for analysis; responses indicating 'more than 7 days' or 'almost every day' indicated the presence of DF<sup>20</sup>.

#### *Independent variables: sleeping habits*

We selected three components as independent variables for sleeping habits (SH) based on their prevalence in existing literature as significant predictors of sleep quality: sleep duration, difficulty initiating sleep, and frequency of nocturnal awakenings. Participants were queried about their sleep patterns over a 2-week

period, focusing on how often they slept more than seven continuous hours at night, experienced trouble falling asleep, and woke up frequently. Response options for sleep duration ranged from “yes” to “no.” We chose to dichotomize the responses – indicating “more than 7 days” or “almost every day” as having sleep disturbances – to clearly differentiate between habitual and non-habitual patterns, simplifying the analysis while maintaining sensitivity to variations in sleep quality<sup>2</sup>.

The measurement instruments used to assess SH and DF were carefully selected for their established validity and reliability in prior studies involving older adults. This ensures that our measures accurately reflect the targeted constructs<sup>1,2,8-12,20</sup>.

### **Correlated factors**

Age, sex, employment, and marital status usage were included as covariates in the analysis.

### **Statistical analysis**

For continuous variables, we report the means and standard deviations (SD), while categorical variables are summarized using percentages. To compare frequencies among groups, the Chi-square ( $\chi^2$ ) Pearson test was applied. We employed multivariate logistic regression analyses to explore the associations between various sleeping habits and the occurrence of DF. Significance was determined at a p-value threshold of <0.05, within confidence intervals set at 95%. Analyses were conducted using the SPSS Statistical Package for the Windows® (SPSS Inc., Chicago, IL v. 20).

## **RESULTS**

Our analysis revealed critical associations between SH and DF in the OP. We assessed 162 individuals, averaging 80 years old (SD = 9), predominantly female (72%). DF was reported by 51% of participants, while marital status appeared unrelated to fatigue levels. Notably, 69% of the cohort achieved over 7 h of sleep nightly.

Further scrutiny of sleep behaviors showed that 85% encountered nocturnal awakenings or nocturia, and 63% reported snoring. About half of the group (46%) recognized having a sleep disorder, and 60.5% indulged in daytime napping. A minority (10%)

resorted to sleep medications, while nearly half (49%) required over half an hour to fall asleep.

Insomnia prevalence stood at 35%, with a corresponding 36% reporting DF, suggesting intricate links between sleep patterns and daytime alertness.

Table 1 illustrates the correlation between SH, sociodemographic factors, and DF prevalence in our participants.

Multivariate logistic regression, controlling for age, sex, employment, and marital status, unveiled a significant inverse relationship between sleeping more than 7 h and experiencing DF (OR = 0.50, 95% CI = 0.23-0.97, p = 0.04), indicating reduced fatigue likelihood with longer sleep duration (Table 2).

## **DISCUSSION**

Our study's findings, with significant female representation (72%) and over half of the participants experiencing DF, illuminate the intricate patterns of SH and their implications in older Mexican adults. The data aligns with established research, confirming that inadequate sleep – reported by 46% of our study's participants – correlates with increased fatigue, mirroring gender-related findings in sleep disorder prevalence<sup>3,9,15,21</sup>. The inverse association between extended sleep and reduced fatigue observed in our study echoes the results of Kaneita et al., while also contrasting with other research employing varying diagnostic criteria, showcasing the impact of methodological approaches on DF prevalence<sup>22,23</sup>. The absence of a standardized definition of DF poses a significant comparative challenge, with the term's heterogeneity leading to varied prevalence rates. This necessitates more comprehensive future studies to establish a more accurate prevalence<sup>24</sup>.

Our results are in concordance with global studies demonstrating that suboptimal sleep quality adversely affects daily life in the OP<sup>5,6,9,12,25</sup>. For example, recent research using a daily diary method found that sleep patterns, including duration and quality, significantly influence next-DF in OP<sup>26</sup>.

Furthermore, the practical implications of our findings suggest that enhancing sleep quality could play a significant role in improving the overall medical care and quality of life for older adults in Mexico. Specifically, healthcare providers could develop targeted interventions that focus on sleep hygiene and the management of sleep disorders among the elderly. Initiatives could include training for caregivers on the importance of sleep routines and the

**Table 1.** Comparative analyses of participant's day-time fatigue

Variable	All (n = 162)	Day-time fatigue No, n = 79 (49%)	Day-time fatigue Yes, n = 83 (51%)	p
Age, years				
60-69	56	15 (27)	41 (73)	< 0.0001
70-79	34	16 (47)	18 (53)	0.623
≥ 80	5	2 (40)	3 (60)	0.548
Sex				
Female	117	57 (49)	60 (51)	0.98
Male	45	22 (49)	23 (51)	0.98
Marital status				
Married	59	24 (41)	35 (59)	0.27
Single	33	19 (58)	14 (42)	0.27
Widowhood	69	36 (52)	33 (48)	0.27
Insomnia				
No	105	58 (55)	47 (45)	0.025
Yes	57	21 (37)	36 (63)	
Sleep disturbance				
No	87	47 (54)	40 (46)	0.14
Yes	75	32 (43)	43 (57)	
Sleep duration (≥ 7 h)				
No	50	18 (36)	32 (64)	0.030
Yes	112	61 (55)	51 (45)	
Fall asleep (≥ 30 min)				
No	83	46 (55)	37 (45)	0.082
Yes	79	33 (42)	46 (58)	
Snore				
No	60	29 (48)	31 (52)	> 0.05
Yes	102	50 (49)	52 (51)	
Night time awakenings				
No	23	14 (61)	9 (39)	0.21
Yes	139	65 (47)	74 (53)	
Nocturia				
No	28	14 (50)	14 (50)	> 0.05
Yes	139	65 (49)	69 (51)	
Daytime napping				
No	64	35 (55)	29 (45)	0.22
Yes	98	44 (45)	54 (55)	
Sleep medications				
No	145	70 (48)	75 (52)	0.54
Yes	16	9 (56)	7 (44)	

**Table 2.** Multivariate regression logistic analyses of day-time fatigue

Variable	OR (95% CI)	P
Sleep duration (> 7 h)	0.50 (0.23-0.97)	0.04
Sleep disturbances	0.50 (0.24-0.93)	0.06

Adjusted by age, sex, employment and marital status.  
OR: odds ratio; CI: confidence interval.

environment conducive to good sleep, and the integration of sleep management strategies into regular health assessments for older adults.

Potential measures to promote healthy SH among the elderly could involve community-based educational programs that emphasize the importance of sleep and its impact on health. In addition, modifications in the sleeping environment, such as reducing

noise and light pollution in residential areas, and promoting regular physical activity tailored to the elderly, can significantly enhance sleep quality<sup>1</sup>.

Nevertheless, it is important to recognize the limitations of our study, such as its incapacity to establish causality and the use of a convenience sample that may not be representative. In addition, our study did not account for potential biological and psychological factors that might contribute to fatigue in the OP. The study emphasizes the pivotal role of sleep hygiene in managing sleep disorders. A notable proportion of our subjects reported nocturnal disturbances, and a significant minority could self-identify sleep disorders. Only a small fraction used sleep medications, while many experienced extended sleep latencies<sup>7,16,26</sup>. These insights underline the necessity for interventions aimed at promoting optimal sleep practices to enhance the health and quality of life for the OP.

In addition, our research corroborates the multifactorial nature of sleep pattern alterations in the aged, with comorbid conditions contributing to sleep disruptions, necessitating comprehensive management strategies<sup>27-32</sup>.

In summary, our research adds to the substantial evidence regarding the impact of SH on DF in the OP.

## CONCLUSION

Our research has shed light on the pivotal role sleep duration plays in mitigating DF among Mexico's OP, where extended sleep – over 7 h – correlates with reduced fatigue symptoms. This reinforces the critical nature of sleep hygiene in the daily well-being of OP and suggests that interventions aimed at enhancing sleep routines may serve as a viable approach to diminish daytime lethargy.

We observed a significant prevalence of sleep disturbances, particularly among females and the advanced age cohort, prompting the need for tailored management strategies. Tailored interventions, especially those addressing nocturnal disruptions and sleep onset challenges, may prove exceedingly advantageous.

Nevertheless, the study's design presents inherent limitations, notably the inability to infer causality and the exclusion of potential confounding factors such as depressive and cognitive disorders, which may influence sleep and fatigue. The dichotomous nature of the SH assessment, as highlighted by methodological critiques, could have constrained the depth of our findings. Highlighting the multifactorial nature

of sleep alterations in the aging population, our findings advocate for a holistic approach in geriatric care encompassing the diverse determinants of sleep health.

This inquiry contributes to a deeper comprehension of the interplay between SH and DF in the OP, underscoring the urgent need for more profound awareness and improved management practices for sleep disorders, considering their complex and diverse underpinnings.

## FUNDING

The authors declare that they have not received funding.

## CONFLICTS OF INTEREST

The authors declare no conflicts of interest.

## ETHICAL DISCLOSURES

**Protection of human and animal subjects.** The authors declare that no experiments were performed on humans or animals for this study.

**Confidentiality of data.** The authors declare that no patient data appear in this article. Furthermore, they have acknowledged and followed the recommendations as per the SAGER guidelines depending on the type and nature of the study.

**Right to privacy and informed consent.** The authors declare that no patient data appear in this article.

**Use of artificial intelligence for generating text.** The authors declare that they have not used any type of generative artificial intelligence for the writing of this manuscript nor for the creation of images, graphics, tables, or their corresponding captions.

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# Impact of retirement on health-related conditions, leisure, and physical activity in older adults

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## Abstract

**Introduction:** Retirement represents a transition in the life of older people. It involves social, physical, and psychological changes that impact the quality of life and well-being. This study aimed to analyze the influence of retirement on biopsychosocial variables and the prevalence of chronic diseases in retired older adults compared with older actively working adults. **Methods:** We obtained data from the Mexican Health and Aging Study. We analyzed the data collected exclusively from people 60 years and older from the 2015 to 2018 waves. First, we compared the demographic characteristics, the prevalence of chronic diseases, frequency of health screenings, and other health-related conditions, as well as biopsychosocial variables, between retired older adults and their working peers in the 2018 wave. Second, we documented and compared their change of status in biopsychosocial variables across the two different time periods (surveys 2015 and 2018). **Results:** Changes in self-perceived health and well-being were not significant after retirement. However, in the comparative analysis, the retired older adults reported less physical activity (30.8% vs. 44.9%,  $p < 0.001$ ), higher prevalence of diabetes and cardiovascular diseases (31.7% vs. 19.6%,  $p < 0.001$ , and 46.6% vs. 38.9%,  $p = 0.011$ ), and more doctor visits (83.8% vs. 76.4%,  $p = 0.005$ ). They also showed more significant involvement in leisure activities ( $p < 0.001$ ) than those working. **Conclusion:** These data demonstrate that retirement is an important checkpoint in life to focus on health care for the detection and prevention of health problems that cause dependence on care and negatively affect the quality of life of older adults.

**Keywords:** Work retirement. Aging. Mexican Health and Aging Study. Health after retirement.

## Impacto de la jubilación en las condiciones relacionadas con la salud, el ocio y la actividad física en adultos mayores

### Resumen

**Introducción:** La jubilación representa una transición en la vida de las personas mayores. Implica cambios sociales, físicos y psicológicos que repercuten en la calidad de vida y el bienestar. Este estudio tuvo como objetivo analizar la influencia de la jubilación sobre variables biopsicosociales y la prevalencia de enfermedades crónicas en adultos mayores jubilados en comparación con adultos mayores que trabajan activamente. **Métodos:** Se obtuvieron datos del Estudio Mexicano de Salud y Envejecimiento (EMSA). Analizamos los datos recolectados exclusivamente de personas de 60 años y más de las oleadas 2015 y 2018. Primero, comparamos las características demográficas, la prevalencia de enfermedades crónicas, la frecuencia de exámenes de salud y otras condiciones relacionadas con la salud, así como variables biopsicosociales, entre adultos mayores jubilados y sus pares trabajadores en la ola 2018. En segundo lugar, documentamos y comparamos su cambio de estado en las variables biopsicosociales a través de los dos periodos de tiempo diferentes (encuestas 2015 y 2018). **Resultados:** Los cambios en la salud y el bienestar autopercebidos no fueron significativos después de la jubilación. Sin embargo, en el análisis comparativo, los adultos mayores jubilados reportaron menos actividad física (30,8% vs. 44,9%,  $p < 0,001$ ), mayor prevalencia de diabetes y enfermedades cardiovasculares (31,7% vs. 19,6%,  $p < 0,001$ , y 46,6% vs. 38,9%,  $p = 0,011$ ), y más visitas al médico (83,8% vs. 76,4%,  $p = 0,005$ ).

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Date of reception: 17-03-2024

Date of acceptance: 08-07-2024

DOI: 10.24875/LAGM.24000008

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También mostraron una participación más significativa en actividades de ocio ( $p < 0,001$ ) que los que trabajaban. **Conclusiones:** Estos datos demuestran que la jubilación es un punto de control importante en la vida para enfocar el cuidado de la salud en la detección y prevención de problemas de salud que causan dependencia de cuidados y afectan negativamente la calidad de vida de los adultos mayores.

**Palabras clave:** Jubilación laboral. Envejecimiento. Estudio Mexicano de Salud y Envejecimiento (EMEA). Salud después de la jubilación.

## INTRODUCTION

The global increase in the older people population has brought many changes, including the rise in the prevalence of chronic diseases, which involves multimorbidity, daily living dependence or disability, and challenges in the economic and social fields of many countries. In addition, labor and the economic sphere have also changed in recent decades, with an increase in the number of working older adults<sup>1</sup>. The demographic shift has led to an increase in the participation of people over 60 years of age in the labor field; according to the Economic Commission for Latin America and the Caribbean and the International Labor Organization in 2018, in Latin America, the participation of adults aged 60 years and over will double, from 7.5% in 2015 to 15% in 2050. In Mexico, data from the National Survey of Occupation and Employment (ENOE) show that a significant proportion of older adults remains in the labor market even after reaching the legal retirement age of 65 years<sup>2</sup>.

Employment reinforces the autonomy of older adults by keeping them collaborating in their community, nevertheless, with the high prevalence of multimorbidity and chronic diseases, retirement becomes a particular and unpredictable phenomenon influenced by economic and health factors. It constitutes a change in daily life, time availability, income streams, social networks, etc., affecting older people's health determinants and quality of life. Retirement can lead to a more sedentary lifestyle, with the advent of new associated diseases. Likewise, retirement is not always planned and can also be precipitated by health problems. The data about how retirement can affect health status and quality of life is heterogeneous. Findings about the impact of retirement on the health of older adults are quite diverse. Oshio and Kan, in their analysis based on The Longitudinal Survey of Middle-aged and Older Adults in Japan, reported favorable changes in health and health behaviors (smoking, heavy alcohol drinking, and leisure-time physical activity), with some gender differences accompanying this transition<sup>3</sup>. On the other hand, findings from Behncke based on the English Longitudinal Study of Ageing, a

panel survey of people born before 1952 who lived in England and previously responded to the Health Survey for England, found that retirement raised the risk of being diagnosed with any chronic condition (e.g., severe cardiovascular disease and cancer) and increased the prevalence of difficulties with activities of daily living<sup>4</sup>. In Mexico, Roman-Sanchez et al., based on data collected from the ENOE, reported that men have twice as much as women's probability of going from an employed status to pensioners, while women are up to 5 times more likely to go from employed to carrying out unpaid household chores. This highlights the fact that in the labor market, women present greater vulnerability than men, considering they have fewer internal and external resources (years of schooling, monetary pensions, other sources of income, social coverage, social support networks, etc.) to face unexpected stressors and changes in overall status, such as job retirement<sup>2</sup>.

For this study, we aimed to analyze the influence of retirement on different biopsychosocial variables, including the prevalence of chronic diseases, involvement in exercise and physical activity, self-perceived health, and social involvement in the Mexican population.

## METHODS

### Study population

This is an observational, longitudinal, retrospective, descriptive, and comparative study. We obtained data from the Mexican Health and Aging Study (MHAS), a nationwide prospective six-wave panel survey. This national longitudinal survey has been conducted in adults 50 years and older in Mexico since 2001 and comprises several surveys (that include sociodemographic variables, health measures, access to health services, and among other measurements) applied in six different waves at the time of the analysis (2001, 2003, 2012, 2015, 2018, and 2021). It has been appraised as a representative sample of Mexican community-dwelling people 50 years and older and their spouses/partners regardless of their age. Its aim and design have been previously published and can be consulted on their

open access webpage<sup>5</sup>. For our study, we focused on analyzing the data collected exclusively from people 60 years and older from the 2015 and 2018 waves. At the time of investigation, the results from the 2021 wave had not yet been published.

### **Definition of retirement and study groups**

We included all subjects 60 years or older who answered “working” or “in search of a job” in the employment status question of the 2015 MHAS wave. Next, we performed a follow-up of all subjects who were surveyed in both the 2015 and 2018 MHAS waves. Subjects were then divided into three categories according to the 2018 MHAS wave responses to the questions “Do you currently work?” (Code I16) and “What is the reason why you do not work?” (Code I26): those who maintained their previous employment status or were looking for a job (W), subjects who reported not to be working because of retirement or pension (R/P), and those who also reported not to be working because of any other reason (dedication to household chores, advanced disease, etc.); the latter were not considered for analysis, to reduce bias. We then approached subjects in two ways. First, we performed a transversal analysis by comparing characteristics between the W and R/P subjects during the 2018 survey. Second, we performed a longitudinal follow-up of the R/P subjects, to identify changes in their status from the 2015 to 2018 wave, based on their own reports.

### **Study variables**

Variables considered in this analysis, as well as their coding within the MHAS surveys, can be consulted in Supplementary Table 1.

First, we compared the demographic characteristics, the prevalence of chronic diseases, frequency of health screenings and other health-related conditions, as well as self-rated health, feelings of loneliness and social isolation, and involvement in physical exercise and other social and leisure activities, between R/P older adults and their peers from the W group on the 2018 wave.

For the second analysis, we documented and compared their change of status in self-reported health, feelings of loneliness and social isolation, and involvement in physical exercise and other social and leisure activities, across the two different time periods

(surveys 2015 and 2018). Due to respondents' related inconsistencies when answering questions related to the prevalence of chronic diseases, the longitudinal analysis related to these variables was not feasible and therefore was discarded (e.g., a respondent might report the presence of a chronic condition, such as diabetes, in the 2015 survey but differ about its presence during the 2018 follow-up).

### **Statistical analysis**

Categorical variables were reported as frequency and proportion and numerical variables as arithmetic mean  $\pm$  standard deviation. For the analysis between R/P and W subjects, age was compared with the independent samples t-test, whereas the remaining categorical variables were analyzed through the Chi-square test. For the intragroup analysis performed within the R/P subjects, we analyzed the change of dichotomous-answer variables (yes/no) between surveys with McNemar's test. For these variables, we descriptively reported results regarding a change in status from a previous positive answer (e.g., we reported the proportions of subjects who affirmed solving puzzles both in 2015 and 2018, *continued*, and the proportion of subjects who denied solving puzzles in 2018 but agreed in the previous survey, *discontinued*), after analyzing each variable with McNemar's test. We compared polychotomous variables (self-rated health and negative feelings, such as loneliness, being ignored, and isolation) using the sign test. For these variables, we also descriptively reported the proportions of changes in previous status (e.g., self-rated health that changed from “poor” to “good” as *positive*, a change from “excellent” to “regular” as *negative*, and a maintained “very good” self-related health as *neutral*), after analyzing each variable with the sign test. Statistical significance was set at  $p < 0.05$  and statistical tests were performed using the IBM SPSS Statistics software, Version 25.0 (Armonk, NY: IBM Corp.).

## **RESULTS**

We analyzed data from 3067 subjects from the 2015 NHAS wave, from which 322 (10.5%) were retired or pensioners (R/P subjects), 1540 (50.2%) continued working or were in search for a job (W subjects), and 1205 (39.3%) were not working for any other reason, at the NHAS 2018 follow-up wave. As previously stated, for this study's purposes, the latter will not be disclosed.

**Table 1.** Demographic, health-related, and health screening characteristics between retired or pensioner and working subjects in the 2018 NHAS wave

Variable	R/P subjects n (%)	W subjects n (%)	p*
Gender (n = 1862)			
Male	257 (79.8)	1153 (74.9)	0.06
Female	65 (20.2)	387 (25.1)	
Age (years, mean $\pm$ standard deviation) (n = 1862)	68.6 $\pm$ 6.1	66.9 $\pm$ 5.2	< 0.001
Marital status (n = 1862)	-		
Single	17 (5.3)	80 (5.2)	0.057
Married	217 (67.4)	977 (63.4)	
Free union	10 (3.1)	108 (7)	
Divorced	4 (1.2)	38 (2.5)	
Separated	15 (4.7)	93 (6)	
Widowed	59 (18.3)	244 (15.8)	
Health-related characteristics	-		
Hypertension (n = 1859)	150 (46.6)	598 (38.9)	0.011
Diabetes (n = 1863)	102 (31.7)	302 (19.6)	< 0.001
Cancer (n = 1847)	11 (3.4)	32 (2.1)	0.146
Lung disease (n = 1876)	16 (5)	70 (4.5)	0.744
Cardiovascular disease (n = 1845)	38 (11.8)	99 (6.5)	0.001
Stroke (n = 1857)	7 (2.2)	20 (1.3)	0.172
Arthritis (n = 1855)	30 (9.3)	164 (10.7)	0.474
Falls in past 2 years (n = 1860)	116 (36)	595 (38.7)	0.376
Bone fractures in past 2 years (n = 1855)	30 (9.3)	118 (7.7)	0.32
Uses eyeglasses (n = 1861)	203 (63)	831 (54)	0.003
Uses hearing aid (n = 1872)	19 (5.9)	31 (2)	< 0.001
Health screening in the past 2 years	-		
Colon cancer (n = 1862)	34 (10.6)	111 (7.2)	0.042
Cholesterol levels (n = 1858)	240 (74.5)	917 (59.7)	< 0.001
Tuberculosis (n = 1851)	65 (20.4)	216 (14.1)	0.004
Diabetes (n = 1858)	251 (78)	983 (64)	< 0.001
Blood pressure (n = 1862)	251 (78)	1021 (66.3)	< 0.001
Mammogram (n = 1436)	40 (67.8)	200 (53.1)	0.034
Cervical screening (n = 1436)	36 (61)	188 (49.9)	0.111
Digital rectal examination (n = 1321)	103 (42.6)	299 (27.7)	< 0.001

R/P: retired or pensioner subjects; W: currently working or in search of a job.

\*Chi-square test of independence for all variables, except "Age," which was analyzed with independent samples t-test.

Table 1 shows the comparison of demographic, health-related, and health-screening characteristics of the subjects from the R/P and W groups included in the study. According to the 2018 MHAS survey, R/P subjects were older (68.6 vs. 66.9,  $p < 0.001$ ) and had a higher prevalence of hypertension (46.6% vs. 38.9%,  $p = 0.011$ ), diabetes (21.7% vs. 19.6%,  $p < 0.001$ ), cardiovascular disease (11.8% vs. 6.5%,  $p = 0.001$ ), the need to use eyeglasses (63% vs. 54%,  $p = 0.003$ ), and hearing aids (5.9% vs. 2%,  $p < 0.001$ ) than their working peers. R/P subjects also had a higher frequency of self-reported doctor visits and screening for chronic diseases.

There was a tendency for higher self-perceived health in R/P subjects (good or higher self-rated

health of 45.7% vs. 38.4%,  $p = 0.024$ ) and fewer reported feelings of loneliness ( $p = 0.049$ ). However, self-related health compared to 2 years prior and to subjects with similar age, and self-perceived feelings of being ignored and isolated were similar between R/P and W subjects (Table 2).

R/P subjects also reported less assistance to religious services (71.9% vs. 78.6%,  $p = 0.014$ ), volunteering for religious, educative, charity, or community purposes (17.5% vs. 23%,  $p = 0.037$ ), doing exercise or heavy physical work  $\geq 3$  times/week in the past 2 years (30.8% vs. 44.9%,  $p < 0.001$ ) but reported more health-care visits in the past 2 years (83.8% vs. 76.4%,  $p = 0.005$ ), assistance to social or sports clubs

**Table 2.** Self-rated health and negative feelings in subjects between retired or pensioner and working subjects in the 2018 NHAS wave

Variable	R/P subjects n (%)	W subjects n (%)	P*
Self-rated health (n = 1761)	-		
Good or higher	138 (45.7)	560 (38.4)	0.024
Regular	140 (46.4)	806 (55.2)	
Poor	24 (7.9)	93 (6.4)	
Self-rated health compared to the past 2 years (n = 1760)	-		
Better	37 (12.2)	165 (11.4)	0.725
Neutral	186 (61.6)	881 (60.4)	
Worse	79 (26.1)	412 (28.2)	
Self-rated health compared to other people their age (n = 1744)	-		
Better	143 (47.4)	725 (50.3)	0.35
Neutral	144 (47.4)	627 (43.5)	
Worse	15 (5)	90 (6.2)	
Feels loneliness (n = 1656)	-		
Rarely	236 (78.4)	1040 (71.5)	0.049
Sometimes	42 (14)	270 (18.6)	
Frequently	23 (7.6)	145 (10)	
Feels ignored (n = 1755)	-		
Rarely	256 (85)	1168 (80.3)	0.162
Sometimes	35 (11.6)	220 (15.1)	
Frequently	10 (3.3)	66 (4.5)	
Feels isolated (n = 1754)	-		
Rarely	259 (86)	1199 (82.5)	0.326
Sometimes	32 (10.6)	190 (13.1)	
Frequently	10 (3.3)	64 (4.4)	

R/P: retired or pensioner subjects; W: currently working or in search of a job.  
\*Chi-square test of independence.

(12.3% vs. 5.8%,  $p < 0.001$ ), reading (64.1% vs. 56.1%,  $p < 0.001$ ), solving puzzles (28.5% vs. 16.3%,  $p < 0.001$ ), and playing board games (20.5% vs. 12.6%,  $p < 0.001$ ) (Table 3).

On the follow-up analysis of subjects who became R/P by 2018, less subjects commenced attending to religious activities than those who quit (6.7% vs. 15.1%,  $p = 0.003$ ); more increased performing exercise or heavy physical work than those who stopped (26.8% vs. 12.1%,  $p < 0.001$ ); R/P subjects also quit, more than they started, assisting to training courses (15.9% vs. 7.4%,  $p = 0.004$ ), reading (15.3% vs. 6.4%,  $p = 0.002$ ), and performing arts and crafts (9.5% vs. 4.1%), when compared to their previous answer on the 2015 survey when they were still actively working (Table 4). Furthermore, in these subjects, self-rated health compared to other people their age had a higher negative change between waves ( $p = 0.047$ ). However, self-rated health compared to the past 2 years, perceived feelings of loneliness, and

feeling ignored and isolated remained statistically unchanged (Table 5).

## DISCUSSION

To the best of our knowledge, this is the first study that addresses the influence of retirement on the elderly Mexican population. With the increase in lifespan under the same retirement norms, some authors have suggested that more people are spending a longer time living in retirement<sup>6</sup>. The transition to retirement can become a prolonged process of adaptation that can include a change in role identity<sup>7</sup>. In this matter, retirement may also have an impact on an individual's well-being. Previous studies have found mixed results regarding the impact of retirement on health in different countries and populations. Some have reported that retirement may be good for health, related to a reduction in physical and psychological stress, whereas others lean toward less favorable outcomes<sup>8</sup>.

**Table 3.** Recreational activities, physical health, and other health-related characteristics between retired or pensioner and working subjects in the 2018 NHAS wave

Variable	2018 wave intergroup analysis*		
	R/P subjects n (%)	W subjects n (%)	p**
Attends to religious services (n = 1757)	217 (71.9)	1144 (78.6)	0.014
Volunteered for religious, educative, charity, or community purposes (n = 1764)	53 (17.5)	336 (23)	0.037
Has sought health-care services in the past 2 years (n = 1762)	253 (83.8)	1114 (76.4)	0.005
Suffers from chronic pain (n = 1759)	88 (29.2)	500 (34.3)	0.092
Depressive symptoms in the past 2 years (n = 1762)	52 (17.2)	289 (19.8)	0.3
Exercise or heavy physical work $\geq 3$ times/week in last 2 years (n = 1761)	93 (30.8)	655 (44.9)	< 0.001
Volunteers for CSO without compensation or reimbursement (n = 1760)	30 (9.9)	185 (12.7)	0.186
Attends any training course (n = 1766)	38 (12.6)	164 (11.2)	0.505
Attends a social or sports club (n = 1749)	37 (12.3)	84 (5.8)	< 0.001
Reads any book, newspaper, or magazine (n = 1760)	216 (71.5)	818 (56.1)	< 0.001
Solves puzzles (n = 1762)	86 (28.5)	238 (16.3)	< 0.001
Plays board games (n = 1763)	62 (20.5)	184 (12.6)	< 0.001
Sews, knits, or does arts and crafts (n = 1756)	35 (11.6)	205 (14.1)	0.255

R/P: retired or pensioner subjects; W: currently working or in search of a job; CSO: civil social organization.

\*Comparison between R/P and W subjects at the 2018 MHAS wave.

\*\*Chi-square test of independence.

As for our study, in the 2018 MHAS survey, R/P subjects were only a median of 1.7 years older than their working peers. However, they also showed a higher prevalence of chronic disease and sensorial disability. These findings are consistent with other reports. Behncke reported a 10% higher risk of being diagnosed with diabetes, angina, having a heart attack or stroke, arthritis, and cancer after being retired in British subjects, who were 5 years older than the working population<sup>4</sup>. In our study, R/P subjects reported a higher frequency of doctor visits and screening tests for chronic diseases, as well as a lower involvement in exercise or heavy physical work. These changes in behavior could add up to their increased prevalence and detection of chronic diseases, in relation to a higher consumption of health services. This highlights the importance of strengthening primary care programs for the prevention and early detection of chronic diseases, even before the subjects go through retirement. In contrast, in the follow-up analysis, a higher proportion of R/P subjects began participating in exercise or heavy physical work after retirement,

than those who stopped doing it. This could signal toward an area of opportunity in a willingness to stay active and carry a healthy lifestyle during this key transitioning moment in life.

Despite the higher prevalence of chronic diseases in this population, R/P subjects also perceived their health better and reported less feelings of loneliness than W subjects on the 2018 MHAS survey. However, half of these subjects maintained the same level of self-rated health, after retirement, a quarter increased it, and the remainder decreased it. Interestingly, there was a tendency toward having a negative change in self-rated health when asked to compare to other people of the same age. These findings contrast with other results. It has been found that self-assessed health declines after retirement, consistent with findings from Tang et al.<sup>9</sup>, while Behncke also reported a 4% increased risk of self-reporting a bad health status after retirement<sup>4</sup>. Stenholm et al. suggested that suboptimal health status was more likely to remain in those with low occupational status; likewise, a low occupational status was associated with a higher prevalence of

**Table 4.** Changes in recreational activities, physical health, and other health-related characteristics after retirement (R/P subjects) from MHAS 2015 to MHAS 2018

Variable	Follow-up (MHAS 2018)		p*
	Yes n (%)	No n (%)	
<b>Baseline (MHAS 2015)</b>			
Attends to religious services (n = 298)	-		
Yes	194 (65.1)	45 (15.1)	0.003
No	20 (6.7)	39 (13.1)	
Volunteered for religious, educative, charity, or community purposes (n = 298)	-		
Yes	34 (11.4)	32 (10.7)	0.065
No	18 (6)	214 (71.8)	
Has sought health-care services in the last 2 years (n = 298)	-		
Yes	229 (76.8)	31 (10.4)	0.272
No	22 (7.4)	16 (5.4)	
Suffers from chronic pain (n = 306)	-		
Yes	43 (14.1)	49 (16)	0.744
No	44 (14.4)	170 (55.6)	
Depressive symptoms in the past 2 years (n = 298)	-		
Yes	19 (6.4)	29 (9.7)	0.798
No	32 (10.7)	218 (73.2)	
Exercise or heavy physical work ≥ 3 times/week in the past 2 years (n = 298)	-		
Yes	12 (4)	36 (12.1)	< 0.001
No	80 (26.8)	170 (57)	
Volunteers for CSO without compensation or reimbursement (n = 296)	-		
Yes	11 (3.7)	29 (9.8)	0.193
No	19 (6.4)	237 (80.1)	
Attends any training course (n = 296)	-		
Yes	16 (5.4)	47 (15.9)	0.004
No	22 (7.4)	211 (71.3)	
Attends a social or sports club (n = 296)	-		
Yes	20 (6.8)	23 (7.8)	0.43
No	17 (5.7)	236 (79.7)	
Reads any book, newspaper, or magazine (n = 295)	-		
Yes	192 (65.1)	45 (15.3)	0.002
No	19 (6.4)	39 (13.2)	
Solves puzzles (n = 295)	-		
Yes	56 (19)	36 (12.2)	0.457
No	29 (9.8)	174 (59)	
Plays board games (n = 285)	-		
Yes	31 (10.5)	36 (12.2)	0.314
No	27 (9.2)	201 (68.1)	
Sews, knits, or does arts and crafts (n = 297)	-		
Yes	22 (7.4)	28 (9.5)	0.017
No	12 (4.1)	234 (79.1)	

R/P: retired or pensioner subjects; W: currently working or in search of a job; CSO: civil social organization; MHAS: Mexican Health and Aging Study.  
\*McNemar test.

diseases. Furthermore, people with a low occupational status before retirement were more likely to have chronic diseases that would stay and impact their health perception after retirement<sup>10</sup>. In our study, R/P subjects tend to participate more in

social and cognitive performance activities. Atalay et al. found that women increased the time spent on mental and household activities after retirement, leading to a modest effect on cognitive functioning<sup>11</sup>. This could be key in establishing health

**Table 5.** Change in self-rated health and negative feelings in the 2018 NHAS retired or pensioner subject from 2015 to 2018

Variable	Positive change n (%)	Neutral n (%)	Negative change n (%)	p*
Self-rated health (n = 298)	71 (23.8)	151 (50.7)	76 (25.5)	0.741
Self-rated health compared to the last 2 years (n = 298)	65 (21.8)	147 (49.3)	86 (28.9)	0.104
Self-rated health compared to other people their age (n = 295)	55 (18.6)	161 (54.6)	79 (26.8)	0.047
Feels loneliness (n = 295)	52 (17.6)	207 (70.2)	36 (12.2)	0.11
Feels ignored (n = 295)	35 (11.9)	234 (79.3)	26 (8.8)	0.206
Feels isolated (n = 295)	32 (10.8)	238 (80.7)	25 (8.5)	0.427

\*Sign test.

interventions that would keep retired individuals healthy and occupied.

This study had several limitations. There was a higher presence of men and an underrepresentation of women in the analysis, explained by work-related gender roles in Mexico. Furthermore, as mentioned before, due to expected inconsistencies when answering the surveys, which were not intentionally paired during recruitment and data collection, it was not possible to accurately measure the epidemiology of chronic diseases among the same subjects across time before and after retirement. We also did not consider the type of work performed during an individual's active years, retirement plans, and other socioeconomic factors that could also impact health after retirement. Furthermore, information regarding functional, cognitive, affective, nutritional, and social status was not considered. These are all factors that could potentially influence the overall well-being of subjects before and after retirement. Because of this, the comparative analysis is unable to accurately establish whether health morbidity acts as either a consequence or a cause for retirement. Matching cohorts that control for gender, as well as other health, social, and labor variables, are required to accurately assess the causative effect of retirement. It is important to understand that with our study, we did not seek to determine causality, especially in a scenario in which we indirectly analyzed the results of a survey that was not created for the sole purpose of studying our objective in a specific and controlled manner, and that we only take advantage of existing data to generate hypotheses from real-world data.

## CONCLUSION

Work retirement is one of the most important transitions in a person's life. Effects on self-perceived health after retirement are still inconclusive. However, less involvement in physical exercise, as well as other social activities, coupled with more frequent visits to the doctor and screening tests, might point toward a less favorable outcome after retirement. More studies are needed to further analyze the many other different factors that might impact life after retirement. However, these results also signal that the transition of retirement is a key point in life to further pursue a healthy lifestyle to promote successful aging in older adults.

## ACKNOWLEDGMENTS AND FUNDING

The authors declare and would like to thank Mrs. María Antonieta Márquez Horta, who financed this research, widow of Mr. José Francisco Pérez Santos<sup>†</sup>, whose original idea inspired this work.

## CONFLICTS OF INTEREST

The authors declare no conflicts of interest.

## ETHICAL DISCLOSURES

**Protection of human and animal subjects.** The authors declare that no experiments were performed on humans or animals for this study.

**Confidentiality of data.** The authors declare that they have followed the protocols of their work center on the publication of patient data.



**Right to privacy and informed consent.** The authors have obtained approval from the Ethics Committee for analysis and publication of routinely acquired clinical data and informed consent was not required for this retrospective observational study.

**Use of artificial intelligence for generating text.** The authors declare that they have not used any type of generative artificial intelligence for the writing of this manuscript nor for the creation of images, graphics, tables, or their corresponding captions.

## SUPPLEMENTARY DATA

Supplementary data are available in *The Journal of Latin American Geriatric Medicine* online (DOI: 10.24875/LAGM.24000008). These data are provided by the corresponding author and published online for the benefit of the reader. The contents of supplementary data are the sole responsibility of the authors.

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# Immunosenescence and inflammaging as physiological processes of aging

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## Abstract

Aging is a complex process, from the biological, social, and psychological point of view, and various definitions have been proposed, however, many of them lack integration, adopting unidirectional reductionist approaches. Aging is associated with chronic low-grade inflammation known as inflammaging, in which factors such as the accumulation of senescent cells, cellular debris, and microbiota dysbiosis have been related. On the other side, immunosenescence is a physiological phenomenon in which the function of the immune system is compromised by personal aging, which can increase susceptibility to infections and decrease the effectiveness of vaccines. These changes in immunity have been considered primarily harmful; at present, they are included in a perspective that goes beyond simple deterioration, giving way to "adaptive theory." Understanding the underlying mechanisms of inflammation and immunosenescence is crucial to subsequently develop therapeutic and preventive approaches for health problems related to the geriatric age group.

**Keywords:** Immunosenescence. Inflammaging. Physiology of aging.

## Inmunosenescencia e inflammaging como procesos fisiológicos del envejecimiento

### Resumen

El envejecimiento es un proceso complejo, desde el punto de vista biológico, social y psicológico, diversas definiciones han sido propuestas, sin embargo, muchas de ellas carecen de integración adoptando enfoques reduccionistas de vía unidireccional. El envejecimiento se asocia a un estado de inflamación crónica de bajo grado conocida como inflammaging en el cual, factores como la acumulación de células senescentes y desechos celulares, así como disbiosis de la microbiota han sido relacionados. Por otra parte, la inmunosenescencia es un fenómeno fisiológico en el que la función del sistema inmunológico se ve comprometida por el mismo envejecimiento del individuo, lo que puede aumentar la susceptibilidad a infecciones y la disminución de la eficacia de las vacunas. Dichos cambios en la inmunidad han sido considerados principalmente perjudiciales; actualmente se incluyen en una perspectiva que va más allá de un simple deterioro dando paso a la "teoría adaptativa". Comprender los mecanismos subyacentes del inflammaging y la inmunosenescencia es crucial para posteriormente desarrollar enfoques terapéuticos y preventivos que aborden problemas de salud relacionados con el grupo etario geriátrico.

**Palabras clave:** Inmunosenescencia. Inflammaging. Fisiología del envejecimiento.

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Date of reception: 29-02-2024

Date of acceptance: 08-07-2024

DOI: 10.24875/LAGM.24000005

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## INTRODUCTION

Aging is a complex process, from the biological, social, and psychological point of view, and various definitions have been proposed, however, many of them lack integration, adopting unidirectional reductionist approaches.

Claudio Franceschi, in his article "Inflammaging: an evolutionary perspective on immunosenescence", used network theory to analyze how stressors affect feedback mechanisms, particularly in the immune system. From then on, inflammaging was recognized as an influential process in immunosenescence, together being considered a fundamental process in the physiology of aging<sup>1</sup>.

Aging is associated with chronic low-grade inflammation known as inflammaging, in which factors such as the accumulation of senescent cells, cellular debris, and microbiota dysbiosis have been related. On the other hand, immunosenescence is a physiological phenomenon in which the function of the immune system is compromised by personal aging, which can increase susceptibility to infections and decrease the effectiveness of vaccines, these processes form a duality resulting in an immunological disorder<sup>2</sup>. Previously, these changes have been considered mainly harmful, at present, they are included in a more complex perspective that goes beyond a simple deterioration giving way to the "adaptive theory"<sup>3</sup>.

Overall, understanding the underlying mechanisms of inflammaging and immunosenescence is crucial to subsequently develop therapeutic and preventive approaches that address health problems for the geriatric age group.

## CELLULAR SENESENCE AND IMMUNOSENESCENCE

Cellular senescence is a state in which cells cannot divide, which acts as a barrier to the transmission of mutations to future generations<sup>4</sup>. It is characterized by a slowed cell cycle (state resistant to apoptosis) which can occur during any stage of life. Senescent cells are eventually eliminated and replaced by optimal tissues. However, during aging, the elimination of these cells by immune mechanisms does not occur efficiently.

Immunosenescence, on the other hand, refers to the alteration of the structure of immune organs (thymic involution, for example) and the dysfunction of immune cellular responses (innate and adaptive)<sup>5</sup>.

Immunosenescence is a dynamic process in which several immunological functions are reduced, while others remain unchanged or increase<sup>6</sup>: these results in a reduction in the ability to fight infections with the consequent reduction in the elimination of infectious agents due to the decrease in the diversity of the immune repertoire and its function<sup>5</sup>.

Although immunosenescence is related to aging, it does not always depend directly on the biological age of the organism since it is possible to identify it in younger adults, called "accelerated immunosenescence", as shown in young patients seropositive for cytomegalovirus and human immunodeficiency virus, responses to stressors (infectious or not) are strong modulators of this process<sup>7</sup>.

## INFLAMMAGING

Inflammaging refers to the state of chronic, low-grade sterile inflammation that develops with age, characterized by elevated serum concentrations of proinflammatory cytokines. It is known that various stressors, from environmental to cellular wear continually stimulate this immune response. The theory of the central adaptive network is an important contribution to this concept since; it integrates reactions at different levels including the neuroendocrine-immune system. Previously, inflammaging was related to worse outcomes of pathological processes; it is currently thought that this process can be adaptive, leading to greater longevity, and maladaptive, resulting in pathological aging characterized by diseases, frailty, and early functional decline<sup>3</sup>.

Inflammaging is a common denominator in individuals experiencing chronic stress, obesity, sleep disorders, intestinal dysbiosis, and chronic infections among others, regardless of age. This can induce elevated levels of C-reactive protein, interleukin-6 (IL-6), tumor necrosis factor- $\alpha$  (TNF- $\alpha$ ), and IL-1b, concluding in impaired immunity. Studies in humans and animals have shown that chronic stress reduces various immune functional capacities<sup>7</sup>.

## IMMUNOSENESCENCE AND MEDULAR MICROENVIRONMENT

The bone marrow (BM), essential for hematopoiesis, undergoes aging-related changes that affect the production and maintenance of immune cells: the original BM tissue gradually transforms into adipose tissue, negatively affecting the generation of immune cells.

Alterations in this tissue also affect the production of cytokines, which increase with age and contribute to inflammation. IL-6 has a dual role; it can act as an anti-inflammatory and pro-inflammatory mediator, affecting lymphocyte maturation and bone resorption. The presence of an inflammatory environment in the BM affects redox homeostasis, generating reactive oxygen species (ROS) and contributing to cellular senescence<sup>5</sup>.

## **IMMUNE SYSTEM AND AGING**

Aging is a multifaceted process, which is biologically related to genetic, hormonal, metabolic, and environmental factors. During aging, senescent cells increase, contributing to immunosenescence and inflammaging<sup>5</sup>. With the presence of immunosenescence, protection against infectious diseases in older people is compromised, making them more susceptible to presenting them. This, combined with the fact that non-specific symptoms frequently occur and that the classic signs of infection are usually absent, make adequate medical care and management be delayed. Furthermore, changes in the immune response may be clinically relevant for the elderly upon vaccination, as cell-mediated immunity is required to drive the humoral response.

## **CHANGES IN THE IMMUNE SYSTEM RELATED TO AGING**

### ***Cellular immunity***

Cellular immunity is affected by aging mainly due to the decrease in function and number of T cells as well as thymic involution. T cells divide into naïve and memory cells, defined by the expression of the CD45RA and CD45RO isoforms, respectively. Naïve cells migrate to lymphoid organs to mount a primary immune response, while memory cells target non-lymphoid organs to initiate secondary immune responses. In old age, virgin cells decrease as well as their response capacity. The absolute number of CD3, CD4, and CD8T cells also decreases with age. With age, there is also a decrease in the production of IL-2, as a result of the reduction in the total number of T cells.

T Helper 1 lymphocytes (Th1) that help the function of CD8 cells and the production of IgG2a and T Helper 2 lymphocytes (Th2) that help B cells and the production of immunoglobulins A, E and G decrease at the same time that the cytokines produced by each

of those cells: Th1 cytokines include IL-2, IFN-gamma, IL-12, and IL-15, while Th2 cytokines are IL-4, IL-5, IL-6, IL-10, and IL-13. These changes also contribute to altered immune responses in older people.

### ***Humoral immunity***

What is observed during aging regarding humoral anomalies ranges from hypergammaglobulinemia to the production of autoantibodies manifesting some autoimmune diseases and lymphoproliferative diseases. The reduced humoral response and altered antibody-mediated defense mechanisms are due to decreased T helper cell function and an intrinsic deficit of primary B cells. Serum levels of immunoglobulins A and G show a significant increase in elderly people while immunoglobulin M does not increase. Thus, age-related changes can be explained by an alteration of B and plasma cells in organs other than the peripheral blood and the germinal centers as well as a different production of immunoglobulins<sup>8</sup>.

## **INNATE IMMUNITY**

The immune system can be divided into an innate part represented mainly by neutrophils, monocytes, natural killers (NK), and dendritic cells (DC) and an adaptive part (B and T lymphocytes)<sup>6</sup>.

- Neutrophils: They represent the first line of defense of the innate immune response, eliminating pathogens by phagocytosis, protein degranulation, and the release of neutrophil extracellular traps (NETs)<sup>6</sup>. The activity of neutrophils in older people is significantly reduced due to the alteration of the capacity for phagocytosis and degranulation as well as an increase in the production of ROS. Older people also show a reduced capacity for NET formation, which explains why older people are more susceptible to invasive bacterial disease.
- Monocytes/macrophages: They suffer a reduction in the production of ROS and in the capacity for phagocytosis. Reduced expression of toll-like receptors (TLRs) is also observed, which play an important role in pathogen detection and activation of innate immunity. Alteration in TLRs in monocytes from older people induces higher levels of the cytokine IL-8 due to alterations in signaling pathways. In addition, a pro-inflammatory environment has been observed, with evidence of higher levels of pro-inflammatory cytokines such

as TNF- $\alpha$ , IL-6, and IL-1 $\beta$ . In summary, aging-related changes in monocytes/macrophages contribute to the pro-inflammatory state<sup>6</sup>.

- NK cells: They are innate lymphoid cells that represent 10-15% of peripheral blood lymphocytes and participate in early defense against pathogens, characterized by the expression of CD56 and/or CD16 with the capacity to produce IFN- $\gamma$ . With aging, there will be an increase in the number of mature NK cells and a reduction in immature NK cells, probably due to the deficient production of new cells<sup>6</sup>.
- Dendritic cells: They are antigen-presenting cells classified as myeloid cells (mDC) or plasmacytoid cells (pDC) that have different functions: mDC produce IL-12, inducing Th1 T cell response and cytotoxic T lymphocytes (CTL), while pDC produces IFN- $\alpha/\beta$  in response to bacteria and viruses. Older people showed a significant impairment in the secretion of IL-6 and IL-12, in addition to the lower release of IFN<sup>6</sup>.

## ADAPTIVE IMMUNITY

Two types of responses constitute the adaptive system: the cell-mediated immune response carried out by T cells and the humoral immune response controlled by activated B cells and antibodies.

Chronic lifelong antigen loading results in a population of T lymphocytes with a late-differentiated phenotype and reduction of the T cell repertoire. The body harbors many latent infections, which can be reactivated from time to time under specific conditions<sup>6</sup>.

The two main features that characterize the aging of the adaptive immune system are:

- Decrease in virgin T cells:
  - Regenerative capacity decreases with age, contributing to the reduction of hematopoietic cells and affecting the production of adaptive immune cells.
  - Thymic involution and decline in function lead to a reduction in the release of new naïve T cells.
  - Homeostatic proliferation attempts to maintain virgin T cells, but the ability to generate new cells is limited.
- Expansion of activated memory T cells:
  - Chronic antigenic load, especially by latent viruses, leads to the expansion of memory T cells, with a late differentiation phenotype.
  - These changes in the T cell repertoire contribute to inflammaging and have implications for the immune response to new pathogens<sup>6</sup>.

## CONCLUSIONS AND PERSPECTIVES

An important characteristic of older people is the heterogeneity presented in terms of their health status (comorbidities, frailty, cognitive impairment, among others) and their different capacities to mount an immune response to pathogens and vaccines, these immunological changes related to age can be a mixture of adaptation and resilience with maladaptation: the intersection between inflammaging and immunosenescence generates a complex network of adaptive mechanisms that can promote longevity when they counteract antigens to which individuals are exposed throughout life or, on the contrary, increase susceptibility to diseases when they are inadequate (poor adaptation) and influences vulnerability.

Therefore, having knowledge of the altered function of the immune system in the aging organism to identify possible consequences such as infectious pathologies with atypical clinical manifestations or an unpredictable disease course is necessary.

The physiological processes related to aging in each organ and system are complex, there is a need to continue studying to try to reach their complete understanding, which may have an impact on various therapeutic options and improvement of functionality as well as quality of life in this age group.

## ACKNOWLEDGMENTS

The authors would like to thank to resident doctors and doctors attached to the Geriatrics Service of the Hospital Central Norte, as well as the other services of the same hospital in where we are allowed to participate.

## FUNDING

The authors declare that they have not received funding.

## CONFLICTS OF INTEREST

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## Peru, Awaken! The alarming lack of information on “Blue Zones”

### *¡Perú, despierta! La alarmante falta de información sobre las ‘Zonas Azules’*

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Dear Editor,

We address the scientific community to highlight a fascinating phenomenon that deserves investigation and understanding in the Peruvian context. The Blue Zones, referring to geographic regions with a high concentration of people living longer and enjoying healthier lives, have been extensively studied by scientists and health experts<sup>1,2</sup>. The lessons from these zones could significantly impact the lives of our elderly population<sup>3</sup>.

In 2004, Poulain et al. evaluated the main factors of longevity in Sardinia, southern Italy, pioneering care and health for older adults<sup>4</sup>. From healthy diets to an active social life and a strong sense of community, they have shown tangible evidence that effective ways exist to increase longevity and satisfaction in the lives of older adults (Fig. 1)<sup>3-5</sup>.

In the Peruvian context, it is alarming to observe that, despite having communities with the potential to become “Blue Zones,” information on how to lead a longer and healthier life is practically non-existent.

The WHOQOL-BREF is an abbreviated version of the WHOQOL-100 that evaluates the quality of life across four dimensions (physical health, psychological health, social relationships, and environment), whereas the WHOQOL-OLD complements this instrument for older adults with six additional dimensions (sensory abilities, autonomy, past, present, and future activities, social participation, death and dying, and intimacy)<sup>6</sup>. In the Hernandez-Huayta et al. report, both instruments use Likert-type response

scales with five options and transform the values into a 0-100 scale, where higher scores indicate better quality of life. They found that older adults in rural areas generally reported better quality of life across most aspects measured by the WHOQOL-BREF and WHOQOL-OLD questionnaires, except for social relationships, where they scored lower compared to urban residents. Conversely, urban dwellers tended to have a higher quality of life specifically in terms of “Death and Dying” and “Intimacy.” Notably, “Sensory Abilities” showed a moderate effect size, indicating its significance in impacting overall quality of life, whereas “Physical Health” and “Social Participation” demonstrated nearly high effect sizes, underscoring their importance as well. After adjusting for age, sex, marital status, employment status, and education level using a multiple linear regression model, the differences remained significant. Rural older adults had 8.4 points higher in physical health ( $p < 0.001$ ), 6.9 points higher in psychological health ( $p < 0.001$ ), and 7.8 points higher in the environment dimension ( $p < 0.001$ ) of the WHOQOL-BREF. On the WHOQOL-OLD, rural residents had 9.3 points higher in sensory abilities ( $p < 0.001$ ), 4.8 points higher in past, present, and future activities ( $p = 0.002$ ), 11.1 points higher in social participation ( $p < 0.001$ ), and 3.3 points higher in the total score ( $p = 0.012$ ), but 7.3 points lower in intimacy<sup>7</sup>. Therefore, these findings could be valuable in identifying rural areas in Peru with a better quality of health-related life, similar to “Blue Zones” elsewhere in the world.

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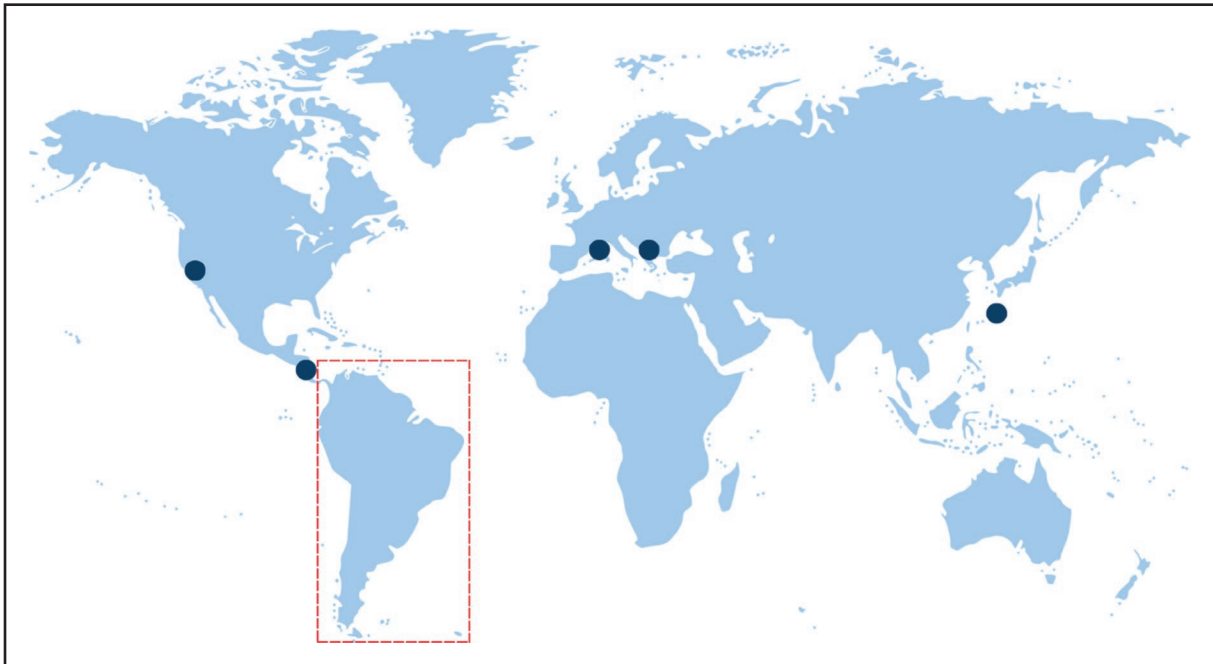
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Date of reception: 11-03-2024

Date of acceptance: 08-07-2024

DOI: 10.24875/LAGM.24000006

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**Figure 1.** Map of Blue Zones Worldwide. In the Americas: Loma Linda (California, USA, North America) and Nicoya (Costa Rica, Central America). European continent: Sardinia (Island, Italy) and Icaria (Island, Greece). Asian continent: Okinawa (Island, Japan). Red-lined rectangle: Represents South America where the absence of “Blue Zones” is evident.

Furthermore, the elderly population in Peru confronts a lack of formal work, considering that only 20% of them have one<sup>8</sup>. This leads us to think that many of them depend financially on their families or a pension provided by the state, e.g., “Pensión 65,” but those who do not fall into these options are usually poor or work in informal establishments until they cannot anymore<sup>9</sup>.

It is time for authorities, health organizations, and society as a whole to recognize the importance of “Blue Zones” and start investing in research, education programs, and public policies that promote healthy aging because the well-being of our elderly population must be a priority. For that, there are many actions to take. First, in Peru, the rights of older people are not assured, which contravenes national regulations such as Supreme Decree No. 006-2021-MIMP<sup>10</sup>. Then, create more recreational sites and entertainment clubs for old people; in this sense, mental and physical health will improve, e.g., “Centro del Adulto Mayor”<sup>11</sup>.

The older population of Peru deserves the opportunity to age with dignity and enjoy a good quality of life, and information along with best practices extracted from “Blue Zones” worldwide could be the

key to achieving this. We cannot allow the lack of information and resources to continue jeopardizing their health and quality of life. Therefore, I urge competent authorities and the scientific community to take immediate action to address this lack of information on “Blue Zones” and ensure that our elderly loved ones have the opportunity to live longer and healthier lives.

Time is of the essence, and we cannot afford to wait any longer to act. Recognizing the challenges faced by the elderly population in Peru is crucial, and addressing these challenges with compassion and urgency is essential to ensure their well-being and happiness in their golden years. We must act with determination and solidarity to overcome these obstacles and secure a better and brighter future for our older adults.

## FUNDING

The authors declare that they have not received funding.

## CONFLICTS OF INTEREST

The authors declare no conflicts of interest.



## ETHICAL DISCLOSURES

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