THE ASSOCIATION OF HEMOGLOBIN CONCENTRATION WITH DISABILITY AND DECREASED MOBILITY AMONG OLDER BRAZILIANS

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Abstract: Objective: To examine the association between hemoglobin concentration and disability and mobility difficulty among older adults living in São Paulo, Brazil. Design: Cross-sectional study. Setting: Population-based study conducted in São Paulo, Brazil. Participants: Adults age 60 and over (n=1,256) from the third data collection wave of the SABE Study (Health, Well-being, and Aging) conducted in 2010. Measurements: Two outcome measures were included in the analyses: 1) a difficulty to perform at least one of the instrumental activities of daily living (IADL) and 2) mobility difficulty, which was assessed using the Short Physical Performance Battery (SPPB). Logistic regression models assessed the association between hemoglobin and each of the outcome measures. All analyses were adjusted for sociodemographic and health characteristics. Results: The prevalence of IADL disability was 26.8% and 10.7% of participants had mobility difficulty. The mean hemoglobin concentration was significantly lower in older adults who already presented disability (13.7g/dL versus 14.4g/dL among independent elderly) or decreased mobility (13.4g/dL versus 14.3g/dL among elderly with preserved mobility). Higher values of hemoglobin concentration were associated with lower the risk of IADL disability (OR=0.88; p=0.04) and mobility difficulty (OR=0.81; p=0.02). Hemoglobin concentrations showed a dose-response effect in the probability of each outcome. Conclusions: Lower hemoglobin concentration was associated with a higher probability of IADL disability and mobility difficulty, showing a clear dose-response effect.

Key words: Hemoglobin, mobility limitation, activities of daily living, older adults, SABE Study.

Introduction

A progressive decrease in erythrogram numbers, which include red blood cell counts, hemoglobin concentration, and erythrocyte indices, is often observed as individuals age. A decrease in the secretion of erythropoietin, a glycoprotein hormone secreted by the kidney that acts on the stem cells of bone marrow to stimulate red blood cell production, and a reduced hematopoietic reserve can lead to anemia (1). Among older adults, anemia has been associated with decreased physical performance (2, 3), more functional dependence (4), reduced mobility (5, 6), decreased cognitive function (7) and increased mortality (6, 8, 9). Common symptoms of anemia, such as fatigue and dyspnea, are directly related to lower quality of life among older adults (10, 11).

In Brazil, major demographic, epidemiological, and nutritional transitions are underway and will impact the disability levels of the older adult population. The older adult population (age 60 and over) has been increasing rapidly as a result of significant demographic transformations related to fast fertility declines and gains in life expectancy in the past decades. Between 2000 and 2025, the number and proportion of older adults is expected to almost double in Brazil (from 14.2 million, or 8.1%, to 35.6 million, or 16.6%) (12). Given this rapid aging of the population, growing numbers of individuals will develop disability and mobility issues in the coming decades. Brazil is also experiencing a major epidemiological transition, and while currently most deaths are related to chronic conditions, there is still a high burden of infectious and parasitic diseases; thus, morbidity and mortality remains high for both standards (13).

In this context, intestinal parasitic infections remain prevalent and may impact iron levels, particularly among children and older adults (14). It is estimated that almost 20% of the anemia cases in older adults are due to iron deficiency (15, 16), and besides the parasites, intestinal occult bleedings can also be caused by chronic diseases like cancer, inflammatory bowel diseases, and other common digestive diseases in older adults that may cause gastrointestinal lesions (17). Anemia of chronic inflammation, a condition that has been traditionally called anemia of chronic disease, is responsible for more than 30% of the cases in older adults. Also frequent in this age group is renal insufficiency, which accounts for about 8% of cases of anemia among older adults, or 12.5% when combined with other chronic conditions (15).

Finally, the rapid nutritional changes underway in Brazil have impacted not only the prevalence of overweight and obesity, but also the consumption of nutrients (18). There is evidence that adiposity among adults in transition countries is associated with decreased iron absorption and iron deficiency (19).

Most of the available literature addressing the role of anemia in health outcomes has dichotomized hemoglobin levels and classified individuals as either having or not having anemia (3, 6, 20); very few researchers have analyzed these associations using continuous levels of hemoglobin concentration (5, 9, 11, 21). We opted to use hemoglobin concentrations rather than
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anemia status for two main reasons: First, continuous data allow the observation of a dose-response pattern when it exists. Classifying individuals as either having anemia or being healthy does not allow the identification of this pattern. Second, there is an ongoing discussion about whether or not the current cutoffs for anemia—12 g/dL for women and 13g/dL for men (22)—are adequate for older adults, because among this population some negative outcomes are observed with mid-low values of hemoglobin, even though the individual is not yet classified as anemic using the current threshold.

Very few studies have analyzed the impact of anemia or hemoglobin concentrations on the well-being of older adults in developing countries; this paper addresses this gap in the literature. We use data from a large population-based study to explore how hemoglobin concentration is related to disability on instrumental activities of daily living (IADL) and mobility difficulty among older adults living in São Paulo, Brazil.

Methods

Sample and procedures
The data originated from the SABE [Saúde, Bem-Estar, e Envelhecimento (Health, Wellbeing, and Aging)] survey, a longitudinal study initiated in 2000 that collected information from a probabilistic sample of older adults (age 60 years or older) residing in the city of São Paulo (n=2,143). The baseline sample (2000 A) was obtained using a two-stage stratified sampling method, following the framework of the 1995 National Household Survey based on geographic areas of the city. Individuals age 75 years and older were oversampled to compensate for the greater mortality rate in this age group. Details on the methodology of the study are described elsewhere (23).

In 2006, a second wave of the study was conducted; 1,115 participants from the first wave (2006 A) were interviewed again, and a new sample (2006 B, n=298) of adults between 60 and 64 years old was added following procedures similar to those used in the first wave. A third wave was conducted in 2010/2011. This wave included 748 respondents from the initial sample (2010 A) and 242 respondents from the 2006 sample (2010 B); in addition, a new sample of adults age 60 to 64 years was added (2010 C, n= 355). The final 2010 sample included 1,345 older adults (≥60 years). Sample weights were recalculated based on Census 2010. Among the 2010 respondents, 89 had incomplete blood count data. The final sample used in the present study is composed of 1,256 respondents, who represent about 1.3 million older adults in São Paulo. Figure 1 summarizes the sample composition.

The 2010 data were collected in five stages. The first stage was a household interview conducted by a single interviewer using a standardized questionnaire addressing the living conditions and health status of the older adult respondent. The second stage was a household visit during which a nutritionist and a dentist measured anthropometric data, determined physical performance and conducted a dental examination. Physiological specimens of blood and urine were collected in the third and fourth stages, respectively. In the fifth stage, an interviewer collected accelerometer data. During the household interview, all eligible older adults received an invitation to participate in the blood collection. Blood samples were collected after an overnight fast of 10 to 12 hours. Samples were taken by trained registered nurses in the respondent’s home in a sitting position by venipuncture. Blood hemoglobin concentrations were determined at the laboratory of the Hospital of the Medical School at the University of São Paulo using an ADVIA 120 system (Siemens Healthcare Diagnostics, Germany).

The third wave of SABE Study was approved by Research Ethics Committee at the Faculty Public Health, University of São Paulo (protocol number 2044). Participation was voluntary, and a signed informed consent form was obtained of all participants in each wave.

Measures and analysis
Two outcome measures were included in the analysis: IADL disability and mobility difficulty. The respondent was classified as having an IADL disability if they reported having difficulty with one or more of the following activities: managing finances, using transportation within the community, shopping, using the telephone, or taking responsibility for their own medications. Mobility difficulty was assessed via the Short Physical Performance Battery—SPPB (24), based on results of three tests: standing balance (the ability to maintain their feet in the side-by-side, semi-tandem, and tandem positions for 10 seconds each), walking speed (for 3 m at their usual pace), and ability to rise from a chair (stand up from a sitting position once with arms folded at the chest). Each test received scores ranging from 0 (could not complete) to 4 (best performance); the final score (ranging from 0 to 12) is the sum of the scores on the three tests. Participants were classified as maintaining mobility (moderate to good performance: 7 to 12 points) or having mobility difficulty (low or very poor performance: 0 to 6 points) (25). Previous research has shown that the SPPB total score is a reliable (ICC=0.83) and valid measure in a population of older adults in Brazil (26).

The analyses included several sociodemographic and health variables. Sociodemographic variables included gender, age, and years of education. Health variables included self-reported chronic conditions diagnosed by a physician (hypertension, diabetes, stroke, and arthritis) and cognitive status. Due to the low level of schooling among the South American older adult population, cognitive status was evaluated using a modified version of the Mini Mental State Exam (MMSE) that had been validated for the SABE Study. The measure includes 13 items that are less dependent upon schooling (than the items on the traditional exam); the cut-off point is a score of 12 or less (27).

Descriptive statistics were included the analysis; mean and standard error values were calculated for the continuous
variables and proportions were calculated for the categorical variables. Between-group differences were estimated using the Wald test of mean equality and the Rao-Scott test. Logistic regressions assessed the association between hemoglobin concentration (used as continuous variable) and each outcome variable. Based on the results of regression models including all variables, we calculated the predicted probabilities of experiencing IADL disability and mobility difficulty given various levels of hemoglobin concentration by gender. All analyses included sample weights and were adjusted for the complex sampling design. The data analysis was performed using Stata® version 11.

Results

Table 1 displays population characteristics. The majority of study participants were women (60.4%), and the average participant was 70.4 years old, had 5.3 years of schooling, and had a hemoglobin blood concentration of 14.2 g/dL. The prevalence of IADL disability was 26.8% and 10.7% of participants had mobility difficulty. Compared to those without IADL limitations, older adults with IADL limitations were
older and less educated, and had lower values of hemoglobin and more chronic conditions and cognitive impairment. A similar pattern was observed for subjects with mobility difficulty.

Table 2 shows the results of logistic regressions models. The associations between hemoglobin concentration and the outcome variables were negative and statistically significant even after adjusting for sociodemographic and health characteristics—the higher the hemoglobin concentration, the lower the risk of IADL disability (OR=0.88; p=0.04) and mobility difficulty (OR=0.81; p=0.02).

**Table 2**

Results of logistic regression models for IADL disability and mobility difficulty of older adults (≥ 60 years old). São Paulo, Brazil, 2010

<table>
<thead>
<tr>
<th>Hemoglobin, g/dL</th>
<th>IADL disability OR [95% CI]</th>
<th>Mobility Difficulty OR [95% CI]</th>
</tr>
</thead>
<tbody>
<tr>
<td>11.5</td>
<td>27.5 [20.0,35.1]</td>
<td>20.6 [11.6,29.5]</td>
</tr>
<tr>
<td>12.0</td>
<td>26.3 [19.9,32.7]</td>
<td>19.5 [11.6,27.5]</td>
</tr>
<tr>
<td>13.0</td>
<td>23.9 [19.4,28.4]</td>
<td>17.6 [11.4,23.9]</td>
</tr>
<tr>
<td>13.5</td>
<td>22.8 [18.9,26.6]</td>
<td>16.7 [11.1,22.3]</td>
</tr>
<tr>
<td>14.0</td>
<td>21.7 [18.2,25.2]</td>
<td>15.9 [10.8,20.9]</td>
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</tbody>
</table>

* p<0.05, ** p<0.01

Table 3 presents the adjusted probabilities of IADL disability and mobility difficulty by gender. These probabilities are predicted values based on the logistic regression models found in Table 2. Results indicate a dose-response effect of hemoglobin concentration on both outcomes—higher blood hemoglobin concentrations were associated with lower likelihoods of having a disability and mobility restriction. For example, a concentration of 12 g/dL was associated with a 26.3% chance of having an IADL disability, whereas the probability of such a disability decreased to 23.9% at 13 g/dL and 21.7% at 14 g/dL. The probability of experiencing mobility difficulty at a concentration of 12 g/dL was estimated at 9.1%, whereas the probability of such a mobility difficulty decreased to 7.4% at 13 g/dL and 6.1% at 14 g/dL.

When we analyzed those probabilities by gender (Table 3), we found that 31.4% of women with a concentration of 12 g/dL (the WHO cutoff point for anemia) (22) reported having an IADL disability, whereas only 26.2% of women with a concentration of 14 g/dL reported having an IADL disability. A comparable decrease occurred for mobility difficulty: at 12 g/dL, the probability of having a limitation was estimated at 11.3%, whereas at 14 g/dL the probability was 7.6%. The pattern for men was similar: among those a concentration of 13 g/dL (the WHO cutoff for anemia) (22), 17.6% and 5.3% had a disability and mobility problems, respectively; at 15g/dL these proportions fell to 14.2% and 3.5%, respectively.

**Table 3**

Adjusted probabilities of IADL disability and mobility difficulty predicted from logistic regression models* for of older adults (≥ 60 years old), according to hemoglobin blood levels and gender. São Paulo, Brazil, 2010

<table>
<thead>
<tr>
<th>Hemoglobin, g/dL</th>
<th>IADL Disability Probability [95% CI]</th>
<th>Mobility Difficulty Probability [95% CI]</th>
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</tbody>
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* Predicted values after estimation of models presented in Table 2, which are adjusted by age, gender, education, cognitive impairment, stroke, hypertension, arthritis and diabetes.

**Discussion**

Our results show that among older adults, hemoglobin levels are related to two measures of functional limitations—IADL and mobility performance. Common symptoms of low hemoglobin levels, such as fatigue and decreased muscle strength, are associated with worse quality of life and difficulty with the activities of daily living. There are several pathways, generally involving decreases in the oxygenation of tissues and reductions in muscle strength, by which reduced hemoglobin could contribute to functional disability (1). First, lower levels of hemoglobin might lead to less oxygen being delivered to skeletal muscles, and thus reductions in VO2max (28). Second, chronic hypoxia may be responsible for several pathophysiological modifications (e.g., peripheral arterial vasodilatation, capillary angiogenesis, myocardial dysfunction, lower blood pressure, activation of the sympathetic and renin angiotensin aldosterone systems, and salt and water retention).
that result in the onset or worsening of disabling diseases (1, 29). The association between anemia and physical performance may also indirectly reflect the effects of low-grade inflammation, which has long been accepted as a major influence on the development of chronic anemia in older adults (30, 31), as well as disability (32), mobility (33) and muscle mass (34).

We found that higher hemoglobin concentrations were associated with lower probabilities of IADL disability and mobility difficulty in both genders. These results align with the previous literature, which has found higher levels of mobility difficulties and disability at lower levels of hemoglobin concentration (5, 9). Specifically, the current findings presented in Table 3 are similar to the ones found by Chaves and colleagues (5) in which the authors found that mobility difficult was higher among women with lower levels of hemoglobin, even when these women were not classified as anemic under WHO criteria. The authors reported that the lowest risk of mobility limitation and disability was found among participants with hemoglobin levels between 13.5 and 14g/dL, and that women with a level of 12g/dL (WHO cutoff) scored worse on these tests than women with higher concentrations of hemoglobin (5). Chaves and colleagues also found that compared to women with hemoglobin levels near 12g/dL, those with an Hb level of 14g/dL had a 24% lower rate of mortality (11). Even though the current study cannot address the impact of anemia on mortality, we contribute to this literature by analyzing the impact of hemoglobin levels on disability among women and men, which were not included in those previous studies, and also by focusing on a sample from an emerging market economy.

In the current sample for this study, the mean levels of hemoglobin were 14.9 (s.e. 0.08) for men and 13.7 (s.e. 0.05) for women. Using the WHO criteria, 7.9% of women and 7.3% of men would be classified as having anemia. Data of anemia among older adults in Brazil are scarce. The few studies found similar frequencies to those presented here, between 4.5% and 12.8% (35-38). Differences in prevalence of anemia can be partially due to different samples and study designs. However, prevalence of anemia seems to be relatively low among older adults in Brazil.

The prevalence of mobility difficulty for the current sample was 10.7%, which is lower than other rates reported in Brazil, possibly because of measurement differences. Using the baseline SABE sample in São Paulo, Alvarado and colleagues (39) estimated that 38.4% of older women and 21.4% of older men reported having difficulty getting up from a chair after sitting for long periods. In the current study, we used an objective measure of mobility difficulty and classified older adults with moderate performance levels as not having mobility difficulty. We opted for this classification for two main reasons: First, the prevalence of having mobility issues would have been very high—54.3%—if we had classified these older adult as having difficulty. Second, a preliminary analysis showed that the prevalence of anemia was very similar (p=0.272) among good and moderate performers—5.2% and 7.0%, respectively. The mean SPPB score in the current sample was 9.1 (9.5 among men and 8.8 among women), which is lower than the mean score of 10.6 (40) found in another study conducted in Brazil. However, Alfieri and colleagues (40) focused on a relatively younger sample of 46 individuals age 60 to 75 years old. Differences in age and sample size may explain the difference in the SPPB scores. The prevalence of IADL disability reached 26.8% in the current sample, which is higher than the 21.8% prevalence found in the first wave of SABE in São Paulo (41), but lower than the rate of 30.1% reported by another study that also used SABE (42). These differences occur because researchers have both included varying numbers of IADL limitations—eight in the case of Zunzunegui and colleagues (41) and five in Santos et al. (42)—and classified answers such as “does not usually do this” differently.

This study has some limitations. First, because the data are cross-sectional, the analyses cannot determine the direction of the association between hemoglobin and the outcomes measures. As discussed above, there are some reasonable pathways that could explain the influence of low hemoglobin levels on disability and mobility difficulty; however, the opposite causal direction is possible as mobility limitations may influence nutrient intake. Another limitation of the study results from the nature of the outcome variables—mobility performance was assessed using a battery of objective tests that are widely used in the research, whereas disability was based on self-reported information. While this is a potential source of bias, methodological studies have demonstrated that self-reported data on functional disability have adequate validity and are consistent with medical diagnoses and/or physical tests (43).

Despite these limitations, the study uses data from a large population study, with a representative sample of community-living older adults of both genders residing in a major city in Brazil. In addition, to our knowledge, this is the first study to assess the association between hemoglobin concentration and mobility and disability outcomes in Latin America, where demographic, epidemiological, and nutritional transitions are occurring at very rapid pace. Like other developing countries, Brazil does not have a sufficiently organized healthcare structure or policies to cope with these rapid transitional processes, which have a considerable impact on healthcare services and consequently the quality of life of older adults.

In conclusion, lower hemoglobin levels were associated with higher probabilities of IADL disability and mobility difficulty, and the analytical results showed a clear dose-response effect. Therefore, physicians and health care practitioners should identify and treat older adults with low hemoglobin concentrations, in order to prevent or postpone outcomes associated with mobility losses and disability.
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References