Protein nutritional status and function are associated with type 2 diabetes in Hispanic elders1–4

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ABSTRACT

Background: Hispanic elders have a high prevalence of diabetes and poor glycemic control, leading to inadequate nutritional status, muscle wasting, and impaired function.

Objective: We examined the association of type 2 diabetes with nutritional status measured by serum albumin concentrations and midupper arm muscle area (MAM) and with function measured by difficulty with at least one activity of daily living.

Design: Health history and disability were assessed by self-report in 556 Hispanics with a mean (±SD) age of 69 ± 7 y and 158 non-Hispanic whites (NHW; aged 71 ± 7 y) from the Massachusetts Hispanic Elders Survey. Energy intake (in MJ/d) and protein intake (in g/d) were estimated with use of a food-frequency questionnaire. Body mass index (BMI; in kg/m²) and C-reactive protein concentrations (in mg/L) were also measured. Multiple logistic regression models by ethnic group were used.

Results: There were no significant differences between Hispanics and NHWs in the proportion of those with low albumin concentrations or low MAM. Hispanic diabetic women had the lowest proportion of low MAM. The risk of low serum albumin concentration was twice as high in Hispanics taking insulin as in their NHW counterparts. Among Hispanics, low albumin concentration and low BMI were associated with low MAM; female sex, low albumin concentration, high BMI, and insulin use were significantly associated with risk of functional impairment.


KEY WORDS Serum albumin, diabetes, Hispanics, nutritional status, disability, midupper arm muscle area, non-Hispanic whites, Massachusetts Hispanic Elders Survey

INTRODUCTION

The concentration of albumin in serum has long been recognized as an indicator, albeit a crude one, of the state of general health and nutrition of an individual (1). Modest to very low serum albumin concentrations are associated with morbidity and all-cause mortality in older persons (2–4). Low serum albumin concentrations have also been found to be significantly associated with reduced muscle mass in relatively healthy, well-nourished elderly men and women (5). Although serum albumin concentration seems to be associated with survival and outcome, it is unclear to what extent it relates to function. The burden of disease on functional limitations has been established for some conditions (6, 7). Specifically, functional limitation has been found to be associated with diabetes mellitus (7, 8). Given that functional limitations influence the quality of life, the likelihood of hospitalization, and survival (9), the search for potentially preventable or treatable causes of declines in serum albumin, regardless of age, is an important public health issue.

The prevalence of diabetes is high in Hispanics (10, 11), particularly in Mexican Americans (12) and Puerto Ricans (13). Hispanic elders report more functional limitations and poorer self-reported health than do non-Hispanic whites (NHWs) (14–16). However, little is known about the association of diabetes with nutritional and functional status among Hispanic elders. Diabetes mellitus is a chronic disease characterized by hyperglycemia and by disturbances of carbohydrate, fat, and protein metabolism (17, 18). Poorly controlled diabetes is associated with altered body protein metabolism (19). Insulin-mediated net protein anabolism occurs largely in skeletal muscle; therefore, the catabolic state resulting from insulin deficiency or resistance may lead to muscle wasting (17). Similarly, decreased synthesis of hepatic plasma proteins (eg, albumin) has been shown with diabetes (19, 20).

Thus, the goal of diabetes management is to improve glycemic control and to provide adequate nutrient intake to help reduce muscle wasting, comorbidity, and the risk of mortality (21).

On the basis of the higher prevalence of diabetes in the Hispanic population, and given that diabetes, particularly with poor glycemic control, leads to protein catabolism, we asked whether Hispanic elders with diabetes are at higher risk of

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poor nutritional status and, therefore, of muscle wasting and disability. We tested the following hypotheses: 1) low serum albumin concentration (as a marker of nutrition and health) is associated with diabetes status; 2) serum albumin concentration is associated with loss of muscle mass [low midupper arm muscle area (MAM)], independent of other health factors that may be associated with serum albumin; and 3) low serum albumin concentration is associated with activities of daily living (ADL) disability in Hispanic and NHW elders.

SUBJECTS AND METHODS

Subjects

The study subjects were a subset of 1030 subjects who were studied in the Massachusetts Hispanic Elders Study (MAHES), a statewide survey conducted between 1993 and 1997 (13, 16). For this analysis, a subset of 714 elders aged 60–92 y, for whom we had health-related information and adequate blood samples for biochemical analyses, was included. This study sample was composed of 556 Hispanic elders from Puerto Rico (49%) and the Dominican Republic (15%) and other Hispanics (14%) from Cuba and Central and South America. One-hundred fifty-eight NHWs represented the neighborhood comparison group, which was located simultaneously in the same census blocks as was the Hispanic elder group. Sociodemographic indicators of the NHW group were closer to those of the population of Hispanic elders than would have been seen with a random sample of NHWs. Subjects were not excluded for health reasons. When subjects could not provide information directly, questionnaires were administered to the primary caregiver. The study was conducted with the approval of the New England Medical Center Human Investigation Review Committee in Boston.

Anthropometric measurements

Body weight was measured with a balance scale (Seca Corporation, Columbia, MD) with a capacity of 150 kg and graduation of 500 g, calibrated regularly with known weights. Stature and knee height were measured with a Harpenden pocket stadiometer (Holtain Ltd, Crymnych, United Kingdom). Body mass index (BMI; in kg/m²) was calculated (22). Midupper arm circumference was measured to the nearest 0.1 cm at the mid-point of the upper left arm (between the acromion process and the tip of the olecranon) with an insert-type measuring tape (Ross Laboratories, Columbus, OH). Triceps skinfold thickness was measured to the nearest 0.5 mm at the midpoint of the back of the upper left arm with a Lange caliper (Cambridge Scientific Industries, Inc, Cambridge, MD). MAM was calculated from triceps skinfold and midupper arm circumference (23). Low MAM was defined as a value below the 75th percentile, equivalent to 63 cm² for men and 47 cm² for women aged >65 y. These cutoff values are based on data for the US population derived from the first National Health and Nutrition Examination Survey (NHANES I; 1971–1974) (24).

Biochemical measurements

Serum albumin concentrations were measured by the dye-binding endpoint reaction using the Cobas Fara II Centrifugal analyzer (25). Modest hypoalbuminemia [albumin concentration ≤40 g/L (26, 27)] has been found to be associated with elevated mortality risk. Population studies have shown that even slightly low serum albumin concentrations, within physiologically acceptable ranges, may be a marker of early mortality (3, 4, 28–30). Thus, for the current study, a low cutoff for albumin concentration of 40 g/L was used. C-reactive protein (CRP) was used as a marker of acute-phase response. CRP concentrations were measured by using a Behring Nephelometer (Behring Diagnostica, Westwood, MA) (31).

Sociodemographic and health status

Information on age, years of education, and income was collected by questionnaire. Income was calculated from employment, public assistance, retirement pensions, and other sources for all members of the household. The presence of type 2 diabetes was determined by using the most recent guidelines of the American Diabetes Association (32). Subjects were classified as having type 2 diabetes if they had a fasting plasma glucose concentration of >7.0 mmol/L, or a random plasma glucose concentration of >11.1 mmol/L, or if they had been prescribed insulin or oral medication for diabetes. Functional limitations and disability were measured with 12 ADL items adapted from the Katz scale (33); a lower ADL score indicates better function whereas a higher ADL score indicates poorer function.

Dietary intake

Dietary data were collected by using a food-frequency questionnaire especially adapted and validated for use with the MAHES cohort (34). Three-dimensional models and measurement aids were used to estimate portion sizes. Dietary analyses were performed by using data from the MINNESOTA NUTRIENT DATABASE (version 25; Nutrition Coordinating Center, University of Minnesota, Minneapolis). Outliers for energy intake were excluded when values were <2.4 or >18.4 MJ/d.

Statistical analysis

Descriptive analyses of subject characteristics and group comparisons were conducted by using general linear models or logistic regression models for continuous and categorical variables, respectively. Residual plots were developed to examine linearity and transformations were made as needed. Pearson correlation analysis was used to determine the simple association between low serum albumin concentration and the sum of ADL scores. Statistical analyses were done by using SPSS for WINDOWS (version 9.0; SPSS Inc, Chicago). First, logistic regression models for each of the primary outcomes (low serum albumin concentration, low MAM, and ADL disability) were developed for the group as a whole, adjusted for sociodemographic variables (age, sex, income, and education level) and ethnicity. Ethnicity alone was not significantly associated with any of the outcome measures, and neither were the interactions between ethnicity and covariates. Because Hispanics were the focus of this analysis, we repeated the analysis for Hispanics only. Dichotomized variables were used to better describe the magnitude of the risk of having values below the reference value for these dependent variables commonly used for clinical assessment and therapy. Models were first run with dummy variables for subjects from the Dominican Republic and for other Hispanics to compare against Puerto Ricans, the largest Hispanic group in MAHES. However, we did not find significant differences in this analysis. Therefore, we present models for Hispanics as one group.
On the basis of our hypotheses, we first ran a model to determine independent predictors of low albumin concentration (<40 g/L). These included energy intake (in MJ/d) and protein intake (in g/d), CRP concentrations (in mg/L), BMI, and dummy variables created for diabetes treatment: 1) diabetes treated with oral hypoglycemic agents alone and 2) diabetes treated with insulin, compared with diabetes not treated with medications. Subjects treated with both oral medications and insulin were placed in the insulin treatment group. Then, we looked at predictors of low MAM (below the 75th percentile) as a function of energy and protein intakes, BMI, low serum albumin concentration, and dummy variables for diabetes treatment. Last, we looked at predictors of ADL disability in relation to BMI, low serum albumin concentration, and diabetes treatment. All 3 models were adjusted for age, sex, education, and income.

RESULTS

Subject characteristics

Characteristics of the study population are presented separately by ethnic group and sex for subjects with diabetes (Table 1) and without diabetes (Table 2) diabetes. Comparisons across sex and ethnic groups were adjusted for age, as appropriate. Among subjects with diabetes (Table 1), NHW men and women were older than were their Hispanic counterparts. Hispanic men and women had significantly fewer years of education and lower incomes than did their NHW counterparts, although the difference was not significant. Hispanic and NHW women had a significantly higher BMI than did men; NHW women had the highest BMI of all groups. MAM was not significantly different across groups. Compared with Hispanic men, Hispanic women were significantly less likely to have low MAM, lower dietary energy and protein intakes, and higher rates of ADL disability. ADL disability was also significantly higher among NHW women than men. Serum albumin, CRP concentration, and the percentage of individuals with low serum albumin concentrations did not differ significantly across groups. Treatment of diabetes with oral medications was also not significantly different across groups. However, there were significantly more cases of diabetes not treated with medications among NHW than Hispanic men. Furthermore, NHW men and women were less likely to use insulin than were their Hispanic counterparts. Detailed information on the prevalence and control of type 2 diabetes in this sample was published elsewhere (13).

Similar results were observed for individuals without diabetes (Table 2) for age, education and income, BMI, MAM, energy and protein intakes, ADL disability, and CRP concentration. Interestingly, mean serum albumin concentrations were significantly lower in NHW women, whereas the proportion of low serum albumin concentrations was not significantly different across groups.

Primary outcomes

The results of the logistic regression models (1) low serum albumin concentrations (<40 g/L), 2) low MAM (below the 75th percentile), and 3) ADL disability (difficulty with at least one ADL) for Hispanics only are presented in Table 3. All the models were adjusted for potentially confounding variables, including age, sex, income, education, and dietary protein and energy intakes, when applicable. The results for models 1 and 2 were not significantly different when the models were run without income and education as covariates. In model 1, independent correlates (P < 0.05) of low serum albumin concentration included high energy intake and elevated CRP concentration. Low serum albumin concentrations were twice as likely among Hispanic elders with diabetes treated with insulin than among their NHW counterparts. In model 2, a higher risk of low MAM among Hispanics was associated with low albumin concentration and low BMI.
TABLE 2
Characteristics of subjects without diabetes

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Men (n = 152)</th>
<th>Women (n = 215)</th>
<th>Men (n = 49)</th>
<th>Women (n = 73)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (y)</td>
<td>68.4 ± 7.5</td>
<td>68.9 ± 6.8</td>
<td>69.9 ± 6.5</td>
<td>72.5 ± 8.0</td>
</tr>
<tr>
<td>Education (y)</td>
<td>5.8 ± 5.2</td>
<td>5.0 ± 4.3</td>
<td>12.6 ± 3.8</td>
<td>11.5 ± 3.3</td>
</tr>
<tr>
<td>Income ($1000)</td>
<td>15 ± 14</td>
<td>13 ± 11</td>
<td>30 ± 66</td>
<td>16 ± 15</td>
</tr>
<tr>
<td>BMI (kg/m²)</td>
<td>26.8 ± 4.8</td>
<td>28.8 ± 6.0</td>
<td>27.1 ± 4.9</td>
<td>26.3 ± 6.4</td>
</tr>
<tr>
<td>Midupper arm muscle area (cm²)</td>
<td>59.2 ± 13.6</td>
<td>50.0 ± 14.9</td>
<td>56.1 ± 12.4</td>
<td>44.1 ± 15.2</td>
</tr>
<tr>
<td>Low midupper arm muscle area (%)</td>
<td>56.6</td>
<td>51.2</td>
<td>67.3</td>
<td>64.4</td>
</tr>
<tr>
<td>Energy intake (MJ/d)</td>
<td>8.1 ± ±2.8</td>
<td>6.9 ± 2.7</td>
<td>8.3 ± 2.9</td>
<td>6.6 ± 2.4</td>
</tr>
<tr>
<td>Energy intake (g/d)</td>
<td>75 ± ±29</td>
<td>63 ± 25</td>
<td>78 ± 28</td>
<td>66 ± 25</td>
</tr>
<tr>
<td>Serum albumin (g/L)</td>
<td>44 ± 0.3</td>
<td>43 ± 0.4</td>
<td>44 ± 0.4</td>
<td>42 ± 0.4</td>
</tr>
<tr>
<td>Serum albumin &lt; 40 g/L (%)</td>
<td>13.8</td>
<td>16.3</td>
<td>20.4</td>
<td>17.8</td>
</tr>
<tr>
<td>C-reactive protein (mg/L)</td>
<td>7.8 ± 5.2</td>
<td>8.3 ± 5.8</td>
<td>9.3 ± 12.3</td>
<td>7.5 ± 5.8</td>
</tr>
</tbody>
</table>

All analyses were adjusted for age by using general linear models and logistic regression models as appropriate.

1Significantly different from Hispanics within sex, P < 0.05.
2Significantly different from men within ethnic group, P < 0.05.
3Below 75th percentile or < 63 and < 47 cm² for men and women, respectively.

TABLE 3
Characteristics associated with poor nutritional and functional status in Hispanics

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Low albumin (&lt; 40 g/L)</th>
<th>Low midarm muscle area (below 75th percentile)</th>
<th>Difficulty with ≥1 activity of daily living</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (y)</td>
<td>1.03 (0.99, 1.07)</td>
<td>1.03 (0.99, 1.06)</td>
<td>1.01 (0.99, 1.04)</td>
</tr>
<tr>
<td>Sex</td>
<td>1.18 (0.71, 1.97)</td>
<td>0.71 (0.47, 1.08)</td>
<td>1.73 (1.19, 2.51)</td>
</tr>
<tr>
<td>Income ($1000)</td>
<td>1.00 (0.98, 1.02)</td>
<td>1.00 (0.98, 1.02)</td>
<td>0.98 (0.94, 1.02)</td>
</tr>
<tr>
<td>Education (y)</td>
<td>1.01 (0.95, 1.07)</td>
<td>0.98 (0.94, 1.03)</td>
<td>0.99 (0.97, 1.00)</td>
</tr>
<tr>
<td>Energy intake (MJ/d)</td>
<td>1.27 (1.07, 1.52)</td>
<td>1.11 (0.96, 1.29)</td>
<td></td>
</tr>
<tr>
<td>Energy intake (g/d)</td>
<td>0.98 (0.97, 1.00)</td>
<td>0.99 (0.97, 1.003)</td>
<td></td>
</tr>
<tr>
<td>C-reactive protein (mg/L)</td>
<td>1.08 (1.04, 1.12)</td>
<td>—</td>
<td></td>
</tr>
<tr>
<td>Serum albumin (g/L)</td>
<td>—</td>
<td>0.53 (0.30, 0.94)</td>
<td>0.64 (0.38, 1.08)</td>
</tr>
<tr>
<td>BMI (kg/m²)</td>
<td>1.04 (0.99, 1.08)</td>
<td>0.80 (0.77, 0.84)</td>
<td>1.06 (1.03, 1.10)</td>
</tr>
<tr>
<td>Diabetes without medications</td>
<td>1.40 (0.61, 3.24)</td>
<td>0.30 (0.13, 0.68)</td>
<td>1.53 (0.77, 3.05)</td>
</tr>
<tr>
<td>Diabetes plus oral agents</td>
<td>1.73 (0.83, 3.60)</td>
<td>0.84 (0.46, 1.55)</td>
<td>1.06 (0.60, 1.88)</td>
</tr>
<tr>
<td>Diabetes plus insulin</td>
<td>2.11 (1.11, 4.01)</td>
<td>0.80 (0.44, 1.47)</td>
<td>2.24 (1.24, 4.04)</td>
</tr>
</tbody>
</table>

1Odds ratios with 95% CIs. Models were evaluated in Hispanics only and adjusted for age, sex (women as reference), income, and education.
2Model included energy and protein intakes based on food-frequency questionnaire, C-reactive protein, BMI, and diabetes treatment modality as independent predictors. When waist circumference was added to the model, the results did not change.
3Model included energy and protein intakes, serum albumin concentrations, BMI, and diabetes treatment modality as independent predictors. When waist circumference was added to the model, the results did not change.
4Model included serum albumin concentrations, BMI, and diabetes treatment modality as independent predictors. When waist circumference was added to the model, the results did not change.
Serum albumin concentrations were inversely associated with the presence of ADL disability (presented as ADL score) for both Hispanics and NHWs (Figure 2). Serum albumin concentrations were also inversely associated with CRP concentrations, but only among Hispanics ($r = -0.22$, $P = 0.001$, data not shown). This association was expected, because the early systemic response to inflammation or infection (the acute phase response) indicated by CRP results in decreased concentrations of visceral proteins such as albumin, transferrin, and transthyretin (referred to as the negative acute phase response) (35). CRP was also found to be positively associated with ADL score in Hispanic elders ($r = 0.19$, $P = 0.001$, data not shown).

DISCUSSION

Our results for Hispanic elders show that low serum albumin concentrations were associated with diabetes and that there was a predicted decline in serum albumin concentrations associated with the acute phase response. Furthermore, low serum albumin concentrations were associated with low MAM and with ADL disability. Insulin treatment was associated with twice the risk of low serum albumin concentrations and disability among Hispanic compared with NHW elders. These findings suggest that the high prevalence of diabetes and poor glycemic control observed in the Hispanic older population place them at a higher risk of morbidity and mortality.

The concentration of albumin in serum has long been recognized as a crude indicator of general health and nutrition (1). Clinical disorders alter albumin homeostasis, so that serum albumin concentrations may be used to assess progression or severity of illness, especially for some catabolic illness in which wasting is a hallmark (36). In this study, we found that greater energy intake, treatment of diabetes with insulin, and inflammation were associated with low serum albumin concentrations. Similar associations between diabetes and low serum albumin were found by using data derived from NHANES I (26). In that population-based sample of subjects aged 55–74 y, diabetes was associated with an almost double risk of having a serum albumin concentration $< 38$ g/L. These associations suggest the importance of these variables as markers of increased risk. Klonoff-Cohen et al (3) found that serum albumin concentrations predicted mortality independent of disease in healthy noninstitutionalized white men and women (aged 50–89 y). The association between albumin and early mortality found by these authors suggests that serum albumin concentrations may also predict subclinical disease in otherwise healthy elders.

Other researchers have described the inverse association between serum albumin and CRP concentrations. The early systemic response to inflammation or infection, known as the acute phase response, results in decreased concentrations of visceral proteins such as albumin, referred to as the negative acute phase response (27, 35, 37). Low serum albumin in the presence of high CRP concentrations seems to have a relation to disease (2, 38). Some researchers did not show an association between acute phase response and serum albumin concentrations in community-dwelling individuals aged $> 60$ y (30). However, the concomitant measurement of an acute phase response reactant along with serum albumin concentrations to determine the role of the latter as a clinical marker (ie, nutrition and disease) may be more accurate (39).

MAM was used in this study as an indirect measure to estimate the muscular component of lean body mass. However,
these results should be interpreted with caution given that anthropometry significantly overestimates actual muscle area, and the amount of error increases systematically with the level of adiposity (40). In contrast, estimates of muscle mass from dual-energy X-ray absorptiometry (DXA; 41) or magnetic resonance imaging (40) are more accurate for in vivo measures of muscle tissue, but these methods are clearly too inconvenient and expensive for population studies. Another limitation of MAM is that, although reference values have been developed for the US white population (24), revised equations have not been validated for elderly, overweight, or minority populations.

In the present study we found low serum albumin concentration and low BMI to be significantly associated with low MAM (estimated by anthropometry) among Hispanic elders, after adjusting for confounders such as age, sex, income, and education. Similarly, Baumgartner et al (5) reported a significant association between low serum albumin and MAM (estimated by DXA) in a cohort of 275 subjects aged 60–95 y from the New Mexico Aging Process Study. These findings suggest the possibility of an underlying association between low serum albumin concentration and muscle mass, which could potentially also be associated with increased risk of disability and chronic disease in the elderly. In contrast, Starling et al (42) did not show an association between serum albumin and appendicular muscle mass by DXA after adjusting for regular physical activity and protein intake. The discrepancy between the data of Starling et al and that from the present study and from Baumgartner et al may be related to the differences in the health status of the study populations. Starling et al’s subjects were generally healthy, whereas the subjects in our study and those from the study by Baumgartner et al had greater prevalences of chronic disease and medication use. Given the well-documented associations between serum albumin and nutrition, general health, disease, and mortality, there is a need for longitudinal studies to better understand the causal relations between low serum albumin and age-related loss of muscle mass.

The association we found between low BMI and low MAM was not surprising. It has been documented that low BMI is a health threat and is associated with sarcopenia or loss of muscle mass and ultimately with mortality risk (43). Elderly individuals with low BMI may be at risk of losing muscle mass, not only because of the age-related changes in body composition but also because of the burden of diseases with aging.

We also asked whether low serum albumin, which is associated with reduced muscle mass and diabetes status, was associated with disability among Hispanics. Our findings show that modestly low serum albumin concentrations (<40 g/L) and insulin treatment, in addition to other known predictors of disability, such as female sex and high BMI (16), were associated with functional impairment. The risk of disability was previously associated with low serum albumin concentrations in the elderly (2, 4). In addition, the positive association of disability with the acute phase response suggests that age-related physiologic changes, inflammation processes, and comorbidity may all contribute to the frailty syndrome of the elderly.

In the Framingham Study elderly cohort (7), diabetes increased the likelihood of inability to climb stairs, walk a mile, or cook. In other recent longitudinal studies, diabetes was found to be a significant factor associated with functional limitations (9, 44, 45). The Established Populations for Epidemiologic Studies in the Elderly showed that noninstitutionalized Mexican Ameri-}


cans aged >65 y with diabetes had a greater likelihood of impairment in ADL tasks and that this association was stronger than those previously published for NHW populations (46). Poor glycemic control (47), which requires more intensive insulin treatment, is also a risk factor for disability in the elderly and deserves further investigation.

In conclusion, despite the observation that the percentage of subjects with serum albumin concentrations <40 g/L was similar between Hispanic and NHW elders, diabetes treated with insulin represents a risk factor for low serum albumin concentrations and functional impairment among Hispanic elders. The association of serum albumin with protein nutrition, muscle mass, and functional status in the context of diabetes is important, particularly among Hispanics who have high prevalences of uncontrolled diabetes and disability. Thus, diabetes interventions seeking to maximize nutritional status and function are needed and should be important public health concerns in this ethnic group.

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REFERENCES


