Relationship between Serum Albumin Level and Aging in Community-Dwelling Self-Supported Elderly Population

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Summary While lower serum albumin concentration is often found in the elderly, a relation between serum albumin and age has not been fully elucidated. We conducted population-based cross-sectional and 5-y longitudinal study to examine the relation. A total of 22,705 male and 40,149 female, aged 65 y and older, living in Gifu, participated in the health check service conducted by Gifu City Medical Association. They were self-supported in the activity of daily living and 3,438 of them were followed up every year from 1999 to 2003. Serum albumin levels decreased with age in both men and women. In the cross-sectional study, median value declined from 4.3 g/dL in males aged 65–69 y to 3.9 g/dL in 90≤ y, and 4.3 g/dL to 4.0 g/dL in females. Incidence of hypoalbuminemia (serum albumin ≤3.5 g/dL) increased in parallel with age from 1.2% (65–69 y) to 6.6% (85–89) in males, and 0.6% to 4.1% in females. In the longitudinal study, regression analysis showed a significant decline in serum albumin of 0.015 g/dL per year (r=−0.716) in males, and 0.012 g/dL per year (r=−0.794) in females. Relative reduction of serum albumin in 5 y was larger in advanced age; 1.2% in females aged 65–69 y and 3.1% in 85–89 y (p<0.05), but not in males. In conclusion, a fall in serum albumin concentration in community-dwelling, self-supported elderly persons was associated significantly with aging.

Key Words serum albumin, hypoalbuminemia, elderly, general population, aging

Most societies worldwide have experienced a marked increase in the aged population in recent years, and malnutrition among them is regarded as an important health care problem. To assess nutritional status, the serum albumin level is commonly used as an indicator. Many studies have shown that low albumin concentration is a reliable predictor of poor outcome such as higher incidence of complications, longer hospital stay, higher readmission rate, and higher mortality (1–8). Although these problems of malnutrition have been well focused in specific populations such as hospitalized patients or nursing home residents, epidemiology of hypoalbuminemia and its significance among community-dwelling elderly persons is obscure. Particularly in this regard, Corti et al. revealed that risk of all-cause mortality increased gradually with decreasing albumin level in 4,116 older persons of a community-setting prospective study (7). Moreover, several cohort studies reported that low albumin concentrations, even above the conventional cutoff, are associated with future loss of muscle mass (9, 10), muscle strength (11), and 10-y survival (6, 12).

As to possible effect of aging on serum albumin level, several investigators have described a substantial age-related decline in albumin (13–19). In contrast, a couple of studies have failed to show a significant effect of age on albumin (20, 21). Thus, there are conflicting findings whether the serum albumin level declines simply with aging. These studies attempted to clarify the relation between age and albumin with efforts to adjust for various factors which could influence serum albumin values, such as infection, inflammation, surgical stress, trauma, and liver and renal disease, or performed a rough sampling to pick out healthy elderly persons. However, it may be quite difficult to control completely for all these potential confounding factors.

The aim of the present study was to elucidate the relation between serum albumin concentration and aging in a cross-sectional and 5-y longitudinal study, using large cohort data from a health check service in a city for the community-dwelling, self-supported population aged 65 y and older.

MATERIALS AND METHODS

Study samples. We conducted both a cross-sectional study and a 5-y longitudinal study. Subjects for the former comprised 62,854 individuals (22,705 males and 40,149 females) aged 65 y and older, living at home in Gifu City. They received a health check service organized for general citizens by Gifu City Medical Association between 1999 and 2003. The participants were...
8,758 persons in 1999, 9,910 in 2000, 11,489 in 2001, 14,410 in 2002 and 18,287 in 2003. The estimated coverage by this service was 10–20% of the aged population over 65 y old in the city.

Subjects for the longitudinal study were 3,438 of the first health check participants in 1999. Thereafter, they were followed-up individually every year until 2003. The subjects were non-institutionalized community dwelling people and were self-supported in their activities of daily living, thus representing the general population of the area.

Serum Albumin. Data on serum albumin were available for all subjects. All samples were managed by the Clinical Examination Center, Gifu City Medical Association. Serum albumin concentrations (g/dL) were determined using the bromcresol green (BCG) procedure with Type 740 automated analyzer (Hitachi, Tokyo, Japan).

Statistical analyses. In view of differences in lifespan or physical function between males and females, all values were stratified by sex. Data analysis was performed using the statistical package SPSS 13.0J for Windows (SPSS Inc, Chicago, USA).

Cross-sectional study. The subjects were divided into 6 generations by every 5 y of age: 65–69, 70–74, 75–79, 80–84, 85–89, and 90 y and older (Table 1). For each gender/generation subgroup, 5, 10, 25, 50, 75, 90 and 95 percentile serum albumin values were calculated. A linear, quadratic, or cubic regression model was used to obtain the best-fit curve of the each percentile value with the age.

The proportion with hypoalbuminemia (conventionally defined as the serum albumin level ≤ 3.5 g/dL) was also compared among age-divided groups using the χ² test.

Table 1. The number of subjects, and distribution by age.

<table>
<thead>
<tr>
<th>Age Group</th>
<th>Male</th>
<th>Female</th>
</tr>
</thead>
<tbody>
<tr>
<td>n (%)</td>
<td>22,705 (36.1)</td>
<td>40,149 (63.9)</td>
</tr>
<tr>
<td>Age (mean±SD)</td>
<td>74.2±5.8</td>
<td>74.8±6.2</td>
</tr>
<tr>
<td>Distribution</td>
<td></td>
<td></td>
</tr>
<tr>
<td>65–69 y old</td>
<td>5,145</td>
<td>9,023</td>
</tr>
<tr>
<td>70–74 y old</td>
<td>8,593</td>
<td>13,441</td>
</tr>
<tr>
<td>75–79 y old</td>
<td>4,876</td>
<td>8,976</td>
</tr>
<tr>
<td>80–84 y old</td>
<td>2,482</td>
<td>5,287</td>
</tr>
<tr>
<td>85–89 y old</td>
<td>1,268</td>
<td>2,612</td>
</tr>
<tr>
<td>90 y old and</td>
<td>341</td>
<td>888</td>
</tr>
</tbody>
</table>

Table 2. The percentile serum albumin levels (g/dL) by gender- and age-defined groups.

<table>
<thead>
<tr>
<th>Age Group</th>
<th>Male</th>
<th>Female</th>
</tr>
</thead>
<tbody>
<tr>
<td>n 5 10 25 50 75 90 95</td>
<td>n 5 10 25 50 75 90 95</td>
<td></td>
</tr>
<tr>
<td>65–69</td>
<td>5,145 3.8 3.9 4.1 4.2 4.4 4.4 4.6 4.7</td>
<td>9,023 3.9 4.0 4.2 4.3 4.5 4.6 4.7</td>
</tr>
<tr>
<td>70–74</td>
<td>8,593 3.8 3.9 4.1 4.2 4.4 4.5 4.7</td>
<td>13,441 3.9 4.0 4.1 4.3 4.4 4.6 4.7</td>
</tr>
<tr>
<td>75–79</td>
<td>4,876 3.7 3.8 4.0 4.2 4.3 4.5 4.6</td>
<td>8,910 3.8 3.9 4.1 4.2 4.4 4.5 4.6</td>
</tr>
<tr>
<td>80–84</td>
<td>2,482 3.6 3.7 3.9 4.1 4.3 4.4 4.5</td>
<td>5,275 3.7 3.8 4.0 4.2 4.3 4.5 4.6</td>
</tr>
<tr>
<td>85–89</td>
<td>1,268 3.5 3.6 3.8 4.0 4.2 4.4 4.5</td>
<td>2,612 3.6 3.7 3.9 4.1 4.3 4.4 4.5</td>
</tr>
<tr>
<td>90≤</td>
<td>341 3.3 3.4 3.7 3.9 4.1 4.3 4.4</td>
<td>888 3.3 3.5 3.7 4.0 4.2 4.3 4.4</td>
</tr>
</tbody>
</table>

Fig. 1. Cubic regression lines as best-fit curves for 5, 50 and 95 percentile value of serum albumin (g/dL). For each percentile value, r² of curve fitting is 0.931, 0.910, and 0.864 in males, and 0.942, 0.913, and 0.850 in females, respectively.
Longitudinal study. Differences in age and serum albumin level between longitudinal subjects and those who entered only into the cross-sectional study in 1999 were examined using Student’s t-test, and differences were considered significant when the two-tailed p-value was less than 0.05.

Changes in serum albumin level from 1999 to 2003 were tested by the paired t-test. Difference in the percent reduction of serum albumin level among subgroups defined by age at 1999 was tested by one-way ANOVA with Scheffe’s multiple comparison procedures.

A linear regression model was used to examine the relationship between aging and serum albumin level for each individual. Then, changes in the serum albumin value starting at the age in 1999 were averaged for every year. Results are presented as a correlation coefficient (r), regression coefficients (β) with standard errors (SIs), and p-value. A regression coefficient of −0.1 can be interpreted as a decline of 0.1 g/dL in serum albumin level per year.

RESULTS

Cross-sectional study

Percentile serum albumin values. The number of participants in each subgroup defined by sex and age is given in Table 1. Five, 10, 25, 50, 75, 90, and 95 percentile serum albumin values for each subgroup are shown in Table 2, and best-fit curves for 5, 50 and 95 percentile values are given in Fig. 1. The curves highly fitted for each percentile (r²=0.931, 0.910 and 0.864 in males, r²=0.942, 0.913 and 0.850 in females for 5 percentile, 50 percentile and 95 percentile, respectively). Thus, the serum albumin level decreased significantly with the progression of age.

Incidence of hypoalbuminemia. According to the conventional definition of hypoalbuminemia (serum albumin of 3.5 g/dL or less), its incidence in each group is calculated. As shown in Fig. 2, 2.4% of all males and 1.5% of all females suffered from hypoalbuminemia. The incidence increased significantly in parallel with age both in males and in females (p overall<0.001, respectively).

Table 3. Changes in serum albumin level during 5 y in longitudinal samples.

<table>
<thead>
<tr>
<th>Age (1999)</th>
<th>Male</th>
<th>Female</th>
</tr>
</thead>
<tbody>
<tr>
<td>n</td>
<td>Serum albumin level in 1999</td>
<td>% Change in 5 y</td>
</tr>
<tr>
<td>65–69</td>
<td>4.29±0.25</td>
<td>−1.8%</td>
</tr>
<tr>
<td>70–74</td>
<td>4.24±0.24</td>
<td>−1.9%</td>
</tr>
<tr>
<td>75–79</td>
<td>4.19±0.24</td>
<td>−2.0%</td>
</tr>
<tr>
<td>80–84</td>
<td>4.11±0.25</td>
<td>−2.0%</td>
</tr>
<tr>
<td>85–89</td>
<td>4.07±0.30</td>
<td>−1.8%</td>
</tr>
<tr>
<td>90+</td>
<td>4.00±0.33</td>
<td>−7.4%</td>
</tr>
<tr>
<td>All</td>
<td>4.22±0.25</td>
<td>−1.9%</td>
</tr>
</tbody>
</table>

Values are expressed as mean±SD.
*p<0.05, **p<0.01, ***p<0.001 compared with serum albumin level in 1999.

Longitudinal study

In comparison between the 3,438 longitudinal study subjects (males: n=1,130, females: n=2,308) and the other participants in 1999, the latter were slightly older (mean±SD: males: 73.4±6.3 y old as compared with 73.4±5.3, p<0.001, females: 75.1±6.5 y old as compared with 73.6±5.4, p<0.001) and had a lower albumin concentration (males: 4.17±0.29 g/dL as compared with 4.22±0.25 g/dL, p<0.001, females: 4.24±0.28 g/dL as compared with 4.28±0.25 g/dL, p<0.001).

The paired t-test showed a significant decrease in serum albumin concentration during 5 y in all groups defined by sex and age in 1999, except 85–89 and 90 y and older males (Table 3).

Percent reduction in serum albumin level for 5 y is shown in Table 3 and Fig. 3. The decline was 2% or less for ages 65–89 in males, and there was no significant difference among the groups. On the other hand, in females, the decline in 85–89 y old was significantly larger than those in 65–69 and 70–74 y old.

The changes in serum albumin from 1999 to 2003 in individual subjects are shown in Fig. 4(a). Averaged changes according to the age in 1999 are shown in Fig. 4(b).
4(b) \( r = -0.716, \beta = -0.015, SE=0.001 \) for males and \( r = -0.794, \beta = -0.012, SE=0.001 \) for females; \( p<0.001 \), and revealed a similar decrease to that in the cross-sectional study. These \( \beta \) values confirm that males and females lose 0.015 and 0.012 g/dL serum albumin, respectively, every year in the aged general population.

DISCUSSION

Serum albumin level is widely used as a nutritional parameter. Several epidemiological and clinical studies have described an association of low serum albumin concentration with increased morbidity and mortality (4–7, 18, 22–25). Functional impairment and disability in elderly people are also reported to be associated with low serum albumin (9–11, 26). Several studies in patients or general population have shown that serum albumin concentration decreases with age, especially in the elderly, although the magnitude of decrease varies considerably among studies (13–18, 23, 27).

This study of a total of 62,854 persons aged 65 y and older in a city suggested that a fall in serum albumin concentration in older persons was associated with aging. In the 5-y follow-up study of 3,438 persons, the slope of the age-albumin regression (\( \beta \) value) of \(-0.015 \) g/dL per year in males and \(-0.012 \) g/dL in females confirms this observation.

However, such slopes were higher than previous reports as \(-0.0054 \) to \(-0.0095 \) per year (13, 16, 27). As a possible explanation for this disagreement, we consider that some previous studies had confounded aging effect on the mixed morbid and healthy cohort. Furthermore, other preceding studies sampled strictly the normal aged by totally excluding morbid subjects, thus presumably giving a milder slope. Salive reported that age was independently associated with lower serum albumin after adjusting for other factors, with the slopes of \(-1.2 \) g/L per decade \((-0.012 \) g/dL/y) as a raw value and \(-0.8 \) g/L per decade \((-0.008 \) g/dL/y) after adjustment (18). In 11,090 hospitalized patients in the Boston Collaborative Drug Surveillance Program, Greenblatt reported that mean serum albumin concentration fell significantly from 3.97 to 3.58 g/dL between the forth and eighth decades of life (0.01 g/dL/y) after stringent selection of the population and stratification by renal function, sex, diagnosis and duration of hospitalization (15). Another possible cause for the discrepancy is the difference in race, since the majority of studies described above were conducted in Western countries.

The strength of our study is the large number of subjects and the 5-y longitudinal data. We demonstrated statistically significant age-albumin relation both in cross-sectional and in longitudinal data. Furthermore, we stress that the speed of decline in serum albumin concentration is different by sex and age, especially in females. The rate of decline was almost consistent around 2% for males throughout 65–89 y old. In contrast, the rate rose in parallel with aging in females (see Fig. 3). Another strength of this study is that the subjects were defined geographically and included only community-dwelling persons. Furthermore, earlier studies had a small number of those over 75 y of age, almost all from a selected cohort such as hospitalized or institutionalized persons.

A limitation of the study is that age-albumin association was not adjusted by background factors. Serum albumin is the main protein synthesized by the liver. A large reduction in protein intake or trauma and infectious diseases may reduce rapidly the serum albumin level. Long-term changes may be induced by chronic renal or liver disease. In addition to disease-related malnutrition, age-related changes such as metabolism, dietary intake, physical activity and body composition are supposed to influence the nutritional status indicated with serum albumin. Several studies excluded patients with malnutrition, protein-losing enteropathies, myeloma, renal or hepatocellular disease to define age-related trends in serum albumin (15, 16). Another study adjusted demographic, health behavior and health status to examine the independent factors of age and serum albumin simultaneously (18). However, it is quite difficult to control completely for all potential confounding factors. In addition, in a 10-y longitudinal study, the rate of change in serum albumin did not differ between the groups with and without disease (12). The elderly live individually with various backgrounds, such as disease, physical activity or disability, health condition, and lifestyle. Therefore we attempted to define practically the trend of age-albumin association based on a large general population in this study. We suggest that our results can be available to refer to for the majority of the elderly without particular conditions.

The second limitation is the lack of outcomes survey in this study. Absolute survival, disease-free survival, ADL, and QOL should be evaluated in association with baseline albumin in future studies.

Finally, our study urges the screening of hypoalbuminemia in the general population. Using the current threshold of 3.5 g/dL, we observed that 2.4% of males and 1.5% of females of the community-dwelling elderly...
Serum Albumin in Aged General Population

had hypoalbuminemia. A number of studies reported a higher incidence of hypoalbuminemia in hospitalized elderly patients and nursing-home elderly people. Thus, it has been thought generally that hypoalbuminemia or malnutrition is a problem peculiar to hospitalized or institutionalized elderly persons. However, Fig. 2 shows clearly that the incidence of hypoalbuminemia changes by age. Hence, we suggest that the surveillance of the aged general cohort for hypoalbuminemia should be made from the preventive perspective of malnutrition.

In conclusion, serum albumin concentration decreased with advanced age in a community-dwelling, self-supported cohort.

REFERENCES


Fig. 4. (A) Individual changes in serum albumin level for 5 y. (B) Averaged changes in serum albumin level for every year starting from the age in 1999. $r = -0.716, \beta = -0.015, SE = 0.001, p < 0.001$ for males and $r = -0.794, \beta = -0.012, SE = 0.001, p < 0.001$ for females.


