Nutrition Research and Practice 2017;11(1):57-63
ⓒ2017 The Korean Nutrition Society and the Korean Society of Community Nutrition
http://e-nrp.org

Serum albumin levels and their correlates among individuals with motor disorders at five institutions in Japan

Hiroko Ohwada[1§], Takeo Nakayama[2], Yuki Kanaya[1] and Yuki Tanaka[1]

[1]Department of Health and Nutrition, Yamagata Prefectural Yonezawa University of Nutrition Sciences, 6-15-1 Torimachi, Yonezawa, Yamagata 992-0025, Japan
[2]Department of Health Informatics, Kyoto University School of Public Health, Yoshida Konoe-cho, Sakyo-ku, Kyoto 606-8501, Japan

BACKGROUND/OBJECTIVES: The level of serum albumin is an index of nourishment care and management. However, the distribution and correlates of serum albumin levels among individuals with motor disorders have not been reported until now. Therefore, we examined the distribution and correlates of serum albumin levels among individuals with motor disorders.
SUBJECTS/METHODS: A cross-sectional study on 249 individuals with motor disabilities (144 men, mean age: 51.4 years; 105 women, mean age: 51.4 years) was conducted at five institutions in Ibaraki Prefecture, Japan in 2008. The results were compared with data from the National Health and Nutrition Survey.
RESULTS: The mean serum albumin levels were 4.0 ± 0.4 g/dL for men and 3.8 ± 0.5 g/dL for women. Overall, 17 (11.8%) men and 25 (23.8%) women had hypoalbuminemia (serum albumin level ≤ 3.5 g/dL); these proportions were greater than those among healthy Japanese adults ($\leq 1\%$). Low serum albumin level was related with female sex, older age, low calf circumference, low relative daily energy intake, low hemoglobin (Hb), low blood platelet count, low high-density lipoprotein cholesterol (HDL-C), low HbA_{1c}, and high C-reactive protein (CRP) levels. The strongest correlates, based on standardized betas, were Hb (0.321), CRP (-0.279), and HDL-C (0.279) levels.
CONCLUSIONS: These results indicate that the prevalence of hypoalbuminemia is higher in individuals with motor disabilities than in healthy individuals and that inflammation is a strong negative correlate of serum albumin levels. Therefore, inflammation should be examined for the assessment of hypoalbuminemia among institutionalized individuals with motor disabilities.

Nutrition Research and Practice 2017;11(1):57-63; https://doi.org/10.4162/nrp.2017.11.1.57; pISSN 1976-1457 eISSN 2005-6168

Keywords: Serum albumin, motor disorders, cross-sectional studies, nutritional status, inflammation

INTRODUCTION

Motor disability (MD) is commonly defined as the partial or entire loss of function of a body part. This frequently results in poor stamina, muscle weakness, lack of muscle control, or total paralysis. MD is commonly noticeable in neurological conditions such as cerebral palsy (CP) and stroke [1]. Individuals with MD often demonstrate abnormal feeding behaviors, leading to reduced food consumption and malnutrition [2-8].

Malnutrition is commonly reported in studies on neurologically impaired children (including those with CP) and is related with inadequate caloric intake, altered nutrient requirements, impaired self-feeding, oral motor dysfunction [3-5], and overall gross motor function [9]. Malnutrition is also common in individuals who have experienced stroke [6-8], in which case poor food and fluid intake may result from swallowing difficulties or other stroke-related physical and functional problems [7]. Weight loss frequently occurs in individuals with CP or stroke and is an important nutritional problem [10,11]. Furthermore, the routine determination of weight changes is among the basic criteria for individuals undergoing long-term care established by the US Joint Commission on Accreditation of Healthcare Organization [12]. Weight loss of $\geq 5\%$ in the elderly is associated with a relative risk of mortality of 2.2 [13].

Albumin is a comparatively small protein synthesized by liver cells and is negatively charged. It accounts for about 70% of plasma colloid osmotic pressure and is the most profuse protein in extracellular fluids. Albumin also plays a critical role in regulating fluid distribution in the body [14]. Due to its relatively long half-life of approximately 14-20 days, albumin is considered a marker of chronic nutritional status [15]. Low albumin concentration has been used as a marker of malnutrition [16] and is the principal nutritional marker in hospitalized patients with chronic kidney disease [17], inflammatory disorders [17,18], chronic infection [18], or burns [19]. It is also related with poor functional status in older persons [20,21] and is predictive of a greater decline in functional status [22].

We previously reported low prevalence (1.3%) of hypoalbumi-

This study was supported by a grant from the Ministry of Health, Labor, and Welfare (grant ID: 2006-disability-general-009). The funders had no role in the study design, data collection and analysis, decision to publish, or preparation of the manuscript. None of the authors have any commercial or financial involvements in connection with this study that represent or appear to represent any conflicts of interest.
§ Corresponding Author: Hiroko Ohwada, Tel. 81-238-22-7330, Fax. 81-238-93-2920, Email. h.ohwada@yone.ac.jp
Received: September 5, 2016, Revised: November 18, 2016, Accepted: December 9, 2016

nemia (serum albumin level ≤ 3.5 g/dL) among individuals with intellectual disabilities (ID) as well as an association between low serum albumin and both inflammation and medication [23]. However, no studies have examined the distributions and correlates of serum albumin levels in institutionalized individuals with MD. Since individuals with MD are mildly to moderately affected by physical disabilities [9,11] as well as problems with oral motor function and feeding, which can also affect nutritional status [2-8], serum albumin levels may be lower than in healthy individuals. Furthermore, onset of MD is widely distributed from the early stage of life (prenatal period, perinatal period, infancy) to adulthood. Earlier onset could extend the length of time with dysphagia and therefore affect serum albumin levels.

In this study, we carried out cross-sectional research on institutionalized individuals with MD to examine serum albumin levels (particularly the prevalence of hypoalbuminemia), correlation of inflammation, medication, and other variables with low serum albumin levels, as well as differences in serum albumin levels according to timing of MD onset.

SUBJECTS AND METHODS

Study subjects

This multi-institutional, cross-sectional research was conducted at five support facilities for individuals with MD (Aiseien, Arisu No Mori, Ikoi, Sakuraen, and Yukarinosato) in Ibaraki Prefecture. This region of Japan is located 109 km north of Tokyo and consists of a population around 3 million. In 2008, 7,149 residents (approximately 1,000 living in support faculties) from the prefecture were identified as having a physical disability. Of these, MD was detected in 3,406 individuals. Of the 261 residents at the five support facilities in this study, 11 individuals without any MD (e.g., visual impairment) and one individual who was hospitalized during this study were excluded, resulting in 249 individuals in the analyses. The research protocol was approved by the Institutional Review Board at Ibaraki Christian University, with which the first author (HO) was affiliated at the time this study was conducted. The ethical approval number is 07-10.

In Japan, regular health check-ups for individuals with MD are conducted at disability support facilities; these are nearly identical to healthy adult check-ups [24]. Anthropometric measurements, calculation of relative intakes of energy and protein, and blood testing were conducted prospectively from September to November 2008. Data on disability, primary diagnosis, and medication were collected retrospectively from medical records. Onset of MD was classified as early stage (e.g., CP, spina bifida) or adulthood and later (e.g., stroke, brain contusion) based on the primary diagnosis.

Anthropometric measurements

Height, weight, triceps skinfold thickness (TSF), mid-arm circumference (MAC), and calf circumference were measured by a trained staff member according to standard procedures [25]. Mid-arm muscle circumference (MAMC) was calculated using the following equation: MAC (cm) - 3.14 × TSF (mm). Mid-arm muscle area (MAMA) was calculated using the following equation: $[\text{MAC (cm)} - 3.14 \times \text{TSF (mm)}]^2/(4 \times 3.14)$. Rates of weight change were calculated using the weights recorded at each facility x (x: 1, 3, or 6) months ago using the following equation: [(weight x months ago - current weight)/weight x months ago] × 100%.

Daily food intake

Rate of meal consumption was calculated using the following equation: [(food provided - food leftover)/food provided] x 100%. This rate was multiplied by the energy and protein (per kg) of each meal provided by each facility's national registered dietitian for each target individual; average daily values for relative intakes of energy and protein (per kg) were calculated.

Analysis of blood components

Fasting blood samples were collected in the early morning and analyzed for red blood cells [RBC, sheath flow direct current (DC)] [26], white blood cells (WBC, flow cytometry method) [27], serum hemoglobin (Hb, sodium lauryl sulfate-Hb) [28], hematocrit (Ht, red blood cell pulse height detection method) [29], blood platelet count (PLT, sheath flow DC) [30], total protein (TP, biuret method) [31], serum albumin (bromocresol green) [32], aspartate aminotransferase (AST), alanine aminotransferase (ALT), and γ-glutamyl transpeptidase (γ-GTP, Japan Society of Clinical Chemistry transferable method) [33], serum total cholesterol (TC, enzyme method) [34], triglycerides (TG, enzyme method) [34], high-density lipoprotein cholesterol (HDL-C, direct method) [35], low-density lipoprotein cholesterol (LDL-C, enzyme method) [34], and HbA_{1c} (latex photometric immunoassay) [36]. Based on findings from previous studies, inflammation markers [C-reactive protein (CRP, latex turbidimetric immunoassay)] [37], medications [major and minor tranquilizers, anticonvulsants, and others (i.e., gastrointestinal medications, medications for the common cold, cardiovascular drugs)], and immunoglobulin G (IgG, turbidimetric immunoassay) [38] were also analyzed.

Frequency of hypoalbuminemia

In Japan, specified albumin levels are used for assessment of malnutrition risks among the elderly (> 65 years old): low risk, ≥ 3.6 g/dL; medium risk, 3.0-3.5 g/dL; high risk, < 3.0 g/dL [39]. Using these criteria, frequency of hypoalbuminemia was determined by sex and age in individuals with MD, and the results were compared with levels in healthy individuals as reported in the annual nationwide National Health and Nutrition Survey (NHNS) in Japan (2008) [40]. A total of 30,135 participants in the NHNS were selected from among approximately 3,838 households and household members using stratified random sampling. Physical condition, nutritional intake status, and daily living habits were analyzed by sex and age cohorts made public by the Ministry of Health, Labor, and Welfare. During the NHNS, blood tests were conducted for 4,451 people (1,819 men, 2,632 women) > 20 years old. Matching of participants in the NHNS with subjects in the present study was not possible. Therefore, the frequencies and mean serum albumin levels for each sex and age group (20-29, 30-39, 40-49, 50-59, 60-69, and ≥ 70 years) were used as a reference.

Statistical analysis

Skewed data (CRP) were log-transformed before analyses. Sex and timing of disability onset were used as binary variables.

Continuous variables are reported as mean ± standard deviation (SD) or median (range). Effect size was used to determine the magnitude of the difference in serum albumin levels between individuals with MD and healthy individuals in the NHNS. The serum albumin levels among individuals with MD were placed into three categories: ≥ 3.6 g/dL, 3.0-3.5 g/dL, and < 3.0 g/dL. The distributions of individuals within these three categories were compared between individuals with MD and healthy individuals in the NHNS. Using sex- and age-adjusted analyses, correlation coefficients were calculated to examine associations between serum albumin levels and each of the following variables: weight, body mass index (BMI), weight change ratio, TSF, MAC, MAMC, MAMA, calf circumference, relative daily energy intake, relative daily protein intake, WBC, RBC, Hb, Ht, PLT, TP, AST, ALT, γ-GTP, TC, HDL-C, LDL-C, TG, HbA_{1c}, CRP, IgG, medication use (anticonvulsants and/or major and minor tranquilizers, others), and timing of disability onset (binary). Significant variables ($P < 0.05$) were used in multivariable analyses using the forced entry method with serum albumin level as the dependent variable and sex, age, BMI, MAMA, calf circumference, relative daily energy intake, Hb, PLT, HDL-C, LDL-C, HbA_{1c}, log CRP, IgG, medication use, timing of disability onset, and facilities as dummy variables. Facility 1 was used as a reference, and four dummy variables were created for Facilities 2 through 5. Ht and MAMC were excluded due to the high cross correlation with Hb and MAMA, respectively. TP and TC were excluded due to containing serum albumin and HDL-C, respectively. Based on the Youden index, the cut-off value in the receiver operating characteristic (ROC) curve was determined as the point at which the value determined by the formula (sensitivity + specificity - 1) becomes the maximum value.

All statistical analyses were carried out using SPSS (ver. 23.0; IBM Corp., Armonk, NY, USA). All statistical tests were two-sided. Significance was fixed at the $P = 0.05$ level.

Table 1. Characteristics of 249 individuals with motor disabilities at five institutions in Ibaraki, Japan

	Individuals with motor disability (n = 249)		*P*-value
	Male (n = 144)	Female (n = 105)	
Age (yrs)	51.4 ± 12.2[1)]	51.4 ± 12.3	0.99[2)]
Height (cm)	160.7 ± 9.3	150.5 ± 8.8	< 0.001[2)]
Weight (kg)	51.4 ± 11.3	46.6 ± 11.6	0.001[2)]
Body mass index (kg/m²)	19.8 ± 3.8	20.6 ± 4.9	0.17[2)]
Mid-arm muscle circumference (cm)	21.4 ± 3.9	20.0 ± 4.0	0.004[2)]
Mid-arm muscle area (cm²)	37.7 ± 12.2	33.0 ± 11.6	0.002[2)]
Relative daily energy intake (kcal/kg)	26.4 ± 8.7	25.2 ± 9.1	0.34[2)]
Relative daily protein intake (g/kg)	1.1 ± 0.3	1.1 ± 0.4	0.39[2)]
Serum albumin (g/dL)	4.0 ± 0.4	3.8 ± 0.5	0.01[2)]
Red blood cells (× 10^6/μL)	4.4 ± 0.6	4.4 ± 3.4	0.95[2)]
White blood cells (× 10^3/μL)	6.1 ± 1.9	6.1 ± 2.1	0.93[2)]
Hemoglobin (g/dL)	13.6 ± 1.7	12.1 ± 1.7	< 0.001[2)]
Total protein (g/dL)	7.0 ± 0.7	6.9 ± 0.6	0.08[2)]
AST (IU/L)	21.2 ± 9.3	19.2 ± 7.3	0.08[2)]
ALT (IU/L)	22.8 ± 15.0	15.0 ± 9.2	< 0.001[2)]
γ-GTP (IU/L)	43.0 ± 37.3	34.5 ± 34.6	0.07[2)]
Total cholesterol (mg/dL)	165.9 ± 31.7	187.1 ± 36.3	< 0.001[2)]
HDL cholesterol (mg/dL)	48.8 ± 14.4	53.5 ± 14.4	0.01[2)]
LDL cholesterol (mg/dL)	97.3 ± 28.0	110.1 ± 28.8	0.001[2)]
Immunoglobulin G (mg/dL)	1,422.7 ± 382.4	1,407.3 ± 374.2	0.75[2)]
C-reactive protein (mg/dL) (raw data)	0.95 ± 2.81	0.66 ± 1.62	0.34[2)]
Log C-reactive protein (mg/dL)	-0.69 ± 0.72	-0.86 ± 0.74	0.07[2)]
Cases using certain medications (n)	137 (95.1%)	97 (92.4%)	0.37[3)]

ALT, alanine aminotransferase; AST, aspartate transaminase; HDL, high-density lipoprotein; LDL, low-density lipoprotein; γ-GTP, gamma-glutamyl transpeptidase.
1) Mean ± SD or n (%)
2) T-test, 3) χ^2-test.

RESULTS

General characteristics

In the NHNS in Japan (2008), 30,135 participants were identified using stratified random sampling, with 7,998 completing physical examinations, 4,451 completing blood tests, 9,129 completing assessment of nutritional intake status, and 8,557 completing assessment of daily living habits. The age distribu-

Table 2. Serum albumin levels among 249 individuals with motor disabilities at five institutions in Ibaraki, Japan

	Total		20-29 yrs		30-39 yrs		40-49 yrs		50-59 yrs		60-69 yrs		≥ 70 yrs	
	Individuals with motor disabilities n (%)	Ref[1)] (%)	Individuals with motor disabilities n (%)	Ref[1)] (%)	Individuals with motor disabilities n (%)	Ref[1)] (%)	Individuals with motor disabilities n (%)	Ref[1)] (%)	Individuals with motor disabilities n (%)	Ref[1)] (%)	Individuals with motor disabilities n (%)	Ref[1)] (%)	Individuals with motor disabilities n (%)	Ref[1)] (%)
Male														
Total	144 (100.0)		8 (100.0)		21 (100.0)		27 (100.0)		43 (100.0)		38 (100.0)		7 (100.0)	
< 3.0 g/dL[2)]	3 (0.0)	(0.0)	0 (0.0)	(0.0)	0 (0.0)	(0.0)	1 (3.7)	(0.0)	1 (2.3)	(0.0)	1 (2.6)	(0.0)	0 (0.0)	(0.3)
3.0-3.5 g/dL[2)]	14 (12.5)	(1.0)	1 (12.5)	(0.0)	2 (9.5)	(0.0)	2 (7.4)	(0.0)	4 (9.3)	(0.3)	5 (13.2)	(0.2)	0 (0.0)	(2.8)
≥ 3.6 g/dL[2)]	127 (88.2)	(99.0)	7 (87.5)	(100.0)	19 (90.5)	(100.0)	24 (88.9)	(100.0)	38 (88.4)	(99.7)	32 (84.2)	(99.8)	7 (100)	(96.9)
Female														
Total	105 (100.0)		3 (100.0)		15 (100.0)		31 (100.0)		26 (100.0)		23 (100.0)		8 (100.0)	
< 3.0 g/dL[2)]	4 (3.8)	(0.0)	0 (0.0)	(0.0)	2 (13.3)	(0.0)	0 (0.0)	(0.0)	0 (0.0)	(0.0)	1 (4.3)	(0.2)	1 (12.5)	(0.0)
3.0-3.5 g/dL[2)]	21 (20.0)	(0.4)	0 (0.0)	(0.7)	1 (6.7)	(0.9)	4 (12.9)	(0.0)	8 (30.8)	(0.2)	7 (30.4)	(0.2)	1 (12.5)	(0.6)
≥ 3.6 g/dL[2)]	80 (76.2)	(99.6)	3 (100.0)	(99.3)	11 (78.6)	(99.1)	27 (87.1)	(100.0)	18 (69.2)	(99.8)	15 (65.2)	(99.6)	6 (75.0)	(99.4)

1) Reference: The National Health and Nutrition Survey for healthy individuals, 2008 [40]
2) In Japan, the following indicators are used to assess the malnutrition risk level among the elderly: low risk, ≥ 3.6 g/dL; medium risk, 3.0-3.5 g/dL; high risk, < 3.0 g/dL [39].

tions of those who completed the blood tests were as follows: 20-29 years, n = 245; 30-39 years, n = 516; 40-49 years, n = 502; 50-59 years, n = 794; 60-69 years, n = 1 108; and ≧ 70 years, n = 1,286.

The sample included 144 men (mean age, 51.4 ± 12.2 years) and 105 women (mean age, 51.4 ± 12.3 years) (Table 1). A median 30 (range: 26-30) men and 20 (range: 18-25) women participated in each institution. The most common primary cause of MD was CP (n = 98), followed by cerebrovascular disease (n = 50) and brain contusion (n = 20). Early-stage MD onset was present in 101 (40.6%) individuals, and 148 (59.4%) individuals had MD onset in adulthood and later. In the present study, approximately 60% of individuals had mastication disorders and dysphagia, and the mean meal consumption rate was 89% (range: 30-100%). Among all target individuals (n = 249), eight (3.2%) had chronic kidney disease, 30 (12.0%) had liver disease, three (1.2%) had thyroid dysfunction, and 20 (8.0%) had bowel disease. Among the 42 individuals with hypoalbuminemia, no participants had any of these conditions.

Serum albumin levels

The mean serum albumin levels were 4.0 ± 0.4 g/dL for men and 3.8 ± 0.5 g/dL for women, which were lower than those in the NHNS for the same age cohort (4.5 ± 0.3 g/dL for men, 4.5 ± 0.2 g/dL for women) (Table 2). When the SD of the serum albumin level in individuals with MD was converted to 0.5, the difference in means between healthy individuals in the NHNS and individuals with MD in the present study was 0.6, which was greater than the SD, indicating a large difference in mean serum albumin levels between these groups. Low serum albumin levels (≦ 3.5 g/dL) were present in 17 (11.8%) of the 144 men and 25 (23.8%) of the 105 women. In the analyses by sex and age, compared with healthy individuals, low serum albumin levels were observed more frequently in all individuals with MD, with the exception of men aged ≧ 70 years and women aged 20-29 years.

Correlates of the serum albumin level

Table 4. Correlates of serum albumin level on multivariable analyses among 249 individuals with motor disabilities at five institutions in Ibaraki, Japan

Correlates	(Dependent variable: Serum albumin)		
	β	*P*-value	VIF
Sex (male: 1, female: 0)	0.143	0.004	1.167
Age (yrs)	-0.005	0.004	1.289
Body mass index (kg/m^2)	-0.007	0.421	3.803
Mid-arm muscle area (cm^2)	0.001	0.740	1.983
Calf circumference (cm)	0.017	0.015	2.797
Relative daily energy intake (kcal/kg)	0.007	0.010	1.551
Hemoglobin (g/dL)	0.076	< 0.001	1.418
Blood platelet count (× 10^3/μL)	0.013	< 0.001	1.253
HDL cholesterol (mg/dL)	0.008	< 0.001	1.248
LDL cholesterol (mg/dL)	0.001	0.054	1.299
HbA_{1c} (%)	0.068	0.022	1.178
Log C-reactive protein (mg/dL)	-0.163	< 0.001	1.351
Immunoglobulin G (mg/dL)	< 0.001	0.348	1.195
Anticonvulsants and/or major tranquilizers	-0.056	0.183	1.197
Onset of disability (early stage: 1, adulthood and later: 0)	0.017	0.699	1.297
Facility 2 dummy[1)]	-0.061	0.338	1.741
Facility 3 dummy[1)]	-0.097	0.129	1.760
Facility 4 dummy[1)]	-0.043	0.517	1.835
Facility 5 dummy[1)]	-0.129	0.043	1.704
Adjusted R-square		0.49	

HbA_{1c}, glycated hemoglobin; HDL, high-density lipoprotein; LDL, low-density lipoprotein; VIF, variance inflation factor.
[1)] Facility 1: reference

Of the 33 variables investigated in the sex- and age-adjusted analyses, 16 were significantly correlated with serum albumin level, including CRP level, medication, and timing of disability onset (Table 3).

In the multivariable analysis, subsequent factors were independently and significantly correlated with low serum albumin levels, including female sex, advanced age, low calf circumference, low relative daily energy intake, low Hb, low PLT, low HDL-C, low HbA_{1c}, and high CRP levels (Table 4). Standardized

Table 3. Sex- and age-adjusted analyses of serum albumin level among 249 individuals with motor disabilities at five institutions in Ibaraki, Japan

Variable	Correlation coefficient	Variable	Correlation coefficient	Variable	Correlation coefficient
Weight (kg)	0.23	Relative daily protein intake (g/kg)	0.25	HDL cholesterol (mg/dL)	0.42**
Body mass index (kg/m^2)	0.27*	White blood cells (× 10^3/μL)	0.25	LDL cholesterol (mg/dL)	0.29*
Weight change ratio for a month (%)	0.25	Red blood cells (× 10^6/μL)	0.26	Triglyceride (mg/dL)	0.27
Weight change ratio for 3 months (%)	0.24	Hemoglobin (g/dL)	0.42**	HbA_{1c} (%)	0.32**
Weight change ratio for 6 months (%)	0.26	Hematocrit (%)	0.43**	C-reactive protein (mg/dL)	-0.48**
Triceps skinfold thickness (mm)	-0.27	Blood platelet count (× 10^3/μL)	0.36**	(logarithmic transformation)	
Mid-arm circumference (cm)	0.26	Total protein (g/dL)	0.62**	Immunoglobulin G (mg/dL)	0.28*
Mid-arm muscle circumference (cm)	0.29*	AST (GOT) (IU/L)	0.25	Anticonvulsants and/or major tranquilizers	-0.31*
Mid-arm muscle area (cm^2)	0.30*	ALT (GPT) (IU/L)	0.26	Minor tranquilizers	-0.25
Calf circumference (cm)	0.29*	γ-GTP (IU/L)	0.25	Other medications[1)]	-0.27
Relative daily energy intake (kcal/kg)	0.28*	Total cholesterol (mg/dL)	0.39**	Onset of disability	0.28
				(early stage:1, adulthood and later: 0)	

ALT, alanine aminotransferase; AST, aspartate transaminase; GOT, glutamic-oxaloacetic transaminase; GPT, glutamic-pyruvate transaminase; HbA_{1c}, glycated hemoglobin; HDL, high-density lipoprotein; LDL, low-density lipoprotein; γ-GTP, gamma-glutamyl transpeptidase.
[1)] Medications other than anticonvulsants and/or major tranquilizers and minor tranquilizers (i.e., gastrointestinal drugs, drugs for the common cold, cardiovascular medication).
** P < 0.001, * P < 0.05.

beta values showed that, among these factors, Hb had the strongest correlation (0.321), followed by CRP (-0.279) and HDL-C (0.279). The cut-off value in the ROC curve using the Youden index was 0.325. Considering the frequency of hypoalbuminemia using this cut-off value, 27 (31.0%) individuals exhibited high CRP levels (≥ 0.325 mg/dL) while 15 (9.3%) individuals exhibited normal CRP levels (< 0.325 mg/dL).

DISCUSSION

This study investigated serum albumin levels and their correlates as well as the effects of onset timing in institutionalized individuals with MD and demonstrated that the prevalence of hypoalbuminemia was greater in both men and women with MD than in healthy individuals. Moreover, inflammation was a strong negative correlate of serum albumin level, whereas MD onset timing did not affect serum albumin level.

There was a large difference in mean serum albumin levels between healthy individuals and individuals with MD, as indicated by the conversion and comparison of the SD. In addition, hypoalbuminemia was observed in 11.8% of men and 23.8% of women in the present sample, which were greater than the proportions of healthy individuals aged 50-59 years (0.3% of men, 0.2% of women) in the NHNS from the same time period. Several factors can reduce serum albumin levels, including insufficient protein intake. Due to mastication disorders and dysphagia, individuals with MD might not have sufficient food and calorie intake [3-7], which could augment degradation of body proteins and lead to reduced serum albumin levels. Moreover, the mean meal consumption rate was approximately 9% lower in those with mastication disorders and dysphagia (approximately 86%) than in those without (approximately 95%). However, all participants in this study received meal support as institutional residents; therefore, no differences in serum albumin level due to swallowing impairments (mastication disorders and dysphagia) were observed.

Second, use of medications, particularly antiepileptic drugs, can decrease the capability to synthesize hepatic albumin, and use anticonvulsants and/or major tranquilizers and other medications has been associated with low serum albumin levels in men with ID [23]; 234 of 249 individuals (94%) in the present study were taking medications. Albumin is synthesized only in liver cells, and its production is quite constant in healthy individuals; therefore, just a small intracellular deposit of protein is needed [14]. However, although the negative correlation between serum albumin levels and use of medications was significant in the sex- and age-adjusted analyses in the present study, it was not significant in the multivariable analysis.

The correlates of low serum albumin level in the present study included female sex, advanced age, low calf circumference, low relative daily energy intake, low Hb, low PLT, low HDL, low HbA_{1c}, and high log CRP levels. The lower serum albumin level in women than in men in the present study might be explained by menopause and aging, which affect total serum albumin levels [41], particularly considering that 57 of the 105 women in the present study were older than 50 years. However, the mean serum albumin levels for both men (4.0 g/dL) and women (3.8 g/dL) in the present study were lower than those of the general Japanese population of similar age (50-59 years) in the NHNS (4.5 g/dL, men and women).

Appropriate Hb, PLT, HDL-C, and HbA_{1c} levels signify overall good nutritional status, and it is reasonable to assume that these factors are not direct causes of low serum albumin levels but rather share the same nutritional basis as serum albumin; however, the individual mechanisms remain unclear.

Appropriate dietary intake is important to maintain good nutritional status. When relative daily energy intake and relative daily protein intake were considered in the sex-age adjusted analyses, only relative daily energy intake was significantly correlated with serum albumin levels. This suggests that relative daily energy intake reflects albumin levels.

CRP is a sensitive marker of inflammation [42], and CRP levels were negatively associated with serum albumin in a number of studies [43-49]. In the present study, the negative correlation between CRP and serum albumin levels was significant in both the sex- and age-adjusted and multivariable analyses, similar to results from a previous study on individuals with ID [23]. A negative correlation with inflammation was also observed in individuals with MD. The cut-off value in the ROC curve using the Youden index was 0.325. The area under the curve was 0.7, and the discernment was mostly favorable. The prevalence of hypoalbuminemia in those with high CRP levels was about three times more frequent as compared to those with normal CRP levels. Participants with hypoalbuminemia individuals may suffer from general malnutrition since 9% had normal CRP levels. Chronic inflammatory disease augments proteolysis in the body, thereby reducing the serum albumin level. In the current study, comorbid chronic inflammatory diseases of the digestive or respiratory system were observed in 50 individuals with lower mean serum albumin levels (3.4 ± 0.4 g/dL) compared to individuals without chronic inflammatory diseases (4.1 ± 0.4 g/dL), suggesting that low serum albumin levels may be due to the presence of chronic inflammatory diseases.

Although the timing of MD onset was not significantly correlated with serum albumin levels in the sex- and age-adjusted analyses in the present study, the mean serum albumin level did not differ by timing of MD onset (3.96 g/dL in the early stage and 3.84 g/dL in adulthood and later).

There were several limitations to this study. First, we compared our data to published data from the general population. Owing to missing details, the characteristics of the study population in the national survey could not be compared with those of the study population. Second, although height, current weight, subcutaneous fat thickness, and circumferences were measured using standard procedures, past weight was not; however, measurement conditions were generally consistent. At each facility, weight was normally measured prior to bathing with all clothes removed. Third, although the types and number of medications used at the time of this study were ascertained, it is possible that temporary medications such as cold medicines were included or that long-term medications ceased just before the study were not included. Fourth, the most common primary cause of MD was CP, followed by stroke and brain contusion. Despite diverse participant backgrounds, determination of the effects of MD on nutritional status was a priority in the present study, regardless of background. Finally, the individuals in the present study were institutionalized and under controlled nutritional management; therefore, generalizing the findings to individuals with MD undergoing home-based care should be undertaken with caution.

The results of this study suggest that institutionalized individuals with MD have lower mean serum albumin levels and higher percentages of hypoalbuminemia than healthy individuals. The correlation assessments indicate that inflammation should be considered for patients with MD. In addition to inflammation, female sex, advanced age, low calf circumference, low relative daily energy intake, as well as low Hb, low PLT, low HDL-C, and low HbA_{1c} levels appear to be correlated with low serum albumin levels. Regarding hypoalbuminemia in institutionalized individuals with MD, women should receive particular consideration. Using the present study as a guideline, further research is necessary to analyze the association between serum albumin levels and prognosis.

ACKNOWLEDGMENTS

The authors wish to thank the department head and staff members of each facility who provided help in conducting this research.

CONFLICTS OF INTEREST

The authors declare no potential conflicts of interests.

REFERENCES

1. International Neuromodulation Society (US). Motor impairment [Internet]. San Francisco (CA): International Neuromodulation Society; 2012 [updated 2014 Jan 29; cited 2016 May 10]. Available from:.
2. Karagiozoglou-Lampoudi T, Daskalou E, Vargiami E, Zafeiriou D. Identification of feeding risk factors for impaired nutrition status in paediatric patients with cerebral palsy. Acta Paediatr 2012;101: 649-54.
3. Rogers B. Feeding method and health outcomes of children with cerebral palsy. J Pediatr 2004;145:S28-32.
4. Reilly S, Skuse D. Characteristics and management of feeding problems of young children with cerebral palsy. Dev Med Child Neurol l992;34:379-88.
5. Sullivan PB, Juszczak E, Lambert BR, Rose M, Ford-Adams ME, Johnson A. Impact of feeding problems on nutritional intake and growth: Oxford Feeding Study II. Dev Med Child Neurol 2002;44: 461-7.
6. Sura L, Madhavan A, Carnaby G, Crary MA. Dysphagia in the elderly: management and nutritional considerations. Clin Interv Aging 2012;7:287-98.
7. Rowat A. Malnutrition and dehydration after stroke. Nurs Stand 2011;26:42-6.
8. Corrigan ML, Escuro AA, Celestin J, Kirby DF. Nutrition in the stroke patient. Nutr Clin Pract 2011;26:242-52.
9. Day SM, Strauss DJ, Vachon PJ, Rosenbloom L, Shavelle RM, Wu YW. Growth patterns in a population of children and adolescents with cerebral palsy. Dev Med Child Neurol 2007;49:167-71.
10. Smith BJ, Bachrach SJ. An unexpected finding in an eight-year-old child with cerebral palsy and weight loss. J Natl Med Assoc 2006;98: 280-3.
11. Jönsson AC, Lindgren I, Norrving B, Lindgren A. Weight loss after stroke: a population-based study from the Lund Stroke Register. Stroke 2008;39:918-23.
12. Patterson CH. Questions & answers from the JCAHO. What new standards are in store for 2000? Nurs Manage 1999;30:9.
13. Wallace JI, Schwartz RS, LaCroix AZ, Uhlmann RF, Pearlman RA. Involuntary weight loss in older outpatients: incidence and clinical significance. J Am Geriatr Soc 1995;43:329-37.
14. Bernardi M, Ricci CS, Zaccherini G. Role of human albumin in the management of complications of liver cirrhosis. J Clin Exp Hepatol 2014;4:302-11.
15. Barron ME, Wilkes MM, Navickis RJ. A systematic review of the comparative safety of colloids. Arch Surg 2004;139:552-63.
16. Naber TH, de Bree A, Schermer TR, Bakkeren J, Bär B, de Wild G, Katan MB. Specificity of indexes of malnutrition when applied to apparently healthy people: the effect of age. Am J Clin Nutr 1997;65:1721-5.
17. Friedman AN, Fadem SZ. Reassessment of albumin as a nutritional marker in kidney disease. J Am Soc Nephrol 2010;21:223-30.
18. Herrmann FR, Safran C, Levkoff SE, Minaker KL. Serum albumin level on admission as a predictor of death, length of stay, and readmission. Arch Intern Med 1992;152:125-30.
19. Eljaiek R, Dubois MJ. Hypoalbuminemia in the first 24h of admission is associated with organ dysfunction in burned patients. Burns 2013;39:113-8.
20. Wu AW, Yasui Y, Alzola C, Galanos AN, Tsevat J, Phillips RS, Connors AF Jr, Teno JM, Wenger NS, Lynn J. Predicting functional status outcomes in hospitalized patients aged 80 years and older. J Am Geriatr Soc 2000;48:S6-15.
21. Jensen GL, Kita K, Fish J, Heydt D, Frey C. Nutrition risk screening characteristics of rural older persons: relation to functional limitations and health care charges. Am J Clin Nutr 1997;66:819-28.
22. Zuliani G, Romagnoni F, Volpato S, Soattin L, Leoci V, Bollini MC, Buttarello M, Lotto D, Fellin R. Nutritional parameters, body composition, and progression of disability in older disabled residents living in nursing homes. J Gerontol A Biol Sci Med Sci 2001;56:M212-6.
23. Ohwada H, Nakayama T. The distributions and correlates of serum albumin levels in institutionalised individuals with intellectual and/or motor disabilities. Br J Nutr 2008;100:1291-6.
24. Hisamichi S. Community screening programs of cancer and cardiovascular diseases in Japan. J Epidemiol 1996;6:S159-63.
25. Lohman TG, Roche AF, Martorell R. Anthropometric Standardization Reference Manual. Champaign (IL): Human Kinetics Books; 1988.
26. Thangawng AL, Kim JS, Golden JP, Anderson GP, Robertson KL, Low V, Ligler FS. A hard microflow cytometer using groove-generated sheath flow for multiplexed bead and cell assays. Anal Bioanal Chem 2010;398:1871-81.
27. Malkiel S, Jeganathan V, Wolfson S, Manjarrez Orduño N, Marasco E, Aranow C, Mackay M, Gregersen PK, Diamond B. Checkpoints for autoreactive B cells in the peripheral blood of lupus patients assessed by flow cytometry. Arthritis Rheumatol 2016;68:2210-20.
28. Jung HJ, Ahn HI, Park JY, Ho MJ, Lee DR, Cho HR, Park JS, Choi YS, Kang MJ. Improved oral absorption of tacrolimus by a solid dispersion with hypromellose and sodium lauryl sulfate. Int J Biol Macromol 2016;83:282-7.
29. Xu L, Meng MQ, Liu R, Wang K. Robust peak detection of pulse

waveform using height ratio. Conf Proc IEEE Eng Med Biol Soc 2008;2008:3856-9.
30. Schiavone NM, Sarver SA, Sun L, Wojcik R, Dovichi NJ. High speed capillary zone electrophoresis-mass spectrometry via an electrokinetically pumped sheath flow interface for rapid analysis of amino acids and a protein digest. J Chromatogr B Analyt Technol Biomed Life Sci 2015;991:53-8.
31. Loh TP, Leong SM, Sethi SK. High concentration of IgM-κ paraprotein causes over-estimation of serum total protein by certain biuret method. Clin Chem Lab Med 2013;51:e205-7.
32. Xu Y, Wang L, Wang J, Liang H, Jiang X. Serum globulins contribute to the discrepancies observed between the bromocresol green and bromocresol purple assays of serum albumin concentration. Br J Biomed Sci 2011;68:120-5.
33. Eto A, Shiki A, Chikaura Y, Oka T, Nakano NI. Multienzyme control serum (Seraclear-HE) containing human enzymes from established cell lines and other sources. 1: preparation and properties. Clin Chem 1995;41:872-80.
34. Music M, Dervisevic A, Pepic E, Lepara O, Fajkic A, Ascic-Buturovic B, Tuna E. Metabolic syndrome and serum liver enzymes level at patients with type 2 diabetes mellitus. Med Arch 2015;69:251-5.
35. Can M, Acikgoz S, Mungan G, Ugurbas E, Ankarali H, Sumbuloglu V, Demirtas S, Karaca L. Is direct method of low density lipoprotein cholesterol measurement appropriate for targeting lipid lowering therapy? Int J Cardiol 2010;142:105-7.
36. Makino M, Hayashi Y, Ito H, Morikawa A. Principal component analysis for microalbuminuria in patients with noninsulin-dependent, maturity-onset diabetes mellitus. Rinsho Byori 1990;38:65-70.
37. Roh EJ, Lim JW, Ko KO, Cheon EJ. A useful predictor of early atherosclerosis in obese children: serum high-sensitivity C-reactive protein. J Korean Med Sci 2007;22:192-7.
38. Alley ML, Haines DM, Smith GW. Short communication: evaluation of serum immunoglobulin G concentrations using an automated turbidimetric immunoassay in dairy calves. J Dairy Sci 2012;95:4596-9.
39. Sugiyama M. The revolution of nutritional care and management in the revised long-term care insurance. J Natl Inst Public Health 2006;55:32-41.
40. Current State of the National Health and Nutrition: The National Health and Nutrition Survey in Japan 2008. Tokyo: Dai-ichi Shuppan Co.; 2011.
41. Sokoll LJ, Dawson-Hughes B. Effect of menopause and aging on serum total and ionized calcium and protein concentrations. Calcif Tissue Int 1989;44:181-5.
42. Ridker PM, Glynn RJ, Hennekens CH. C-reactive protein adds to the predictive value of total and HDL cholesterol in determining risk of first myocardial infarction. Circulation 1998;97:2007-11.
43. Ikizler TA, Wingard RL, Harvell J, Shyr Y, Hakim RM. Association of morbidity with markers of nutrition and inflammation in chronic hemodialysis patients: a prospective study. Kidney Int 1999;55:1945-51.
44. Nakamura K, Moriyama Y, Kariyazono H, Hamada N, Toyohira H, Taira A, Yamada K. Influence of preoperative nutritional state on inflammatory response after surgery. Nutrition 1999;15:834-41.
45. Fein PA, Mittman N, Gadh R, Chattopadhyay J, Blaustein D, Mushnick R, Avram MM. Malnutrition and inflammation in peritoneal dialysis patients. Kidney Int Suppl 2003:S87-91.
46. Danielski M, Ikizler TA, McMonagle E, Kane JC, Pupim L, Morrow J, Himmelfarb J. Linkage of hypoalbuminemia, inflammation, and oxidative stress in patients receiving maintenance hemodialysis therapy. Am J Kidney Dis 2003;42:286-94.
47. Fernández-Reyes MJ, Alvarez-Ude F, Sánchez R, Mon C, Iglesias P, Díez JJ, Vázquez A. Inflammation and malnutrition as predictors of mortality in patients on hemodialysis. J Nephrol 2002;15:136-43.
48. Kaysen GA, Greene T, Daugirdas JT, Kimmel PL, Schulman GW, Toto RD, Levin NW, Yan G; HEMO Study Group. Longitudinal and cross-sectional effects of C-reactive protein, equilibrated normalized protein catabolic rate, and serum bicarbonate on creatinine and albumin levels in dialysis patients. Am J Kidney Dis 2003;42:1200-11.
49. Haupt W, Holzheimer RG, Riese J, Klein P, Hohenberger W. Association of low preoperative serum albumin concentrations and the acute phase response. Eur J Surg 1999;165:307-13.