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# In addition to malnutrition and renal function impairment, anemia is associated with hyponatremia in the elderly

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#### ABSTRACT

Hyponatremia is the most common electrolyte abnormality among the elderly living in long-term care facilities. In this study, we investigate the associated factors of hyponatremia, and its association with anemia in the institutionalized elderly in Taiwan. A total of 414 participants aged 65 years and above were recruited from eight long-term care facilities in 2002-2003. Baseline characteristics, medical records, and biomarkers were obtained. Hyponatremia was defined as a serum Na-concentration < 135 mmol/l. Relationships between hyponatremia and the demographic and laboratory characteristics were tested using multiple logistic and linear regression analyses. The prevalence of hyponatremia and anemia was 14.7% and 56.0%, respectively. Anemia, hypouricemia, and the placement of tubes (including nasogastric tube, tracheostomy tube, and Foley catheter) were significantly associated with hyponatremia after adjustment for potential confounders using multiple logistic regression analysis. The adjusted odds ratios (OR) and 95% confidence interval (95%CI) for these three factors were 3.28 (1.40-7.69), 4.98 (2.18-11.36), 9.15 (3.33-25.12), respectively. Multiple linear regression analyses also showed that serum Na concentration was significantly associated with hemoglobin, uric acid, and number of tubes. In conclusion, it was found that anemia, the placement of tubes, and hypouricemia were associated with hyponatremia in the institutionalized elderly. In those with the above conditions, serum Na concentration should be monitored.

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#### 1. Introduction

Population aging is a global phenomenon which progresses more rapidly and significantly in East and Southeast Asian countries, including Taiwan (Kinsella et al., 2001). It is estimated that the percentage of population aged 65 and over in Taiwan is 10.8% in 2010, which will reach 20% in 2025 (Council for Economic Planning and Development, 2010). The rapid population aging have caused expanding burden of care and demand for long-term care facilities. According to the survey among Taiwanese in 2000, nearly 10% of the elderly needs long-term care (Directorate-

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General of Budget Accounting and Statistics, 2000). As a result, issues regarding elderly in long-term care facilities are increasingly important.

Hyponatremia has been reported as the most common electrolyte abnormality in the elderly, and the prevalence of hyponatremia is higher among those indwelling in long-term care facilities than those living in community (Oh et al., 2005; Chua et al., 2007). Elderly patients are more prone to hyponatremia as a result of co-morbidities such as heart failure, chronic liver disease, renal insufficiency, gastrointestinal losses, chest infection, polypharmacy, and poor nutritional status (Chen et al., 2006; Chua et al., 2007; Yawar et al., 2008). Although being usually asymptomatic, hyponatremia is associated with poor long-term prognosis, in both institutionalized elderly and community-dwelling subjects (Chua et al., 2007; Sajadieh et al., 2009). Besides, hyponatremia is found to be associated with increased mortality in hospitalized individuals, and resolution of hyponatremia can

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attenuate the increased mortality risk conferred by hyponatremia (Waikar et al., 2009). Therefore, it is important to identify potential risk factors of hyponatremia.

Anemia is also frequent in the elderly, especially those who lived in long-term care facilities (Artz et al., 2004). In the anemic elderly, the possible etiologies include malnutrition, renal insufficiency, chronic inflammation, primary disorders of hematopoiesis, undiscovered blood loss, or age-associated reduction in bone marrow cellularity (Mitrache et al., 2001; Steensma and Tefferi, 2007). The clinical importance of anemia is highly related to the poor outcomes such as prolonged hospitalization or higher mortality rate (Endres et al., 2009; Riva et al., 2009).

Since previous studies evaluating hyponatremia and anemia in the elderly are little (Chen et al., 2006), the purpose of this study was to investigate the associating factors of hyponatremia in the institutionalized elderly, and the possible relationship between hyponatremia and anemia.

#### 2. Subjects and methods

#### 2.1. Study subjects

We conducted a cross-sectional study of institutionalized elderly in 2002–2003. The target population was residents living in eight long-term care facilities in Taichung City, Taiwan, as in the previous report (Lin et al., 2010). Subjects aged 65 years and older (age range: 65–101 years) were recruited. Thus, a total of 414 participants were enrolled (men = 180, mean age = 77.0  $\pm$  6.7 years; women = 234, mean age = 79.8  $\pm$  7.1 years). Ethics approval for patient recruitment and data analyses was obtained from the Institutional Review Board of the China Medical University Hospital. All participants gave their written informed consent.

### 2.2. Anthropometric measurements

All of the demographic information and health care records were collected by trained staffs as previous study. In brief, they measured body weight (to the nearest 0.1 kg), body height and waist circumference (WC) (to the nearest 0.1 cm). WC was taken at the midway point between the inferior margin of the rib cage and the iliac crest in a horizontal plane. Body mass index (BMI) was calculated as body weight (kg) divided by height squared (m²). The presence of pressure ulcer was evaluated by registered nurse using the National Pressure Ulcer Advisory Panel (NPUAP) staging system (NPUAP, 1997). The placement of any tubes (nasogastric tube, tracheostomy tube, or Foley catheter) was also recorded by the same staff.

#### 2.3. Laboratory examinations and performance status

A venous blood sample was taken after a 12-h fast for the determination of hemoglobin, albumin, total cholesterol (TC), triglyceride (TG), serum creatinine, uric acid, and electrolytes (Na, K, and Cl) concentration. The laboratory data was obtained using a biochemical autoanalyzer (Beckman Coulter, Fullerton, CA, USA) at the Clinical Laboratory Department, China Medical University Hospital, Taichung, Taiwan. The performance status was assessed according to the definition of the Eastern Cooperative Oncology Group (ECOG) (Oken et al., 1982) in terms of five categories, from 0 (fully active) to 4 (completely disabled).

In this study, hyponatremia was defined with the serum Na concentration < 135 mmol/l. Following the definition of the World Health Organization (WHO) criteria, anemia was set as serum hemoglobin concentration < 13 g/dl in men or <12 g/dl in women. Central obesity was defined as WC  $\geq$  90 cm in men and/or WC  $\geq$  80 cm in women. Characteristics indicating malnutri-

tion were judged as follows: hypoalbuminemia (albumin <3.5~g/ dl), hypocholesterolemia TC <160~mg/dl), under-weight (BMI  $<18.5~kg/m^2)$ . Hypouricemia was defined as serum uric acid concentration <4~mg/dl (Musch and Decaux, 2001). The estimated glomerular filtration rate (eGFR) was calculated by using the modified Modification of Diet in Renal Disease Study (MDRD) equation for Chinese people, as follows:  $186\times serum$  creatinine  $[mg/dl]^{-1.154}\times age[years]^{-0.203}\times (0.742$  if female)  $\times$  (1.227 if Chinese) (Ma et al., 2006). Renal function impairment was determined by the eGFR  $<60~ml/min/1.73~m^2$ . Poor performance status was defined as ECOG score  $\geq 3$ .

#### 2.4. Statistical analysis

Data are presented as means  $\pm$  S.D. for continuous variables. Student's t-test was used to compare mean values between two groups. Proportions and categorical variables are presented as percentages; they were tested for statistical significance by using the  $\chi^2$ -test and the two-tailed Fisher's exact test. The variables with statistical significance were further tested with multiple logistic and linear regression. All statistical tests were two-sided at the p < 0.05 significance level. These statistical analyses were performed by using the PC version of the SPSS statistical software (version 13.0, SPSS Inc., Chicago, IL, USA).

#### 3. Results

The age of the participants was  $78.6 \pm 7.1$  years. The prevalence of hyponatremia was 14.7% (men: 16.7%; women: 13.2%). Table 1 shows comparisons for the anthropometric indices and biomedical markers between subjects with hyponatremia and non-hyponatremia. Subjects with hyponatremia had lower body weight, BMI, WC, hemoglobin, albumin, uric acid, and higher prevalence of underweight, anemia, hypoalbuminemia, hypocholesterolemia, hypour-

**Table 1** Baseline characteristics according to hyponatremic status, n, %, mean  $\pm$  S.D.

	0 71		
Subjects	With	Without	p
	hyponatremia	hyponatremia	
Number	61	353	
Male gender	49.2	42.5	0.331
Age (years)	$\textbf{80.0} \pm \textbf{7.1}$	$78.4 \pm 7.1$	0.107
Body height (cm)	$152.3 \pm 8.5$	$153.1 \pm 7.7$	0.436
Body weight (kg)	$46.3 \pm 9.3$	$51.1 \pm 10.8$	0.001
BMI (kg/m <sup>2</sup> )	$20.1 \pm 4.0$	$21.8 \pm 4.1$	0.003
WC (cm)	$\textbf{78.6} \pm \textbf{10.6}$	$82.5 \pm 10.6$	0.010
Hemoglobin (g/dl)	$11.2\pm1.8$	$12.0\pm1.9$	0.002
Albumin (g/dl)	$2.96 \pm 0.49$	$\textbf{3.21} \pm \textbf{0.44}$	< 0.001
TC (mg/dl)	$170.1 \pm 63.4$	$176.4 \pm 43.8$	0.348
TG (mg/dl)	$77.3 \pm 43.7$	$115.1 \pm 180.1$	0.115
BUN (mg/dl)	$19.0\pm14.9$	$18.5 \pm 11.8$	0.781
Creatinine (mg/dl)	$1.34\pm1.61$	$\boldsymbol{1.22 \pm 0.96}$	0.567
eGFR (ml/min/1.73 m <sup>2</sup> )	$97.4 \pm 52.7$	$84.5 \pm 36.1$	0.069
Uric acid (mg/dl)	$\textbf{4.70} \pm \textbf{1.97}$	$5.60 \pm 1.69$	< 0.001
K (mmol/l)	$\textbf{4.76} \pm \textbf{1.03}$	$\boldsymbol{4.23 \pm 0.72}$	< 0.001
Cl (mmol/l)	$97.6 \pm 4.7$	$106.6 \pm 3.7$	< 0.001
Underweight	34.4	19.4	0.008
Anemia	75.4	52.7	0.001
Central obesity	28.6	42.0	0.057
Hypoalbuminemia	86.9	69.4	0.005
Hypocholesterolemia	50.9	36.8	0.042
Renal function impairment	24.6	24.4	0.970
Hypouricemia	40.4	14.0	< 0.001
ECOG	$\boldsymbol{3.44 \pm 0.98}$	$2.46 \pm 1.27$	< 0.001
Poor performance status	83.6	57.2	< 0.001
Placement of any tubes	80.3	36.5	< 0.001
With nasogastric tube	76.8	27.9	< 0.001
With tracheostomy tube	19.6	6.1	0.001
With Foley catheter	32.1	15.8	0.003
Presence of pressure ulcer	10.9	3.1	0.007

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