The Journal of Nutrition, Health & Aging©
Volume 17, Number 3, 2013

SELENIUM IS INVERSELY ASSOCIATED WITH INTERLEUKIN-6 IN THE ELDERLY

C.-K. TSENG[1,7], C.-T. HO[1], H.-S. HSU[1,7], C.-H. LIN[1], C.-I. LI[2], T.-C. LI[2,4,6], C.-S. LIU[1,3,5], C.-C. LIN[1,3,5,6], W.Y. LIN[1,3,5]

1. Department of Family Medicine; 2. Medical Research, China Medical University Hospital, Taichung, Taiwan; 3. School of Medicine; 4. Graduate Institute of Biostatistics; 5. Graduate Institute of Clinical Medical Science, China Medical University, Taichung, Taiwan; 6. Institute of Health Care Administration, Asia University, Taichung, Taiwan. 7. Equal as first author; Correspondence and reprint request to: Wen-Yuan Lin MD, PhD, Department of Family Medicine, China Medical University Hospital, 2, Yuh-Der Road, Taichung 404, Taiwan. Tel.: +886-4-22052121 Ext. 4507; fax: +886-4-22361803, E-mail: wylin@mail.cmu.edu.tw

Abstract: *Background:* Selenium is an essential trace element with antioxidant property. Decreased serum selenium concentration with aging had been found in previous report. In this study, we aim to investigate the association between serum selenium and the inflammatory cytokine interleukin-6 in the elderly living in long-term care facilities in Taiwan. *Materials and Methods:* A total of 336 subjects aged 65 years and older (range of age: 65 – 101 years) were recruited from eight long-term care facilities in 2002-2003. Baseline characteristics, anthropometric indices, and biochemical data were obtained. Selenium deficiency was defined as serum selenium concentration < 80 μg/L. Multiple logistic and linear regression analyses were used to examine the relationships between selenium deficiency and interleukin-6 (divided into quartiles). *Results:* The prevalence of selenium deficiency was 35.6% in men and 43.2% in women, respectively. After adjusting for potential confounders using multiple logistic regression analysis, interleukin-6 quartiles were significantly associated with selenium deficiency. Compared to the interleukin-6 quartile I, the adjusted odds ratios of having selenium deficiency for interleukin-6 quartile II, III, IV were 1.00(0.50~2.01), 1.24 (0.62~2.50), and 2.35(1.15~4.83), respectively. The increasing odds ratios for selenium deficiency in higher interleukin-6 quartiles revealed dose-response effects ($p < 0.05$). Moreover, multiple linear regression analysis showed that serum selenium was significantly inversely associated with interleukin-6 after adjusting for potential confounders. *Conclusions:* Serum selenium was inversely associated with inflammatory cytokine interleukin-6 among elderly living in long-term care facilities in Taiwan. Monitoring serum selenium should be considered in these institutionalized elderly.

Key words: Selenium, interleukin-6, elderly, long-term care, Taiwan.

Introduction

Selenium is an essential trace element and dietary nutrient. As the key component of some antioxidant enzymes, selenium is considered to be protective against oxidative damage (1). Serum selenium concentration tends to be lower in the elderly (2, 3), especially in those with cancer and chronic diseases (4). Low serum concentration of selenium in community-dwelling elderly has been reported to be associated with increased cancer (5) and all-cause mortality (6-8). It is also found that low selenium concentration correlates to decrease performance in coordination and Alzheimer's disease among elderly (9, 10). As above, low selenium level is an important issue for elderly.

The aging process has been demonstrated to be associated with oxidative damage and increased production of inflammatory cytokines (11, 12). The inappropriate presentation of inflammatory cytokines, including tumor necrosis factor-alpha, interleukin (IL)-1, and IL-6, characterizes a chronic inflammatory state in the elderly (13). Meanwhile, it has been reported that the increase in serum inflammatory cytokines, especially IL-6, is related to the development of sarcopenia, functional disability, frailty, and increased morbidity and mortality (14-17). Elevated serum IL-6 concentration seems to be originated from declines in sex hormones, increased fat mass with age, and increased free radical generation (15).

With the antioxidant property, selenium may assist in deactivation of the inflammatory process through eliminating free radicals (18). To our knowledge, few studies have evaluated the correlations between serum selenium concentration and inflammation, as measured by serum IL-6 level, among elder population (19). Therefore, we aimed to investigate the associations of serum selenium with IL-6 in the institutionalized elderly, who are more prone to malnutrition, co-morbidities, and poor health outcomes (20).

Materials and Methods

Subjects

This cross-sectional study of institutionalized elderly was conducted in 2002-2003. Our target population was elder residents living in eight long-term care facilities in Taichung City, Taiwan, as previous reports (20-22). A total of 336 subjects aged 65 years and older (146 men and 190 women, mean age = 77.3 ± 6.9 and 80.4 ± 7.2 years, respectively) were recruited. Ethics approval for participant recruitment and data analyses was obtained from the Institutional Review Board of the China Medical University Hospital. All subjects gave their written informed consent.

Received March 23, 2012
Accepted for publication July 18, 2012

Anthropometric measurements and lifestyle behaviors

All of the demographic information, basic characteristics, and lifestyle behaviors were collected by trained staffs, as previous studies (20-22). Body weight was measured to the nearest 0.1 kilogram (kg), and body height was measured to the nearest 0.1 centimeter (cm). Body mass index (BMI) was calculated as body weight (kg) divided by height squared (m2) by the same trained staffs. Blood pressure (BP) was measured on the right arm using an appropriately sized cuff and a standard mercury sphygmomanometer in a seated position. Mean arterial blood pressure (MAP) was calculated as [(2 × diastolic BP) + systolic BP] / 3. Smoking, alcohol drinking, and betel nut chewing history were divided into 3 classes as follows: never, former and current, according to self-reported questionnaire.

Laboratory examinations

A venous blood sample was taken after a 12-hour fast for determination of white blood cell count (WBC), total cholesterol (TCHOL), triglyceride (TG), high-density lipoprotein cholesterol (HDL-C), fasting glucose, insulin, IL-6, high sensitivity C-reactive protein (hsCRP), and selenium concentration. The biochemical data was obtained using a biochemical autoanalyzer (Beckman Coulter, Fullerton, CA, USA) at the Clinical Laboratory Department, China Medical University Hospital, Taichung, Taiwan. The hsCRP levels were examined by nephelometry, a latex particle-enhanced immunoassay (TBA-200FR, Tokyo, Japan), and the inter-assay and intra-assay coefficients of variation were less than 2.0% and less than 1.9%, respectively. Selenium was measured using atomic absorption spectrophotometer (Hitachi model SSC-300 for Cr, Se), and IL-6 was measured using enzyme-linked immunosorbent assay (ELISA) kit. Selenium deficiency was defined as serum selenium concentration < 80 μg/L (23). IL-6 was divided by quartiles: < 3.86; 3.87 – 9.47; 9.48 – 32.00; > 32.01 pg/ml. The homeostasis model assessment was used to estimate the degree of insulin resistance (Homeostasis model assessment for insulin resistance, HOMA-IR = fasting insulin × fasting glucose / 22.5, where insulin in μU/ml, and glucose in mmol/l).

Units of measure

For unit conversion of total cholesterol and high-density lipoprotein cholesterol, values from mg/dl multiply by 0.0259 to receive mmol/l; for conversion of triglyceride, values from mg/dl multiply by 0.0113 to receive mmol/l; for conversion of fasting glucose, values from mg/dl multiply by 0.0555 to receive mmol/l; for conversion of insulin, values from μU/ml multiply by 6.945 to receive pmol/l; for conversion of interleukin-6, values from pg/ml multiply by 0.131 to receive IU/ml; for conversion of high sensitivity C-reactive protein, values from mg/dl multiply by 9.524 to receive nmol/l; for conversion of selenium, values from μg/l multiply by 0.0127 to receive μmol/l.

Statistical analysis

The data are presented as means and standard deviations for continuous variables. Student's t-test was used to compare mean values of variables between two groups. Proportions and categorical variables are presented as percentages, and they were tested for statistical significance using the χ2-test. Analysis of variance (ANOVA) test was used to compare the continuous variables across IL-6 quartiles. Multiple logistic and linear regression analyses were used to evaluate the association between selenium and IL-6 with adjusting for potential confounders, including age, gender, lifestyle behaviors, blood pressure, and insulin resistance. Statistically significance was set at p value < 0.05 at two sides. The SPSS statistical software (version 17.0, SPSS Inc., Chicago, IL, USA) was used to perform all these statistical analyses.

Results

The prevalence of selenium deficiency was 39.9% (men: 35.6%; women: 43.2%). Table 1 shows the differences of anthropometric indices, biomedical markers, and lifestyle behaviors between participants with or without selenium deficiency. Subjects with selenium deficiency were younger and had higher serum IL-6 level. The comparisons for basic characteristics of the participants by quartiles of IL-6 are presented in Table 2. Statistically significant differences were found among BMI, WBC, hsCRP, and serum selenium by IL-6 quartiles. Lower serum selenium concentration was found among participants in the subgroup with highest IL-6 quartile. Multiple logistic and linear regression analyses were used to adjust potential confounders relating to selenium and IL-6. After adjustment for age, gender, smoking, alcohol drinking, betel nut chewing, BMI, MAP, and HOMA-IR using multiple logistic regression analyses, the IL-6 IV group was significantly associated with selenium deficiency, as shown in Table 3 (Model 1-4). Compared to the lowest IL-6 quartile (I), the adjusted odds ratio for the highest IL-6 quartile (IV) was 2.35 (95% confidence interval: 1.15-4.83) (Table 3 Model 4). The increasing odds ratios of selenium deficiency with higher IL-6 quartile revealed dose-response effects (p = 0.015). Furthermore, we used multiple linear regression analyses to assess the relationship between IL-6 level and serum selenium level. After adjusting for potential confounders, IL-6 was inversely associated with selenium, as shown in Table 4.

Discussion

In the present study, high prevalence of selenium deficiency among elderly living in long-term care facilities in Taiwan was identified. Furthermore, we have demonstrated that serum selenium level is inversely associated with serum IL-6 level using multiple logistic and linear regression analyses. The increasing odds ratios of selenium deficiency with higher IL-6 quartile revealed dose-response effects. Population aging has

become a global phenomenon and caused increasing residents in long-term care facilities. Our findings are important for health-care providers and policy-makers because both selenium deficiency and increased IL-6 level have negative health effects in elder population.

Table 1
Baseline characteristics by selenium deficiency status

	With selenium deficiency (n = 134)	Without selenium deficiency (n = 202)	P value
Gender, male (%)	38.8	46.5	0.162
Age (year)	78.0 ± 6.9	79.8 ± 7.3	0.019
Height (cm)	152.4 ± 7.9	153.2 ± 7.9	0.318
Wight (kg)	50.6 ± 10.6	50.9 ± 11.1	0.834
BMI (kg/m^2)	21.7 ± 3.8	21.6 ± 4.4	0.884
Systolic BP (mmHg)	125.3 ± 14.6	124.2 ± 14.5	0.497
Diastolic BP (mmHg)	74.2 ± 9.5	74.7 ± 11.5	0.697
MAP (mmHg)	91.3 ± 9.9	91.2 ± 11.4	0.963
WBC (109/l)	6.69 ± 2.15	6.79 ± 2.08	0.675
TCHOL (mg/dl)	171.3 ± 40.2	176.0 ± 44.8	0.324
TG (mg/dl)	98.2 ± 57.7	121.4 ± 232.3	0.258
HDL-C (mg/dl)	51.9 ± 13.3	52.3 ± 13.8	0.826
Fasting glucose (mg/dl)	100.3 ± 27.9	103.2 ± 3.1	0.392
Insulin (μU/ml)	5.32 ± 5.50	11.64 ± 52.13	0.094
HOMA-IR	1.44 ± 2.10	4.41 ± 28.51	0.150
IL-6 (pg/ml)	75.95 ± 154.40	30.78 ± 68.68	0.002
hsCRP (mg/dl)	1.18 ± 3.01	1.30 ± 2.58	0.689
Selenium (μg/l)	48.01 ± 20.07	123.94 ± 36.03	< 0.001
Smoking			0.261
Never (%)	84.4	81.4	
Former (%)	14.8	14.9	
Current (%)	0.8	3.7	
Alcohol drinking			0.395
Never (%)	86.7	91.5	
Former (%)	11.7	7.4	
Current (%)	1.6	1.1	
Betel nut chewing			0.162
Never (%)	93.0	97.3	
Former (%)	6.3	2.1	
Current (%)	0.8	0.5	

Abbreviation: BMI, body mass index; BP, blood pressure; MAP, mean arterial blood pressure; WBC, white blood cell count; TCHOL, total cholesterol; TG, triglyceride; HDL, high-density lipoprotein cholesterol; HOMA-IR, homeostasis model assessment for insulin resistance; IL-6, interleukin-6; hsCRP. high sensitivity C-reactive protein.

Serum selenium status is sensitive to changes in dietary intake. The reference range of serum selenium concentration is quite narrow, and both excessive and insufficient selenium levels are pathogenic (23). Although experts expressed great interest in reduced selenium level and associated health issues in the past decades, most of them used a relatively low selenium value, such as dividing into quartiles, for comparison and investigation (8, 9). To our knowledge, no consistent definition regarding the cutoff value of selenium deficiency had been made yet. In our study, we decided to adopt serum selenium level at 80 μg/L for the definition of selenium deficiency according to the reference range of serum selenium concentration (23), which had been applied in some previous studies (24-26). With this definition, nearly 40% of our study population has selenium deficiency. The high prevalence of selenium deficiency corresponds to the result of previous report, that institutionalized elderly had significantly lower serum levels of selenium compared with those living in the community (2).

An inverse association between serum selenium and IL-6 is shown in this study. Elderly in subgroup of the highest IL-6 quartile had significantly lower serum selenium concentration, and the increase of selenium deficiency with higher IL-6 quartiles showed dose-response effects. Besides, we also identified a significant difference among IL-6 by selenium quartiles, and higher serum IL-6 level was found among the subgroup with lowest serum selenium quartile (data not shown). It had been found that participants with high serum selenium levels were less likely to be in the highest tertile of IL-6 concentration among community-dwelling older women (19). Our study, focusing on the institutionalized elder population, reveals a similar result to the previous research.

The association of serum selenium and IL-6 demonstrated from our findings may be derived from the anti-inflammatory and antioxidant property of selenium (18). This hypothesis could be supported by the fact that both decreased serum selenium concentration and increased serum IL-6 level are correlated to the chronic diseases with inflammatory characteristics, such as hypertension and cardiovascular disease. Previous studies showed that IL-6 is connected with hypertension through the effect of renin-angiotensin system activity (27), and it is related to the inflammatory process and mortality in patients with cardiovascular disease (28, 29). On the other hand, previous studies revealed that selenium deficiency contributes to hypertension and myocardial ischemia through an accumulation of lipid peroxides (30). Also, low serum selenium concentration was found to be associated with cardiovascular mortality in patients with acute coronary syndrome (31). Moreover, being similar to the above relationships with hypertension and cardiovascular disease, selenium and IL-6 may have connection through insulin resistance. It was found that serum IL-6 level has an inverse relationship with insulin sensitivity (32), and former researches revealed the possible association among selenium deficiency and insulin resistance (24, 33). Even though serum selenium and IL-6 are associated with some comorbidities in common, our study results indicated that the correlation between selenium and IL-6 remained significant after adjustment for blood pressure, insulin resistance, and specific lifestyle behaviors (including smoking, alcohol drinking, and betel nut chewing history). Meanwhile, chronic inflammatory diseases may be the consequences, rather than the origins of the connection between serum selenium and IL-6. Selenium deficiency may play a role on chronic inflammatory diseases through the inflammatory process, represented by activation of inflammatory cytokines such as IL-6.

Despite our findings, there are some limitations in this study. Firstly, owning to the cross-sectional nature of our study

Table 2
Characteristics among quartiles of IL-6 concentration

	IL-6 I	IL-6 II	IL-6 III	IL-6 IV	P value
Gender, male (%)	48.7	35.2	49.4	41.2	0.194
Age (year)	79.5 ± 6.7	78.7 ± 7.5	79.7 ± 7.6	78.5 ± 7.0	0.646
Height (cm)	153.5 ± 8.6	152.1 ± 7.5	153.3 ± 8.2	152.8 ± 7.3	0.659
Wight (kg)	50.8 ± 10.8	51.0 ± 11.7	52.7 ± 11.2	48.5 ± 9.5	0.085
BMI (kg/m^2)	21.5 ± 4.0	21.9 ± 4.4	22.5 ± 4.6	20.7 ± 3.5	0.047
Systolic BP (mmHg)	124.1 ± 13.9	124.8 ± 15.5	122.9 ± 4.5	127.0 ± 14.1	0.309
Diastolic BP(mmHg)	74.1 ± 11.0	73.6 ± 10.9	73.2 ± 10.0	77.2 ± 10.8	0.065
MAP (mmHg)	90.8 ± 10.6	90.6 ± 11.2	89.8 ± 10.3	93.8 ± 10.8	0.082
WBC (103/μl)	6.14 ± 1.75	6.43 ± 2.31	7.17 ± 2.07	7.21 ± 2.05	0.001
TCHOL (mg/dl)	175.8 ± 47.9	180.4 ± 44.9	175.0 ±40.5	165.2 ± 37.9	0.127
TG (mg/dl)	144.2 ±366.2	105.8 ± 61.6	106.6 ±77.8	95.4 ± 55.9	0.363
HDL-C (mg/dl)	53.4 ± 11.8	52.4 ± 13.8	51.3 ± 13.8	51.4 ± 14.7	0.754
Fasting glucose (mg/dl)	100.7 ± 23.7	103.6 ± 32.3	104.9 ±34.9	98.7 ± 25.9	0.518
Insulin (μU/ml)	9.47 ± 33.12	7.74 ± 15.98	13.25±70.73	5.69 ± 7.90	0.670
HOMA-IR	2.95 ± 12.77	2.25 ± 4.93	5.94 ± 41.27	1.61 ± 2.84	0.600
IL-6 (pg/ml)	1.60 ± 1.17	6.01 ± 1.74	16.82 ± 5.98	168.01 ± 178	<0.001
hsCRP (mg/dl)	0.66 ± 1.63	1.06 ± 2.61	1.12 ± 1.60	2.12 ± 4.13	0.005
Selenium (μg/l)	101.4 ± 53.9	103.8 ± 50.3	92.1 ± 41.8	77.9 ± 43.2	0.002
Smoking					0.704
Never (%)	81.9	87.2	78.6	82.4	
Former (%)	13.9	11.6	17.9	16.2	
Current (%)	4.2	1.2	3.6	1.4	
Alcohol drinking					0.482
Never (%)	87.5	94.2	88.1	87.8	
Former (%)	9.7	4.7	11.9	10.8	
Current (%)	2.8	1.2	0.0	1.4	
Betel nut chewing					0.551
Never (%)	93.1	97.7	96.4	94.6	
Former (%)	6.9	2.3	2.4	4.1	
Current (%)	0.0	0.0	1.2	1.4	

design, the causal relationship between serum selenium and IL-6 could not be explored. It should depend on further longitudinal cohort research. Secondly, our target subjects were Taiwanese elderly living in long-term care facilities. The generalization of these results to the community-dwelling elderly, adults, or population of other races should be cautioned. Thirdly, although the inverse relationship between serum selenium and IL-6 disclosed in our study remained significant even after additional adjustment for hypertension, diabetes mellitus, malignancies, and WBC using logistic and linear regression analyses (data not shown), we were unable to obtain and include all possible confounders, such as dietary supplement of selenium, inflammatory and infectious diseases, and other major systemic medical diseases for analyses and adjustment. Further investigation is necessary for advanced understanding of the mechanisms linking selenium and IL-6.

In conclusion, high prevalence of selenium deficiency was found among Taiwanese elderly living in long-term care facilities, and serum selenium concentration was significantly and inversely associated with serum IL-6 level. The results of the present study suggested the importance of monitoring serum selenium level in the institutionalized elderly. Future studies should aim to further clarify the linkage between selenium and IL-6, and possible benefits and disadvantages of intervention.

Table 3
The odds ratio and 95% confidence interval of having selenium deficiency according to quartiles of IL-6 concentration after adjustment for potential confounders

	Model 1	Model 2	Model 3	Model 4
IL-6 I	1.00 (reference)	1.00 (reference)	1.00 (reference)	1.00 (reference)
IL-6 II	1.15 (0.61-2.19)	1.03 (0.52-2.04)	1.03 (0.52-2.04)	1.00 (0.50-2.01)
IL-6 III	1.12 (0.59-2.13)	1.19 (0.60-2.36)	1.20 (0.60-2.41)	1.24 (0.62-2.50)
IL-6 IV	1.97 (1.04-3.72)#	2.12 (1.06-4.23)#	2.11 (1.05-4.23) #	2.35 (1.15-4.83)#

Model 1: unadjusted; Model 2: adjusted for age, gender, smoking, alcohol drinking, betel nut chewing; Model 3: Model 2 plus BMI, MAP; Model 4: Model 3 plus HOMA-IR; #: $p < 0.05$

Table 4
The coefficients (± standard error) of IL-6 level to serum selenium concentration after adjustment for potential confounders using multiple linear regression analysis

	Model 1	Model 2	Model 3	Model 4
IL-6	-0.10 (± 0.02)$	-0.11 (± 0.03)$	-0.12 (± 0.03)$	-0.12 (± 0.03)$
Age	-	0.45 (± 0.38)	0.47 (± 0.39)	0.48 (± 0.39)
BMI	-	-	-0.30 (± 0.67)	-0.20 (± 0.68)
MAP	-	-	0.45 (± 0.25)	0.45 (± 0.26)
HOMA-IR	-	-	-	0.01 (± 0.12)

Model 1: unadjusted; Model 2: adjusted for age, gender, smoking, alcohol drinking, betel nut chewing; Model 3: Model 2 plus BMI, MAP; Model 4: Model 3 plus HOMA-IR; $: $p < 0.001$

Acknowledgments: The authors declare that they have no conflicts of interest. The authors would like to than Drs. Lai, Ming-Mei and Dr. Lai, Shih-Wei for their kind assistance in subject recruitment. This study was financially supported by grants from the Department of Health, Executive Yuan, Taiwan (DOH92-TD-1024), National Science Council of Taiwan (NSC 93-2314-B-039-031), and China Medical University Hospital (DMR-96-061, DMR-98-090, and DMR-101-109).

References

1. Klein EA. Selenium: epidemiology and basic science. J. Urol. 2004;171:S50-3; discussion S3.
2. Campbell D, Bunker VW, Thomas AJ and Clayton BE. Selenium and vitamin E status of healthy and institutionalized elderly subjects: analysis of plasma, erythrocytes and platelets. Br J Nutr 1989;62:221-7.
3. Berr C, Nicole A, Godin J, Ceballos-Picot I, Thevenin M, Dartigues JF et al. Selenium and oxygen-metabolizing enzymes in elderly community residents: a pilot epidemiological study. J. Am. Geriatr. Soc. 1993;41:143-8.
4. Bates CJ, Thane CW, Prentice A and Delves HT. Selenium status and its correlates in a British national diet and nutrition survey: people aged 65 years and over. J. Trace Elem. Med. Biol. 2002;16:1-8.
5. Kornitzer M, Valente F, De Bacquer D, Neve J and De Backer G. Serum selenium and cancer mortality: a nested case-control study within an age- and sex-stratified sample of the Belgian adult population. Eur J Clin Nutr 2004;58:98-104.
6. Akbaraly NT, Arnaud J, Hininger-Favier I, Gourlet V, Roussel AM and Berr C. Selenium and mortality in the elderly: results from the EVA study. Clin. Chem. 2005;51:2117-23.
7. Ray AL, Semba RD, Walston J, Ferrucci L, Cappola AR, Ricks MO et al. Low serum selenium and total carotenoids predict mortality among older women living in the community: the women's health and aging studies. J Nutr 2006;136:172-6.
8. Lauretani F, Semba RD, Bandinelli S, Ray AL, Ruggiero C, Cherubini A et al. Low plasma selenium concentrations and mortality among older community-dwelling adults: the InCHIANTI Study. Aging Clin Exp Res 2008;20:153-8.
9. Shahar A, Patel KV, Semba RD, Bandinelli S, Shahar DR, Ferrucci L et al. Plasma selenium is positively related to performance in neurological tasks assessing coordination and motor speed. Mov Disord 2010;25:1909-15.
10. Cardoso BR, Ong TP, Jacob-Filho W, Jaluul O, Freitas MI and Cozzolino SM. Nutritional status of selenium in Alzheimer's disease patients. Br J Nutr 2010;103:803-6.
11. Bruunsgaard H and Pedersen BK. Age-related inflammatory cytokines and disease. Immunol Allergy Clin North Am 2003;23:15-39.
12. Ferrucci L, Corsi A, Lauretani F, Bandinelli S, Bartali B, Taub DD et al. The origins of age-related proinflammatory state. Blood 2005;105:2294-9.
13. Krabbe KS, Pedersen M and Bruunsgaard H. Inflammatory mediators in the elderly. Exp. Gerontol. 2004;39:687-99.
14. Ferrucci L, Harris TB, Guralnik JM, Tracy RP, Corti MC, Cohen HJ et al. Serum IL-6 level and the development of disability in older persons. J. Am. Geriatr. Soc. 1999;47:639-46.
15. Ershler WB and Keller ET. Age-associated increased interleukin-6 gene expression, late-life diseases, and frailty. Annu. Rev. Med. 2000;51:245-70.
16. Harris TB, Ferrucci L, Tracy RP, Corti MC, Wacholder S, Ettinger WH, Jr. et al. Associations of elevated interleukin-6 and C-reactive protein levels with mortality in the elderly. Am J Med 1999;106:506-12.
17. Cesari M, Kritchevsky SB, Baumgartner RN, Atkinson HH, Penninx BW, Lenchik L et al. Sarcopenia, obesity, and inflammation--results from the Trial of Angiotensin Converting Enzyme Inhibition and Novel Cardiovascular Risk Factors study. Am J Clin Nutr 2005;82:428-34.
18. Fang YZ, Yang S and Wu G. Free radicals, antioxidants, and nutrition. Nutrition 2002;18:872-9.
19. Walston J, Xue Q, Semba RD, Ferrucci L, Cappola AR, Ricks M et al. Serum antioxidants, inflammation, and total mortality in older women. Am J Epidemiol 2006;163:18-26.
20. Lin WY, Huang HY, Liu CS, Li CI, Lee SD, Lin CC et al. A hospital-based multidisciplinary approach improves nutritional status of the elderly living in long-term care facilities in middle Taiwan. Arch. Gerontol. Geriatr. 2010;50 Suppl 1:S22-6.
21. Tseng C-K, Lin C-H, Hsu H-S, Ho C-T, Huang H-Y, Liu C-S et al. In addition to malnutrition and renal function impairment, anemia is associated with hyponatremia in the elderly. Arch. Gerontol. Geriatr. 2011.
22. Lin WY, Albu J, Liu CS, Huang HY, Pi-Sunyer FX, Li CI et al. Larger body mass index and waist circumference are associated with lower mortality in Chinese long-term care facility residents. J. Am. Geriatr. Soc. 2010;58:2092-8.
23. Mahan LK and Escott-Stump S. Krause's food & nutrition therapy. St. Louis, Mo.: Saunders/Elsevier: 2008 pp. xxiv, 1352 p.
24. Ozkaya M, Sahin M, Cakal E, Gisi K, Bilge F and Kilinc M. Selenium levels in first-degree relatives of diabetic patients. Biol. Trace Elem. Res. 2009;128:144-51.
25. Rafraf M, Mahdavi R and Rashidi MR. Serum selenium levels in healthy women in Tabriz, Iran. Food Nutr Bull 2008;29:83-6.
26. Lee O, Moon J and Chung Y. The relationship between serum selenium levels and lipid profiles in adult women. J Nutr Sci Vitaminol (Tokyo) 2003;49:397-404.
27. Chamarthi B, Williams GH, Ricchiuti V, Srikumar N, Hopkins PN, Luther JM et al. Inflammation and hypertension: the interplay of interleukin-6, dietary sodium, and the renin-angiotensin system in humans. Am J Hypertens 2011;24:1143-8.
28. Patterson CC, Smith AE, Yarnell JW, Rumley A, Ben-Shlomo Y and Lowe GD. The associations of interleukin-6 (IL-6) and downstream inflammatory markers with risk of cardiovascular disease: the Caerphilly Study. Atherosclerosis 2010;209:551-7.
29. Volpato S, Guralnik JM, Ferrucci L, Balfour J, Chaves P, Fried LP et al. Cardiovascular disease, interleukin-6, and risk of mortality in older women: the women's health and aging study. Circulation 2001;103:947-53.
30. Oster O and Prellwitz W. Selenium and cardiovascular disease. Biol. Trace Elem. Res. 1990;24:91-103.
31. Lubos E, Sinning CR, Schnabel RB, Wild PS, Zeller T, Rupprecht HJ et al. Serum selenium and prognosis in cardiovascular disease: results from the AtheroGene study. Atherosclerosis 2010;209:271-7.
32. Kern PA, Ranganathan S, Li C, Wood L and Ranganathan G. Adipose tissue tumor necrosis factor and interleukin-6 expression in human obesity and insulin resistance. Am J Physiol Endocrinol Metab 2001;280:E745-51.
33. Himoto T, Yoneyama H, Kurokohchi K, Inukai M, Masugata H, Goda F et al. Selenium deficiency is associated with insulin resistance in patients with hepatitis C virus-related chronic liver disease. Nutr Res 2011;31:829-35.