Table 1 Comparison of Hb, SpO_2, BMI, BP and glucose intolerance in Han and Mongolian elderly people compared with Tibetan people in Qinghai

	Qinghai in China	Han	Mongolian	Tibetan	*P*
n	393	247	49	97	
Age (years old)	66.2 (5.3)	65.9 (5.3)	67.4 (5.8)	66.7 (5.1)	NS
Sex, Male (%)	47.1	44.9	57.1	47.4	NS
Hematological					
Hematocrit (%)	46.7 (7.6)	47.8 (8.0)**	44.8 (6.4)	44.8 (6.5)	0.0008
Hemoglobin (g/dL)	16.3 (2.6)	16.6 (2.8)*	16.1 (2.2)	15.9 (2.5)	0.045
Excessive polycythemia (%)	7.9	10.1	6.1	3.1	0.0009
Mild polycythemia (%)	23.7	28.3	18.4	14.4	
Normal (%)	66.2	59.1	69.4	82.5	
Anemia (%)	2.3	2.4	6.1	0	
SpO_2 (%)	89.6 (4.2)	89.4 (4.6)	89.4 (3.9)	90.4 (3.4)	NS
$SpO_2 \leq 85\%$ (%)	13.2	13.8	16.3	10.3	NS
Obesity					
BMI	23.7 (4.0)	23.4 (3.6)**	23.7 (3.6)	24.7 (4.3)	0.03
BMI ≥ 22 (%)	63.6	60.3	61.2	73.2	NS
BMI ≥ 25 (%)	34.1	31.2	42.9	38.1	NS
Blood pressure					
SBP (mmHg)	137.4 (24.8)	140.6 (24.5)**	137.2 (21.5)	130.2 (25.6)	0.0025
DBP (mmHg)	83.9 (13.9)	85.8 (13.5)**	84.4 (12.3)†	79.4 (14.8)	0.0007
HT (%)	51.1	57.5	49.0	36.1	0.0017
DBP ≥ 85 (%)	42.0	49.4	40.8	23.7	0.0001
DBP ≥ 90 (%)	31.3	35.6	30.6	20.6	0.016
Glucose intolerance (%)	17.7	19.7	9.4	17.1	NS
IGT (%)	9.9	11.8	0	10.5	
DM (%)	7.6	7.9	9.4	6.6	
Smoking (%)					NS
Current	16.8	16.7	22.4	14.3	
Past	10.7	8.5	20.4	11.1	
No	72.3	74.5	57.1	74.6	
History of stroke (%)	14.5	15.4	10.5	14.4	NS
History of heart disease (%)	59.5	53.0	71.4	70.1	0.029
ADL					
Scores in basic ADL (0–21)	19.9 ± 2.7	20.1 ± 2.4**	20.1 ± 2.5	19.0 ± 3.6	0.015
Independence rate of basic ADL (%)	74.0	78.1	79.6	60.8	0.023
Scores in instrumental ADL (0–5)	3.6 ± 1.5	3.9 ± 1.4**	3.6 ± 1.2	3.4 ± 1.4	0.03
Scores in intellectual activities (0–4)	1.5 ± 1.4	1.6 ± 1.4**	1.5 ± 1.4	1.0 ± 1.3	0.0029
Scores in social role (0–4)	3.0 ± 1.1	2.9 ± 1.1	3.2 ± 1.0	2.8 ± 1.3	NS
Scores in TMIG (0–13)	8.0 ± 3.1	8.5 ± 2.9**	8.3 ± 2.6†	7.2 ± 3.1	0.0084

**$P < 0.01$, *$P < 0.05$: Han vs Tibetan in post-hoc test (Fisher's protected least-significant difference [PLSD]). †$P < 0.05$: Mongolian vs Tibetan in post-hoc test (Fisher's PLSD). Excessive polycythemia: Hb ≥ 20 g/dL. Mild polycythemia: 20 > Hb ≥ 18 (men), ≥16 g/dL (women). Normal (%). Anemia: <13 (men), <12 g/dL (women). ADL, activities of daily living, *P*, ANOVA or χ^2-test; BMI, body mass index; DBP, diastolic blood pressure; HT, hypertension; SBP/DBP >140/90 or on antihypertensive medication; NS, not significant; SBP, Systolic blood pressure; SpO_2, O_2 saturation by pulse oximetry; TMIG, Tokyo Metropolitan Institute of Gerontology.

There was the significant correlation of Hb with age in women ($R = 0.22$, $P < 0.01$), SpO_2 in the both sexes (men: $R = -0.20$, $P < 0.05$; women: $R = -0.26$, $P < 0.01$), BMI in men ($R = 0.26$, $P < 0.01$) and DBP in men ($R = 0.19$, $P < 0.05$) in the analysis of all the subjects in Qinghai. Age was positively correlated with Hb in Hans ($R = 0.21$, $P < 0.05$) and Tibetans only in women ($R = 0.28$, $P < 0.05$). SpO_2 was negatively correlated with Hb in Han women ($R = -0.32$, $P < 0.01$) and Mongolian men ($R = -0.43$, $P < 0.05$) but not in Tibetans. BMI was

Table 2 Comparison of hemoglobin in Han and Mongolian elderly people compared with Tibetan people in Qinghai, respectively, in men and women

	Male				Female			
	Han	Mongolian	Tibetan	*P*	Han	Mongolian	Tibetan	*P*
n	111	28	46	ANOVA	136	21	51	ANOVA
Age (years old)	65.9 (5.3)	67.4 (5.8)	66.7 (5.1)	NS	65.9 (5.3)	67.4 (5.8)	66.7 (5.1)	NS
Hematological								
Hematocrit (%)	51.7 (8.1)***	48.0 (5.6)	46.6 (5.2)	0.0002	44.6 (6.3)	40.6(4.8)	43.2 (7.1)	0.023
Hemoglobin (g/dL)	18.1 (2.9)**	17.1 (2.3)	16.9 (1.8)	0.014	15.3 (2.1)	14.4 (1.7)	15.0 (1.2)	NS (0.086)
Excessive polycythemia (%)	20.7	10.7	6.5	0.0064	1.5	0	0	NS (0.084)
Mild polycythemia (%)	26.1	25.0	13		30.1	9.5	15.7	
Normal (%)	52.3	57.3	80.5		64.7	85.7	84.3	
Anemia (%)	0.9	7.1	0		3.7	4.8	0	

***$P < 0.0001$, **$P < 0.01$, *$P < 0.05$: Han vs Tibetan in post-hoc test (Fisher's protected least-significant difference). *P*, ANOVA or χ^2-test.

positively correlated with Hb in all ethnicities only in men (Han, $R = 0.29$; Mongolian, $R = 0.41$; Tibetan, $R = 0.34$, $P < 0.05$).

Table 4 shows the comparison of prevalence of low SpO_2, hypertension, prevalence of elderly with glucose intolerance, obesity, smoking, ethnicity, history of stroke or heart disease and ADL in people with excessive polycythemia compared with those without excessive polycythemia. Excessive polycythemia was defined as over 20 mg/dL of Hb and there were 31 people (7.9%). Of those, 79.3% were Han people. People with excessive polycythemia had a much higher prevalence of men compared with those without excessive polycythemia (93.3% vs 43.2%). They had also significantly higher prevalence of low SpO_2 (<85%; 27.6% vs 10.7%), higher score in intellectual ADL (2.2 vs 1.4) and higher DBP (90.1 vs 83.3 mmHg) compared with those without excessive polycythemia. They also had higher prevalence of obesity and higher scores in the TMIG index but not significantly. In the separate analysis in sex, there was no difference in any of the scores in basic and higher functional ADL between people with excessive polycythemia and those without it.

Table 5 shows the associated factors for excessive polycythemia (Hb ≥ 20 g/dL) by logistic regression. Male sex, SpO_2 of less than 85%, DBP of 85 mmHg or more, BMI of 25 or more and Han ethnicity (vs Tibetan) were associated factors for excessive polycythemia in monovariate logistic regression. High scores in basic or higher ADL seem mildly associated with excessive polycythemia in monovariate analysis, but they have no significant association after adjustment by sex.

Male sex, BMI of 25 or more, SpO_2 of less than 85%, DBP of 85 mmHg or more, and Han ethnicity (vs Tibetan) were independent associated factors for excessive polycythemia in multiple logistic regression.

Discussion

Diseases specific at high altitudes, those closely associated with hypoxic environments, may be regarded as one of the environmental issues that affect the human body. High-altitude peoples are burdened with physiological adaptations to hypoxia. Some high-altitude people with the failure of adaptation suffer from CMS, which is characterized by an abnormally high concentration of Hb.[3–10] Excessive erythrocytosis was defined as over 21 mg/dL of Hb for men and over 19 mg/dL for women and it is the most important criterion of CMS.[8] This study showed the association of polycythemia with lifestyle-related diseases (hypertension and obesity) among the three ethnicities. Those associations with excessive polycythemia defined as Hb of 20 g/dL and more were analyzed by multiple logistic regression in this study.

Table 3 Comparison of averaged hemoglobin concentrations (g/dL) in the differences of SpO_2, DBP, BMI and glucose intolerance in the elderly in the three ethnicities in Qinghai by separate analysis in sex

	Qinghai in China	*P*	Han	*P*	Mongolian	*P*	Tibetan	*P*
Sex								
Male	17.6 (2.6)	<0.0001	18.1 (2.9)	<0.0001	17.1 (2.3)	<0.0001	16.9 (1.8)	<0.0001
Female	15.1 (1.9)		15.3 (2.1)		14.4 (1.7)		15.0 (1.2)	
SpO_2								
Male								
$SpO_2 \le 85$	19.4 (2.1)	0.0051	20.6 (1.7)	0.018	19.4 (1.3)	0.014	17.3 (1.7)	NS
$SpO_2 > 85$	17.4 (2.6)		17.9 (2.9)		16.5 (2.1)		16.8 (1.8)	
Female								
$SpO_2 \le 85$	16.5 (2.5)	<0.0001	17.2 (2.5)	<0.0001	15.2 (0.1)	NS	14.8 (2.0)	NS
$SpO_2 > 85$	14.8 (1.7)		14.9 (1.8)		14.2 (1.8)		15.0 (1.1)	
DBP								
Male								
DBP ≥ 85	18.2 (3.0)	0.02	18.7 (3.2)	NS	16.8 (2.1)	NS	17.3 (2.2)	NS
DBP < 85	17.2 (2.2)		17.5 (2.4)	(0.051)	17.4 (2.5)		16.7 (1.7)	
Female								
DBP ≥ 85	15.4 (1.7)	NS	15.4 (1.8)	NS	14.7 (1.2)	NS	15.6 (0.9)	0.017
DBP < 85	14.9 (2.0)	(0.092)	15.2 (2.4)		13.9 (2.1)		14.7 (1.2)	
BMI								
Male								
BMI ≥ 25	18.5 (2.5)	0.0015	19.3 (2.8)	0.008	17.9 (2.1)	NS	17.6 (2.0)	0.049
BMI < 25	17.2 (2.5)		17.6 (2.8)		16.4 (2.3)		16.5 (1.6)	
Female								
BMI ≥ 25	15.1 (1.6)	NS	15.2 (1.8)	NS	14.5 (1.0)	NS	15.1 (1.2)	NS
BMI < 25	15.1 (2.0)		15.4 (2.2)		14.1 (1.9)		14.8 (1.1)	
75-g OGTT								
Male								
Glucose intolerance	17.5 (2.5)	NS	17.8 (3.3)	NS	16.3 (1.1)	NS	17.5 (1.4)	NS
Normal	17.3 (2.3)		17.5 (1.4)		17.0 (2.6)		16.9 (2.2)	
Female								
Glucose intolerance	15.5 (1.6)	NS	15.6 (1.7)	NS	–		15.0 (0.1)	NS
Normal	15.2 (1.9)		15.4 (2.2)		14.4 (1.9)		15.1 (1.2)	

75-g OGTT, 75 g oral glucose tolerance test; BMI, body mass index; DBP, diastolic blood pressure; mean (standard deviation), averaged hemoglobin concentration (g/dL); NS, not significant; SpO_2, O_2 saturation by pulse oximetry.

Of the highlanders in Qinghai, 7.9% had excessive polycythemia (Hb ≥ 20 g/dL). The independent associated factors for excessive polycythemia were male sex, hypoxia, obesity, high DBP and Han ethnicity. In our analysis of 294 people in Qinghai who had chest-Xp and electrocardiography, there were 14 people with excessive polycythemia and all of them were diagnosed as having CMS. As excessive polycythemia (Hb ≥ 20 g/dL) is close to excessive erythrocytosis, the associated factors for excessive polycythemia in this study may be closely regarded as the risk for CMS.

The risk factors of CMS were reported previously and they were male sex, postmenopausal state, aging, being overweight, lower respiratory tract disease and sleep apnea.[8,10,27–31] The risk factors of HAPH were also reported to be of male sex, a Han immigrant and a child.[8,10,27,28] It remained unknown how lifestyle-related diseases are related to suffering from CMS. In this study, male sex and obesity were the associated factors as in the previous reports.[28,29] Obesity is associated with other conditions that may increase Hb such as hypoventilation syndromes.[32] The strong association of male sex with Hb was shown in all ethnicities of highlanders and that of obesity was shown in all ethnicities in men. Male sex was markedly associated with polycythemia in the highlanders mainly due to hypoxic environments.

Chronic pulmonary diseases such as chronic obstructive pulmonary diseases (COPD) are risk factors for polycythemia and may cause secondary CMS.[8,10,30]

Table 4 Comparison of prevalence of low SpO_2, hypertension, glucose intolerance, obesity, smoking and ethnics in people with excessive polycythemia compared with those without excessive polycythemia

	Excessive polycythemia		*P*
	Positive 31	Negative 362	
Age	66.0 (4.9)	66.3 (5.3)	NS
Sex, male (%)	93.3	43.2	<0.0001
SpO_2 (%)	88.4 (4.8)	89.9 (4.1)	0.076
$SpO_2 \leq 85\%$ (%)	27.6	10.7	0.0077
Hemoglobin (g/dL)	22.1 (1.7)	15.8 (1.9)	<0.0001
HT (%)	62.3 (6.2)	45.3 (6.0)	<0.0001
SBP (mmHg)	142.7 (26.6)	136.9 (24.5)	NS
DBP (mmHg)	90.1 (14.6)	83.3 (13.8)	0.01
Ht (%)	63.3	49.4	NS
Glucose intolerance: IGT or DM (%)	18.8	17.6	NS
BMI	25.0 (4.1)	23.7 (3.8)	0.082
BMI ≥ 22 (%)	80.0	63.7	0.073
BMI ≥ 25 (%)	50.0	33.6	0.071
Smoking (%)			NS
Current or past smoker	42.9	27.6	
No	57.1	72.4	
Ethnicity			0.084
Han (%)	79.3	59.2	
Tibetan (%)	10.3	13.2	
Mongolian (%)	10.3	27.6	
History of stroke (%)	4.8	15.5	NS
History of heart disease (%)	68.4	66.2	NS
ADL			
Scores in basic ADL (0–21)	20. ± .6	19. ± .7	NS
Independence rate of basic ADL (%)	90.5	74.3	0.098
Scores in instrumental ADL (0–5)	3.9 ± 1.4	3.5 ± 1.5	NS
Scores in intellectual activities (0–4)	2.2 ± 1.3	1.4 ± 1.3	0.0047
Scores in social role (0–4)	2.9 ± 1.3	2.9 ± 1.1	NS
Scores in TMIG (0–13)	9.0 ± 3.2	7.9 ± 3.1	0.09

ADL, activities of daily living; BMI, body mass index; DBP, diastolic blood pressure; Ht, hematocrit; HT, hypertension; NS, not significant; SBP/DBP > 140/90 or on antihypertensive medication; SBP, systolic blood pressure; SpO_2, O_2 saturation by pulse oximetry; TMIG, Tokyo Metropolitan Institute of Gerontology.

Smoking is the most important risk factor for COPD.[31] But current and past smoking was not directly associated with polycythemia in the separate analysis of men and women in this study. In this study, forced vital capacity or forced flow volume over 1.0 s was not examined in respiratory function. This is a study limitation and further research is needed to disclose the association between COPD, polycythemia and CMS.

In this report, it was found that high DBP was associated with excessive polycythemia. High DBP was independently associated with excessive polycythemia after adjustment of other confounding factors in all Qinghai highlanders in this report. Erythropoietin is effective for patients with severe orthostatic hypotension and their blood pressure will be augmented by red blood cell increase.[33,34] High DBP may be caused by the increase of blood volume accompanying the increase of Hb volume aggravated by hypoxia with aging. From another viewpoint, high DBP itself may be the risk factor for excessive polycythemia and for CMS. Further longitudinal study will be needed to disclose its association.

Table 5 Associated factors for excessive polycythemia (Hb ≥ 20 g/dL)

	Odds ratio	*P*
	(logistic regression, monovariate)	
Age	1.0	NS
Male (vs female)	16.5	0.0002
BMI 22–24 (vs BMI < 22)	2.1	NS
BMI ≥ 25 (vs BMI < 22)	3.1	0.035
SpO_2 < 85%	2.8	0.031
DBP ≥ 85 mmHg	3.1	0.0065
Han people (vs Tibetan)	3.8	0.032
Mongolian people (vs Tibetan)	1.5	NS
Glucose intolerance	0.9	NS
Current and past smoker	1.9	NS
History of stroke	0.3	NS
History of heart disease	1.1	NS
Full score of basic ADL	3.3	NS (0.12)
Full score of instrumental activities	1.8	ns
Full score of intellectual activities	2.6	NS (0.06)
Full score of social Role	1.0	ns
Scores in TMIG ≥ 10	2	NS (0.13)
	(logistic regression, multiple)	
Age	1.03	NS
Male (vs female)	36.3	<0.0001
BMI 22–24 (vs BMI < 22)	2.8	0.10
BMI ≥ 25 (vs BMI < 22)	4.5	0.013
SpO_2 < 85%	5.9	0.005
DBP ≥ 85 mmHg	3.5	0.011
Han people (vs Tibetan)	4.1	0.043
Mongolian people (vs Tibetan)	0.8	NS

ADL, activities of daily living; BMI, body mass index; DBP, diastolic blood pressure; NS, not significant; SpO_2, O_2 saturation by pulse oximetry; TMIG, Tokyo Metropolitan Institute of Gerontology.

In order to compensate for hypoxia at high altitude, the human body undergoes a number of physiological changes. It was shown that there are differences in adaptation among the three highlands of the Tibetan Plateau, the Andes and the Ethiopian Highland and a diversity of biological and evolutionary strategies for adaptation to high-altitude environments. The Hb concentration in native Tibetans was lower than in native Andean people. The difference was speculated to be due to Tibetans undergoing a much longer period of adaptation of 20 000–30 000 years than Andean people of 10 000 years.[1,2,35,36] It was previously reported that Han people who immigrate to the Qinghai Tibetan Plateau have Hb concentrations higher than native Tibetans.[37] It was also reported that Han people who were born and raised at high altitude in the Qinghai Tibetan Plateau have Hb concentrations higher than native Tibetans.[38] In this study, Han people had higher prevalence of polycythemia than Tibetan people in spite of the same SpO_2 level. Han ethnicity was independently associated with excessive polycythemia even after adjustment of other confounding factors such as male sex, high DBP, obesity and hypoxia in all of the Qinghai highlanders in this report. The study site in Haiyan County is located at the ecological boundary area (3000–3500 m a.s.l.) between agricultural area inhabited by Han people and pastoral area inhabited by native Tibetan.[39] Han subjects in this area are not immigrants and have lived there over many generations with a history of 2000 years from the early Western Han dynasty. While native Tibetan people are estimated to have lived in the Qinghai Tibetan Plateau area for much longer, namely 6000–20 000 years.[40–42] The difference of Hb concentration may be due to Tibetans undergoing a much longer period of adaptation than Han people, as in the difference in adaptation to hypoxia between Tibetan and Andean people shown by Beall *et al.*[1,35,36] This hypothesis will be supported by the following result in this study; SpO_2 was associated with polycythemia in Han and Mongolian people but not in Tibetan people. So, Tibetan people may have adapted to hypoxia differently.

Polycythemia was associated with obesity and high DBP in this study. Polycythemia is a risk factor of stroke and high DBP is that of ischemic heart disease.[43–45] Neither history of heart disease nor stroke was directly associated with polycythemia after adjustment of sex in this study. Neither were basic ADL nor higher functional abilities directly associated with polycythemia. Prognosis in those people with polycythemia should be disclosed in longitudinal follow-up studies.

In conclusion, there was close association of polycythemia with lifestyle-related diseases (obesity and high DBP) in high-altitude elderly people. Han people had higher Hb concentration after adjustment of age, sex and lifestyle-related diseases compared with Tibetan people. The difference of Hb concentration may be due to Tibetans undergoing a much longer period of adaptation than Han people. A further and longitudinal study may be needed to disclose the association between the different means of hypoxic adaptation with susceptibility to lifestyle-related diseases (not only obesity and hypertension but also dyslipidemia, metabolic syndrome, heart diseases and stroke). It should also be disclosed how lifestyle-related diseases would increase the risk of CMS. The prevention of lifestyle-related diseases may be important for the prevention of CMS in highlanders.

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ORIGINAL ARTICLE

Comprehensive geriatric assessment of elderly highlanders in Qinghai, China, III: Oxidative stress and aging in Tibetan and Han elderly highlanders

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Background: Although there are several factors which may contribute to oxidative stress at high altitude, little is known about the association between oxidative stress and aging in the community-dwelling elderly in the Tibetan Plateau.

Methods: Reactive oxygen species (ROS) and comprehensive geriatric functions were examined among 235 community-dwelling elderly subjects aged 60 years or more (146 Hans and 89 Tibetans). As a marker of ROS, the levels of reactive oxygen metabolites (ROM) were measured using the d-ROM test.

Results: The rate of dependence of basic activities of daily living (basic ADL) among Tibetan elderly highlanders was significantly higher than that among Han elderly highlanders. The d-ROM level was higher among the Tibetan elderly than those among the Han elderly (Tibetan 465.6 ± 97.9 Carr U, Han 415.3 ± 72.0 Carr U, $P = 0.003$). The ROM level was higher among women than those among men. Stepwise multiple regression analysis showed that being Tibetan, female, and oxygen saturation were independent predictors of increasing d-ROM level (Tibetan β, 0.241; female β, 0.206; oxygen saturation β, 0.218). The high levels of ROM (d-ROM >500 Carr U) were significantly associated with dependence of basic ADL after adjustment for age, sex and ethnicity (odds ratio = 2.51, $P = 0.028$).

Conclusion: The findings of this study imply the possibility that ROS is higher among Tibetan elderly highlanders than that of Han, which related to the geriatric items.

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Further studies are needed to show the impact of oxidative stress on the aging of highlanders.

Keywords: aging, elderly highlanders, oxidative stress, reactive oxygen species.

Introduction

An unbalance between production of reactive oxygen species (ROS) and the antioxidant defense system associates with oxidative stress. Oxidative stress is widely recognized as being associated with various disorders including diabetes, hypertension, atherosclerosis, and so on. Oxidative stress is also hypothesized to be one of the main causes of aging.[1,2] Several reports suggest that hypoxia is associated with oxidative stress. In highlands, there are several environmental factors which may contribute to the oxidative stress such as hypoxia, ultraviolet light and cold exposure. Lower dietary intake of antioxidants such as fruits and vegetables could also contribute to higher level of oxidative stress.[3,4] The aim of this study was to investigate the effects of level of ROS on aging among community-dwelling highlanders.

Tibetans are reported to have higher blood flow and higher circulating nitric oxide (NO) products than people living at sealevel to adapt to high altitude hypoxia.[5] But excessive NO production can cause oxidative stress. Our hypothesis is that the level of ROS and the way of aging are different between Tibetan and Han elderly highlanders and ROS levels are associated with aging in elderly highlanders.

Methods

Subjects

The study population consisted of 235 community-dwelling elderly subjects aged 60 years or more (male : female = 97:138; mean age, 66.3 years) living in Haiyan County in Qinghai Province, China. Haiyan County is located at 3000–3200 m a.s.l. and 30 km northwest of Xining which is the capital of Qinghai Province. These subjects were elderly volunteers who hoped to be examined and who responded to our announcement of geriatric examination. The survey for community-dwelling elderly living in Haiyan County in Qinghai Province was carried out in August 2008.

Colorimetric determination of ROS

To measure serum hydroperoxides, the analytic method d-ROMs (Diacron, Parma, Italy) was used. It is based on Fenton's reaction or on radical formation during lipid peroxidation. The oxyradical species are trapped by alchylamine, a phenolic compound that forms a colored, stable radical detectable spectrophotometrically at 505 nm. The concentration of the colored complex is directly correlated to the concentration of hydroperoxides. We mixed 10 μL of serum and 1 mL of buffered solution (R2 reagent of kit, pH 4.8) in a cuvette, and then added 10 μL of chromogenic substrate (R1 reagent of kit) into the cuvette. After mixing, the cuvette was centrifuged for 60 s at 37°C and immediately incubated in the thermostatic block of the analyzer for 5 min at 37°C. The results were expressed as Carr U. It has been established that 1 Carr U corresponds to 0.08 mg/100 mL H_2O_2.[6–8] It has been reported that replicate measures on the same serum sample showed a within-assay coefficient of variation (CV) of less than 0.5% and a between-assay CV of less than 2.9%.[9]

Items of comprehensive geriatric assessment

Items of the comprehensive geriatric assessment included activities of daily living (ADL), anthropometric indicators, and so on.[10–16] For basic ADL assessment, each subject was rated by interview on his/her independency in seven items (walking, ascending and descending stairs, feeding, dressing, making his/her toilet, bathing and grooming) as to the help needed, and was rated from 3 to 0 as follows: 3, completely independent; 2, need some help; 1, need much help; and 0, completely dependent. The items were added to give scores ranging 0–21, with low scores indicating disability.[17–21]

For higher-level functional capacity, each subject was rated on his/her independence by the Tokyo Metropolitan Institute of Gerontology Index of Competence (TMIG-IC).[22,23] We assessed neurobehavioral function using two items of tests including the Up & Go test[24] and functional reach.[25]

Blood pressure was measured twice in sitting position by auto-sphygmomanometer (HEM 757; Omron, Kyoto, Japan). Hypertension was defined as 140 mmHg or higher in systolic blood pressure, 90 mmHg or higher in diastolic blood pressure or taking antihypertensive medication. Blood tests were taken twice at fasting and 2 h after drinking 75 g glucose among participants who provided informed consent. Diabetes mellitus and impaired glucose tolerance were defined according to the criteria of the World Health Organization: diabetes (fasting blood sugar [FBS] $\geq$126 mg/dL or 2-h oral glucose tolerance test [OGTT] $\geq$200 mg/dL), impaired glucose tolerance (110 mg/dL $\leq$ FBS < 126 mg/dL or 140 $\leq$ 2 h OGTT < 200 mg/dL) or taking antidiabetic medication. Blood chemical analysis was carried out in the central laboratory of Qinghai University Hospital.

Ankle Brachial Pressure Index (ABI) and Cardio Ankle Vascular Index (CAVI) were measured using a VaSera instrument (Fukuda Denshi, Tokyo, Japan). Carotid plaques were examined by carotid ultrasound. We defined plaque as a focal structure that encroached into the arterial lumen of at least 0.5 mm or 50% of the surrounding intima-media thickness value or demonstrated a thickness of 1.5 mm as measured from the media-adventitia interface to the intima-lumen interface. Smoking habit, diet, working or gardening were assessed by questionnaire.[26]

Ethical approval

These surveys were approved by the Ethical Committee of Research Institute for Humanity and Nature and Medical Institute of Qinghai University, and written informed consent was obtained from each participant.

Statistical methods

The data analysis was performed with SPSS ver. 15.0 for Windows. Baseline data are presented as mean ± standard error or percentages. Stepwise multiple regression analyses (to $P < 0.05$) were used to assess the association of ROM and other variables. Standardized β-coefficients were used because they allow for direct comparison of the strength of associations between ROM and other variables. In the multivariate model, factors of $P < 0.05$ were considered in the univariate analysis. $P < 0.05$ was considered statistically significant. Logistic regression analysis (to $P < 0.05$) was used to assess the relations of ROM to geriatric items. In the logistic regression analysis, the covariates considered were age, sex and ethnicity.

Results

Comparison between Tibetan and Han elderly highlanders

The elderly participants consisted of 89 Tibetans and 146 Hans. Table 1 shows comparison of characteristics between Tibetan and Han elderly highlanders in Haiyan County in Qinghai Province. There was no significant difference in mean age, sex ratio, exercise or smoking habits. The d-ROM level was higher among the Tibetan elderly than those among the Han elderly (Tibetan 465.6 ± 97.9 Carr U, Han 415.3 ± 72.0 Carr U, $P = 0.003$). Tibetan elderly highlanders had lower blood pressure, lower hemoglobin level and lower ABI. In geriatric functions, Tibetan elderly highlanders took longer in the Up & Go test, and had lower basic ADL and lower TMIG-IC than Han elderly highlanders.

Table 1 Comparison of characteristics between Tibetan and Han elderly highlanders

Characteristic	Tibetan ($n = 89$)†	Han ($n = 146$)†	P‡
Age (year)	66.8 ± 5.2	66.0 ± 5.5	NS
Sex (M/F)	41/48	56/90	NS
Systolic blood pressure (mmHg)	131.0 ± 26.3	142.1 ± 23.8	0.001
Diastolic blood pressure (mmHg)	79.5 ± 15.2	86.1 ± 13.1	0.001
Pulse rate	76.5 ± 10.7	78.0 ± 14.5	NS
SpO_2 (%)	90.3 ± 3.5	89.5 ± 4.8	NS
Hemoglobin (mg/dL)	15.9 ± 1.8	16.6 ± 2.8	0.036
Fasting blood sugar (mg/dL)	90.6 ± 29.3	87.4 ± 34.7	NS
HOMA-IR	1.64 ± 2.00	1.26 ± 1.17	NS
CAVI	9.2 ± 1.5	9.3 ± 1.4	NS
ABI	1.07 ± 0.09	1.11 ± 0.12	0.007
d-ROM (Carr U)	465.6 ± 97.9	415.3 ± 72.0	0.003
Functional reach (cm)	28.2 ± 10.3	26.5 ± 10.3	NS
Up & Go test (s)	19.5 ± 13.4	14.1 ± 4.0	0.003
Basic activities of daily living	19.1 ± 3.4	20.2 ± 2.2	0.041
TMIG-IC	7.0 ± 3.3	8.2 ± 3.0	0.017
Current smoker (%)	11.9	15.0	NS
Vegetables intake more than 5 times a week (%)	62.7	64.7	NS
Fruits intake more than once a week (%)	47.5	57.9	NS
Work or gardening more than 5 times a week (%)	47.5	60.0	NS

†Data are given as the number (%) or as mean ± standard deviation. ‡P-values were calculated using Student's t-test or χ^2-test. ABI, Ankle Brachial Pressure Index; CAVI, Cardio Ankle Vascular Index; HOMA-IR, Homeostasis Model Assessment Insulin Resistance; SpO_2, oxygen saturation of hemoglobin; NS, not significant; TMIG-IC, Tokyo Metropolitan Institute of Gerontology Index of Competence.

Table 2 Factors associated with levels of d-ROM by regression analysis

Factor	Univariate analysis		Multivariate analysis‡	
	Standardized coefficient β	*P*-value	Standardized coefficient β	*P*-value
Age (year)	0.142	0.03	–	NS
Female (vs male)	0.271	<0.001	0.206	0.009
Tibetan (vs Han)	0.196	0.003	0.241	<0.001
Systolic blood pressure (mmHg)	−0.11	NS		
Diastolic blood pressure (mmHg)	−0.076	NS		
SpO_2 (%)	−0.242	<0.001	−0.218	0.002
Hemoglobin (mg/dL)	−0.232	0.001	−0.154	0.05
Fasting blood sugar (mg/dL)	0.039	NS		
Postprandial blood sugar (mg/dL)	0.038	NS		
Low-density lipoprotein cholesterol (mg/dL)	0.151	0.03	–	NS
Current smoker	−0.12	NS		
Vegetable intake more than five times a week	−0.083	NS		
Fruits intake more than once a week	−0.135	NS		
Working or gardening more than five times a week	−0.075	NS		

‡Stepwise multiple regression analysis (to $P < 0.05$) was used. Multivariate model considered factors with $P < 0.05$ in the univariate analysis. NS, not significant; SpO_2, oxygen saturation of hemoglobin.

Factors associated with the level of d-ROM by regression analysis

Univariate analysis showed that age, female sex, Tibetan ethnicity, oxygen saturation of hemoglobin, hemoglobin, total cholesterol and low-density lipoprotein cholesterol were the associated factors with d-ROM level. By stepwise multiple regression analysis, Tibetan ethnicity, female sex and oxygen saturation were independent predictors of increasing d-ROM level (Tibetan β, 0.241; female β, 0.206; oxygen saturation β, −0.218) (Table 2).

Relations of high ROS on geriatric items

The high level of ROM (d-ROM >500 Carr U) was significantly associated with dependence of basic activities of daily living after adjustment for age, sex and ethnicity (odds ratio [OR] = 2.51; 95% confidence interval [CI], 1.10–5.72; $P = 0.028$). It was also significantly associated with higher Homeostatic Model Assessment of Insulin Resistance (HOMA-IR; ≥1.6; OR = 2.32; 95% CI, 1.12–4.84; $P = 0.024$) and detection of carotid plaque (OR = 2.09; 95% CI, 1.03–4.26; $P = 0.042$) after adjustment for age, sex and ethnicity (Table 3). The cut-off level of d-ROM was determined based on the cut-off point of 75%.

Discussion

The present study showed that Tibetan elderly highlanders had higher level of ROS, took a longer time in the Up & Go test, and had lower basic ADL and lower TMIG-IC than Han elderly highlanders. The high level of ROS was significantly associated with the higher HOMA-IR score (≥1.6), detection of carotid plaque by carotid ultrasound and dependent basic ADL. These findings imply the possibility that higher levels of ROS among Tibetan elderly highlanders relate to their aging acceleration.

The results of this study indicated that Tibetan elderly highlanders have higher levels of ROS than Han elderly highlanders. Although the definite the pathological mechanisms have not been established, it can be speculated that the difference both in lifestyles and evolutionary genetic backgrounds between Tibetans and Hans affected the level of ROS. There are many factors which are known to relate to the oxidative stress such as smoking habit, vegetable or fruit intake, low-oxygen, ultraviolet light, coldness, and so on.[3,4,27,28] Presently, we are particularly interested in the effect of NO. It was reported that one of the Tibetan ways to adapt to high-altitude hypoxic environment was to increase NO. They had higher forearm blood flow and higher plasma nitrite levels as compared with sealevel US residents.[5] Higher blood flow and circulating NO products can offset high-altitude hypoxia in a sense of adaptation to hypoxia.[5] As to oxidative stress, nitroxides are known to have dual activities as pro- and antioxidants.[29] Reactive metabolites of NO, especially $ONOO^-$, may induce oxidative stress.[30] Further studies are needed to disclose the association between NO and aging indicators in Tibetan elderly highlanders. We need to check both physiological and cultural factors in more detail.

Table 3 Relations of high reactive oxygen metabolites (ROM) (d-ROM ≥500 Carr U) to geriatric items

	Odds ratio†	95% confidence interval	*P*-value
Hypertension	–	–	NS
Hyperlipidemia	–	–	NS
Diabetes	–	–	NS
HOMA-IR ≥1.6	2.32	1.12–4.84	0.024
Carotid plaque	2.09	1.03–4.26	0.042
CAVI ≥9.0	–	–	NS
ABI <1.0	–	–	NS
Functional reach <28 cm	–	–	NS
Up & Go test ≥16 s	1.90	0.89–4.06	0.096
Dependent basic activities of daily living	2.51	1.10–5.72	0.028
TMIG-IC < 8	–	–	NS

†Logistic regression analysis (to $P < 0.05$) were used. Covariates considered were age, sex and ethnicity. ABI, Ankle Brachial Pressure Index; CAVI, Cardio Ankle Vascular Index; HOMA-IR, Homeostasis Model Assessment Insulin Resistance; NS, not significant; TMIG-IC, Tokyo Metropolitan Institute of Gerontology Index of Competence.

There are considerable studies reporting an increased production of indicators of oxidative stress of laboratory rats in response to hypoxia.[31] But a limited number of studies have been conducted investigating hypoxia and oxidative stress of human.[32] In addition, although oxidative stress is hypothesized to be one of the main causes of aging, as far as we know, there is no study which investigates the association between ROS and geriatric assessments in the elderly living at high altitude.

Our study also shows that ROS is an independent predictor for the higher HOMA-IR score (≥1.6) among elderly highlanders. This result agrees with a study of laboratory rats that states that oxidative stress induces insulin resistance by impairing insulin receptor substrate-1 (IRS-1) phosphorylation and PI 3-kinase activation in the low-density microsome (LDM) fraction.[33,34]

There are several limitations in this study. This cross-sectional study suggests the association between ROS and aging but a cause-and-effect relationship remains unknown. As an indicator of ROS, this study focused on only the level of d-ROM, and multilateral methods were needed to examine the consequences of ROS generation which can be detected by formation of various oxidatively-altered biomolecules, including DNA, lipids and protein. From the aspect of the antioxidant defense system, there is a report that the concentration of glutathione-S-transferase P1-1, an enzyme catalyzing and detoxifying cytoprotective reactions, was high in high-altitude Tibetans and we cannot make hasty conclusions.[35]

The Tibetan Plateau and adjacent ranges have the most extensive inhabited land area above 2500 m a.s.l.[36] Some of this high altitude land is populated by indigenous people who have adapted to high-altitude environments over the generations. Tibetan and Han people have evolved mechanisms of oxygen supply in different ways.[37,38] It is known that the patterns of adaptation to high-altitude hypoxia are different among Andean, Tibetan and Ethiopian highlanders.[5,39–41] Andean highlanders have higher hemoglobin concentration and Tibetan highlanders have higher blood flow than people living at sealevel.[5] Ethiopian highlanders have high oxygen saturation of hemoglobin inspite of thin air.[39] The findings of this study imply the possibility that the level of ROS is different according to the patterns of adaptation to high-altitude hypoxia.

Human activities are necessarily accompanied by the generation of oxidative stress. If produced in excess, however, these stresses may contribute to the acceleration of aging. The ways of aging should be various in each individual as well as each region or ethnicity. Further studies focused on the individual human life are needed to show the impact of ROS on the aging of highlanders.

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ORIGINAL ARTICLE

Comprehensive geriatric assessment of elderly highlanders in Qinghai, China IV: comparison of food diversity and its relation to health of Han and Tibetan elderly

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Aim: To examine the association between food diversity and health status of Han and Tibetan elderly highlanders in Qinghai Plateau, China.

Methods: The study population consisted of 240 community-dwelling elderly subjects aged 60 years or more (176 Han elderly subjects, 64 Tibetan ones). Food diversity was determined using an 11-item Food Diversity Score Kyoto (FDSK-11). Subjects were interviewed on health status including activities of daily living (ADL), screening-based depression and quality of life (QOL). Blood chemical investigation was carried out in association with food diversity.

Results: ADL was significantly lower in both Han and Tibetan elderly with lower food diversity than those with higher diversity. In Han elderly with lower food diversity, QOL was significantly lower in the items of subjective sense of health, relationship with family and subjective happiness, but not significant in Tibetan elderly. A close association was found between lower food diversity and lower financial satisfaction in both Han and Tibetan subjects. No association was found between food diversity and age or body mass index. Higher food diversity was associated with lower blood glucose level in Han elderly subjects, but the opposite association was found in Tibetan ones.

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Conclusion: Food diversity was associated with ADL and QOL in highlanders in Qinghai, China. Food assessment is very important as a useful indicator to establish the actual condition of diet and its relation to health status of community-dwelling elderly as well as the change of economic background in the Qinghai highlands.

Keywords: activities of daily living, elderly highlanders, food diversity, Qinghai Plateau in China, quality of life.

Introduction

In highlands, with their harsh natural environments, food resources are limited and the supply of various foods seem to be insufficient. However, in recent years, food availability has changed with the transition to a market economy and highlanders have become able to obtain various foods at the market. This economic change might have affected the food diversity of daily meals. (Fig. 1)

Dietary diversities have been reported to be closely associated with prolonged longevity[1,2] and also several dietary guidelines have long emphasized the value of eating a variety of foods.[3,4] Moreover, food diversity is reported to decline with aging and is related to disability in the elderly.[5–7] However, most of those previous studies have been researched in developed countries and the actual condition of food diversity in highlanders seems to be unclear.

Based on this background, we carried out a comprehensive geriatric survey in Qinghai Province (3000–3300 m a.s.l.) in China to research highlanders' diet and its relation to health status from a view point of food diversity.

Methods

Subjects

The study population consisted of 240 community-dwelling elderly subjects living in Haiyan County (Qinghai, China), aged 60 years or older (male : female = 111 : 129; mean age, 65.9 years, standard deviation [SD] 6.1) who completed the interview for food diversities. These subjects were elderly volunteers who hoped to be examined in response to our announcement of geriatric examination. The geriatric survey for

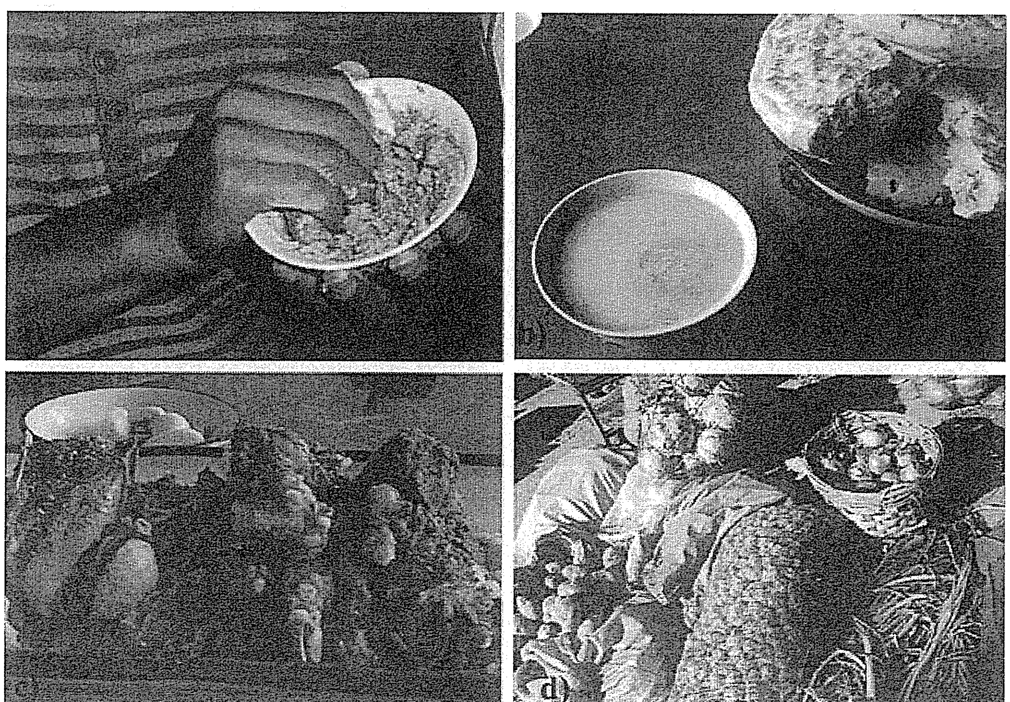

Figure 1 Foods in Qinghai, China. (a) Tsampa: Tibetan traditional staple food made of roasted barley flour mixed with butter tea. (b) Butter tea: common Tibetan drink made by adding butter to milk tea, usually with salt, and bread. (c) Boiled lamb meat. (d) Various vegetables can be seen in the market.

scommunity-dwelling elderly living in Haiyan County, Qinghai Province, was carried out in August 2008.

Food diversity

Food diversity was determined using an 11-item Food Diversity Score Kyoto (FDSK-11).[8] The FDSK-11 consists of 11 main food groups (grain, meat, fish and shellfish, eggs, milk, beans and bean products, potatoes, vegetables, seaweed, nuts and fruits) and each participant was interviewed on the frequency of eating these foods over a week. Participants were asked whether they had taken each of the 11 food groups once or more (a score of 1) a week, or less (a score of 0). Scores were summed to provide a FDSK-11 ranging 0–11, with a higher score indicating higher food diversity.

In this assessment by FDSK-11, we used food groups from the National Nutritional Survey, Japan (NNS-J). To adjust these food groups to the elderly living in Qinghai, China, we changed and added several examples of certain foods eaten in Chinese and Tibetan daily meals for each food group. Interviewers were Chinese or Tibetan speakers and able to explain the foods in each food groups.

Geriatric functions

Geriatric functions were assessed by measuring activities of daily living (ADL), depression and quantitative subjective quality of life (QOL).

For the assessment of basic ADL, the scores for seven items (walking, ascending and descending stairs, feeding, dressing, using the toilet, bathing, and grooming) were summed using a rating scale from 0 (completely dependent) to 3 (completely independent) to obtain a basic ADL score (0–21).[9,10] For higher-level functional capacity, each subject was rated on his/her independence on the Tokyo Metropolitan Institute of Gerontology Index of Competence (TMIG-IC) rating scale of 0–13. This scale includes instrumental self-maintenance (0–5), intellectual activity (0–4) and social role (0–4).[11]

Depressive symptoms were screened using the 15-item Geriatric Depression Scale (GDS-15)[12,13] translated into Chinese version.[14,15]

Quality of life was assessed using a 100-mm visual analog scale (worst QOL on the left end of the scale, best on the right) in the following five items: subjective sense of health, relationship with family, relationship with friends, financial status and subjective happiness.[16]

In addition to these assessments, the interviewer asked about economic condition with the question "How do you feel about your economic condition?" and each subject chose from among three choices: "rich", "moderate" or "poor".

Medical examination

Body mass index (BMI) was calculated as weight divided by square of height (kg/m^2).

Blood chemical check-up (including albumin, high-density lipoprotein cholesterol, total cholesterol, triglyceride, low-density lipoprotein cholesterol, hemoglobin, blood urea nitrogen, blood glucose, 75 g-OGTT) was carried out for each participant who gave informed consent. Blood chemical analysis was carried out in the central laboratory of Qinghai University Hospital.

These surveys were approved by the Ethical Committee of the Research Institute of Humanity and Nature and Medical Institute of Qinghai University, and written informed consent from each participant was obtained.

Statistical analysis

Statistical analysis was performed using SPSS. We compared the results of these surveys between the elderly with high/low food diversity using the Student's t-test for continuous variables and χ^2-tests for categorical variables. $P < 0.05$ indicated statistical significance.

Results

The elderly participants consisted of 176 Han elderly subjects, and 64 Tibetan ones by ethnical classification. The mean score of FDSK-11 was 7.8 (standard deviation 2.1) in Han, and 7.3 (SD 2.1) in Tibetan elderly. Based on this mean score, we classified subjects as one of two groups by using 7/8 as the cut point.

Table 1 shows the comparison of health status between Han and Tibetan elderly with high and low scores in food diversity. In both Han and Tibetan elderly subjects, each TMIG-IC score was significantly lower in the elderly with lower food diversity than those with higher diversity. A close association was also found between lower food diversity and lower financial satisfaction in subjective QOL in both Han and in Tibetan ones. QOL items of subjective sense of health, relationship with family and subjective happiness were significantly lower in elderly with lower food diversity than those with a higher one in Han people, but not in Tibetan elderly. No association was found between food diversity and age or BMI.

Figure 2 shows the relation between food diversity and subjective economic condition. The FDSK-11 scores declined with the economic condition from "rich" to "poor" in both Han and Tibetan elderly.

Table 2 shows the comparison of blood chemical indicators between Han and Tibetan elderly with high and low scores in food diversity. In Tibetan elderly subjects, triglyceride was significantly higher in the elderly with higher food diversity than those with lower, but not in Han elderly. Higher food diversity was associated

Table 1 Comparison of scores in ADL, Geriatric Depression Scale and QOL between the Han and Tibetan elderly with high and low food diversity score

	Han			Tibetan		
	High (n = 102)	Low (n = 74)	P-Value	High (n = 31)	Low (n = 33)	P-Value
FDSK-11, mean ± SD (range 0–11)	9.3 ± 1.0	5.7 ± 1.2	<0.001	9.2 ± 1.0	5.7 ± 1.5	<0.001
Age, mean ± SD	65.9 ± 5.5	65.2 ± 4.0	NS	65.9 ± 3.9	66.6 ± 6.1	NS
Sex (male/female)	50/52	29/45	NS	16/15	16/17	NS
Body mass index, mean ± SD	23.4 ± 4.0	23.9 ± 3.5	NS	25.8 ± 4.7	23.8 ± 4.07	NS (0.067)
ADL, mean ± SD						
Basic ADL score (range 0–21)	20.4 ± 1.5	19.9 ± 2.6	NS	19.7 ± 2.4	18.3 ± 4.3	NS
TMIG-IC (range 0–13)	9.0 ± 2.6	7.6 ± 2.8	0.001	9.0 ± 2.6	5.6 ± 2.6	<0.001
Self-maintenance (range 0–5)	4.1 ± 0.9	3.5 ± 1.5	0.006	4.1 ± 1.1	2.8 ± 1.5	<0.001
Intellectual activity (range 0–4)	1.9 ± 1.4	1.3 ± 1.2	0.009	1.5 ± 1.4	0.5 ± 0.8	0.001
Social role (range 0–4)	3.1 ± 1.1	2.8 ± 1.1	NS (0.06)	3.4 ± 1.0	2.3 ± 1.3	0.001
Depression, mean ± SD (range 0–15)						
Geriatric Depression Scale	5.3 ± 2.6	6.0 ± 2.9	NS	5.7 ± 2.2	5.3 ± 2.3	NS
QOL, mean ± SD (range 0–100)						
Subjective sense of health	59.1 ± 25.4	39.9 ± 29.7	<0.001	57.3 ± 27.6	56.1 ± 26.4	NS
Relationship with family	90.1 ± 15.5	81.6 ± 23.9	0.006	87.9 ± 29.0	89.0 ± 18.3	NS
Relationship with friends	87.6 ± 16.1	82.3 ± 23.4	NS (0.088)	96.3 ± 26.5	89.0 ± 19.8	NS (0.073)
Financial satisfaction	50.9 ± 26.8	39.5 ± 28.4	0.009	79.4 ± 23.6	56.8 ± 23.4	<0.001
Subjective happiness	80.4 ± 20.2	59.6 ± 29.6	<0.001	87.8 ± 15.5	77.2 ± 27.3	NS (0.069)

P-Values were calculated using the Student's t-test for continuous variables, and χ^2-tests for categorical variables. ADL, activities of daily living; FDSK-11, 11-item Food Diversity Score Kyoto; QOL, quality of life; NS, not significant; SD, Standard Deviation; TMIG-IC, Tokyo Metropolitan Institute of Gerontology Index of Competence.

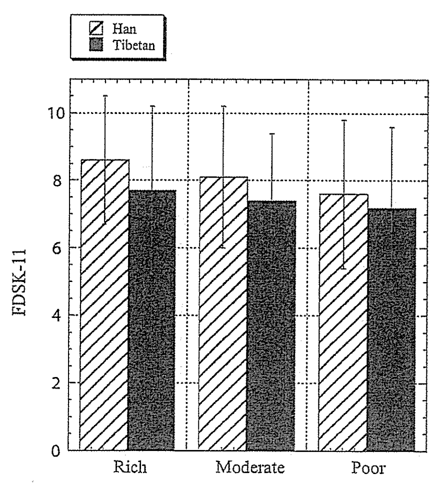

Figure 2 Relation between food diversity and subjective economic condition. Mean scores ± standard deviation of 11-item Food Diversity Score Kyoto were: Han, "rich" (n = 8) 8.6 ± 1.9; "moderate" (n = 81) 8.1 ± 2.1; and "poor" (n = 58) 7.6 ± 2.2. Tibetan, "rich" (n = 12) 7.7 ± 2.5; "moderate" (n = 33) 7.4 ± 2.0; and "poor" (n = 14) 7.2 ± 2.4.

with lower blood glucose in Han elderly subjects, but the opposite association was found in Tibetan ones.

We also checked each food in the FDSK-11 separately to find out the difference of the variety of food intake between Han and Tibetan elderly. Table 3 shows the percentage of elderly subjects who ate each food more than once a week between the subjects with high and low food diversity. The percentage of the Han elderly subjects who ate meat was 95% in the high food diversity group and 68% in the lower one, which was significantly different. However, no significant difference was found in the Tibetan subjects who ate meat between the high and low food diversity groups. In addition to meat, there was no significant difference of milk and vegetable intake between the Tibetan elderly subjects with high and low food diversity while there was in the Han elderly.

Discussion

Earlier studies reported that nutritional adequacy of a diet can be predicted by counting the number of food groups eaten.[4,17] In this study, we used the food groups from NNS-J with examples of Chinese and Tibetan

Table 2 Comparison of blood chemical indicators between the Han and Tibetan elderly with high and low food diversity score

	Han			Tibetan		
	High ($n = 102$)	Low ($n = 74$)	*P*-Value	High ($n = 31$)	Low ($n = 33$)	*P*-Value
Albumin (g/dL)	4.5 ± 0.3	4.4 ± 0.6	NS	4.5 ± 0.3	4.3 ± 0.3	0.09
HDL cholesterol (mg/dL)	51.1 ± 13.4	50.2 ± 17.5	NS	53.2 ± 12.5	54.0 ± 9.1	NS
Total cholesterol (mg/dL)	196 ± 45.5	194 ± 37.2	NS	228.4 ± 71.3	230.1 ± 41.8	NS
Triglyceride (mg/dL)	65.4 ± 30.6	64.1 ± 28.9	NS	55.2 ± 29.7	42.0 ± 11.5	0.026
LDL cholesterol (mg/dL)	130.1 ± 39.4	134.9 ± 36.8	NS	168.1 ± 40.7	171.2 ± 62.8	NS
Atherogenic Index	2.9 ± 0.9	3.2 ± 1.0	0.082	3.3 ± 0.8	3.5 ± 1.3	NS
Hemoglobin Level (g/dL)	16.7 ± 2.8	16.4 ± 2.7	NS	16.1 ± 1.7	15.6 ± 1.6	NS
Blood urea nitrogen (mg/dL)	16.8 ± 5.0	15.2 ± 4.3	0.063	17.0 ± 4.3	21.0 ± 5.5	0.008
Fating blood sugar (mg/dL)	81.9 ± 15.3	92.4 ± 42.6	0.029	96.2 ± 40.3	81.5 ± 5.8	0.036
2-h blood sugar (mg/dL)	108.4 ± 41.3	131.9 ± 87.8	0.039	132.7 ± 82.2	92.4 ± 26.7	0.049

Mean ± standard deviation. *P*-Values were calculated using the Student's *t*-test for continuous variables. HDL, high density lipoprotein; LDL, low-density lipoprotein.

Table 3 Percentage of the elderly subjects who ate each food more than once in a week between high and low food diversity

Food groups	Han			Tibetan		
	High	Low	*P*-value	High	Low	*P*-Value
Grain	100	100	NS	100	100	NS
Potatoes	96.1	87.5	0.042	96.8	69.7	0.006
Meat	95.1	68.1	<0.001	100	87.9	NS
Fish and Shellfish	65.3	9.6	<0.001	38.7	0	<0.001
Egg	81.2	36.2	<0.001	90	41.9	<0.001
Milk	93.1	70.8	<0.001	100	93.5	NS
Vegetables	99.1	92.2	0.047	100	87.9	NS
Seaweed	53.5	6.9	<0.001	37.9	0	<0.001
Beans	88.7	34.3	<0.001	87.1	15.2	<0.001
Nuts	85.7	25.0	<0.001	87.1	12.1	<0.001
Fruits	93.1	54.9	<0.001	96.2	78.1	0.053

daily foods and have found a significant health-related difference between subjects with high and low scores in the FDSK-11. This suggests that the FDSK-11 could serve as a useful indicator to screen food diversity, even in elderly living in the highlands in China.

The mean score of the FDSK-11 was higher in the Han elderly than Tibetan ones (7.8 vs 7.3). According to our previous study conducted in Tosa, Kochi Prefecture, Japan, in 2008, the mean score of the FDSK-11 was 9.9 in the Japanese elderly.[8] We showed that highlanders have still lower food diversity compared to Japanese elderly. Especially, Tibetans have traditionally less varied diets in their culture and living environment until now.

Food diversity is considered to decrease with aging[5,7] because of the changes in health status with aging such as deterioration in chewing ability.[18] Our previous study also revealed that the Japanese elderly participants with lower food diversity scores were significantly older than those with higher scores.[8] However, no association was found between food diversity and age in either the Han or Tibetan elderly highlanders. Instead, a close association was found between food diversity and financial satisfaction, although this was not seen in the Japanese elderly. Economic status was supposed to greatly influence food diversity in the elderly highlanders in Qinghai, China, with the background of a developing market economy which made them able to get various foods if they were affordable.

Lower food diversity was associated with lower ADL in both Han and Tibetan elderly subjects. This might be explained by insufficient nutritional intake affecting level of disability. QOL scores in subjective sense of health, relationship with family and subjective happiness were related to food diversity in the Han elderly subject, but not Tibetan ones. Tibetans have traditionally simple diets so food diversity might not affect subjective sense of QOL. Also, depression was not associated with food diversity in the Han and Tibetan elderly highlanders although we found a close association between them in the Japanese elderly. Eating various foods was not related to their subjective mood in elderly highlanders in Qinghai, China.

We also performed multivariate analysis and confirmed that the association between food diversity and ADL or QOL was independent of the economic status in the Han elderly while economic status and ADL or QOL were significantly related. In the case of Tibetan elderly, there was no significant relation between economic status and ADL or QOL.

Blood chemical indicators suggested a difference between the Han and Tibetan elderly. In Han elderly subjects, higher food diversity was associated with lower blood glucose levels, but the opposite association was found in Tibetan ones. In considering the theory that healthy diets are those that are the most varied,[1,4] in the case of Han elderly that higher food diversity was associated with lower blood glucose levels might be more reasonable. However, in the case of Tibetan elderly, the rapid change to consumption of a variety of foods from simple traditional food might lead to a rise in the blood glucose levels as well as obesity as a result of high BMI (Table 1). Azadbakht *et al.* reported that obesity could be increased with total food diversity scores.[19] We may be able to discuss the possibility that the amount of dietary intake might be higher in the Tibetan elderly with high food diversity compared to low food diversity and results in relatively higher blood sugar levels as well as higher BMI. Also, from Table 3, we can see that Tibetans have a particular food culture of frequent milk and meat consumption and this difference might also affect the discrepancy the relationship between food diversity and blood sugar level in the Han and Tibetan subjects.

In conclusion, food diversity was associated with ADL and QOL even in highlanders in Qinghai, China, although there were several differences between the Han and Tibetan subjects. Food assessment is very important as a useful indicator to know the actual condition of diet and its relation to health status of the community-dwelling elderly as well as the change of economic background in Qinghai highland, China. It can be predicted to become more diverse as a market economy develops in the highland. Increasing food diversity might have a good aspect in maintaining higher ADL and QOL. However, it might bring about a negative health impacts of obesity and high blood glucose levels in the case of Tibetans experiencing a drastic change from traditional food culture to a more diverse diet.

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