on the GDS-15). Random number generation and group allocation were conducted concomitantly by an independent epidemiologist not involved in the participant recruitment, intervention, or assessments. Written informed consent was then obtained from those assigned to the intervention group, from July to August, 2013.

There were 1734 residents over 65 years old in the town as of 2013. Of those, 127 residents were in hospital or geriatric care institutions, leaving 1607 residents to whom we had sent questionnaires for our annual observational study. A total of 893 people responded to the questionnaire. For the current study, we enrolled 184 eligible participants, with 93 in the intervention arm and 91 in the control arm (Fig. 1).

2.6. Consent to intervention and dropout from the analysis

The number of participants who consented to the intervention was 42 (45.2%). One participant dropped out from the intervention before it started, because her family wished her not to receive the letter. A total of 19 participants who consented to the intervention sent us non-obligatory replies to our letters. We sent 328 letters and received non-obligatory 62 replies. Those who did not respond to the annual questionnaire in 2014 numbered 20 (21.5%) in the intervention arm and 15 (16.5%) in the control arm. In all, 73 participants in each arm (78.5% in the intervention arm and 73.5% in the control arm) were included in the analysis (Fig. 1).

2.7. Intervention

Letters written on two pieces of A4 paper, including illustrations or photos, were sent in a sealed envelope once a month for eight months, from August, 2013, to March, 2014. The letter was composed of two parts: the first part was a handwritten message, with the aim of increasing social connectedness; the second part included computer-printed seasonal greetings or news of the month from Kyoto, where the study authors were located and one of the most famous cultural centres in Japan. Non-mandatory self-addressed stamped reply letters were enclosed with the letter. It was explicitly expressed in the reply letters that reply was not mandatory. Any treatment outside the trial was permitted.

2.8. Outcomes and measures

Self-reported outcomes were measured at baseline (at April, 2013) and post-intervention (from April to June, 2014), using self-reported questionnaires.

2.8.1. Primary outcomes

The primary outcome was the difference in GDS-15 scores at post-intervention, comparing the two groups as a measure of effectiveness.

The GDS-15 is a validated depression scale comprised of 15 items. This scale was developed to exclude the effects of non-specific symptoms such as anorexia and insomnia, which are frequently observed in elderly populations (Sheikh and Yesavage, 1986; Yesavage et al., 1982). Each item have two answers: yes or no. The highest possible score is 15, indicating the most severe depressive state. Using a cut-off point of 5, the GDS-15 has a sensitivity of 92% and a specificity of 81% to detect major depression as diagnosed through structured clinical interview (Lyness et al., 1997).

2.8.2. Secondary outcomes

Secondary outcomes were the differences in QOL, as assessed using self-rated visual analogue scales, self-rated basic ADLs (BADLs), and self-rated advanced ADLs (AADLs), between the two groups post-intervention.

Subjective QOL was assessed using a 100-mm visual analogue scale (the lowest QOL on the left end of the scale and the highest on the right) for the following five items: subjective sense of health, relationship with family, relationship with friends, financial state, and subjective happiness (Matsubayashi et al., 1997; Morrison, 1983).

Each participant rated his or her independence with respect to seven items corresponding to BADLs. Specifically, these items are as follows: walking, ascending and descending stairs, feeding, dressing, going to the toilet, bathing, and grooming. Each BADL item is evaluated based on four levels of competence: 3 = completely independent; 2 = requiring some assistance; 1 = requiring much assistance; 0 = completely dependent. The total score ranges from 0 to 21 (Matsubayashi et al., 1996; Pace, 1989).

For AADLs, the Tokyo Metropolitan Institute of Gerontology Index of Competence rating scale was used to measure competence (Ishizaki et al., 2000; Koyano et al., 1991). This scale consists of 13 items encompassing three sublevels of competence: (i) instrumental ADLs (five items: the ability to use public transport, buy daily necessities, prepare a meal, pay bills, and handle banking matters); (ii) intellectual activities (four items: the ability to complete forms, read newspapers, read books or magazines, and show interest in television programs or news articles on health-related matters); and (iii) social roles (four items: the ability to visit friends, give advice to relatives and friends in confidence, visit someone at the hospital, and initiate conversation with younger people). Because each item is rated as 'yes' or 'no', instrumental ADLs have a score range of 0–5, intellectual ADLs 0–4, and social role ADLs 0–4.

2.8.3. Other outcomes

The subjective sense of effectiveness of the intervention (4-point scale from 1 = *not effective* to 4 = *very effective*), recollection of the number of intervention mailings received, and the number of mailed replies were evaluated to measure acceptability of the postcard intervention. We also asked about the frequency of letters ('What frequency do you think is appropriate for the postcard intervention?': 1. Once per month; 2. Once per two months; 3. Once per three months; 4. Once per four months; 5. Once per six months; 6. Once per year), quantity of content ('What quantity of content do you think is appropriate per one letter?': 1. More than twice the present content, 2. About twice the present, 3. Same as present, 4. Half the present, 5. One-fourth the present, 6. Less than one-fourth the present).

2.8.4. Sociodemographic and other information

Data on age, sex, eating alone, and living alone were obtained through a self-reported questionnaire.

2.9. Statistical analysis

The difference in scores between the two groups at post-intervention was analysed using Student's *t*-test. Sensitivity analysis was conducted using data imputed by a multiple imputation method as well as completers' data. Statistical analysis was performed using SPSS ver. 20.0 (IBM Inc., Armonk, NY). Analysis of the primary outcome was conducted by an independent analyst who was blind to group allocation.

2.10. Sample size

To detect an effect size of 0.5 with $p = 0.05$ at 80% power, 63 participants were required per group. Assuming a non-consent and dropout rate of 30%, a total of 180 subjects were needed.

2.11. Ethical approval

The Institutional Review Board (IRB) of the Graduate School of Medicine, Kyoto University, reviewed and approved the study protocol and informed consent documents (E1658, February 12th, 2013). Written informed consent for data usage was obtained from all the participants and written informed consent for intervention was obtained from all the participants in the intervention arm.

3. Results

3.1. Baseline characteristics

The baseline characteristics of the participants are shown in Table 1. There were no substantial differences in important clinical characteristics between the two groups. The percentage of males was 28.0% in the intervention arm and 25.3% in the control arm. Mean age (S.D.) was 82.2 (7.9) in the intervention arm and 80.4 (7.4) in the control. The mean (S.D.) GDS-15 score was 8.2 (3.0) in the intervention arm and 8.2 (2.8) in the control arm.

3.2. Primary outcome

There was no significant difference in the mean GDS-15 score post-intervention of completers of the intervention arm ($M = 7.7$, S.D. $= 3.7$, $n = 73$) compared to the controls ($M = 7.5$, S.D. $= 3.5$, $n = 73$). A sensitivity analysis was performed after multiple imputations for missing data, and the result did not change; there was no significant difference with respect to the primary outcome between the intervention arm (pooled mean $= 8.1$, $n = 93$) and the control arm (pooled mean $= 7.5$, $n = 91$) (Table 2).

3.3. Secondary outcomes

Of the self-rated QOL ratings, there were no significant differences between the two groups in terms of friend relationships,

Table 1
Characteristics of participants at baseline.

	Intervention (n=93)	No treatment (n=91)
Male, %	28.0	25.3
Age, mean (S.D.)	82.2 (7.9)	80.4 (7.4)
Loss of spouse, %	73.9	72.1
Living alone, %	65.9	58.8
Medications		
Antidepressant, %	8.9	8.3
Hypnotic, %	44.1	43.7
Antihypertensive, %	62.0	73.3
Antidiabetic, %	14.3	18.8
Past medical history		
Cerebrovascular disease, %	9.9	14.5
Cardiovascular disease, %	23.9	17.6
Osteoarthropathy, %	58.7	53.5
GDS-15 (0–15), mean (S.D.)	8.2 (3.0)	8.2 (2.8)
BADLs (0–21), mean (S.D.)	19.7 (2.5)	19.8 (2.1)
IADLs (0–5), mean (S.D.)	4.2 (1.4)	4.3 (1.3)
Intellectual ADLs (0–4), mean (S.D.)	3.0 (1.1)	3.0 (1.1)
Social role ADLs (0–4), mean (S.D.)	3.0 (1.3)	3.1 (1.1)

ADLs: activities of daily living, GDS-15: 15-item geriatric depression scale, BADLs: basic activities of daily living, IADLs: instrumental activities of daily living.

Table 2
Geriatric Depression Scale (GDS-15) scores at post-intervention.

			Mean (S.D.)	n	p (t-test)
GDS-15 score	Completer	Intervention	7.7 (3.7)	73	0.664
		No treatment	7.5 (3.5)	73	
	Imputation[a]	Intervention	8.1	93	0.366
		No treatment	7.5	91	

[a] Multiple imputations.

family relationships, and subjective happiness, whereas there were significant differences in subjective health ($p=0.02$) and economic satisfaction ($p=0.04$). However, the significance disappeared in the sensitivity analysis after multiple imputations for missing data (Table 3).

There were no significant differences in the BADLs, IADLs, intellectual ADLs, and social role ADLs. The result did not change after multiple imputations for missing data (Table 4).

3.4. Other outcomes

We sent follow-up questionnaires about the intervention to participants who completed the intervention ($n=41$), and we received 24 replies (58.5%). As for the subjective effectiveness of the postcard intervention, 14 (58%) thought it was very effective, six (25%) thought it was a little effective, and four (17%) thought it was not very effective. As an index of fidelity of the postcard intervention, we asked participants how many letters they had received. Participants who replied with the correct answer (eight letters) numbered 18 (75%). Other answers were seven letters ($n=2$, 8%), four letters ($n=1$, 4%), five letters ($n=1$, 4%), six letters ($n=1$, 4%), and nine letters ($n=1$, 4%). Regarding the participants' preference in terms of frequency and quantity of content for the letter intervention, the frequencies participants thought appropriate were once a month ($n=11$, 46%), once in two months ($n=7$, 29%), once in three months ($n=3$, 13%), and once in four months ($n=2$, 8%). One participant answered that she did not want to receive letters. Almost all the replies answered that the present quantity of content in the letter intervention was appropriate ($n=22$, 92%). One participant replied that half of the present quantity was appropriate, and one participant did not reply to the question.

Table 3
Quality of life at post-intervention.

			Mean (S.D.)	n	p (t-test)
Subjective health	Completer	Intervention	42.8 (18.7)	73	0.021
		No treatment	51.4 (19.6)	73	
	Imputation[a]	Intervention	15.2	93	0.249
		No treatment	24.2	91	
Friend relationships	Completer	Intervention	64.6 (22.0)	73	0.644
		No treatment	66.5 (20.7)	73	
	Imputation[a]	Intervention	59.1	93	0.607
		No treatment	61.6	91	
Family relationships	Completer	Intervention	69.2 (20.8)	73	0.233
		No treatment	63.6 (25.2)	73	
	Imputation[a]	Intervention	70	93	0.437
		No treatment	66.7	91	
Economic satisfaction	Completer	Intervention	43.8 (25.2)	73	0.041
		No treatment	53.7 (24.6)	73	
	Imputation[a]	Intervention	43.2	93	0.120
		No treatment	50.6	91	
Subjective happiness	Completer	Intervention	53.6 (24.0)	73	0.715
		No treatment	55.2 (21.3)	73	
	Imputation[a]	Intervention	47.0	93	0.837
		No treatment	48.1	91	

[a] Multiple imputations.

Table 4
Basic and advanced activities of daily living at post-intervention.

			Mean (S.D.)	n	p (t-test)
BADLs	Completer	Intervention	13.3 (9.5)	73	0.514
		No treatment	14.2 (9.1)	73	
	Imputation	Intervention	13.4	93	0.547
		No treatment	14.2	91	
IADLs	Completer	Intervention	4.1 (1.4)	73	0.567
		No treatment	4.2 (1.4)	73	
	Imputation	Intervention	4.1	93	0.566
		No treatment	4.2	91	
Intellectual ADLs	Completer	Intervention	2.8 (1.3)	73	0.343
		No treatment	3.0 (1.2)	73	
	Imputation	Intervention	1.6	93	0.362
		No treatment	1.9	91	
Social role ADLs	Completer	Intervention	3.2 (1.2)	73	0.701
		No treatment	3.3 (1.0)	73	
	Imputation	Intervention	2.0	93	0.440
		No treatment	2.3	91	

ADLs: activities of daily living, BADLs: basic activities of daily living, IADLs: instrumental activities of daily living.

4. Discussion

The present study is the first postcard intervention for depression in community-dwelling elderly people. We found that the intervention was neither acceptable nor effective in our population.

The percentage of people who consented to the intervention was low (45.2%), although the percentage of completers was high; 97.6% of people who consented to the intervention completed the intervention. Two reasons may explain the low consent rate. First is the influence of widespread fraud against elderly people in Japan, in which victims are told to pay money to criminals pretending to be their acquaintances. As a result, elderly people have become cautious with strangers such as the present researchers. Second is the stigmatisation associated with depression. In recruitment, some people said "I'm not depressed and don't need such an intervention." Even if the questionnaire results indicated that people were depressed, some people did not admit that explicitly. Other research indicates that 26.8% of people in Japan reported they would not tell anyone if they had depression (Griffiths et al., 2006). Given these factors, a population approach may be a better way to meet the objectives. That is, setting only older age as the eligibility criterion may be a better choice. Once people consent to the intervention, they are likely to be willing to accept it, considering the high completion rate in the current study. Fidelity of the intervention was also good, as indicated by the recollection of the number of postcards received; 87% of replies were correct plus or minus one, although the low response rate lowered the quality of results.

As for the effectiveness, the present study showed that the postcard intervention was not effective in improving depression among community-dwelling elderly people, although previous studies using postcard interventions have reported effectiveness against self-harm or suicide (Beautrais et al., 2010; Carter et al., 2005, 2007; Hassanian-Moghaddam et al., 2011; Motto, 1976). The differences between the present and previous studies are likely related to the participants and the outcome variables. Our inclusion criteria and outcome variables were relatively undefined compared with the previous studies. We used GDS-15 scores as the inclusion criteria. Although there are studies comparing GDS-15 scores and the diagnosis rate of major depression (Mitchell et al., 2010), the GDS-15 can only evaluate depressive mood. Participants in the present study were more heterogeneous, including not only major depression but also other disorder accompanied with depressive mood such as anxiety disorders. This may have led to a different result from previous studies. The primary outcome of the present study was also based on the GDS-15 score, whereas previous studies used more tangible outcomes. As we mentioned previously, stigmatisation may have prevented participants from expressing honest answers. Using more tangible outcomes such as hospital visits and suicide could change the results. However, that approach would have required a much larger sample size, which was not feasible in the present setting. Another consideration is the quality of the intervention. According to the present results, the majority of responders thought the intervention was effective and appropriate in frequency and quantity. Given these results, the present intervention was not necessarily of low quality.

In addition to the primary outcome, we could not find evidence of effectiveness in any of the secondary outcomes: subjective QOL, BADLs, and AADLs. Depressive mood has been shown to erode QOL and lead to disability (Kivelá and Pahkala, 2001; Penninx et al., 1998; Unutzer, 2009). It is reasonable to think that the intervention did not improve QOL and ADLs because it failed to improve depressive mood. However, another possible reason for the negative results is the timing of the evaluation. There was a time lag between the end of the intervention and the evaluation. It was one month after the end of the intervention when we sent out the annual health check questionnaire, and it took approximately two months to collect the answers. The time lag could have lessened the effect, if the intervention was indeed effective at its conclusion.

One limitation of the present study relates to its external validity. First, as the setting was a town in Japan, cultural background should be considered. As aforementioned, the acceptability of unsolicited letters may differ between cultures. Some participants felt burdened by the need to respond to the letters, even if it was explicitly expressed that reply was not mandatory. This may be related to Japanese culture. Second, the participants were elderly people. The results may be different when the intervention is applied to younger individuals. Some elderly people may have difficulty writing or seeing.

Another limitation is the low consent rate for the intervention. Approximately half of the people randomised to the intervention arm did not consent to the intervention. However, the present study reflects a realistic portrayal of the intervention, that is, how readily participants would accept the intervention and how effective it is, including people who did not accept it. This information is valuable from the viewpoint of policymakers or related persons.

In spite of these limitations, the results of the present study are robust, in that this was a pragmatic study with a careful sample size calculation. By using Zelen's design, the study was more realistic than an ordinary randomised controlled trial. Typically, an intervention conducted by the local government starts with recruitment of participants. The present study was a realistic evaluation of the feasibility and effectiveness of a postcard intervention in the community.

5. Conclusion

Postcard intervention for depression in elderly people in a rural setting in Japan is neither feasible nor effective. However, the descriptive results suggest that the intervention may be effective given different parameters. In future research, studies in different settings and with different participants should be conducted.

6. Conflict of interests

TAF has received honoraria for speaking at CME meetings sponsored by Asahi Kasei, Eli Lilly, GlaxoSmithKline, Mochida, MSD, Otsuka, Pfizer, Shionogi, and Tanabe-Mitsubishi. He is a diplomate of the Academy of Cognitive Therapy. He has received royalties from Igaku-Shoin, Seiwa-Shoten, and Nihon Bunka Kagaku-sha. He is on the advisory board for Sekisui Chemicals and Takeda Science Foundation. The Japanese Ministry of Education, Science, and Technology, the Japanese Ministry of Health, Labour and Welfare, and the Japan Foundation for Neuroscience and Mental Health have funded his research projects. All the other authors report no conflict of interests.

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ORIGINAL RESEARCH

Oxidized Low Density Lipoprotein Among the Elderly in Qinghai-Tibet Plateau

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Objective.—Several environmental factors including hypoxia have been reported to contribute to oxidative stress in individuals living in the highlands. However, little is known about the role of oxidized low-density lipoprotein (ox-LDL) among community-dwelling elderly in the Qinghai-Tibet plateau.

Methods.—The study population comprised 168 community-dwelling elderly subjects aged 60 years or older (male to female ratio, 70:98; mean age, 65.8 years) living in Haiyan County, located 3000 to 3200 m above sea level, 30 km northwest of Xining, Qinghai. The subjects were volunteers who joined a Comprehensive Geriatric Assessment. Plasma ox-LDL was measured in 168 community-dwelling elderly subjects aged 60 years or older (23 Tibetans and 145 Hans) with a monoclonal antibody-based enzyme-linked immunosorbent assay.

Results.—Mean ox-LDL level was higher among Tibetan elderly than Han elderly (Tibetan, 79.0 ± 29.6 U/L; Han, 62.8 ± 23.5 U/L; $P = .003$). Tibetan ethnicity was significantly associated with ox-LDL levels after adjusting for LDL cholesterol levels. In addition, high ox-LDL levels (≥70 U/L) were significantly associated with a homeostasis model assessment insulin resistance index of at least 1.6 (odds ratio [OR], 2.82; 95% confidence interval [95% CI], 1.11 to 7.15; $P = .029$) and ankle brachial pressure index of less than 1.0 (OR, 4.85; 95% CI, 1.14 to 10.00; $P = .028$), after adjusting for age, sex, and ethnicity.

Conclusions.—Our findings support the hypothesis that ox-LDL levels are higher among Tibetan elderly highlanders compared with those among Han elderly. As ox-LDL levels can affect insulin resistance and arteriosclerosis, further research is needed to determine how oxidative stress influences the health situation among elderly individuals at high altitudes.

Key words: Oxidative stress, Ox-LDL, High altitude, Elderly people, Tibetan, Han

Introduction

Inspired oxygen pressure decreases with altitude. Compared with values at sea level, this pressure is roughly 89% at an altitude of 1000 m, 79% at 2000 m, 69% at 3000 m, 60% at 4000 m, and 52% at 5000 m.[1] Several environmental factors including hypoxia may contribute to oxidative stress in individuals living in the highlands.[2,3] In general, ultraviolet radiation increases by approximately 4% per 300 m because of decreases in clouds, dust, and water vapour.[4] In addition, as much as 75% of ultraviolet radiation can be reflected back by snow.[4] Low temperature stress contributes significantly to oxidative stress, and temperature decreases with increasing altitude at a rate of approximately 6.5°C per 1000 m.[4,5] Lower dietary intake of antioxidants such as fruits and vegetables could also result in higher levels of oxidative stress.[6–8] Oxidative stress is widely recognized as being associated with various disorders including atherosclerosis, diabetes mellitus, hypertension, and hypercholesterolemia, to name a few.[9–13] Many studies have pointed out the advantageous points of the Tibetan

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adaptation to high altitude. However, our previous study, which measured serum hydroperoxides with the Diacron reactive oxygen metabolites test (d-ROMs; Diacron, Parma, Italy), showed the Tibetan elderly had higher levels of reactive oxygen metabolites (ROM) than the Han elderly.[14] The present study aimed to investigate oxidized low-density lipoprotein (ox-LDL) level as a reliable measure of oxidative stress and its association with other cardiovascular and metabolic variables among community-dwelling elderly individuals living at high altitudes.[15–19]

Materials and methods

SUBJECTS

Our study population comprised 168 community-dwelling elderly subjects aged 60 years or older (male/female ratio, 70:98; mean age, 65.8 years) living in Haiyan County (Qinghai, China). Haiyan County is located 3000 to 3200 m above sea level, 30 km north-west of Xining, which is the capital of Qinghai province in China. Our subjects were elderly volunteers who joined our medical and geriatric examination camp. The survey for community-dwelling elderly living in Haiyan County was conducted in August 2008.

OX-LDL LEVELS

In February 2009, concentrations of ox-LDL in cryopreserved plasma samples at Affiliated Hospital of Qinghai University, China, were measured by a competitive enzyme-linked immunosorbent assay (ELISA) kit using a specific murine monoclonal antibody, mAb-4E6 (Mercodia, Uppsala, Sweden). The results were interpreted in accordance with the manufacturer's instructions. The mAb-4E6 is directed against a conformational epitope in the apolipoprotein B-100 (apoB-100) moiety of low-density lipoprotein (LDL) that is generated as a consequence of the substitution of at least 60 lysine residues of apoB-100 with aldehydes. The substituting aldehydes can be produced by peroxidation of LDL lipids, which generates ox-LDL. The results were interpreted in accordance with the manufacturer's instructions.

Comprehensive Geriatric Assessments

Blood pressure was measured twice with the subject in a sitting position using an autosphygmomanometer (HEM 757, Omron, Japan). Hypertension was defined as 140 mm Hg or greater for systolic pressure, 90 mm Hg or greater for diastolic pressure, or if the subject was taking antihypertensive medication. Blood chemical tests were conducted twice, at fasting and 2 hours after drinking 75 g of glucose, among subjects who provided informed consent. Diabetes mellitus and impaired glucose tolerance were defined according to World Health Organization criteria. Specifically, diabetes mellitus was defined as a fasting blood sugar (FBS) of 126 mg/dL or greater or 2-hour oral glucose tolerance test (OGTT) of 200 mg/dL or greater, or if the subject was taking diabetes medication, and impaired glucose tolerance was defined as an FBS from 110 mg/dL to 126 mg/dL or an OGTT from 140 to 200 mg/dL. Insulin resistance was assessed using the homeostasis model assessment insulin resistance index (HOMA-R) and was calculated as fasting plasma glucose $\times$ fasting serum insulin / 405.[20] Blood chemical analyses were conducted in the central laboratory of Qinghai University Hospital. Ankle brachial pressure index (ABI) and the cardio ankle vascular index (CAVI) were measured using a VaSera instrument (Fukuda Denshi, Tokyo, Japan). Carotid plaques were examined by carotid ultrasound. Plaques were defined as focal structures that encroached into the arterial lumen at least 0.5 mm, comprised 50% of the surrounding intima-media thickness value, or that for which the thickness was 1.5 mm from the media-adventitia interface to the intima-lumen interface.

ETHICAL APPROVAL

These surveys were approved by the Ethics Committee of the Research Institute for Humanity and Nature (2007-02) and Medical Institute of Qinghai University. Written informed consent was obtained from each subject.

STATISTICAL ANALYSIS

Data were analyzed with SPSS 15.0 for Windows (IBM Corp, Armonk, NY). Baseline data are presented as mean $\pm$ SE or percentages. Stepwise multiple regression analyses (to $P < .05$) were used to assess associations between ox-LDL and other variables. Standardized β coefficients were used, as they allow for a direct comparison of the strength of associations between ox-LDL and other variables. Any factors significant in the univariate model were used in the multivariate analysis, and a probability value of less than 0.05 was considered statistically significant. Logistic regression analysis (to $P < .05$) was used to assess associations between ox-LDL and geriatric variables. The logistic regression analysis incorporated covariates of age, sex, and ethnicity.

Results

COMPARISON OF TIBETAN AND HAN ELDERLY HIGHLANDERS

Our elderly study population consisted of 23 Tibetans and 145 Hans. Table 1 compares basic characteristics of Tibetan and Han elderly highlanders in Haiyan County

Table 1. Comparison of basic characteristics between Tibetan and Han elderly highlanders

Characteristic	*Tibetan (n = 23)*[a]	*Han (n = 145)*[a]	*P value*[b]
Age (years)	65.7 (65.0–66.6)	65.8 (63.9–67.5)	.919
Sex (female)	11 (47.8)	87 (60.0)	.363
Current smoker (no, yes, unknown)	12 (52.2), 3 (13.0), 8 (34.8)	87 (60.0), 23 (15.9), 35 (24.1)	.552
Vegetables intake more than 5 times a week (no, yes, unknown)	4 (17.4), 11 (47.8), 8 (34.8)	31 (21.4), 80 (55.2), 34 (23.4)	.504
Fruits intake at least once a week (no, yes, unknown)	5 (21.7), 10 (43.5), 8 (34.8)	55 (37.9), 53 (36.6), 37 (25.5)	.309
Meat intake more than 2 times a week (no, yes, unknown)	3 (13.0), 12 (52.2), 8 (34.8)	56 (38.6), 54 (37.2), 35 (24.1)	.058
Eggs intake at least once a week (no, yes, unknown)	3 (13.0), 11 (47.8), 9 (39.1)	48 (33.1), 57 (39.3), 40 (27.6)	.143
Dairy products intake at least once a week (no, yes, unknown)	4 (17.4), 11 (47.8), 8 (34.8)	66 (45.5), 45 (31.0), 34 (23.4)	.039
Work or gardening more than 5 times a week (no, yes, unknown)	5 (21.7), 10 (43.5), 8 (34.8)	42 (29.0), 68 (46.9), 35 (24.1)	.522

[a] Data are given as the number (percentage) or as mean (95% confidence interval).
[b] P values were calculated using Student's t test or χ^2 test.

(Qinghai province). Mean age and sex ratios did not differ significantly, but dairy product intake was higher among Tibetans. Table 2 compares cardiovascular and metabolic variables of the 2 ethnic groups. No significant difference was found in mean systolic blood pressure, oxygen saturation, hemoglobin concentration, fasting

Table 2. Comparison of cardiovascular and metabolic items between Tibetan and Han elderly highlanders

Item	*Tibetan (n = 23)*[a]	*Han (n = 145)*[a]	*P value*[b]
Systolic blood pressure (mm Hg)	130.4 (119.5–141.4)	139.0 (134.8–143.3)	.130
Diastolic blood pressure (mm Hg)	78.8 (73.7–84.0)	85.3 (83.0–87.6)	.034
Hypertension	11 (47.8)	76 (52.4)	.657
SpO_2 (%)	90.1 (88.6–91.6)	89.9 (89.1–90.6)	.799
Hemoglobin (g/dL)	15.8 (15.0–16.7)	16.1 (15.7–16.5)	.679
Fasting blood sugar (mg/dL)	92.6 (76.1–109.1)	84.5 (80.0–89.0)	.216
IFG, IGT, or diabetes	4 (17.4)	22 (15.2)	.758
HOMA-R	1.08 (0.66–1.50)	1.14 (0.97–1.30)	.799
HOMA-R $\geq$ 1.6	1 (4.3)	23 (15.9)	.197
Triglyceride (mg/dL)	63.2 (45.1–81.3)	61.4 (57.2–65.6)	.836
HDL cholesterol (mg/dL)	53.6 (46.8–60.3)	48.2 (46.3–50.1)	.054
LDL cholesterol (mg/dL)	175.9 (157.5–194.3)	137.9 (131.9–143.9)	<.001
Dyslipidemia	18 (78.3)	80 (55.2)	.006
ox-LDL (U/L)	79.0 (65.9–92.1)	62.8 (58.9–66.6)	.003
ox-LDL $\geq$ 70 U/L	14 (39.1)	42 (29.0)	.004
Carotid plaque	10 (43.5)	37 (25.5)	.132
CAVI	9.3 (8.7–9.9)	9.3 (9.0–9.6)	.895
CAVI $\geq$ 9.0	13 (56.5)	74 (51.0)	1.000
ABI	1.06 (0.99–1.13)	1.10 (1.08–1.13)	.162
ABI < 1.0	2 (8.7)	14 (9.7)	1.000

SpO_2, oxygen saturation of hemoglobin; IFG, impaired fasting glucose; IGT, impaired glucose tolerance; HOMA-R, homeostasis model assessment insulin resistance index; HDL, high-density lipoprotein; LDL, low-density lipoprotein; ox-LDL, oxidized low-density lipoprotein; CAVI, cardio ankle vascular index; ABI, ankle brachial pressure index.

[a] Data are given as the number (percentage) or as mean (95% confidence interval).
[b] P values were calculated using Student's t test or χ^2 test.

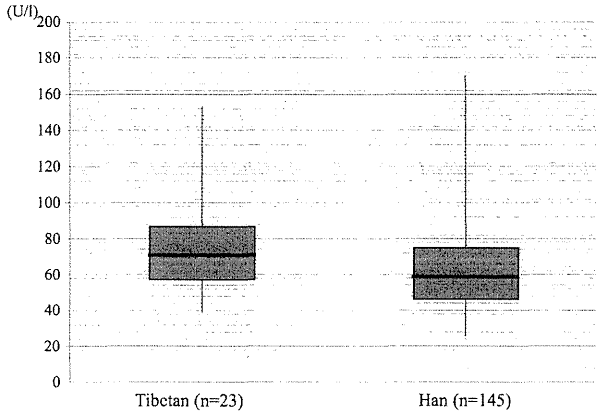

Figure. Level of oxidized low-density lipoprotein (LDL) in Tibetan and Han elderly highlanders. The thick horizontal lines represent medians, boxes represent interquartile ranges, and whiskers represent extreme values. The oxidized LDL levels differed significantly between Tibetan and Han after adjustment for LDL levels ($P = .025$).

blood glucose, HOMA-R, triglycerides, high-density lipoprotein (HDL) cholesterol, CAVI, and ABI levels between Tibetan and Han individuals. Mean diastolic blood pressure was lower in Tibetan elderly than in Han elderly, whereas LDL cholesterol was higher in Tibetan elderly than in Han elderly. The ox-LDL levels differed significantly between Tibetan and Han after adjustment for LDL levels ($P = .025$; Figure). The prevalence of dyslipidemia and ox-LDL of 70 U/L or greater was significantly higher in Tibetan elderly than in Han elderly.

OX-LDL LEVELS, ASSOCIATED FACTORS, AND PROBLEMS

The univariate analysis demonstrated that being Tibetan, LDL cholesterol levels, and frequency of vegetable intake and meat intake were associated with ox-LDL levels. The stepwise multiple regression analysis found that being Tibetan and LDL cholesterol levels were independent predictors of increasing ox-LDL levels (Table 3).

High ox-LDL levels ($\geq$70 U/L) were significantly associated with prevalence of dyslipidemia, HOMA-R of 1.6 or greater, impaired fasting glucose (IFG), impaired glucose tolerance (IGT), diabetes, carotid plaque, and ABI of less than 1.0 in Han elderly highlanders by χ^2 test (Table 4). High ox-LDL levels ($\geq$70 U/L) were significantly associated not only with dyslipidemia but also with HOMA-R of 1.6 or greater, IFG, IGT, or diabetes, after adjusting for age, sex, and ethnicity by logistic regression analysis (Table 5). The cutoff level for ox-LDL was defined as the cutoff at the 70th percentile.

Discussion

The present study showed that Tibetan elderly highlanders had higher ox-LDL levels than Han elderly highlanders. High ox-LDL levels were significantly associated with high HOMA-R ($\geq$1.6) and low ABI ($<$1.0) levels, and are associated with insulin resistance

Table 3. Factors associated with levels of oxidized low-density lipoprotein by regression analysis

Factor	*Univariate analysis*		*Multivariate analysis*[a]	
	Standardized coefficient β	*P value*	*Standardized coefficient β*	*P value*
Age (years)	.024	.758		
Female (vs male)	–.029	.705		
Tibetan (vs Han)	.225	.003	.267	.004
Systolic blood pressure (mm Hg)	–.092	.239		
Diastolic blood pressure (mm Hg)	–.146	.063		
SpO_2 (%)	.082	.314		
Hemoglobin (g/dL)	–.101	.212		
Fasting blood sugar (mg/dL)	.02	.804		
HDL cholesterol (mg/dL)	.064	.427		
LDL cholesterol (mg/dL)	.394	<.001	.206	.029
Current smoker	–.051	.569		
Vegetables intake more than 5 times a week	–.19	.034	–.076	.388
Fruits intake at least once a week	.122	.178		
Meat intake more than 2 times a week	.266	.003	.126	.163
Eggs intake at least once a week	.136	.140		
Dairy products intake at least once a week	.027	.761		
Work or gardening more than 5 times a week	.082	.364		

SpO_2, oxygen saturation of hemoglobin; HDL, high-density lipoprotein; LDL, low-density lipoprotein.

[a] Multiple regression analysis was used. Multivariate model considered factors with $P < .05$ in the univariate analysis.

Table 4. Relations of high oxidized LDL (≥70 U/L) to cardiovascular and metabolic problems in Tibetan and Han elderly highlanders

	Tibetan (n = 23)[a]			*Han (n = 145)*[a]		
Variable	*ox-LDL < 70 U/L (n = 9)*	*ox-LDL ≥ 70 U/L (n = 14)*	*P value*[b]	*ox-LDL < 70 U/L (n = 103)*	*ox-LDL ≥ 70 U/L (n = 42)*	*P value*[b]
Hypertension	2 (22.2)	9 (64.3)	.089	56 (54.4)	20 (47.6)	.578
Dyslipidemia	6 (66.7)	12 (85.7)	1.000	49 (47.6)	31 (73.8)	.001
HOMA-R ≥ 1.6	0 (0.0)	1 (7.1)	1.000	12 (11.7)	11 (26.2)	.043
IFG, IGT, or diabetes	1 (11.1)	3 (21.4)	1.000	11 (10.7)	11 (26.2)	.038
Carotid plaque	2 (22.2)	8 (57.1)	.070	31 (30.1)	6 (14.3)	.048
CAVI ≥ 9.0	4 (44.4)	9 (64.3)	.203	53 (51.5)	21 (50.0)	1.000
ABI < 1.0	1 (11.1)	1 (7.1)	1.000	6 (5.8)	8 (19.0)	.024

ox-LDL, oxidized low-density lipoprotein; HOMA-R, homeostasis model assessment insulin resistance index; IFG, impaired fasting glucose; IGT, impaired glucose tolerance; CAVI, cardio ankle vascular index; ABI, ankle brachial pressure index.

[a] Data are given as the number (percentage).

[b] P values were calculated using χ^2 test.

and arteriosclerosis. Although the precise pathophysiologic mechanisms have not been established, we speculate that differences in lifestyles and evolutionary genetic backgrounds between Tibetans and Hans affected ox-LDL levels. Factors known to affect ox-LDL include living in hypoxic environments, ultraviolet light, smoking habits, vegetable or fruit intake, and coldness.[6] In addition, one that we find particularly interesting is the effect of the natural selection of endothelial Per-Arnt-Sim domain protein 1 (*EPAS1*).[21]

Several ways by which Tibetans have adapted to high altitudes have been reported as advantageous. For example, Tibetans tend to have lower hemoglobin (Hb).[22,23] A mild increase in Hb is advantageous for oxygen transport to tissues, but too much Hb increases the risk of morbidities from pulmonary hypertension, stroke, and intrauterine growth restriction.[24] A study of individuals in the Andes found that ideal Hb concentrations are actually not so high.[25] Compared with Andeans, Tibetans have been reported to have higher ventilation volume at rest, lower pulmonary vasoconstriction under low oxygen, fewer low-birth-weight babies, and lower Hb.[26,27] One other way that Tibetans adapt to high altitude hypoxic environments is increased nitric oxide (NO) production.[28–30] Tibetans has been reported to have higher forearm blood flow and higher plasma nitrite levels compared with residents at sea level in the United States.[30] Higher blood flow and circulating NO products can offset high altitude hypoxia, and serve as a type of adaptation to hypoxia.[30] However, nitroxides are known to have dual activities as pro-oxidants and antioxidants.[31] Increased reactive oxygen species (ROS) reduce the amount of bioactive NO by chemical inactivation to form toxic peroxynitrite. In turn, peroxynitrite can uncouple endothelial NO synthase to become a dysfunctional superoxide-generating enzyme that contributes to vascular oxidative stress.[32]

Table 5. Relations of high oxidized low-density lipoprotein (≥70 U/L) to cardiovascular and metabolic problems

Variable	*Odds ratio*[a]	*95% confidence interval*	*P value*
Hypertension	1.01	0.52–1.98	.978
Dyslipidemia	4.97	2.00–12.35	.001
HOMA-R ≥ 1.6	2.82	1.11–7.15	.029
IFG, IGT, or diabetes	2.68	1.08–6.64	.034
Carotid plaque	0.56	0.24–1.31	.180
CAVI ≥ 9.0	1.05	0.48–2.30	.901
ABI < 1.0	4.85	1.14–10.00	.028

HOMA-R, homeostasis model assessment insulin resistance index; IFG, impaired fasting glucose; IGT, impaired glucose tolerance; CAVI, cardio ankle vascular index; ABI, ankle brachial pressure index.

[a] Logistic regression analysis (to $P < .05$) was used. Covariates considered were age, sex, and ethnicity.

Our study found that Tibetan elderly highlanders have higher ox-LDL levels compared with those of Han elderly highlanders, but pathophysiological mechanisms in convincing detail remain to be identified. Several interesting reports have been published with regard to natural selection of *EPAS1*, egl nine homolog 1 (*EGLN1*), and peroxisome proliferator-activated receptor alpha (*PPARA*), identified as being involved in the adaptational process to hypoxia that has occurred in Tibetans over generations.[21,33,34] They are highly involved in gene regulation with regard to angiogenesis and metabolism of carbohydrates and fat. One study found that after exposure to hypoxic conditions, heterozygous *EPAS1*-deficient mice were protected against pulmonary hypertension and right ventricular hypertrophy.[35] Yet another study found that in such mice, oxidative stress was increased.[36] Indeed, as mentioned above, compared with Andeans, Tibetans have lower pulmonary hypertension under low oxygen. According to the results of the present study, Tibetan elderly individuals had higher levels of ox-LDL, an indicator of oxidative stress, relative to their Han counterparts. In Yushu County located at 3700 m above sea level, we detected increased weight, hypertension, and impaired glucose tolerance in relatively high prevalence among the Tibetan elderly.[37] We should be more concerned about the relationships among hypoxia, selected genes, oxidative stress, and metabolic problems. Although the data remain somewhat inconclusive, it is certainly possible that selected genes of Tibetans may partially contribute to the levels of ox-LDL.[21,30,35,36,38,39] It should be noted that advantages under certain conditions may become disadvantageous from different aspects.

LIMITATIONS

This cross-sectional study may suggest an association between ox-LDL levels and cardiovascular and metabolic indicators, but a cause-and-effect relationship cannot be concluded here. This study focused only on ox-LDL levels as an indicator of oxidative stress, but multilateral methods were needed to examine the consequences of ROS generation, which can be detected by formation of biomolecules altered by oxidation, including DNA, lipids, and proteins. To determine ethnicity, we used identification cards that included a description of ethnicity, but were unable to determine the precise duration for which an individual and his or her ancestors had resided at high altitude. The population-genetic mixture between Tibetans and Hans could not be determined by our data. The single-county location limits the generalizability. In addition, the study has a small and unequal sample size. The statistical power to detect the difference of ox-LDL between Tibetan and Han was approximately 0.83.

Conclusions

Our findings support the hypothesis that ox-LDL levels are higher among Tibetan elderly highlanders relative to those among Han elderly. As ox-LDL levels can affect insulin resistance and arteriosclerosis, further research is needed to determine how oxidative stress occurs among elderly individuals at high altitudes.

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0.69 (95% CI=0.68–0.71) and for NH placement was 0.77 (95% CI=0.75–0.78).

CONCLUSIONS

A risk index devised in 1962[1] to predict and measure rehabilitation outcomes on inpatient units also predicts adverse outcomes in community-living older adults in the modern era. This finding underscores the central importance of functional and cognitive status in older adults across settings and historical eras. Use of this score in clinical practice is not advocated—in particular, there is a ceiling effect, with most community-living older adults scoring high on the scale. Nonetheless, the cumulative effect of cognitive and functional loss remains important in the clinical care, administration, and research into the health of older adults. This early risk score also demonstrates the historical roots of some of the current frailty models. Although not defined as frailty, the notion has deep roots in geriatric medicine.

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COMMUNITY-BASED COMPREHENSIVE GERIATRIC ASSESSMENT OF SHORT- AND LONG-TERM PREDICTORS OF COGNITIVE DECLINE IN ELDERLY ADULTS

To the Editor: Only little is known regarding successful approaches to primary or secondary prevention of most dementia. There is a need for detecting and modifying specific risk factors assessable in the community. From a combined global and local viewpoint, a community-based comprehensive geriatric assessment (CGA) of older adults in a rural Japanese town was performed to investigate its association with cognitive status.

Recent investigations have shown that physical performance is an important predictor of change in cognitive function[1–3] and that blood pressure (BP) is associated with cognitive performance.[4–6] How changes in cognitive function may relate to changes in physical assessments, brachial and central systolic BP and other cardiovascular and clinical endpoints was investigated after 3 and 5 years of follow-up.

Annual community-based CGA of elderly adults living in Tosa (Kochi prefecture) has been performed since 2004. Of health check participants aged 75 to 99 in 2005 (reference; second year of project), 133 (94 women, 39 men, mean 2005 age 80.1) were followed up in 2008 and 108 (77 women, 31 men, mean 2005 age 79.9) again in 2010.

Left brachial BP and right radial arterial pulse waves were noninvasively measured using oscillometry and tonometry (HEM-9000AI, Omron Healthcare Co., Ltd., Kyoto, Japan).[7] SBP2 (radial augmentation index (AI) × (brachial SBP–brachial DBP) + brachial DBP) and AI were determined using pulse wave analysis.[8]

Because central SBP by direct measurement is reportedly closely associated with radial SBP2,[8] radial SBP2 was used as the derived central aortic pressure. Subjects grouped in terms of declining, unchanged, or improving cognitive function were compared using one-way analysis of variance or chi-square tests, complemented by Student *t*-tests. $P < .05$ was considered statistically significant.

In 2005, mean Mini-Mental State Examination (MMSE) score was 27.5 (range 24–30), mean Hasegawa Dementia Rating Scale—Revised (HDS-R) score was 26.8 (range 19–30), mean modified Kohs' block design test score was 21.7 (range 2–46), and mean Clock Drawing Test (CDT) score was 8.5 (range 1–10) (Table 1).

Improvement (or decline) in cognitive function was defined as an increase (or decrease) of three points on the MMSE. In 2008 (3-year follow-up), men were more likely to have declined than women ($P = .04$), CDT was larger ($P = .01$), Timed Up and Go was faster ($P = .02$), and serum creatinine was higher in the improved than in the unchanged group ($P = .04$). In 2010 (5-year follow-up), central systolic BP was higher in the declined than in the unchanged group ($P = .02$), and hemoglobin was higher in

Table 1. Association Between Comprehensive Geriatric Assessment and Alterations in Cognitive Performance at 3- and 5-Year Follow-Up in Older Adults in a Rural Japanese Town

	2008 (3-Year Follow-Up Since 2005)					2010 (5-Year Follow-Up Since 2005)				
Characteristic	Total, N = 133	Declined, n = 15	Unchanged, n = 76	Improved, n = 42[a]	P-Value[b]	Total, N = 108	Declined, n = 31	Unchanged, n = 55	Improved, n = 22[a]	P-Value[b]
Age, mean ± SD	80.1 ± 4.2	79.5 ± 3.3	80.4 ± 4.8	79.9 ± 3.4	.71	79.9 ± 4.0	79.7 ± 3.4	80.3 ± 4.6	79.0 ± 2.8	.38
Sex, n (%)										
Female	94 (70.7)	7 (46.7)	59 (77.6)	28 (66.7)	.04	77 (71.3)	22 (71.0)	39 (70.9)	16 (72.7)	.99
Male	39 (29.3)	8 (53.3)	17 (22.4)	14 (33.3)		31 (28.7)	9 (29.0)	16 (29.1)	6 (27.3)	
Body mass index, kg/m², mean ± SD	23.4 ± 0.2	23.3 ± 2.5	23.3 ± 3.0	23.5 ± 3.0	.94	23.5 ± 3.1	23.4 ± 2.5	23.1 ± 3.5	24.6 ± 2.5	.15
Mini-Mental State Examination, mean ± SD (range 0–30)[c]	27.5 ± 1.9	28.4 ± 1.6	27.2 ± 1.8	27.6 ± 2.1	.06	27.7 ± 1.8	28.2 ± 1.7	27.6 ± 1.7	27.2 ± 1.9	.08
HDS-R, mean ± SD (range 0–30)[c]	26.8 ± 2.7	27.0 ± 2.7	26.5 ± 2.6	27.2 ± 2.7	.40	27.2 ± 2.3	26.9 ± 2.8	27.4 ± 1.9	27.2 ± 2.3	.69
Modified Kohs' block design test, mean±SD (range 0–47)[c]	21.7 ± 10.9	23.4 ± 10.0	19.9 ± 10.8	24.3 ± 11.2	.09	23.1 ± 11.0	20.0 ± 8.6	23.9 ± 10.9	25.6 ± 13.0	.14
Clock Drawing Test, mean ± SD, range 0–10	8.5 ± 2.1	8.9 ± 1.8	8.0 ± 2.2	9.2 ± 1.7[d]	.01	8.7 ± 2.0	8.2 ± 2.0	8.9 ± 1.9	8.8 ± 2.0	.25
Frequency of hypertension, n (%)	99 (74.4)	12 (80.0)	54 (71.1)	33 (78.6)	.58	76 (70.4)	25 (80.6)	36 (65.5)	15 (68.2)	.32
Systolic blood pressure, mean ± SD, mmHg	149.0 ± 18.7	149.1 ± 12.6	147.7 ± 20.9	151.5 ± 16.5	.57	147.3 ± 19.1	152.0 ± 15.7	144.0 ± 20.9	148.5 ± 17.5	.16
Diastolic blood pressure, mean ± SD, mmHg	81.5 ± 10.0	78.9 ± 9.1	81.5 ± 10.5	82.4 ± 9.6	.53	81.2 ± 0.3	83.4 ± 10.3	79.2 ± 10.9	83.3 ± 9.7	.12
Central aortic blood pressure, mean ± SD, mmHg	130.8 ± 18.8	133.3 ± 21.5	129.8 ± 19.8	131.8 ± 16.0	.75	129.9 ± 17.6	137.2 ± 17.7[e]	126.6 ± 17.7	127.8 ± 14.4	.02
Augmentation Index, mean ± SD	91.0 ± 11.2	89.8 ± 10.3	91.7 ± 11.4	90.4 ± 11.2	.74	91.4 ± 11.9	94.6 ± 14.1	91.0 ± 11.1	87.7 ± 9.2	.11
Heart rate, beats/min, mean ± SD	70.5 ± 10.9	68.7 ± 8.9	70.6 ± 11.0	70.7 ± 11.5	.81	69.7 ± 10.3	69.3 ± 11.0	69.9 ± 10.4	69.8 ± 9.4	.96
Atrial fibrillation, n (%)	5 (3.8)	0 (0.0)	4 (5.3)	1 (2.4)	.53	3 (2.8)	1 (3.2)	0 (0.0)	2 (9.1)	.89
Cardio-Ankle Vascular Index, mean ± SD, m/s	10.2 ± 1.1	10.5 ± 1.1	10.1 ± 1.2	10.4 ± 1.1	.27	10.2 ± 1.2	10.1 ± 1.1	10.3 ± 1.2	10.1 ± 1.1	.54
Ankle-brachial index, mean ± SD	1.05 ± 0.11	1.06 ± 0.15	1.05 ± 0.11	1.07 ± 0.08	.59	1.07 ± 0.09	1.07 ± 0.07	1.07 ± 0.11	1.07 ± 0.08	.89
Timed Up and Go Test, seconds, mean ± SD	14.1 ± 4.1	14.1 ± 3.4	14.9 ± 4.4	12.6 ± 3.5[d]	.02	14.0 ± 4.3	14.5 ± 5.3	14.2 ± 4.2	12.8 ± 2.7	.33
Functional reach, cm, mean ± SD	27.5 ± 9.2	29.3 ± 9.0	27.2 ± 9.4	27.6 ± 8.9	.71	27.9 ± 9.1	25.0 ± 9.1	29.1 ± 9.7	28.9 ± 6.9	.12
Button test score, mean ± SD	13.1 ± 3.4	13.8 ± 4.2	13.2 ± 3.4	12.5 ± 3.3	.41	13.1 ± 3.9	13.7 ± 4.9	13.5 ± 3.6	11.5 ± 2.8	.08
Serum albumin, g/dL, mean ± SD	4.3 ± 0.2	4.2 ± 0.2	4.3 ± 0.3	4.3 ± 0.2	.60	4.3 ± 0.2	4.3 ± 0.2	4.3 ± 0.2	4.3 ± 0.3	.50
Hemoglobin, g/dL, mean ± SD	12.7 ± 9.2	12.7 ± 1.5	12.6 ± 1.2	12.8 ± 1.4	.76	12.6 ± 1.2	12.7 ± 1.3	12.3 ± 1.2	13.3 ± 0.8[d]	.002
Serum glucose, mg/dL, mean ± SD	109.5 ± 24.7	106.7 ± 13.2	108.1 ± 24.4	113.2 ± 28.3	.51	110.1 ± 26.5	109.5 ± 27.3	109.8 ± 27.4	111.9 ± 24.1	.94
Serum total cholesterol, mg/dL, mean ± SD	193.6 ± 31.8	191.2 ± 24.4	192.2 ± 32.6	197.0 ± 33.1	.71	190.9 ± 34.0	190.4 ± 35.0	189.3 ± 33.8	195.6 ± 34.4	.76
Serum high density lipoprotein, mg/dL, mean ± SD	54.5 ± 14.3	50.1 ± 13.7	54.9 ± 14.0	55.3 ± 15.0	.46	53.0 ± 13.6	50.6 ± 11.3	53.1 ± 14.2	55.8 ± 14.9	.39
Serum triglyceride, mg/dL, mean ± SD	126.0 ± 67.9	118.4 ± 61.0	123.0 ± 70.0	133.1 ± 67.1	.69	126.6 ± 67.2	123.8 ± 63.0	127.1 ± 71.9	129.4 ± 63.6	.95
Serum creatinine, mg/dL, mean ± SD	0.80 ± 0.25	0.75 ± 0.14	0.77 ± 0.16	0.88 ± 0.37[d]	.04	0.8 ± 0.3	0.8 ± 0.2	0.8 ± 0.3	0.8 ± 0.2	.65

SD = standard deviation.

Three hundred sixteen citizens were examined in 2005.

[a]Including subjects who scored 30 in 2008 or 2010 and had a Mini-Mental State Examination (MMSE) score of 29 or 30 in 2005 (reference).

[b]One-way analysis of variance or chi-square test.

[c]2005 scores.

$P < .05$ from Student t-test comparing [d]improved or [e]declined with unchanged group.

the improved than in the unchanged group (P = .002) (Table 1).

Anemia in older adults is reportedly associated with greater risk of dementia in the next 11 years,[9] perhaps related to chronic brain hypoxia. In the current study, central systolic BP was a predictor of cognitive decline at 5-year follow-up, and physical activity assessed according to the Timed Up and Go test was a short-term predictor of cognitive function. Slow gait was also a strong and early risk factor for cognitive decline in a study of 767 participants aged 70 and older studied over 36.5 months (dementia hazard ratio = 3.27, 95% confidence interval (CI) = 1.55–6.90).[2]

Other investigations also suggest that high BP in midlife increases the risk of dementia and Alzheimer's disease in older age. High systolic BP was a risk factor for dementia in younger elderly adults (<75) but not in older adults in a less-than-10-year prospective community-based cohort study.[4] In a transverse investigation, central BP, but not brachial BP, was a sensitive indicator of cognitive function.[6] This is in keeping with the current investigation confirming in older adults that central systolic BP, but not brachial systolic BP, was a statistically significant predictor of cognitive decline at five but not 3 years.

Central hemodynamic variables are independently associated with organ damage and incident cardiovascular disease, suggesting that central BP may be different from BP measured on the arm.[6,10] It may thus be more relevant to the study of cognitive function, given that blood is delivered to the brain through the large central arteries.

In conclusion, central BP is a long-term predictor of cognitive decline in older adults, whereas preserved physical activity, represented by the Timed Up and Go test is a short-term predictor of cognitive improvement.

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DISTRIBUTION OF SURVIVAL TIMES IN A REAL-WORLD COHORT OF OLDER ADULTS WITH CHRONIC KIDNEY DISEASE: THE MEDIAN MAY NOT BE THE MESSAGE

To the Editor: The population-based approach to chronic kidney disease (CKD) recommended in clinical practice guidelines relies on levels of estimated glomerular filtration

BMJ Open

Prevalence of hypertension at high altitude: cross-sectional survey in Ladakh, Northern India 2007–2011

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ABSTRACT

Objective: Prevalence of hypertension was examined in a widely dispersed (45 110 km^2) representative group of Ladakhi in Northern India. The influence of hypoxic environment of wide-ranged altitude (2600–4900 m) and lifestyle change on hypertension was studied.

Methods: 2800 participants (age 20–94 years) were enrolled. Systolic blood pressure ≥140 mm Hg and/or diastolic blood pressure of ≥90 mm Hg and/or taking current anti-hypertensive medicine was defined as hypertension. Height and weight for body mass index and SpO_2 were examined. The rural population comprised six subdivisions with a distinct altitude, dietary and occupational pattern. Participants in the urban area of Leh consist of two groups, that is, migrants settled in Leh from the Changthang nomadic area, and dwellers born in Leh. The prevalence of hypertension in the two groups was compared with that in the farmers and nomads in rural areas. The effects of ageing, hypoxia, dwelling at high altitude, obesity, modernised occupation, dwelling in an urban area, and rural-to-urban migration to hypertension were analysed by multiple logistic regression.

Results: The prevalence of hypertension was 37.0% in all participants and highest in migrants settled in Leh (48.3%), followed by dwellers born in Leh town (41.1%) compared with those in rural areas (33.5). The prevalence of hypertension in nomads (all: 27.7%, Tibetan/Ladakhi: 19.7/31.9%)) living at higher altitude (4000–4900 m) was relatively low. The associated factors with hypertension were ageing, overweight, dwelling at higher altitude, engagement in modernised sedentary occupations, dwelling in urban areas, and rural-to-urban migration. The effects of lifestyle change and dwelling at high altitude were independently associated with hypertension by multivariate analysis adjusted with confounding factors.

Conclusions: Socioeconomic and cultural factors play a big role with the effect of high altitude itself on high prevalence of hypertension in highlanders in Ladakh.

Strengths and limitations of this study

- This study examined most of the socioeconomic environmental factors known to influence hypertension in a population of different distinct geographical subdivisions of a high-altitude region. Though we did not carry out a nutritional survey in all the participants, overweight was a decisive factor for hypertension according to lifestyle change.
- This study showed the influence of ageing, overweight, modernised sedentary occupations, rural-to-urban migration and dwelling in urban areas to hypertension as well as the effect of altitude by multivariate analysis.
- This study did not look into the genetic factors, as environmental and genetic factors may contribute to regional and racial variations of blood pressure and the prevalence of hypertension.

INTRODUCTION

Systemic arterial hypertension at high altitude has evoked great interest among high-altitude researchers as well as in sojourners and natives. There have been conflicting reports with investigators generally reporting a slight increase in the blood pressure level soon after arrival at high altitude[1 2] and investigators reporting no such change[3 4] or a decrease followed by an increase.[5 6] There is no standard way of treating hypertension at high altitude for sojourners till now.[7 8] Similar contradictory views also exist between the investigators of the two high-altitude continents regarding the blood pressure status of the high-altitude natives. Studies done in Spiti India (4000 m) show a lower prevalence of hypertension.[9] Andean residents are reported to have low prevalence of hypertension[1 10 11] while the prevalence of hypertension in Tibet Lhasa was found to be higher than that of Han migrants residing in Tibet.[12] Recent reports showed that the prevalence of hypertension was higher in Tibetan highlanders[13 14] than in Chinese lowlanders.[15]

The risk of developing hypertension may depend on socioeconomic factors, as well as geographic and racial differences. It is in the backdrop of this difference in opinion that we planned this study in Ladakh, one of the highest inhabited regions in the northernmost part of India. The population of the two districts of Ladakh (Leh and Kargil) was about 270 000 (Leh: 130 000, Kargil: 140 000) in 2011 by Census.[16] 77% of the population in Leh are Buddhists and 80% of the Kargil population are Muslims. Spread over 45 110 km^2, sandwiched between Karakoram in the north and Trans-Himalaya in the south and 80% comprising of a rural population with many villages high up in the mountains remaining inaccessible during winter, logistics for conducting a comprehensive epidemiological study representative of the whole population is formidable. The purpose of the study is twofold: first, to determine the prevalence of hypertension in different geographical subdivisions of this widely dispersed high-altitude district (from a median high 2500~ to very high ~4500 m), and second, which factors among the altitude, occupation, socioeconomic and lifestyle play a predominant role in association with hypertension.

METHODS

This cross-sectional epidemiological study was carried out from 2007 to 2011. A total of 2800 participants aged between 20 and 94 years were examined. Figure 1 shows the map of Ladakh region showing all the villages in the subdivisions where the study was conducted. A two-stage stratified sampling method was used to select a representative sample of the adult population over 20 years of age. The population was first stratified as urban versus rural and then in the rural sector into six geographical areas (subdivisions). Each geographical subdivision has different characteristics in altitude, occupation, dietary habits and socioeconomic conditions as well as separate administrative blocks (table 1). Migrants from the rural

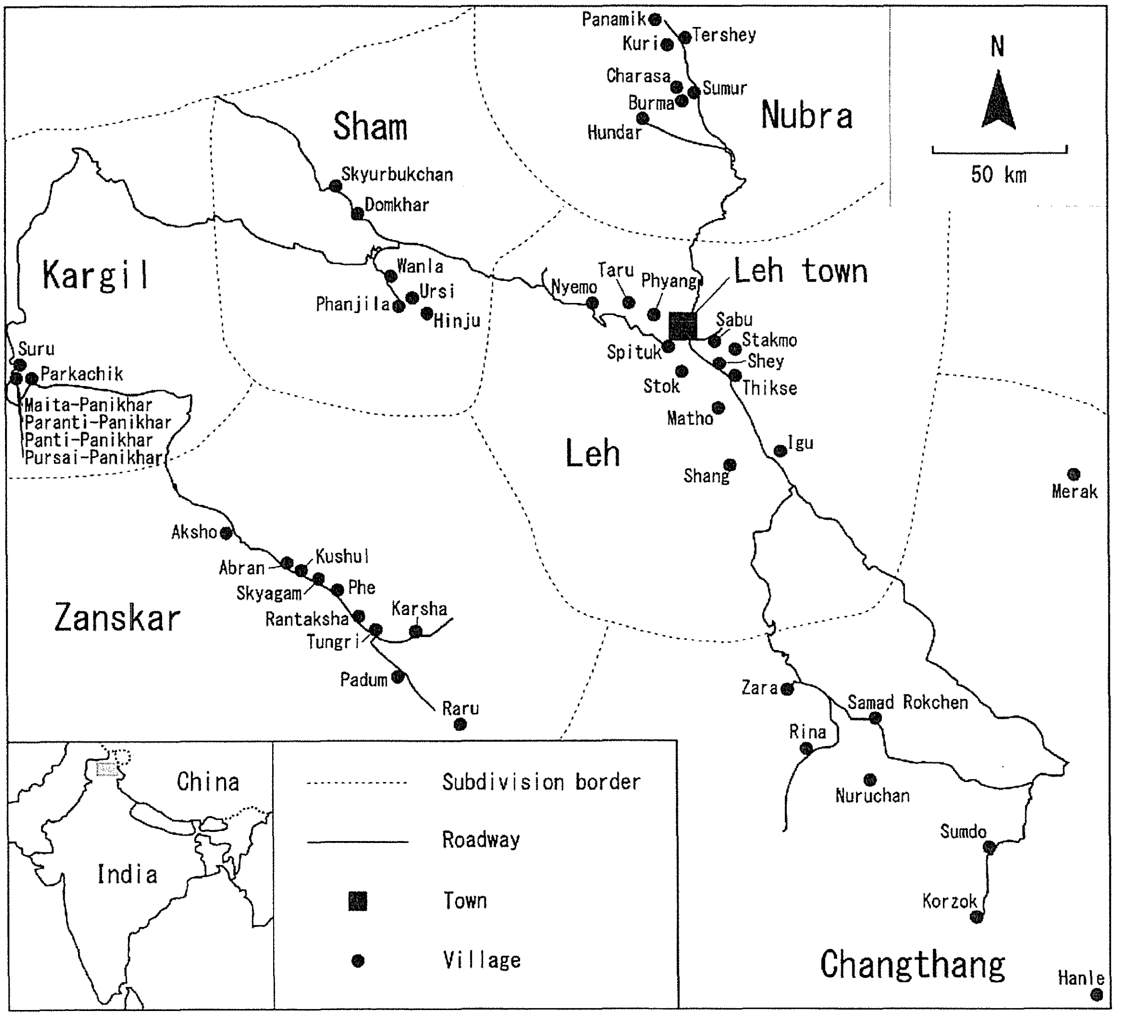

Figure 1 Map of Ladakh Region showing all the field sites. The map of Ladakh region showing all the villages in the subdivisions where the study was conducted.

Table 1 Characteristics of the subdivisions

Urban/rural	Subdivision	Altitude (metres above MSL)	Livelihood
Urban	Leh town (including colonies of migrants)	3300–3600	Urban lifestyle
Rural	Leh block villages	3000–3700	Farmer
	Nubra	2600–3000	Farmer
	Kargil (Panikhar and Parkachik)	2600–3100	Farmer
	Sham	2700–3900	Farmer
	Zanskar	3500–3900	Farmer and cattle rearing
	Changthang	4000–4900	Livestock rearing nomads

MSL, mean sea level.

population now settled in the Leh town subdivision since the 1970s were included in the urban population as they have adopted a lifestyle similar to the city dwellers. The Tata Institute of Social Sciences Mumbai (TISS) and Ladakh Autonomous hill development council (LAHDC) conducted a house-to-house survey of the total population of Leh (urban population) in 2007 for developing Ladakhi villages in the region.[17] Since the data from this census were the latest, we corrected and used this population survey list (age group 20–90 years) to draw our sample of urban population for the study. The list of 2000 eligible participants was representative of the age and gender structure of a Ladakhi family and they were invited as the volunteer participants to the research centre in Leh town. In the rural villages, all men and women aged 20 years or more were announced in the collaboration of health staff and village leaders. We carried out health checks on the volunteer participants in health centres or community halls in the rural villages.

There were no criteria for exclusion except absentees and critical and terminal illness patients who cannot report to the study centre to complete the study. Participants in *Leh town subdivision* were classified into two groups, that is, migrants settled in Leh town from Changthang area, and dwellers in Leh town. The former consisted of Tibetan and Ladakhi nomads. The latter consisted of Tibetans born in Leh, and other Ladakhi people, almost of whom were born in Leh, including some migrants from rural areas (non-Changthang).

The rural population was subdivided into six subdivisions as each subdivision had distinct characteristics which could influence the outcome.

Leh block subdivision comprises nearly 12 villages within 40 km of Leh town at an altitude varying between 3000 and 3700 m. The occupations of those living here are a mix of farming and modernised sedentary work. *Nubra subdivision* is in the north of Ladakh about 120 km from Leh after crossing Khardong Pass (5400 m), one of the highest motorable roads in the world. We studied the population of seven villages here. The subdivision is located on the banks of Shyok and Nubra rivers between the Karokoram and Ladakh ranges of mountains. People are predominantly farmers and the altitude of the valley generally is around 2600–3000 m. *Kargil subdivision (Panikhar and Parkachik)* is a green belt in Kargil district and is a fertile farming area on the Suru river. However, fruit trees are not cultivated here. The population is mainly Muslim and the altitude is 2600–3100 m. We studied the population of six villages representative of this subdivision. *Sham (Khalse) subdivision* is wide-ranged in altitude (2700–3900 m), generally more fertile and many of the villages have fruit trees like apricot, apple and almond. We studied six representative villages in this subdivision. *Zanskar subdivision* is a remote region on the trans Himalayan range of mountain which remains closed from the rest of the world for 6 months in a year due to heavy snowfall. Though people do farming, yet the harsh weather is not conducive for productive farming. Fresh fruit and vegetables are very meagre here. People rear cattle, which forms their secondary source of income by selling dairy products. The altitude of the subdivision is 3500–3900 m. We studied 10 villages representative of this subdivision. *Changthang subdivision* is the biggest and highest plateau (Altitude 4000–4900 m). The population is generally nomadic, moving from pasture to pasture every 3 months along with their cattle and livestock and living in Yak wool woven tents. Life is very hard for them because of the high altitude and severe cold. Farming is not possible, and fresh fruit and vegetables fruits are not available to them throughout the year. Meat, barley flour and local tea are their staple diet. We studied six villages representative of the subdivision.

The occupation was interviewed from all the participants and classified into four groups: farmer, nomad, sedentary worker and others (housewife, manual labourer, monk, retired sedentary worker and no job). A full-time housewife was regarded as a housewife. A housewife who also worked as a nomad or farmer was classified as a nomad or farmer. People engaged in work closely associated with an urban lifestyle are classified into sedentary workers consisting of office worker, business person, shopkeeper, taxi driver, government officer, travel agent, teacher and so on.

The procedure for obtaining informed consent was approved by the Institutional review board of the Ladakh institute of prevention and the District ethical committee, Leh, Ladakh and Research Institute for Humanity and Nature, Kyoto, Japan. The participants attended the village medical aid centre or the village community centre. Anthropometric measurements including weight and height were obtained using standard techniques. The body mass index (BMI) was calculated using the formula, weight(kg)/(height(m))^2. Blood pressure was measured in an arm using an automatic device (HEM 7000; OMRON Life Science Co. Ltd, Kyoto, Japan) based on the cuff oscillometric principle, and its accuracy has been validated in previous studies.[18–20] Oxyhaemoglobin saturation (SpO_2) was measured by a pulse oximeter (PULSOX-300; KONICA MINOLTA Co. Ltd, Tokyo, Japan). Blood pressure and SpO_2 were measured twice after taking at least a 5 min rest in a sitting position and the mean of systolic blood pressure (SBP), diastolic blood pressure (DBP) and SpO_2 was calculated. SBP ≥140 mm Hg and/or DBP of ≥90 mm Hg and/or taking current anti-hypertensive medicine was defined as hypertension.[21] The mean rate of current antihypertensive medication was 2.1%.

The age of the participants was confirmed with reference to a carefully prepared cross tabulation correlating their date of birth with the animal year, which the rural population always remembered, and to historical sentinel events in case of elderly participants.

Statistical analysis

χ^2 Test, Student's t-test and one-way analysis of variance were conducted for the analysis of the prevalence rate of hypertension or overweight (BMI ≥25), mean SBP, DBP, BMI and SpO_2. The associations of hypertension with the above confounding factors including altitude, ageing, sex, obesity, occupation and dwelling area were analysed by multiple logistic regression. Hypertension as the dependent variable was defined as SBP ≥140 mm Hg and/or DBP of ≥90 mm Hg and/or taking current anti-hypertensive medicine.[21] SPSS V.17.0 (SPSS Inc., Chicago, Illinois, USA) was used for the analysis. A statistically significant level was $p<0.05$.

RESULTS

A total of 2800 participants aged between 20 and 94 years were examined between 2007 and 2011.

Table 2 shows the characteristics of all variables and those associated with hypertension were overviewed. We found a 37.0% crude prevalence rate in the total Ladakhi population of both men and women. Male and older people, as well as those with overweight, had more prevalence of hypertension, but SpO_2 was not associated with hypertension. Dwelling at an altitude of 3000–3999 m had more prevalence of hypertension compared with altitude below 3000 or above 4000 m. People dwelling in urban areas had more prevalence of hypertension compared with those in rural areas. Nomads had lower prevalence of hypertension compared with farmers or sedentary workers.

Table 3 shows the participants surveyed and the prevalence rates of hypertension, mean SBP, DBP, BMI, rate of overweight (BMI ≥25) and mean SpO_2 according to sex and age groups in Ladakh region. Prevalence rates of hypertension, mean SBP and DBP increased significantly with ageing in men and women. Up to the age of 60 years, men tend to have higher blood pressure than women; however, there were no significant differences between men and women aged 60 years or above. The prevalence of overweight was highest (28.5%) in the 40–59 age group and men had a higher prevalence rate of overweight than women up to 75 years. Mean SpO_2 decreased significantly with ageing in both men and women.

Table 4 shows the crude and age-standardised prevalence rates of hypertension, and overweight (%) in seven subdivisions in Ladakh region in each age group. As the mean age was different among the participants of the seven subdivisions (ANOVA, analysis of variance; $p<0.0001$), age-standardised prevalence rates were calculated.

Leh town subdivision, which is inhabited by an urban population, had a higher crude prevalence rate of hypertension (43.4%) with age-standardised prevalence rate (45.5%) than any other subdivisions comprising a rural population (crude; 24.3–39.1, age-standardised; 24.6–36.8) (ANOVA, $p<0.0001$). The prevalence of hypertension, especially in the younger age group of 40–59 years, was extremely high in Leh town (41.6%) compared with other rural subdivisions (19.6–30.7%) (ANOVA, $p<0.0001$). Also in the old population above 60 years, the prevalence of hypertension was highest in Leh town (61.7%) compared with other rural subdivisions (34.1–56.0%) (ANOVA, $p=0.0001$). There was no significant difference in prevalence of hypertension in the young age group of 20–39 among the seven subdivisions (ANOVA; ns, not significant). Prevalence rates of hypertension increased significantly with ageing in all subdivisions (ANOVA, $p<0.01$~ $p<0.0001$) except Kargil. Prevalence of overweight (BMI≥25) was highest in the middle age group of 40–59 in Leh town subdivision.

Table 5 shows the prevalence rate of hypertension at different altitude levels according to age and occupation group. Up to the altitude of 4000 m, the prevalence of hypertension rose with altitude and the participants surveyed at altitude ranging from 3500 to 3999 m had a higher prevalence rate of hypertension (40.8%) than the other altitude ranges in all participants (ANOVA, $p<0.0001$). In the age group of 20–59 years, people at altitude ranging from 3000 to 3499 m had a higher prevalence rate of hypertension than others, while in the age group of 60–74 years, up to the altitude of 4499 m, the prevalence rate of hypertension rose with altitude, and people at altitude ranging from 4000 to 4499 m had the highest prevalence rate of hypertension (55.8%) (ANOVA, $p<0.05$). In the age group of 75 years and more, the prevalence of hypertension was highest and there was no difference among altitude levels.

According to occupation group, the prevalence of hypertension rose closely with altitude remarkably in agriculture ($p<0.001$), mildly in sedentary workers ($p=0.09$) and insignificantly in nomads.

Table 2 Characteristics of all variables and those associated with hypertension in Ladakh region

	All	Hypertension (+)	Hypertension (−)	p Value
n	2800	1037	1763	
Per cent		37.0 (35.2 to 38.8)	63.0 (61.2 to 64.8)	
Male (%)	44.3 (41.8 to 46.8)	46.9 (43.9 to 49.9)	42.8 (40.5 to 45.1)	0.03
age (years)	53.8±15.0	60.1±13.8	50.1±14.4	<0.0001
weight (kg)	55.3±11.1	57.4±12.2	54.1±10.2	<0.0001
BMI	22.6±3.6	23.6±3.9	22.0±3.3	<0.0001
Overweight (BMI ≥25) (%)	24.4 (22.8 to 26.0)	34.9 (32.0 to 37.8)	18.2 (16.4 to 20.0)	<0.0001
SpO_2 (%)	89.7±5.2	89.5±5.4	89.8±5.2	ns
SpO_2 <89 (%)	32.5 (30.8 to 34.2)	32.1 (29.3 to 34.9)	32.7 (30.5 to 34.9)	ns
SBP (mm Hg)	130.9±23.2	153.8±19.9	117.5±11.7	<0.0001
DBP (mm Hg)	82.5±13.4	94.6±11.2	75.4±8.5	<0.0001
Altitude (m)	3514.4±432.2	3524.6±388.6	3508.3±455.9	ns
	n			
Altitude (n=2800), m		Per cent	Per cent	<0.0001
2500–2999	417	27.1 (22.8 to 31.4)	72.9 (68.6 to 77.2)	
3000–3499	428	37.4 (32.8 to 42.0)	62.6 (58.0 to 67.2)	
3500–3999	1604	40.8 (38.4 to 43.2)	59.2 (56.8 to 61.6)	
4000–4499	174	30.5 (23.7 to 37.3)	69.5 (62.7 to 76.3)	
4500–4999	177	32.2 (25.3 to 39.1)	67.8 (60.9 to 74.7)	
Dwelling area (n=2800)		Per cent	Per cent	<0.0001
Rural areas	1798	33.5 (31.3 to 35.7)	66.5 (64.3 to 68.7)	
Leh block (3000–3700 m)	349	33.0 (28.1 to 37.9)	67.0 (62.1 to 71.9)	
Nubra (2600–3000 m)	248	27.8 (22.2 to 33.4)	72.2 (66.6 to 77.8)	
Kargil (2600–3100 m)	115	24.3 (16.5 to 32.1)	75.7 (67.9 to 83.5)	
Sham (2700–3900 m)	451	39.2 (34.7 to 43.7)	60.8 (56.3 to 65.3)	
Zanskar (3500–3900 m)	284	36.3 (30.7 to 41.9)	63.7 (58.1 to 69.3)	
Changthang (4000–4900 m)	351	31.3 (26.4 to 36.2)	68.7 (63.8 to 73.6)	
Urban area: Leh town (3300–3600 m)	1002	43.4 (40.3 to 46.5)	56.6 (53.5 to 59.7)	
Dwellers in Leh town*	683	41.1 (37.4 to 44.8)	58.9 (55.2 to 62.6)	
Migrants from Changthang	319	48.3 (42.8 to 53.8)	51.7 (46.2 to 57.2)	
Occupation (n=2800)		Per cent	Per cent	<0.0001
Farmer	1247	36.6 (33.9 to 39.3)	63.4 (60.7 to 66.1)	
Nomad	220	27.7(21.8 to 33.6)	72.3 (66.4 to 78.2)	
Sedentary worker	549	37.3 (33.3 to 41.3)	62.7 (58.7 to 66.7)	
Others	784	40.2 (36.8 to 43.6)	59.8 (56.4 to 63.2)	
Housewife	325	42.5 (37.1 to 47.9)	57.5 (52.1 to 62.9)	
Manual labourer	63	14.3 (5.7 to 22.9)	85.7 (77.1 to 94.3)	
Monk	157	36.9 (29.4 to 44.4)	63.1 (55.6 to 70.6)	
No job	138	44.2 (35.9 to 52.5)	55.8 (47.5 to 64.1)	
Retired sedentary	101	48.5 (38.8 to 58.2)	51.5 (41.8 to 61.2)	

Mean±SD, % (95% CI).
p; χ^2 Test for the comparison of the rate of variables, and Student's t test for the comparison of the mean of variables between hypertension and non-hypertension.
*Almost born in Leh with some migrants from no-Changthang areas.
BMI, body mass index; DBP, diastolic blood pressure; ns, not significant; SBP, systolic blood pressure; SpO_2, oxyhaemoglobin saturation measured by a pulse oximeter.

Table 6 shows the prevalence rate of hypertension at different altitude levels in each subdivision. In the only Sham subdivision, where altitude ranging is as wide as 2700–3900 m, the prevalence rate of hypertension increased (29.1, 36.2, 46.4%, p=0.0067) in accord with the elevation of altitude (2500–2999, 3000–3499, 3500–3999 m) in spite of the decrease in overweight (23.3, 18.9, 12.6%, p=0.040) with the altitude. In the other subdivisions, there was no difference in the prevalence rate of hypertension among different altitudes.

Table 7 shows the prevalence rate of hypertension and overweight in people with different occupations. In the age group of 40–59 years, sedentary workers had the highest prevalence of hypertension (48.3%) and obesity (43.9%), while nomads (hypertension/obesity; 19.6%/22.5%) and manual labourers (11.3%/20.8%) had a lower prevalence of hypertension compared with other workers (27.3–36.1%/20.1–61.1%) (ANOVA, p<0.0001). In the other age groups, there was no or little significant difference in the prevalence of hypertension among different occupations.

Table 3 Prevalence of hypertension and related variables according to sex and age groups in Ladakh region

	Age group (years)					
	20–39	40–59	60–74	75–	p†	All
Male (n)	217	489	396	138		1240
Female (n)	288	709	448	115		1560
All (n)	505	1198	844	253		2800
Hypertension (%)						
Male	18.4 (13.2–23.6)	34.2 (30.0–38.4)	48.2 (43.3–53.1)	63.8 (55.8–71.8)	<0.0001	39.2 (36.5–41.9)*
Female	12.5 (8.7–16.3)	29.9 (26.5–33.3)	50.4 (45.8–55.0)	67.0 (58.4–75.6)	<0.0001	35.3 (32.9–37.7)
All	15.1 (12.0–18.2)	31.6 (29.0–34.2)	49.4 (46.0–52.8)	65.2 (59.3–71.1)	<0.0001	37.0 (35.2–38.8)
SBP (mm Hg)						
Male	122.2±14.3****	127.7±18.0*	138.9±22.6	149.0±26.1	<0.0001	132.7±21.7***
Female	116.0±14.2	125.3±19.5	138.8±25.5	153.7±32.8	<0.0001	129.5±24.2
All	118.7±14.5	126.3±18.9	138.8±24.2	151.1±29.4	<0.0001	130.9±23.2
DBP (mm Hg)						
Male	78.5±11.4	83.4±12.5***	85.2±12.8	87.5±14.2	<0.0001	83.6±12.9***
Female	76.4±11.9	80.9±12.0	84.5±14.9	88.4±17.3	<0.0001	81.7±13.7
All	77.3±11.7	81.9±12.3	84.9±14.0	87.9±15.7	<0.0001	82.5±13.4
BMI						
Male	22.4±3.2***	23.3±3.6*	23.2±3.4****	22.4±3.4	0.0017	23.0±3.5****
Female	21.4±3.3	22.8±3.7	22.1±3.7	22.1±3.7	<0.0001	22.3±3.7
All	21.8±3.3	23.0±3.7	22.6±3.6	22.3±3.5	<0.0001	22.6±3.6
BMI ≥25 (%)						
Male	22.6 (17.0–28.2)*	31.7 (27.6–35.8)*	28.4 (24.0–32.8)**	19.6 (13.0–26.2)	0.0098	27.7 (25.2–30.2)***
Female	14.6 (10.5–18.7)	26.2 (23.0–29.4)	19.5 (15.8–23.2)	20.9 (13.5–28.3)	0.0003	21.8 (19.8–23.8)
All	18.0 (14.6–21.4)	28.5 (25.9–31.1)	23.6 (20.7–26.5)	20.2 (15.3–25.1)	<0.0001	24.4 (22.8–26.0)
SpO_2 (%)						
Male	90.8±4.4*	90.4±4.6	89.1±5.3**	89.0±5.4**	<0.0001	89.9±5.0
Female	91.6±3.6	90.3±4.8	87.7±6.4	86.6±6.5	<0.0001	89.5±5.0
All	91.2±4.0	90.4±4.7	88.3±5.9	87.9±6.0	<0.0001	89.7±5.2
SpO_2 <89 (%)						
Male	25.7 (19.9–31.5)*	29.0 (25.0–33.0)	37.1 (32.3–41.9)**	39.4 (31.2–47.6)*	0.0029	32.2 (29.6–34.8)
Female	17.7 (13.3–22.1)	27.2 (23.9–30.5)	46.3 (41.7–50.9)	52.2 (43.1–61.3)	<0.0001	32.8 (30.5–35.1)
All	21.1 (17.5–24.7)	27.9 (25.4–30.4)	42.0 (38.7–45.3)	45.2 (36.1–54.3)	<0.0001	32.5 (30.8–34.2)

p†; χ^2 Test for the comparison of the prevalence of hypertension and BMI ≥25 (%) among the 4 age groups, and ANOVA for the comparison of mean of SBP, DBP, BMI and SpO_2 among the 4 age groups in the whole population (n=2800).
*p<0.05, **p<0.01, ***p<0.001, ****p<0.0001; χ^2 test for the comparison of the prevalence of hypertension and BMI ≥25 (%) and SpO_2 <89 (%) between men and women, and Student's t test for the comparison of mean of SBP, DBP, BMI and SpO_2 between men and women in each age group.
ANOVA, analysis of variance;BMI, body mass index; DBP, diastolic blood pressure; SBP, systolic blood pressure; SpO_2, oxyhaemoglobin saturation measured by a pulse oximeter.