

1 Altitude of residential area affects salt intake in a rural area in Japan: Shimane CoHRE Study

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9 Running head: Association between altitude and salt intake.

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37 **Abstract**

38 **BACKGROUND** There has been increasing evidence for an association between residential
39 environment and hypertension. As shown in our previous study, inconvenience due to the
40 residential area might be one of the factors influencing blood pressure in habitants. Salt intake is
41 one of likely mediators between inconvenience and hypertension. In this study, we therefore
42 evaluated the association between altitude of residential area and salt intake in a Japanese rural
43 region because altitude may be one of the proxies for inconvenience.

44 **METHODS** In this cross-sectional study, 1016 participants living in a mountainous region in
45 Japan were recruited at health examinations. Altitude of the living place was estimated with a
46 geographical information system according to the address of each participant. Subjects were
47 divided into quartile groups according to the altitude of their living place. To evaluate salt intake,
48 we employed the 24h salt intake estimated according to Kawano et al. (e24h salt intake) and
49 urinary sodium-to-potassium ratio (uNa/K).

50 **RESULTS** Linear regression analyses indicated that the altitude was an independent factor
51 influencing both the e24h salt intake and uNa/K after adjustment with age, sex, body mass
52 index, physical activity, drinking, triglyceride and the county the participants lived. The same
53 result was observed when the subjects without antihypertensive medication were employed
54 (N=633).

55 **CONCLUSIONS** The present study indicated that the altitude of living place had a significant
56 positive influence on salt intake in a rural area of Japan.

57

58 **Introduction**

59 There is a growing interest in the association between residential environment and
60 hypertension.¹⁻⁵ Residential environment has both physical (e.g. climate and geography) and
61 social (e.g. socioeconomic condition and social capital) aspects that may attribute to individual
62 health.⁶ Inconvenience in daily life may be one of such factors. Japan has wide mountainous
63 regions (hilly and mountainous areas occupy approximately 70% of the land), in which people
64 have much less accessibility to facilities supporting their health and daily life (food shops,
65 hospitals, etc.).⁷⁻⁹

66 In the previous study, we showed that distance from a city area influenced blood pressure (BP)
67 of habitants.¹⁰ Considering the mechanisms underlying this observation, we hypothesized that
68 inconvenience determined by the geographic feature may influence salt intake, which may
69 result in increase in BP.¹¹ Evidence from the previous studies showed detrimental effects of high
70 salt intake on BP both among hypertensive and normotensive individuals.¹² Furthermore, a
71 recent study in UK reported that salt intake differed among subjects according to their socio-
72 economic status and the geographic feature of the living area.¹³

73 In this study, we therefore examined the association of altitude of living place, which is a
74 possible index of inconvenience in Japan, with salt intake in a rural area.

75

76 **Materials and Methods**

77 1) Participants

78 This cross-sectional population-based study was conducted as a part of Shimane CoHRE Study, a
79 cohort study designed to determine factors of lifestyle-related diseases including hypertension.
80 Health examinations were performed in 6 counties (Takeya, Mitoya, Daito, Kamo, Yoshida and
81 Kisuki) located in Un-nan city in 2012. Un-nan city is located in a rural mountainous area in the
82 eastern part of Shimane prefecture, Japan. Participants of the health examination were invited
83 to the study, and were involved in the study when they gave a written informed consent. After
84 excluding individuals with missing data, we recruited 1016 individuals in the study. This study
85 was approved by the local ethics committee of Shimane University.

86 2) Measurement

87 BP was measured twice after a 15-min resting at sitting position with automatic
88 sphygmomanometers, and the lower value was taken as a representative BP. History of
89 hypertension was asked in the interview and usage of antihypertensive drugs was checked on
90 prescriptions. Regular physical activity, drinking and smoking habit were asked in the interview
91 as well. Subjects taking one hour or more of physical activities (e.g. walking) per day were
92 categorized to those with high physiological activity. Drinkers were defined as those taking
93 alcohol once a week or more.

94 High-density and low-density lipoprotein cholesterol (HDL-C and LDL-C, respectively),
95 triglyceride (TG) and fasting blood glucose (FBG) were measured in serum by standard methods.

96 Altitude of the living place was estimated with a geographical information system (GIS)
97 according to the address of each participant (ESRI Japan Corp, Tokyo, Japan). In the analysis,
98 subjects were divided into quartile groups according to the altitude of their living place; the first

99 (29 - 44 m, N=261), the second (45 - 68 m, N=237), the third (69 - 195 m, N=245) and the fourth
100 quartile (196 - 485 m, N=250).

101 To evaluate salt intake, we employed two different parameters; 1) estimated 24 hours salt intake
102 (e24h salt intake) calculated with the formula proposed by Kawano *et al.*¹⁴ and 2) urinary
103 sodium-to-potassium ratio (uNa/K). The uNa/K was reported to be an index of salt intake,¹⁵⁻¹⁷
104 and, in fact, a significant correlation was observed between the e24h salt intake and the log-
105 transformed uNa/K in the present study (Pearson's $r=0.72$; $p<0.0001$, see Fig. S1). Spot urine
106 samples were collected at the site of the health examination, and the concentration of sodium
107 and potassium was measured using the electrode method (TBA-c16000, Toshiba Medical System
108 Corporation, Tochigi, Japan).

109 3) Statistical analysis

110 All the measures were represented as mean \pm SD. Parameters influencing salt intake were
111 analyzed by the linear regression analysis. $P<0.05$ was considered statistically significant. All
112 statistical analyses were performed using JMP 11 (SAS Institute, Cary, NC, USA).

113

114 **Results**

115 Characteristics of the studied population are shown in Table 1. We found significant differences
116 in the e24h salt intake as well as in the uNa/K among the quartiles according to the altitude of
117 living place. A post-hoc analysis indicated that the e24h salt intake and the uNa/K significantly
118 differed between the quartile (Q) 1 and the others (Dennett's test under Q1 was the reference).

119 Factors influencing the salt intake were listed in Table 2. By the Spearman's non-parametric
120 correlation analysis, sex, age, body-mass index (BMI), systolic and diastolic BP (SBP and DBP,
121 respectively), HDL-C, TG and the drinking status showed a significant correlation with the salt
122 intake in addition to the altitude. Besides the factors included in this univariate analysis, we
123 took into account effects of the county that the subjects lived in; as shown in the Figure, the
124 county seemed to have an effect on the e24h salt intake independently to their altitude.

125 We therefore performed a linear regression analysis on the e24 salt intake including the county
126 as a nominal variance. As BP was probably the result of salt intake, we excluded SBP/DBP from
127 the model. The result was summarized in Table 3. Even if the county was included in the model,
128 the highest quartile of the altitude (Q4) showed an independent effect on the salt intake in
129 addition to sex, age, BMI and the physical activity. Collinearity was not estimated to be high
130 when variance inflation factors (VIFs) were calculated (the maximal VIF was 3.7 for the county
131 Kakeya). When the analysis was performed on the uNa/K, the altitude was a significant
132 independent factor influencing it in parallel with sex and the county as well (see Table S1).
133 Further, addition of SBP (or DBP) in the model did not affect the result; the altitude was still an
134 independent factor affecting the salt intake (data not shown).

135 In the participants, we had 383 who were under the treatment with antihypertensive drugs. We
136 therefore performed the same analysis on those who had no antihypertensive drugs (N=633) to
137 avoid potential perturbation by antihypertensive treatment. The results indicated that the
138 effect of the altitude was significant in this population as well (see Table S2).

139

140 **Discussion**

141 To the best of our knowledge, this is the first study to examine the association between altitude
142 of living place and salt intake. The major finding of our study was that the salt intake was
143 associated with increased altitude in a rural area of Japan. This association seemed robust even
144 after adjustment with the county that the subjects lived in (see Table 3). Further, the same
145 significant association was observed after excluding the subjects taking antihypertensive drugs
146 (Table S2), and between the altitude and the uNa/K, another estimate of the daily salt intake
147 (see Table S1).

148 Previous studies pointed out that climbing up to high altitude increased BP acutely.^{18, 19} Several
149 factors in addition to lower air pressure were suggested to be responsible, such as hypoxia, low
150 temperature, wind, stress and dehydration.^{20, 21} In contrast, chronic effect of living at high
151 altitude was controversial.²² In anyway, however, the subjects employed in this study lived in a
152 range between 29 and 485 m in height, which was much less than that in the previous studies
153 (mostly, higher than 2000 m). Accordingly, the effect of altitude observed in this study was
154 probably not through physical effects of altitude *per se*.

155 In this context, it is of interest that Tyrovolas *et al.* reported that people living in mountainous
156 regions (upper than 400 m in height) in Mediterranean islands showed a greater incident of the
157 metabolic syndrome including hypertension.²³ They argued that people living in mountainous
158 regions had less opportunity to use health-promoting facilities due to inconvenience or
159 remoteness. To examine whether the similar inconvenience was indeed observed in our
160 population, we checked a number of food shops and bus stops in the studied counties according

161 to the altitude using the GIS. As expected, the result indicated that number of these facilities
162 decreased according to the altitude, suggesting that the living place in high altitude was more
163 inconvenient (Fig. S1). Based on the analysis above, it is possible to hypothesize that people
164 living higher altitude in this area might have more preserved food containing more salt because
165 of the less accessibility to fresh food. This hypothesis needs to be examined in future studies.

166 In contrast to salt intake, the altitude did not influence BP. When factors influencing SBP were
167 evaluated by a linear regression analysis, the e24h salt intake was a strong independent risk
168 factor increasing SBP ($B \pm SE = 1.1 \pm 0.2$, $p < 0.0001$) along with age and BMI (data not shown). This
169 result indicated that, although the altitude indeed affected salt intake in this population, many
170 factors other than the altitude, especially those related to an individual life style, probably had
171 larger influence on salt intake as well as on BP of each subject. In the previous study, we
172 showed that a distance from a city area was an independent risk factor for hypertension.¹⁰ In
173 that report, we argued that the distance from a city area was a parameter representing
174 'inconvenience' as well. At the moment, we cannot provide any good interpretation about the
175 reason why the altitude and the distance from a city area gave different results on hypertension.
176 Further analyses may be essential to solve this inconsistency between the two parameters.

177 It is of interest that the county had an independent effect on the salt intake in addition to the
178 altitude. Many potential factors such as difference in urbanization might attribute to this
179 observation. In fact, the counties with higher adjusted salt intake are more urbanized (as far as
180 the central area of the county is concerned) than the others (see Table S3). Further analyses
181 would be warranted on this issue as well.

182 Our study has several limitations. First, due to a cross-sectional study design, it was, in general,
183 difficult to argue the causal relationship between independent and dependent parameters.
184 However, in the present case, it seemed reasonable to assume that the altitude of living place
185 causally influence salt intake as the opposite was not likely. Second, our data did not allow the
186 assessment of other important socioeconomic factors for hypertension, such as income,
187 education and occupation. In spite of those limitations, this is a unique study evaluating the
188 altitude of living place as a factor influencing dietary habits of people. Implementation of such
189 a geographical factor as a risk factor may be warranted in future studies of life-style related
190 diseases.

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192 **Disclosure**

193 The authors declared no conflict of interest.

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コメントの追加 [並河1]: abbreviation?

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283 **Figure legends**

284 Figure. The altitude and the e24h salt intake in each county

285 A closed circle indicates the median of altitude and the mean of the e24h salt intake of each
286 county. Vertical lines and horizontal broken lines are for the S.D. of the e24h salt intake and for
287 the 25/75 percentile of the altitude, respectively.

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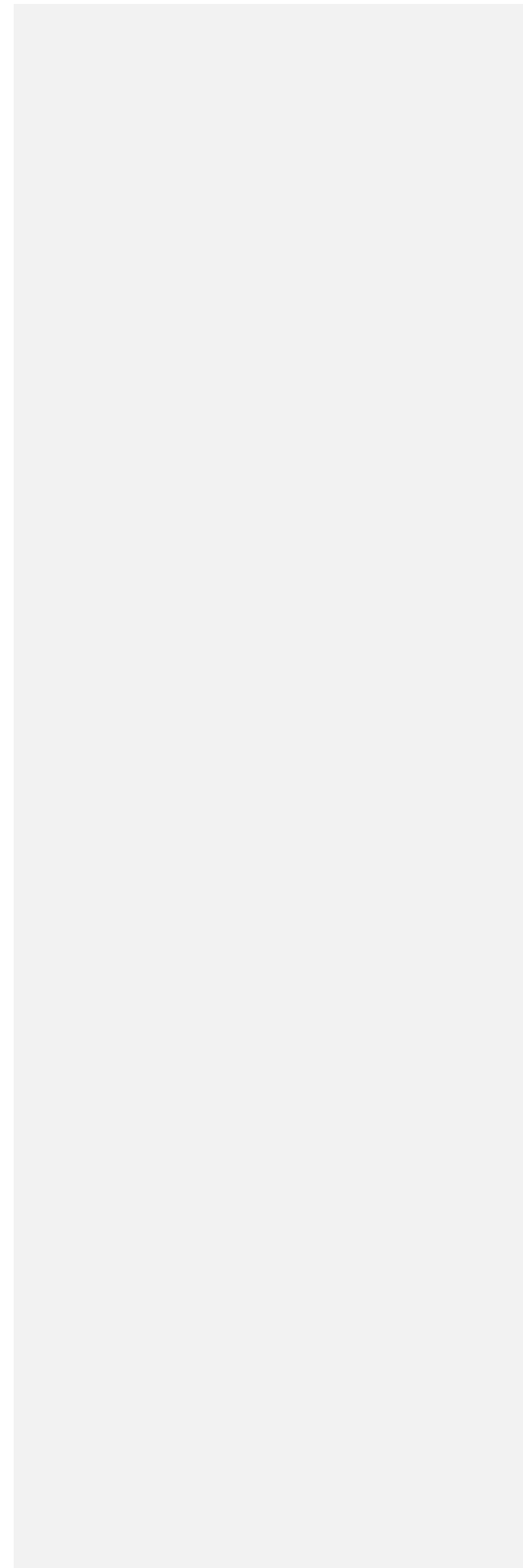


Table 1 Demographic data of the studied subjects

	Quartile 1	Quartile 2	Quartile 3	Quartile 4	p
Number	261	237	245	250	
Altitude, m	38±5	53±6	125±38	307±82	<0.0001
Sex, % male	37.2	38.8	40.4	40.8	0.8
Age, years	71±7	70±8	70±7	71±7	0.02
BMI, kg/m ²	22.2±3.2	22.3±3.5	21.9±2.7	22.6±2.9	0.06
SBP, mmHg	129±16	128±15	127±15	128±15	0.8
DBP, mmHg	77±10	78±10	76±10	77±10	0.3
Physical activity, %yes	47.3	46.6	47.5	51.2	0.7
Drinking, %	44.7	42.5	54.5	46.8	0.04
Smoking, %	5.3	6.5	4.3	5.2	0.8
e24h salt intake, g/day	9.2±2.0	9.7±2.0	9.6±2.2	9.7±2.0	0.02
uNa/K	2.3±1.6	2.6±1.6	2.6±1.7	2.6±1.7	0.01
HDL-C, mg/dL	66±14	64±17	66±15	63±16	0.2
LDL-C, mg/dL	123±28	124±27	118±29	122±30	0.1
TG, mg/dL	85±1.5	89±1.5	83±1.5	83±1.5	0.3
FBG, mg/dL	96±15	95±13	96±13	96±13	0.8

Log-transformed uNa/K and TG were used in the analysis. The means and the SDs calculated back to the untransformed form were shown in the table.

Table 2 Factors correlated with e24h salt intake

	ρ	p
Sex, M vs. F	0.11	0.0003
Age	-0.11	0.0008
BMI	0.18	<0.0001
SBP	0.17	<0.0001
DBP	0.16	<0.0001
HDL-C	-0.06	0.05
LDL-C	-0.03	0.3
TG	0.08	0.006
FBS	-0.05	0.09
Smoking, Y vs. N	0.004	0.9
Drinking, Y vs. N	0.10	0.002
Physical activity, Y vs. N	0.05	0.08
Altitude, quartile	0.10	0.002

Spearman's ρ was employed in the analysis.

Table 3 Linear regression analysis on the e24h salt intake

	B±SE	t	p
Sex, M vs. F	0.37±0.15	2.43	0.02
Age	-0.02±0.009	-2.51	0.01
BMI	0.11±0.02	4.89	<0.0001
Physical act, y vs. n	0.27±0.12	2.13	0.03
Altitude			
Q2 vs. 1	0.23±0.19	1.23	0.2
Q3 vs. 2	0.20±0.18	1.07	0.3
Q4 vs. 3	0.48±0.21	2.27	0.02
County			
Takeya	-0.60±0.20	-3.10	0.002
Yoshida	-0.50±0.20	-2.53	0.01
Mitoya	0.29±0.13	2.18	0.03
Kamo	0.06±0.19	0.30	0.8
Kisuki	0.07±0.15	0.43	0.7
Daito	0.69±0.13	5.42	<0.0001

HDL-C, TG, drinking status and FBS were excluded from the independent factors by the analysis,

Table S1 Linear regression analysis on the urinary Na/K ratio

	B±SE	t	p
Sex, M vs. F	0.05±0.016	3.06	0.002
Altitude			
Q2 vs. 1	0.04±0.02	2.03	0.04
Q3 vs. 2	0.01±0.02	0.67	0.5
Q4 vs. 3	0.06±0.02	2.55	0.01
County			
Takeya	-0.06±0.02	-2.81	0.005
Yoshida	-0.08±0.02	-3.48	0.0005
Mitoya	0.05±0.01	3.70	0.0002
Kamo	0.0003±0.02	0.13	0.9
Kisuki	0.02±0.02	1.35	0.18
Daito	0.06±0.01	4.01	<0.0001

Log transformation of Na/K ratio was done before the analysis due to a skewed distribution of the ratio. Age, BMI, HDL-C, TG, FBS, drinking status and the physical activity were excluded from independent factors by the analysis.

Table S2. Linear regression analysis on the e24h salt intake in the subjects without using antihypertensive drugs (N=633)

	B±SE	t	p
Sex, M vs. F	0.32±0.17	1.88	0.06
Age	-0.03±0.01	-2.87	0.004
BMI	0.14±0.03	5.04	<0.0001
Physical activity, y vs. n	0.30±0.14	2.10	0.04
Altitude			
Q2 vs. 1	0.26±0.21	1.25	0.2
Q3 vs. 2	0.15±0.21	0.71	0.5
Q4 vs. 3	0.68±0.26	2.65	0.008
County			
Takeya	-0.54±0.24	-2.21	0.03
Yoshida	-0.54±0.24	-2.29	0.02
Mitoya	0.35±0.15	2.30	0.02
Kamo	0.12±0.22	0.54	0.6
Kisuki	-0.10±0.18	-0.55	0.6
Daito	0.71±0.14	4.98	<0.0001

HDL-C, TG, FBS and drinking status were excluded from the independent factors by the analysis. Sex had a marginal effect on the e24h salt intake.

Table S3. e24h salt intake and uNa/K according to the altitude and the county adjusted by the linear regression analysis

A) Altitude

altitude	e24h salt intake, g/day	log uNa/K
Q1	9.07±0.15	0.34±0.016
Q2	9.30±0.15	0.39±0.016
Q3	9.50±0.13	0.40±0.015
Q4	9.96±0.16	0.46±0.017

B) County

county	e24 salt intake, g/day	log uNa/K
Takeya	8.47±0.28	0.29±0.03
Yoshida	8.56±0.29	0.27±0.03
Mitoya	9.35±0.18	0.40±0.02
Kamo	9.12±0.19	0.35±0.02
Kisuki	9.13±0.18	0.37±0.02
Daito	9.75±0.19	0.40±0.02

The e24h salt intake and the uNa/K were adjusted with sex, age, BMI, HDL-C, TG, FBS and the physical activity.

