INTRODUCTION

There is growing interest in the association between residential environment and hypertension. Residential environment includes both physical (e.g. climate and geography) and social (e.g. socioeconomic conditions and social capital) aspects that may contribute to individual health. Inconvenience in daily life may be one of such factors. In a previous study, we showed that the distance from an urban area influenced the average blood pressure (BP) of inhabitants. Concerning the mechanisms underlying this observation, we hypothesized that inconvenience due to geographic features might influence salt intake, which might result in increased BP. In this study, we therefore examined the association between altitudes of residence, which is a possible index of inconvenience in Japan, and salt intake in a rural area.

MATERIALS AND METHODS

This is a population-based cross-sectional study. We analyzed data collected in the Shimane CoHRE Study conducted in six counties (Kakeya, Mitoya, Daito, Kamo, Yoshida and Kisuki) located in Un-nan City in 2012. A total of 1016 subjects were recruited in health examinations. All the participants gave informed consent and the study was approved by the local ethical committee in Shimane University. Altitude of residence was estimated with a geographic information system (GIS) based on the addresses of the participants (ESRI Japan,
Tokyo, Japan). In the analysis, subjects were divided into quartile groups according to their altitudes of residence: Quartile 1 (Q1): 29–44m, N= 261; Q2: 45–68m, N= 237; Q3: 69–195m, N= 245 and Q4: 196–485m, N= 250. We used two different parameters to evaluate salt intake: (1) estimated 24-h salt intake (e24-h salt intake), which was calculated with the formula proposed by Kawano et al., and (2) the urinary sodium-to-potassium ratio (uNa/K). Spot urine samples were collected at the site of the health examination, and the concentrations of sodium and potassium were measured using the electrode method (TBA-c16000, Toshiba Medical System Corporation, Tochigi, Japan). Regular physical activity, alcohol consumption and smoking habits were obtained in the interview. High-density and low-density lipoprotein cholesterol (HDL-C and LDL-C, respectively), triglycerides (TG) and fasting blood glucose were measured in serum by standard methods. Parameters influencing salt intake were analyzed by the linear regression analysis. All of the statistical analyses were performed using JMP 11 (SAS Institute, Cary, NC, USA) and SPSS (v.23, IBM, Armonk, NY, USA).

RESULTS AND DISCUSSION

We found significant differences in the e24-h salt intakes (p=0.02) as well as in the uNa/K (p=0.01) among the quartiles according to the altitude of residence. A post-hoc analysis indicated that the e24-h salt intakes and the uNa/K were significantly different between Q1 and other quartiles (Dunnett’s test using Q1 as the reference). In Spearman’s non-parametric correlation analysis, age, sex, body mass index, systolic and diastolic BP (SBP and DBP, respectively), HDL-C, TG and alcohol consumption were found to have significant correlations with salt intake in addition to the altitude of residence. Besides the factors included in this univariate analysis, the county of residence appeared to have an effect on the e24-h salt intake independent of the altitude. Therefore, we performed a linear regression analysis on the e24-h salt intake with the county of residence as an independent variance. Even after the county of residence was included in the model, the altitude displayed an independent effect (B=0.27±0.08, p=0.001) on the salt intake. When the analysis was performed on the uNa/K measurements, the altitude was a significant independent factor as well (B=0.03±0.009, p=0.0001). The addition of SBP (or DBP) in the model did not affect the results; the altitude was still an independent factor affecting the salt intake. Three hundreds and eighty-three subjects were receiving antihypertensive drugs. Therefore, we performed the same analysis on those who were not taking antihypertensive drugs (N=633) to avoid potential perturbation by antihypertensive treatment. The results indicated that the effect of altitude was significant (p=0.001) in this population as well.

The major finding of our study was that salt intake was associated with altitude in a rural area of
Japan. This association seemed robust because the same significant association was observed with uNa/K, and after excluding the subjects taking antihypertensive drugs.

As the subjects in this study lived at altitudes between 29 and 485m in height, which seemed to too low to impose physical influence (e.g., lower pressure, lower concentration of oxygen) on BP. Accordingly, the effects of altitude observed in this study were probably due to inconvenience or remoteness. To examine whether inconvenience was indeed present in our population, we assessed the number of food shops and bus stops in the studied counties according to their altitudes. As expected, the number of these facilities decreased with increasing altitudes, suggesting that living at high altitudes is more inconvenient. Based on the above analysis, it is possible to hypothesize that people living at a higher altitude in this area might consume more processed food with high salt contents because of the reduced access to fresh food. This hypothesis needs to be examined in future studies.

In contrast to salt intake, altitudes did not influence BP. When factors influencing SBP were evaluated by a linear regression analysis, the 24-h salt intake was a strong independent risk factor for increased SBP ($B = 1.1 \pm 0.2$, $P < 0.0001$), along with age and body mass index. This indicated that although the altitude indeed affected salt intake in this population, many other factors, especially those related to the individual's lifestyle, probably had a larger influence on BP of each subject. In addition, it is of interest that the county of residence had an independent effect on the salt intake in addition to the altitude. Potential confounding factors, such as differences in urbanization, might contribute to this observation. Further analyses are warranted on this issue as well.

**CONCLUSION**

To the best of our knowledge, this is the first study to examine the association between altitude of residence and salt intake. Our study indicated that altitude of residence had a significant positive influence on salt intake in a rural area of Japan.
論文審査及び最終試験又は学力の確認の結果の要旨

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<tbody>
<tr>
<td>学位論文名</td>
<td>Altitudes of Residential Areas Affect Salt Intake in a Rural Area in Japan: a Shimane CoHRE Study</td>
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<td>学位論文審査委員</td>
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<td>神田 秀幸</td>
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<td>田邊 一明</td>
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<td>副査</td>
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</tbody>
</table>

論文審査の結果の要旨

本論文は高血圧症発症に関して、居住地の地域的・社会的要因に関する研究は多くみられない。申請者は、居住地の地域的要因が住民の食塩摂取量に影響を与え、居住地の標高が高血圧発症の要因のひとつになり得るという仮説を検証することを目的として、一般住民を対象として、居住地の標高と食塩摂取量の関連を、横断的研究を用いて研究を行った。

居住地の標高は、健康調査受診者993名の住所情報をもとに地理情報システムを用いて検索し、標高別に4群に分けた。食塩摂取量を反映する変数として、スポット尿中のナトリウム量とクレアチニン値から既存の推定式を用いて算出した24時間尿中ナトリウム排泄量（24h uNa）と尿Na/K比を用いた。年齢、喫煙等の調整を行った多重線形回帰分析の結果、居住地の標高は、24h uNa、尿Na/K比のいずれも有意な正の影響を及ぼす独立因子であり、標高が高い群ほど推定食塩摂取量が多くなることが明らかとなった。また、居住する地区（旧町村）も食塩摂取量に有意な関連要因であることを示した。

申請者の研究は、居住地の地域的要因が生活習慣病の危険因子となり得ることを示唆した貴重な報告である。

最終試験又は学力の確認の結果の要旨

申請者は、居住地の標高と推定食塩摂取量について調査研究した。有効回答993人の地域住民から得た回答を統計解析し、居住地の標高と推定食塩摂取量が正の相関を持つ、推定一日食塩摂取量と社会的背景とも関連する等の結論であった。研究背景や方法、結果の解釈等についての質問に対し、適切な回答が得られた。学位授与に関して、博士（医学）に値すると評価できた。

（主査）神田 秀幸

申請者は雲南省の住民健診から一日塩摂取量と居住地区、居住地の高度との関係を分析し、高血圧リスク因子に地域的因子も加えることの必要性を示した。関連分野の知識も十分に有し、学位授与に値すると判断した。

（副査）田邊 一明

申請者は島根県雲南省の複数地域住民のデータを用いて居住地の標高と推定一日食塩摂取量の関連に有意な相関があることを見出し、その意義付けを行い、生活習慣病の危険因子についての新たな一助とした。公開審査での質疑応答も的確であり、学位授与に値する高い学識と研究能力を示した。

（副査）竹下 治男

（備考）要旨は、それぞれ400字程度とする。