Original Article

Increased salt intake is associated with diabetes and characteristic dietary habits: a community-based cross-sectional study in Japan

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We investigated the association of salt intake with lifestyle-related diseases and also the association of habitually consumed foods with salt intake. A cross-sectional study was conducted using data from a baseline survey of 2,129 residents of Yonezawa city (980 males and 1,149 females), Yamagata prefecture. The residents were divided into three groups based on their estimated daily salt intake: low, medium, and high. In both genders, the prevalence of hypertension and diabetes increased in the order of high > medium > low salt intake (trend *p*<0.001). Similar trends were observed in the prevalence of hyperlipidemia in females and metabolic syndrome in males. The prevalence of diabetes in the high salt intake group was significantly higher than that in the control group (matched from the low and medium salt intake groups), even when confounding factors were excluded by propensity score matching (*p*<0.01). Network analysis showed that the low salt intake group had a greater tendency to habitually consume various vegetables than the high salt intake group. Our findings reveal that the prevalence of lifestyle-related diseases increased with higher salt intake. We speculate that a dietary shift to multiple vegetable consumption could have salt-lowering effects.

Key Words: **community-based study, salt intake, lifestyle-related diseases, dietary habit, network analysis**

Sodium ions (Na^+) play vital physiological roles such as maintenance of body osmolality, nerve and muscle cell excitation, and absorption of nutrients in the gastrointestinal tract.(1) However, excessive salt intake leads to elevated blood pressure, thus increasing the risk of cerebrocardiovascular events and kidney disease,(2) and is implicated in a variety of other conditions such as gastric cancer, asthma, and osteoporosis.(3–5) A technical report by the World Health Organization (WHO) and the Food and Agriculture Organization of the United Nations has recommended a salt consumption level of less than 5 g per day as a nutrient intake goal. In Japan, the number of patients with metabolic syndrome and diabetes mellitus has increased with the westernization of dietary habits. Although excessive salt intake has gained consensus as a risk factor for hypertension, the association between excessive salt intake and obesity, dyslipidemia, and diabetes has remained controversial.(6–9) Although the Japanese diet is well recognized to be one of the world's healthiest, overconsumption of soy sauce, miso, pickles and salted fish can be responsible for excessive salt intake.(10) To avoid excessive salt intake, it is necessary to clarify the dietary habits that are associated with it.

We have conducted a regional study, the Yamagata Study, involving a cohort of residents of Yonezawa city, Yamagata prefecture.(11) Most residents of Yamagata Prefecture have lived there for many generations, with little migration. Using such a cohort, therefore, it is possible to obtain accurate data that reflect the natural history of various diseases. Yamagata is located in the Tohoku region of Japan, and the average daily salt intake of local residents in Yamagata prefecture is 12.4 g/day for males and 10.5 g/day for females, which is higher than the Japanese average level (average daily salt intake for Japanese: 11.3 g for males and 9.6 g for females). In the present study, we examined the associations of salt intake with obesity, diabetes, and dietary habits among citizens of Yonezawa. To obtain a grasp of their dietary habits, we employed network analysis, an approach that is widely used for pathway analysis of metabolism, genes and social networks, and whose usefulness has been well validated.(12,13) The purposes of the present study were to clarify the association between excessive salt intake and metabolic diseases, which is still a controversial issue, and to examine salt intake in relation to dietary habits using network analysis.

Materials and Methods

Participants. The Yamagata Study was established through the 21st Century Center of Excellence (COE) program and the Global COE program in Japan, and is managed by the Institute for Promotion of Medical Science Research, Yamagata University Faculty of Medicine.(11) In this study, a cross-sectional analysis was performed using data from a baseline survey of Yonezawa city included in the Yamagata Study. From May to December 2015, we recruited 2,129 Yonezawa citizens (980 males and 1,149 females) aged over 40 years who had received a community-based annual health checkup and agreed to participate in the Yamagata Study. Written informed consent for the study was obtained from all participants. This study was approved by the Ethic Committee of Yamagata University Faculty of Medicine. Supplemental Fig. 1* shows a participant flow diagram.

Anthropometric measurements and blood examinations. Participants' height and weight were measured in 0.1-cm and 0.1-kg units, respectively. Body mass index (BMI) was calculated as weight (kg) divided by height squared (m^2). Waist

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circumference was measured at the umbilical level to the nearest 0.1 cm in the standing position using a tape measure after normal expiration. Blood pressure was measured from the right arm in a seated position after resting for at least 5 min. Hypertension was defined as a systolic blood pressure of ≥140 mmHg or a diastolic blood pressure of ≥90 mmHg at the time of the health checkup. Hyperlipidemia was defined as either triglycerides ≥150 mg/dl, low-density lipoprotein (LDL) cholesterol ≥140 mg/dl, or high-density lipoprotein (HDL) cholesterol <40 mg/dl. Diabetes was defined as a fasting glucose level of ≥126 mg/dl or glycated hemoglobin level (HbA1c) ≥6.5. Routine laboratory examinations were conducted using standard automated analyzers. Diagnoses of hypertension, hyperlipidemia, and diabetes were made on the basis of blood data and also medical history at the time of the health checkup. Metabolic syndrome was diagnosed according to the Japanese diagnostic criteria.[14] To determine whether salt intake in subjects with diabetes was high in comparison with that in non-diabetic subjects, we matched age, sex, height, weight, and medication history (mainly for hypertension) by propensity scoring to determine whether higher salt intake was related to increased diabetes prevalence.

Estimation of daily salt intake and grouping. Estimated daily salt intakes were determined by measuring urinary sodium and urinary creatinine in spot-urine obtained at the time of the survey and were calculated using the method of Kawasaki *et al.*[15] Estimated daily salt intakes tabulated as histograms in 1-g widths for males and females separately were used for grouping.

Questionnaire. In the baseline survey for the Yamagata Study, we utilized a self-administered questionnaire, the "questionnaire on health and lifestyle habits", inquiring about lifestyle habits, eating habits, presence of stress in daily life, exercise habits, medical history, current medications, family history, clinical symptoms, drinking habits, and smoking habits. We distributed the questionnaire during a community health checkup and collected it later. Data from the questionnaire were used for analysis. We chose moderate sleep duration, alcohol abstinence, currently non-smoking, moderate physical activity, and green-yellow vegetable consumption as healthy lifestyle behaviors.[16]

For analysis of dietary habits, 45 food items were examined by a validated food frequency questionnaire,[17] including rice, miso soup, bread, vegetables, and fruits, and food items consumed 3–4 times or more per week were considered habitual.[18] All data from the questionnaire were anonymized so that individuals could not be identified.

Network analysis. Network analysis is represented by nodes and edges. Epidemiological analyses were conducted by applying human relationship network analysis.[19] In order to clarify the relationship between dietary habits and salt intake, two groups, low salt intake and high salt intake, were subjected to network analysis with intake food items as nodes and edges between the nodes. We expressed the networks as undirected graphs produced by Cytoscape, a software platform that has been commonly used to visualize metabolic pathway networks and gene expression profiles.[20] The Jaccard coefficient is an index representing the similarity of the two aggregates and represents the strength of co-occurrence between nodes. If the Jaccard coefficient was large and showed strong co-occurrence, the width of the edges between the nodes was displayed thicker. Edges below a Jaccard coefficient of 0.45 were removed and nodes with strong associations were extracted.

Statistical analysis. Continuous variables were expressed as mean ± SD. Trend tests were performed using the Jonckheere-Terpstra test for continuous values and the Cochran-Armitage test for ratios. Comparison of salt intake and diabetes prevalence was performed by propensity score matching for age, gender, height, weight, and medication history (mainly hypertension), and the significance of differences between two groups was examined by the Mantel-Heanszel test. R was used for statistical analysis. Statistical significance was set at $p<0.05$ for all analyses.

Results

Grouping based on estimated daily salt intake. In males, the estimated daily salt intake peaked at 11–12 g and showed an almost normal distribution (Fig. 1A). In females, it peaked at 10–11 g/day and also showed an almost normal distribution (Fig. 1B). We divided the subjects into three groups: low salt intake (<mean − 0.5 SD), medium salt intake (from ≥mean − 0.5 SD to <mean + 0.5 SD), and high salt intake (≥mean + 0.5 SD). Among the males, 331 were in the low salt intake group (≤11.0 g/day), 365 were in the medium salt intake group, and 284 were in the high salt intake group (≥14.5 g/day). Among the females, 363 were in the low salt intake group (≤9.9 g/day), 485 were in the medium salt intake group, and 301 were in the high salt intake group (≥13.2 g/day). For both genders, the mean age was significantly higher in the order high > medium > low salt intake (p for trend<0.001).

Salt intake and prevalence of lifestyle-related diseases. Table 1 shows the association between the amount of salt intake and prevalence of hypertension, dyslipidemia, diabetes, and metabolic syndrome. In both genders, body weight and BMI increased in proportion to increased salt intake (p for trend<0.001). Systolic and diastolic blood pressures increased and the prevalence of hypertension increased with increasing salt intake (p for trend<0.001). In females, triglycerides level increased with higher salt intake (p for trend<0.001). In addition, blood glucose and HbA1c increased along with increased salt intake and the prevalence of diabetes increased in both genders (p for trend<0.001). The prevalence of metabolic syndrome increased with increasing salt intake in males (p for trend<0.001), but not in females (p for trend<0.09).

The propensity score-matching method was used to exclude confounding factors for comparison of diabetes prevalence with the amount of salt intake (Table 2). Pairs matching with the high salt intake group was conducted using individuals selected from the low and medium salt intake groups (control group). The prevalence of diabetes in the high salt intake group was significantly higher than that in the control group ($p<0.01$).

Relationship of salt intake with lifestyle, stress, educational background, and salt reduction awareness. In males, the proportion of individuals with adequate sleep duration increased with higher salt intake (Table 3), whereas the proportion of nonsmokers decreased with higher salt intake (p for trend<0.001). There was no clear association between the amount of salt intake and alcohol consumption, exercise habits, and intake of green and yellow vegetables.

Among females, the proportion of those who had received higher education decreased with increasing salt intake (p for trend<0.001). The proportion of individuals with stress increased with decreasing salt intake (p for trend<0.05).

In addition, the percentage of subjects receiving medication increased with increasing salt intake (males; p for trend<0.05, females; p for trend<0.01) in both genders. Importantly, salt reduction awareness—as assessed by responses to the questionnaire—was unassociated with decreased salt intake in both genders.

Association of habitually consumed foods with salt intake. We examined the relationship between dietary habits and the amount of salt intake (Table 4). Many males and females regularly ate rice, miso soup, fish and green and yellow vegetables. Habitual intake of rice and miso soup was associated with increased salt intake in females (p for trend<0.04 and p for trend<0.03, respectively). Other dietary habits showed no significant association with salt intake (Table 4).

Network analysis of dietary habits in relation to salt intake. As shown in Table 4, there were no marked differences

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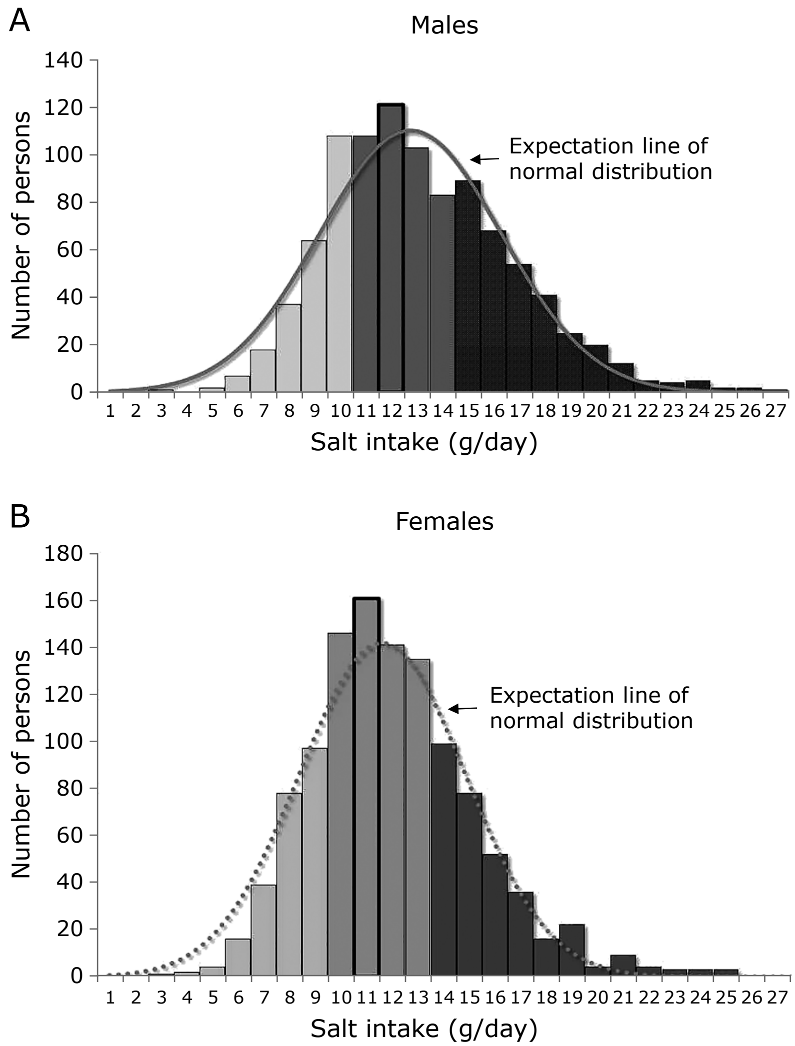

Fig. 1. Histograms of estimated daily salt intake in males (A) and females (B). In both genders, the estimated daily salt intake showed an almost normal distribution.

in dietary habits between males and females. We conducted a network analysis of the low salt group (331 males and 353 females) and the high salt group (284 males and 301 females) using habitually consumed food items as nodes and the strength of their association as edges. Fig. 2A and B present a visualized network of the food item preferences according to the amounts of salt intake for both males and females. Rice and miso soup were strongly connected in both the low and high salt intake groups (Jaccard coefficients of 0.77 and 0.81, respectively). In the low salt intake group, light yellow vegetables, green leaves, green and yellow vegetables, and cabbage were strongly interconnected (Fig. 2A and B).

Discussion

In the present study, we examined whether the prevalence of lifestyle-related diseases was associated with higher salt intake by dividing the participants into three groups according to their estimated daily salt intake. We also investigated food items and their various combinations associated with excess salt intake by analysis of dietary habits. As salt intake became higher, blood pressure and the prevalence of hypertension increased. In females, the prevalence of hyperlipidemia increased as salt intake became higher. For both genders, increased salt consumption resulted in higher levels of blood glucose and HbA1c and also a higher prevalence of diabetes. The proportion of males with metabolic syndrome also increased with higher salt intake. For both genders, awareness of the need for reduced salt intake, as assessed from questionnaire responses, did not necessarily lead to a decrease in salt intake. Network analysis showed that the low salt intake group had tended to consume different kinds of vegetables to a greater degree than the high salt intake group.

Many epidemiological, clinical and experimental studies have shown that salt intake is related to hypertension.[2,6,21] The increase in blood pressure with excess salt intake varies among individuals and the mechanism involved it is not yet clear. Various factors, including genetic background, race, age, renal function, and neurohumoral factors, contribute to salt-sensitive increases in blood pressure. Excessive salt intake is thought to increase cardiac output and vascular resistance due to an increase in circulating blood volume, resulting in an elevation of blood pressure. Many epidemiological studies have shown that increased salt intake is positively correlated with elevated blood pressure.[21] In addition, intervention trials have shown that a reduction in salt intake is directly linked to a reduction

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Table 1. Association between the amount of salt intake amount and hypertension, hyperlipidemia, diabetes, and metabolic syndrome

Characteristics	Males (*n* = 980)				Females (*n* = 1,149)			
	Low	Medium	High	*p* for trend	Low	Medium	High	*p* for trend
Number (%)	331 (33.8)	365 (37.2)	284 (29)		363 (31.6)	485 (42.2)	301 (26.2)	
Age, years	61.8 ± 9.4	63.9 ± 8.1	64.1 ± 7.5	0.015	59.8 ± 9.5	62.3 ± 8.2	64.8 ± 6.7	0.001
Height, cm	165.8 ± 6.4	166.0 ± 6.3	167.0 ± 5.7	0.02	154.0 ± 5.8	153.6 ± 5.9	153.3 ± 6.0	0.12
Body weight, kg	62.9 ± 9.6	64.3 ± 9.4	66.9 ± 9.1	0.001	52.0 ± 7.8	52.6 ± 8.0	55.2 ± 9.5	0.001
BMI (body mass index), kg/m^2	22.8 ± 2.9	23.3 ± 3.0	24.0 ± 3.0	0.001	21.9 ± 3.2	22.3 ± 3.2	23.5 ± 3.8	0.001
BMI ≥30 (%)	6 (1.8)	8 (2.2)	9 (3.2)	0.274	8 (2.2)	11 (2.3)	17 (5.6)	0.015
Hypertention								
Systolic blood pressure (mmHg)	125.9 ± 16.8	130.5 ± 17.5	132.7 ± 15.0	0.001	120.1 ± 16.6	123.3 ± 17.0	127.1 ± 16.9	0.001
Diastolic blood pressure (mmHg)	78.8 ± 10.6	80.8 ± 10.6	81.9 ± 9.2	0.001	72.9 ± 10.0	74.9 ± 10.7	75.9 ± 10.5	0.001
Hypertention (treated) (%)	121 (36.6)	139 (38.1)	131 (46.1)	0.018	100 (27.5)	143 (29.5)	105 (34.9)	0.044
Hypertention (diagnosed at baseline survey) (%)	84 (25.4)	117 (32.1)	100 (35.2)	0.008	46 (12.7)	78 (16.1)	69 (22.9)	0.001
Hypertention (treated or diagnosed at baseline survey) (%)	162 (48.9)	203 (55.6)	174 (61.3)	0.002	122 (33.6)	182 (37.5)	135 (44.9)	0.003
Hyperlipidemia								
Triglyceride (mg/dl)	132.7 ± 94.3	130.2 ± 91.0	148.1 ± 142.7	0.6	101.2 ± 107.3	98.0 ± 49.1	108.0 ± 61.8	0.001
LDL cholesterol (mg/dl)	122.5 ± 28.8	125.7 ± 32.0	121.6 ± 30.5	0.89	126.7 ± 32.2	130.8 ± 31.4	127.3 ± 30.0	0.54
HDL cholesterol (mg/dl)	57.9 ± 16.0	57.7 ± 14.3	58.0 ± 15.4	0.87	69.8 ± 16.8	67.4 ± 15.4	64.7 ± 15.6	0.001
Hyperlipidemia (treated) (%)	53 (16.0)	64 (17.5)	58 (20.4)	0.16	76 (20.9)	131 (27.0)	88 (29.2)	0.013
Hyperlipidemia (diagnosed at baseline survey)	156 (47.1)	172 (47.1)	137 (48.2)	0.79	136 (37.5)	202 (41.6)	127 (42.2)	0.202
Hyperlipidemia (treated or diagnosed at baseline survey)	184 (55.6)	194 (53.2)	160 (56.3)	0.88	187 (51.5)	287 (59.2)	181 (60.1)	0.021
Diabetes								
Fasting plasma glucose (mg/dl)	98.4 ± 16.5	99.0 ± 16.8	103.0 ± 24.0	0.031	93.6 ± 13.7	94.3 ± 13.1	97.6 ± 18.6	0.003
HbA1c (%)	5.7 ± 0.7	5.8 ± 0.7	5.9 ± 0.9	0.001	5.6 ± 0.6	5.7 ± 0.5	5.8 ± 0.6	0.001
Diabetes (treated) (number, %)	27 (8.2)	36 (9.9)	43 (15.1)	0.006	9 (2.5)	22 (4.5)	34 (11.3)	0.001
Diabetes (diagnosed at baseline survey)	31 (9.4)	42 (11.5)	41 (14.4)	0.051	18 (5.0)	24 (4.9)	33 (11.0)	0.003
Diabetes (treated or diagnosed at baseline survey)	37 (11.2)	55 (15.1)	60 (21.1)	0.001	23 (6.3)	32 (6.6)	44 (14.6)	0.001
Metabolic syndrome (number, %)	38 (11.5)	49 (13.4)	62 (21.8)	0.001	11 (3.0)	14 (2.9)	17 (5.6)	0.087

Low, low salt intake group; Medium, medium salt intake group; High, high salt intake group. Hyperlipidemia was defined as either triglycerides >150 mg/dl, LDL cholesterol >140 mg/dl, or HDL cholesterol <40 mg/dl. Continuous values are expressed as the mean ± SD. Trend test is performed using Jonckheere-Terpstra test.

Table 2. Comparison of the amount of salt intake and prevalence of diabetes by propensity score matching method

	High salt intake group (*n* = 585)	Matching from medium and low salt intake groups (*n* = 585)	*p* value
Age, years	64.45 ± 7.13	64.34 ± 7.17	NS
Number of men/women	284/301	275/310	NS
Height, cm	159.94 ± 9.01	159.90 ± 8.66	NS
Body weight, kg	60.85 ± 10.98	60.55 ± 10.99	NS
Antihypertensive medication, %	74.40	73.30	NS
Prevalence of diabetes, %	17.78	12.14	<0.01

in blood pressure.[6] The data from the present cross-sectional study appear to support an association between salt intake and hypertension.

Obesity and metabolic syndrome are increasing worldwide. A combination of unhealthy factors constituting metabolic syndrome leads to health impairment. Excessive salt intake is reportedly associated with obesity and metabolic syndrome.[22] One possible mechanism is that excess salt intake causes thirst, which in turn leads to increased consumption of sugar-containing beverages.[23] It has also been proposed that salt increases body fat directly or via adipokines such as leptin.[24,25] An epidemiological study from Finland conducted over 18 years concluded that excess salt intake was a risk factor for diabetes independent of confounding factors such as physical activity, obesity and hypertension.[8] Recently, a Finnish research group reported by having twice the sample size, a longer follow-up, and a wider

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Table 3. Baseline characteristics derived from the habitual life questionnaire based on the amount of salt intake

	Low		Medium		High		*p* for trend
	Yes	No	Yes	No	Yes	No	
Males							
Sleep 5.5–7.5 h/day	55% (171)	45% (141)	61% (203)	39% (129)	64% (173)	36% (98)	0.02
Nondrinker	79% (250)	21% (67)	84% (282)	16% (54)	84% (228)	16% (45)	0.13
Nonsmoker	64% (199)	36% (114)	80% (266)	20% (68)	85% (224)	15% (41)	0.001
Exercise ≥1 h/day	41% (136)	59% (194)	43% (157)	57% (206)	41% (117)	59% (167)	0.98
Stress	85% (266)	15% (46)	88% (294)	12% (41)	87% (236)	13% (35)	0.50
Eating between meals	82% (253)	18% (57)	80% (264)	20% (64)	81% (215)	19% (52)	0.73
College or higher education	30% (92)	70% (215)	30% (96)	70% (225)	31% (81)	69% (179)	0.77
Medication status	57% (171)	43% (128)	60% (196)	40% (129)	65% (173)	35% (92)	0.05
Awareness of salt intake reduction	63% (198)	37% (128)	62% (209)	38% (126)	67% (181)	33% (91)	0.37
Refraining from sweets	44% (137)	56% (175)	47% (156)	53% (176)	50% (136)	50% (136)	0.14
Awareness of dietary fat restriction	48% (151)	52% (161)	50% (163)	50% (166)	51% (140)	49% (132)	0.46
Refraining from of excessive calories intake	48% (151)	52% (161)	48% (159)	52% (175)	55% (149)	45% (122)	0.12
Females							
Sleep 5.5–7.5 h/day	72% (246)	28% (94)	72% (326)	28% (128)	70% (198)	30% (86)	0.48
Nondrinker	49% (166)	51% (172)	40% (183)	60% (270)	43% (119)	57% (160)	0.08
Nonsmoker	93% (306)	7% (24)	90% (391)	10% (42)	95% (251)	5% (14)	0.45
Exercise ≥1 h/day	47% (170)	53% (191)	51% (242)	49% (237)	51% (153)	49% (147)	0.30
Stress	70% (237)	30% (104)	72% (326)	28% (127)	77% (218)	23% (65)	0.04
Eating between meals	54% (183)	46% (154)	54% (247)	46% (210)	57% (159)	43% (119)	0.49
College or higher education	37% (123)	63% (213)	28% (128)	72% (327)	23% (64)	77% (212)	0.001
Medication status	57% (189)	43% (142)	61% (276)	39% (175)	67% (185)	33% (119)	0.01
Awareness of salt intake reduction	69% (238)	31% (106)	73% (334)	27% (126)	73% (209)	27% (78)	0.30
Refraining from sweets	45% (155)	55% (186)	50% (231)	50% (228)	60% (173)	40% (113)	0.001
Awareness of dietary fat restriction	60% (206)	40% (135)	62% (287)	38% (174)	69% (196)	31% (90)	0.04
Refraining from of excessive calories intake	53% (182)	47% (159)	56% (258)	44% (201)	63% (180)	37% (106)	0.02

Low, low salt intake group; Medium, medium salt intake group; High, high salt intake group. Numbers in parentheses represent the number of persons. Trend test is performed using Cochran-Armitage trend.

sodium excretion range that high salt intake was associated with an increased incidence of cardiovascular disease and diabetes mellitus.[26] In animal experiments, excess salt intake has been shown to induce insulin resistance by decreasing insulin sensitivity, suppressing insulin mRNA expression, attenuating insulin signaling, and increasing angiotensin II production.[27–29] A previous clinical study has shown that excess salt intake results in increased production of glucocorticoid and insulin resistance.[30] In the present study, propensity score matching excluding confounders showed that increased salt intake led to higher diabetes prevalence. Although further studies of gene-environmental interactions are required, we have been able to clearly demonstrate an association between excessive salt intake and diabetes, which has been a controversial issue to date, in community populations.

We examined whether healthy lifestyle habits (adequate sleep duration, non-drinking, non-smoking, or moderate exercise) were associated with salt intake. Among males, a higher proportion of individuals with adequate sleep duration had increased levels of salt intake. Because increased salt intake also reflects high caloric intake, further investigation will be required to determine whether acquisition of adequate sleep is purely attributable to salt intake. Ma *et al.*[31] reported that alcohol consumption, smoking, and education level were associated with increased salt intake. In the present study, neither non-drinking nor non-smoking was associated with a decrease in salt intake. In support of our data, one report has indicated that smoking prevalence increases with decreasing salt intake.[32] Genetic difference by race and the degree of alcohol consumption and smoking may also need to be considered in this context. The proportion of females without higher education increased with higher salt intake. Since females often perform housework including cooking, health guidance is considered to be necessary so that cooking habits can aim to reduce salt intake. One important observation was that awareness of salt intake did not necessarily lead to a decrease in salt intake, despite the fact that a high percentage of both males and females were aware of the need for salt reduction. As Takahashi *et al.*[33] have reached a similar conclusion, appropriate salt reduction guidance seems to be necessary in order to achieve the salt reduction target advocated by WHO.

Network analysis has been adapted to social and biological networks and has played an important role in clarifying various complex life and biological events.[34] It is also used in marketing strategies by identifying consumption preferences through information browsing and purchasing histories on the internet. Here we applied network analysis for investigating dietary habits for the first time. Because co-occurrence between vegetable consumption was stronger in the low salt intake group than in the high salt intake group, the former group appeared to exhibit habitual consumption of various vegetables, which could not have been revealed by the trend test, as shown in Table 4. As vegetable consumption is a key component of the DASH diet proposed by WHO for hypertensive patients, we speculated that habitual consumption of various types of vegetables may have resulted in a reduction of salt intake.[35] Having a lower vegetable intake could be a marker of unhealthier dietary habits in general

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Table 4. Dietary characteristics from the food frequency questionnaire according to the amount of salt intake

Food items	Males				Females			
	Low	Medium	High	*p* for trend	Low	Medium	High	*p* for trend
Rice	89.7%	88.2%	91.5%	0.195	88.2%	89.7%	89.4%	0.037
Bread	23.6%	20.3%	15.8%	0.149	33.9%	28.9%	29.2%	0.25
Noodle	23.3%	26.6%	28.5%	0.1	20.7%	24.3%	17.9%	0.88
Soba	4.2%	7.1%	4.9%	0.327	3.0%	3.1%	3.0%	0.523
Margarine	11.5%	7.9%	7.0%	0.054	12.7%	8.2%	10.3%	0.329
Butter	3.6%	2.2%	2.1%	0.272	1.9%	1.9%	2.0%	0.811
Milk	37.5%	38.6%	37.7%	0.982	46.8%	47.8%	44.2%	0.942
Yogurt	31.1%	32.1%	33.8%	0.524	48.2%	50.7%	45.8%	0.851
Miso soup	74.3%	78.1%	77.1%	0.06	70.8%	76.1%	75.7%	0.028
Tofu	31.4%	37.0%	35.6%	0.178	43.8%	38.4%	38.9%	0.45
Natto or soybeans	42.3%	51.0%	47.2%	0.147	47.9%	48.2%	52.2%	0.233
Egg	37.2%	44.1%	43.0%	0.057	50.4%	46.8%	42.2%	0.033
Chicken	15.7%	17.5%	12.3%	0.384	23.7%	21.0%	20.3%	0.338
Beef or pork	27.5%	25.5%	25.0%	0.466	39.9%	40.0%	41.5%	0.68
Liver	0.3%	1.6%	0.7%	0.502	0.6%	1.4%	0.7%	0.752
Ham or sausage	14.5%	16.4%	12.7%	0.788	21.8%	19.8%	21.9%	0.9
Fish	47.4%	51.2%	50.4%	0.37	54.3%	62.9%	60.5%	0.053
Small fish with bones	7.3%	6.6%	9.5%	0.348	12.9%	13.2%	13.0%	0.907
Canned tuna	1.8%	1.1%	2.8%	0.364	1.1%	3.7%	5.3%	0.002
Squid	3.6%	4.7%	3.9%	0.822	2.5%	5.4%	6.6%	0.009
Shellfish	1.8%	2.2%	3.5%	0.171	0.6%	2.1%	3.0%	0.016
Cod roe	3.9%	3.8%	6.7%	0.125	3.9%	4.5%	5.3%	0.332
Chikuwa	5.7%	5.5%	6.3%	0.797	8.3%	12.8%	16.3%	0.001
Ganmodoki	3.9%	6.0%	6.0%	0.303	16.8%	18.6%	20.9%	0.131
Potato	18.1%	17.3%	16.2%	0.518	28.7%	31.1%	34.2%	0.089
Pumpkin	6.0%	6.3%	5.3%	0.688	11.6%	9.9%	10.6%	0.737
Carrot	23.0%	26.6%	21.1%	0.598	48.5%	49.1%	44.5%	0.36
Broccoli	13.0%	12.9%	10.9%	0.436	22.0%	19.4%	18.3%	0.255
Green leaves	47.1%	45.2%	47.9%	0.889	57.9%	61.0%	56.8%	0.997
Green and yellow vegetables	32.6%	34.5%	33.8%	0.742	44.4%	42.5%	45.5%	0.606
Cabbage	38.1%	42.2%	43.7%	0.183	56.7%	53.4%	52.5%	0.257
Radish	21.5%	26.3%	27.8%	0.081	38.0%	37.3%	35.2%	0.791
Dried radish	1.8%	2.7%	1.4%	0.757	4.1%	4.1%	5.3%	0.437
Burdock	4.5%	5.8%	4.9%	0.763	8.3%	8.2%	8.0%	0.943
Other vegetables	48.6%	59.5%	56.0%	0.131	77.7%	72.4%	72.4%	0.109
Mushroom	23.9%	30.1%	24.3%	0.966	48.8%	49.7%	52.5%	0.229
Seaweed	24.5%	27.4%	25.4%	0.835	32.2%	30.5%	31.9%	0.998
Mayonnaise	25.1%	24.9%	27.1%	0.664	25.9%	28.5%	24.9%	0.93
Fried food	26.0%	26.3%	23.9%	0.489	19.0%	22.3%	17.3%	0.767
Stir fried food	31.4%	35.9%	33.5%	0.709	46.0%	51.8%	43.2%	0.755
Orange	12.7%	13.7%	12.3%	0.95	24.2%	22.7%	25.6%	0.749
Other fruits	19.6%	23.8%	24.3%	0.178	41.9%	41.6%	39.5%	0.712
Peanuts	10.0%	7.9%	10.2%	0.932	14.0%	13.8%	9.3%	0.096
Western confectionery	3.6%	3.6%	3.5%	0.996	6.3%	5.8%	3.0%	0.07
Japanese confectionery	5.4%	5.5%	5.6%	0.855	11.8%	12.8%	9.3%	0.462

Low, low salt intake group; Medium, medium salt intake group; High, high salt intake group. Trend test is performed using Cochran-Armitage test.

and further study will be required to clarify this aspect. This is the first reported study to have examined dietary habits through network analysis and examined their significance.

Although salt alone is unlikely to cause diabetes, we were able to clarify a relationship between high salt intake and diabetes, which has been a controversial issue to date. Salt intake is defined by the salt content of the diet, and thus analysis of overall dietary habits is essential. For the first time, we employed network analysis to clarify dietary habits in a community-based population. We believe that simultaneous consumption of more vegetables will also increase the potassium intake thus decreasing the sodium to potassium ratio which may be even

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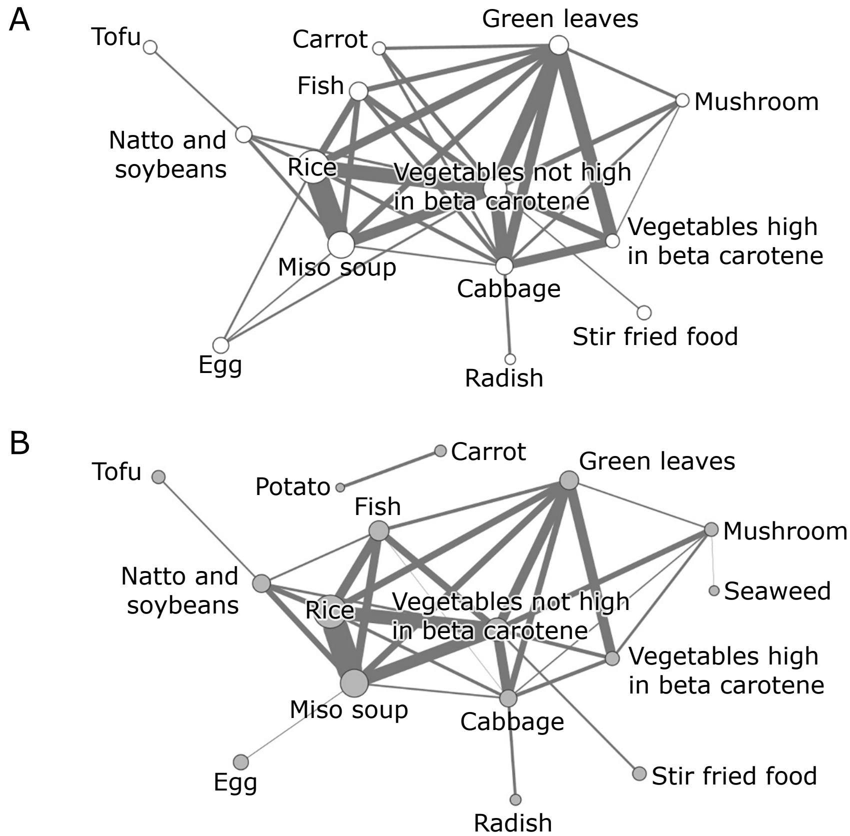

Fig. 2. The network of food items for the low salt intake group and the high salt intake group displayed using Cytoscape. In the low salt intake group (A), the edges connecting vegetables (Jaccard coefficient) are depicted as thick compared to the high salt intake group (B).

more important than sodium intake alone with respect to its effect on living body including blood pressure.

The potential limitations of this study should also be noted. The first is related to estimation of daily salt intake, for which various methods have been proposed. We employed daily spot urine samples for this purpose, as the method is simple and allows coverage of large local populations. Estimated salt intakes obtained using the Kawasaki equation are widely used in epidemiological studies.[15] Estimation of daily salt intake from a single spot urine is considered to be a good indicator for assessing salt intake in a population.[36] The second potential limitation was the appropriateness of the items in the food frequency questionnaire for different dietary habits. The food frequency questionnaire does not include a question on sugar-containing beverages. The Japanese are not in the habit of drinking sugar-containing beverages with their meals. During the follow-up process, therefore, we would like to investigate changes in dietary habits, including the consumption of sugar-containing beverages. The third potential limitation is that Japan is a country with a relatively high salt intake. The current study was a cross-sectional study, which would have limited evaluation of the results. In particular, the low salt intake group would have corresponded to a relatively low salt intake. Although the present study was an analysis of the residents with high salt intake and would needs to be validated in countries with low salt intake, our results may be appreciable to countries and regions with a relatively high salt intake, such as Japan.

In conclusion, we conducted a cross-sectional study of residents in Yonezawa city (980 males and 1,149 females) who had been included in the Yamagata Study based on baseline blood tests and lifestyle questionnaires. We examined lifestyle-related diseases associated with increased salt intake and dietary habits that contributed to reduced salt intake. Increased salt intake was associated with higher blood pressure (both systolic and diastolic), higher BMI, and higher diabetes prevalence. Salt reduction awareness did not necessarily lead to a decrease in salt intake. Network analysis showed that the low salt intake group habitually consumed various kinds of vegetables more often than the high salt intake group.

Author Contributions

HT, TKonta, KN, HY, and TKayama designed research (project conception, development of overall research plan, and study oversight). NI, AT, and HK analyzed and interpreted the data. NI, AT, and HT wrote the manuscript. TKonta, KN, HY, and TKayama critically revised the manuscript.

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Abbreviations

BMI	body mass index
HbA1c	glycated hemoglobin level
HDL	high-density lipoprotein
LDL	low-density lipoprotein

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Conflicts of interest

No potential conflicts of interest were disclosed.

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