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Factors Associated with Oral Dryness in Women: An Analysis by Age

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Abstract

Aim: Factors associated with oral dryness have not been clarified, although it affects people's quality of life. Few reports have discussed the relationship between climacteric symptoms and oral dryness. This study aimed to explore factors associated with oral dryness by age.

Methods: We recruited 372 participants. Data were collected using a web-based questionnaire that covered medical history, climacteric symptoms, and dryness of the eyes, nose, mouth, skin and vagina. Data were collected in May 2018. Univariate and multiple logistic regression analyses were performed to examine the relationships between oral dryness and other factors.

Results: The prevalence of oral dryness was 29%–46%. The number of dryness regions was significantly higher in participants with oral dryness in all age groups. Oral and climacteric symptoms were observed in the oral dryness group. The multiple logistic regression analysis showed the number of dryness regions was a significant explanatory variable for oral dryness.

Conclusion: Considering factors associated with oral dryness will support early detection and may contribute to improved quality of life.

Keywords: Menopause; Oral Dryness; Xerostomia; Quality of Life; Web-Based Survey

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Introduction

Xerostomia is defined as a subjective complaint of a dry mouth [1], whereas hyposalivation is an objective reduction in salivary secretion [2]. The causes of hyposalivation are diverse, and include Sjögren's syndrome, head and neck radiotherapy, adverse effects of medications on oral dryness (xerogenic medications), systemic disease and psychological stress [1,3]. The tolerance for dryness varies from person to person [4]. Therefore, the presence of subjective oral dryness does not always match a person's salivary secretion. A previous study reported a 47.1% agreement rate between the subjective complaint of a dry mouth and the objective measurement of unstimulated salivary flow [5]. Another report demonstrated that 75% of female patients with burning mouth syndrome complained of a dry mouth, whereas only 46.4% showed less than 0.1 mL/min of unstimulated saliva secretion [6]. In dry mouth clinic at Niigata University Medical and Dental Hospital, the volume of unstimulated and stimulated salivary secretion was not decreased in 14.5% of patients who were diagnosed with xerostomia [7]; 78.4% of these patients were female. Previous analyses by age showed that xerostomia was reported more often in women aged ≤55 years; with rates of 21.3% in women aged ≤55 years, 10.6% in women aged 56–64 years, and 10.3% in women aged ≥65 years. The mean age of menopause in Japan is 50.5 years, and the 10 years from age 45–55 years are considered to represent the menopause. The reason for xerostomia being commonly observed in women aged ≤55 years may be related to the decrease of female hormones [8,9]. Compared with hyposalivation, the causes of xerostomia have not yet been clarified. It is also possible that risk factors for xerostomia differ from those for hyposalivation. Clarifying the causes of xerostomia may lead to early detection and treatment.

People who feel dryness in a certain region of the body (e.g. oral dryness) also tend to feel dryness in other regions. Recently, this has been called 'dryness syndrome' [8,10] or 'dry X syndrome' [11]. A recent survey among Japanese women showed that approximately half felt dryness in more than two regions of the body (e.g. eyes, nose, mouth, skin and vagina) [8]. This appeared to result in decreased quality of life (QOL) [12]. Determining factors related to xerostomia may lead to early detection of dryness in other regions of the body, which in turn may contribute to improvement in QOL. This study

aimed to explore factors related to xerostomia according to age using a web-based survey.

Methods

Participants

The present authors have conducted web-based surveys in Japan covering systemic body symptoms every 3 years from May 2012, using an internet research company (Macromill, Tokyo, Japan). This study was conducted as part of these surveys. The research company has a proprietary "Automatic Internet Research System," which instantly collects consumer response data on products and services provided by a variety of companies. The sample size was calculated using an estimated 20% prevalence of oral dryness. Based on a α-value of 0.05 and a 0.05% confidence interval (CI) for true prevalence, 372 subjects were needed for this analysis [8]. We recruited women aged in their 20s, 30s, 40s, 50s, 60s and 70s (n=62 in each age group).

Questionnaires

A web-based survey covering systemic body symptoms was administered to participants. The survey comprised 45 items that investigated participants' characteristics, feelings of dryness, oral symptoms, climacteric symptoms and health related quality of life (HRQOL). All questions were in Japanese. Participants' characteristics included sex, age, employment, household income, personal income, medical history and medication. Feelings of dryness of the skin, eyes, nose, mouth and vagina were assessed using four levels: none, mild, moderate and severe. Oral symptoms included burning sensation of the tongue, dysgeusia, phantogeusia, gum bleeding, temporomandibular joint pain, globus syndrome (sensation of a lump in the throat), difficulty swallowing and vagina symptoms (e.g. vaginal discharge and itchiness). These symptoms were also assessed using the four levels. The climacteric symptom checklist for Japanese women was used to evaluate climacteric symptoms [13]. This checklist includes 21 items: 'hot flashes of face or upper body (become hot)', 'sweat easily', 'unable to fall asleep at night', 'fall asleep but often wake at night', 'easily excitable, often irritable', 'always anxious', 'worry about minor things', 'worry and often become depressed', 'lack of energy, easily tired', 'tired feeling of eyes', 'difficulty remembering things or often forgetful', 'dizziness', 'heart pounds quickly', 'tight feeling of chest', 'heavy feeling of the head or frequent headache', 'shoulder or neck stiffness', 'back or low back pain', 'painful joints of hands and feet', 'cold feeling of low back or hands and feet', 'numbness of hands and feet (fingers, toes)' and 'recently sensitive to sound'. These symptoms were evaluated using the same four levels.

We used the Japanese version of the eight-item Short-Form Health Survey (SF-8) to evaluate HRQOL [14]. The SF-8 assesses eight health concepts: physical functioning, role (physical), bodily pain, general health, vitality, social functioning, role (emotional) and mental health. A higher score indicates better HRQOL. The standard score in the Japanese population is 50 [14]. In addition, sleeping hours and menopause status were investigated.

Statistical analysis

The Japanese national drug database 2018 was used to categorise effects and adverse effects. In the analysis of symptoms, participants who reported 'severe', 'moderate' or 'mild' for a symptom were considered to have that symptom. The number of body parts in which the feeling dryness was reported was counted as dryness regions. In the SF-8 analysis, physical component summary (PCS) and mental component summary (MCS) scores were calculated using the scoring method previously described [14]. For both PCS and MCS, a higher score indicates better HRQOL.

We divided participants into four age groups: <45 years, 45–55 years, 56–64 years and ≥65 years. Participants who reported an oral dryness symptom level from severe to mild were classified as the oral dryness group. The remaining participants were considered the non-oral dryness group.

Univariate analysis was performed to investigate the relationship between the presence of oral dryness and each evaluation item. Variables not normally distributed (as assessed using the Shapiro-Wilk normality test) were analysed using non-parametric tests. Mann-Whitney U tests were used to compare the number of dryness regions, sleeping hours, duration since menopause, PCS and MCS between the oral dryness and non-oral dryness groups. Chi-square and Fisher's exact tests were applied for other evaluation items (e.g. oral and climacteric symptoms). The top three medications were analysed for medicinal efficacy.

A multiple logistic regression model yielding odds ratios (OR) and 95% CIs was used to identify factors associated with oral dryness. The model included variables that showed an association in the univariate analysis ($p<0.05$). A stepwise method was used to develop an optimal multivariable logistic model. All analyses were performed using SPSS version 24.0 (IBM, Japan). Statistical significance was set at $p<0.05$.

Results

Participants' characteristics and prevalence of oral dryness

One of the 372 participants were excluded because their answers to the questionnaire were inconsistent. The prevalence of oral dryness by age is shown in Table 1. In all age groups, 29%-46% of participants felt oral dryness. Women aged 45–55 years demonstrated the highest prevalence of oral dryness (46.2%).

In total, 146 participants (39.4%) had some medical histories. The common diseases were uterine disease (n=52; 14.0%) and hypertension (n=40; 10.8%). There were 111 (30.0%) women that were taking prescribed medications. The top three medications categorised by effect were: cardiovascular agents (n=32; 8.6%), central nervous system agents (n=16; 4.3%), and digestive organ agents (n=8; 2.2%).

Univariate analysis of oral dryness and other evaluation items by age

The results of the univariate analysis of oral dryness and characteristics, medical history, medication, sleeping duration, menopause status, and HRQOL are shown in Table 2. Women who had uterine disease in the group aged <45 years (p=0.047) and hyperlipidemia in the group aged 45–55 years (p=0.040) had a high prevalence of oral dryness. There were significant differences between the presence of medication and oral dryness in women aged <45 years (p=0.048 and p=0.019, respectively). The PCS scores for women aged

Table 1: Prevalence of oral dryness by age.

		Non-oral dryness		Oral dryness	
Age	**n**	**n**	**%**	**n**	**%**
total	371	225	60.6	146	39.4
<45	157	90	57.3	67	42.7
45-55	65	35	53.8	30	46.2
56-64	65	46	70.8	19	29.2
≥65	84	54	64.3	30	35.7

Table 2: Univariate analysis of oral dryness and characteristics, medical history, medication, sleeping duration, menopause status, and quality of life.

	Total (n=371)			<45 years (n=157)			45–55 years (n=65)			56–64 years (n=65)			over 65 years (n=84)		
	Non-oral dryness n=225	Oral dryness n=146	P-value	Non-oral dryness n=90	Oral dryness n=67	P-value	Non-oral dryness n=35	Oral dryness n=30	P-value	Non-oral dryness n=46	Oral dryness n=19	P-value	Non-oral dryness n=54	Oral dryness n=30	P-value
Characteristics															
Married	158 (70.2)	95 (65.1)	0.298	56 (62.2)	35 (52.2)	0.21	23 (65.7)	22 (73.3)	0.507	37 (80.4)	17 (89.5)	0.377	42 (77.8)	21 (70.0)	0.43
Children	150 (66.7)	83 (56.8)	0.056	48 (53.3)	25 (37.3)	0.047	22 (62.9)	17 (56.7)	0.612	34 (73.9)	15 (78.9)	0.668	46 (85.2)	26 (86.7)	0.853
Household income >6MM	55 (32.0)	34 (31.2)	0.89	21 (35.0)	10 (23.8)	0.227	14 (51.9)	14 (56.0)	0.764	10 (27.8)	7 (43.8)	0.257	10 (20.4)	3 (11.5)	0.334
Personal income >2MM	49 (27.5)	29 (23.8)	0.466	3.2±1.4	3±1.2	0.315	10 (35.7)	7 (25.9)	0.432	10 (26.3)	1 (5.3)	0.058	8 (16.3)	6 (21.4)	0.577
Job	102 (45.3)	73 (50.0)	0.379	53 (58.9)	44 (65.7)	0.387	21 (60.0)	17 (56.7)	0.786	21 (45.7)	4 (21.1)	0.064	7 (13.0)	8 (26.7)	0.116
Medical history															
Uterine disease	26 (11.6)	26 (17.8)	0.063	**7 (7.8)**	**12 (17.9)**	**0.047**	6 (17.1)	7 (23.3)	0.757	5 (10.9)	1 (5.3)	0.584	8 (14.8)	5 (16.7)	0.527
Hypertension	23 (10.2)	17 (11.6)	0.666	1 (1.1)	2 (3.0)	0.39	2 (5.7)	2 (6.7)	0.873	5 (10.9)	3 (15.8)	0.429	15 (27.8)	10 (33.3)	0.594
Hyperlipidemia	13 (5.8)	11 (7.5)	0.292	0 (0.0)	1 (2.1)	0.427	**0 (0.0)**	**4 (13.3)**	**0.04**	4 (8.7)	2 (10.5)	0.571	7 (13.0)	4 (13.3)	0.604
Respiratory disease	7 (3.1)	4 (2.7)	0.551	0 (0.0)	2 (3.0)	0.181	1 (2.9)	1 (3.3)	0.912	1 (2.2)	0 (0.0)	0.708	5 (9.3)	1 (3.3)	0.297
Dysautonomia	6 (2.7)	8 (5.5)	0.165	2 (2.2)	4 (6.0)	0.214	1 (2.9)	1 (3.3)	0.912	2 (4.3)	2 (10.5)	0.346	1 (1.9)	1 (3.3)	0.59
No disease	**147 (65.3)**	**78 (53.4)**	**0.022**	**75 (83.3)**	**46 (68.7)**	**0.03**	24 (68.6)	17 (56.7)	0.321	26 (56.5)	7 (36.8)	0.149	22 (40.7)	8 (26.7)	0.197
Medication															
N. medication data	219	142		89	66		34	30		44	18		52	28	
Medication	67 (29.8)	44 (30.1)	0.941	**12 (13.3)**	**19 (28.4)**	**0.019**	7 (20.0)	3 (10.0)	0.223	16 (34.8)	8 (42.1)	0.578	32 (59.3)	14 (46.7)	0.267
Xerogenic medication	37 (16.9)	23 (16.2)	0.862	6 (6.7)	9 (13.6)	0.151	1 (2.9)	2 (6.7)	0.452	9 (20.5)	4 (21.1)	0.877	21 (40.4)	8 (28.6)	0.294
Cardiovascular agent	22 (10.0)	10 (7.0)	0.327	0 (0.0)	1 (1.5)	0.426	0 (0.0)	2 (6.7)	0.216	5 (11.4)	2 (11.1)	0.674	17 (32.7)	5 (17.9)	0.123
CNS agent	**5 (2.3)**	**11 (7.7)**	**0.014**	**0 (0.0)**	**5 (7.6)**	**0.013**	1 (2.9)	0 (0.0)	0.531	2 (4.5)	1 (5.6)	0.65	**2 (3.8)**	**5 (17.9)**	**0.041**
Digestive organ agent	6 (2.7)	2 (1.4)	0.327	0 (0.0)	1 (1.5)	0.426	1 (2.9)	0 (0.0)	0.531	2 (4.5)	1 (5.6)	0.65	3 (5.8)	0 (0.0)	0.269
Menopause															
Menopause	107 (48.0)	55 (38.5)	0.074	0 (0.0)	0 (0.0)	—	8 (22.9)	9 (30.0)	0.449	45 (100.0)	17 (89.5)	0.085	54 (100.0)	30 (100.0)	—
Menopause years	13.8±7.4	13.8±8	0.829	0	0	—	5.3±4.2	3.8±1.5	0.549	**8.1±4**	**10.8±3.8**	**0.017**	19.6±4.6	19.4±6.8	0.548
Sleeping duration (min)	**389.2±60.5**	**374±62.5**	**0.032**	**392.6±66.0**	**370.6±65.0**	**0.003**	379.7±64.6	369.5±60.1	0.471	385.0±56.8	388.4±43.0	0.691	393.5±51.2	377.0±70.3	0.225
Health related quality of life															
PCS	**49.7±6.0**	**47.9±7.0**	**0.006**	**49.4±6.8**	**47.7±6.8**	**0.013**	50.4±5.3	48.2±8.2	0.269	50.3±5.4	48.7±6.3	0.276	49.3±5.4	47.5±6.8	0.207
MCS	**49.4±6.9**	**46±8.9**	**<0.001**	47.8±6.4	43.2±9.4	0.135	47.6±8.1	46.1±7.8	0.216	50.2±7.1	48.5±6.9	0.352	52.7±5.1	50.3±7.8	0.191

Household income >6MM: household income > 6,000,000 Japanese yen per year
Personal income >2MM: household and personal income > 2,000,000 Japanese yen per year
N. medication data: number of participants whose medication information was obtained
CNS: central nervous system
Menopause years: years since menopause
PCS: physical component summary
MCS: mental component summary

<45 years were significantly lower in the oral dryness group compared with the non-oral dryness group.

The results of the univariate analysis of oral dryness and dryness in other regions, oral symptoms, and climacteric symptoms by age are shown in Table 3. In all age groups, the number of dryness regions was significantly higher in those with oral dryness than in the non-oral dryness group ($p \leq 0.001$). Oral and climacteric symptoms were more commonly observed in the oral dryness group than the non-oral dryness group.

Multiple logistic regression analysis of oral dryness by age

Multiple logistic regression analysis was performed using the presence of dryness as the objective variable and factors that showed significant relationships in the univariate analysis as explanatory variables (Table 4). A noteworthy finding was that in all age groups, the number of dryness regions was an explanatory variable for oral dryness with high ORs.

Discussion

This survey revealed that factors associated with oral dryness differed by age, with the number of dryness regions of the body being the only common factor across all age groups. This supported the concept of dryness syndrome or dry X syndrome; in other words, people who feel dryness in certain regions of the body may feel dryness in other regions. The cause of dryness of the eyes, nose, mouth, skin and vagina may be complex. For example, an important factor that contributes to the onset of dry eye disease is meibomian gland dysfunction, which causes a disruption in the tear film lipid layer and affects the rate of tear evaporation [15]. Symptoms of dryness of the nose range from the purely subjective sensation of a rather dry nose to visible crusting of the (inner) nose (nasal mucosa), and there are various nasal dryness combinations. Relevant diseases are rhinitis sicca anterior, primary and secondary rhinitis atrophicans, rhinitis atrophicans with foetor (ozena) and empty nose syndrome [16]. The occurrence of dry skin depends on various extrinsic factors including: climate; environment;

Table 3: Univariate analysis of oral dryness and dryness of other regions, oral symptoms, and climacteric symptoms by age.

	Total (n=371)			<45 years (n=157)			45–55 years (n=65)			56–64 years (n=65)			over 65 years (n=84)		
	Non-oral dryness n=225	Oral dryness n=146	P-value	Non-oral dryness n=90	Oral dryness n=67	P-value	Non-oral dryness n=35	Oral dryness n=30	P-value	Non-oral dryness n=46	Oral dryness n=19	P-value	Non-oral dryness n=54	Oral dryness n=30	P-value
Dryness															
Dryness of skin	**101 (44.9)**	**103 (70.5)**	**<0.001**	**48 (47.8)**	**48 (71.6)**	**<0.001**	**17 (48.6)**	**23 (76.7)**	**0.02**	**20 (43.5)**	**14 (73.7)**	**0.027**	**16 (29.6)**	**18 (60.0)**	**0.007**
Dryness of eyes	**93 (41.3)**	**116 (79.5)**	**<0.001**	**43 (47.8)**	**57 (85.1)**	**<0.001**	**13 (37.1)**	**24 (80.0)**	**0.001**	**12 (26.1)**	**13 (68.4)**	**0.001**	**25 (46.3)**	**22 (73.3)**	**0.017**
Dryness of nose	**28 (12.4)**	**67 (45.9)**	**<0.001**	**12 (13.3)**	**29 (43.3)**	**<0.001**	**5 (14.3)**	**19 (63.3)**	**<0.001**	**4 (8.7)**	**10 (52.6)**	**<0.001**	7 (13.0)	9 (30.0)	0.057
Dryness of vagina	**10 (4.4)**	**29 (19.9)**	**<0.001**	**1 (1.1)**	**9 (13.4)**	**0.002**	**2 (5.7)**	**10 (33.3)**	**0.004**	5 (10.9)	2 (10.5)	0.968	**2 (3.7)**	**8 (26.7)**	**0.002**
N. dryness regions	**1.0±1.0**	**2.2±1.2**	**<0.001**	**1.2±0.9**	**2.1±1.1**	**<0.001**	**1.1±1.1**	**2.5±1.3**	**<0.001**	**0.9±1.1**	**2.1±1.3**	**0.001**	**0.9±1.0**	**1.9±1.3**	**0.001**
Oral Symptoms															
Burning sensation of tongue	**8 (3.6)**	**26 (17.8)**	**<0.001**	**3 (3.3)**	**11 (16.4)**	**0.004**	2 (5.7)	6 (20.0)	0.081	2 (4.3)	2 (10.5)	0.346	**1 (1.9)**	**7 (23.3)**	**0.001**
Dysgeusia	**14 (6.2)**	**27 (18.5)**	**<0.001**	4 (4.4)	6 (9.0)	0.252	**1 (2.9)**	**9 (30.0)**	**0.002**	4 (8.7)	4 (21.1)	0.168	**5 (9.3)**	**8 (26.7)**	**0.035**
Phantogeusia	**10 (4.4)**	**28 (19.2)**	**<0.001**	**3 (3.3)**	**9 (13.4)**	**0.018**	**0 (0.0)**	**9 (30.0)**	**<0.001**	3 (6.5)	4 (21.1)	0.086	4 (7.4)	6 (20.0)	0.088
Gum bleeding	**64 (28.4)**	**68 (46.6)**	**0.001**	**34 (37.8)**	**38 (56.7)**	**0.018**	7 (20.0)	11 (36.7)	0.134	14 (30.4)	6 (31.6)	0.928	**9 (16.7)**	**13 (43.3)**	**0.008**
TMJ pain	**11 (4.9)**	**26 (17.8)**	**<0.001**	**5 (5.6)**	**14 (20.9)**	**0.004**	2 (5.7)	5 (16.7)	0.156	2 (4.3)	0 (0.0)	0.356	**2 (3.7)**	**7 (23.3)**	**0.005**
Globus syndrome	**21 (9.3)**	**41 (28.1)**	**<0.001**	11 (12.2)	14 (20.9)	0.142	**2 (5.7)**	**11 (36.7)**	**0.002**	3 (6.5)	4 (21.1)	0.086	**5 (9.3)**	**12 (40.0)**	**0.001**
Difficulty swallowing	**10 (4.4)**	**36 (24.7)**	**<0.001**	**4 (4.4)**	**11 (16.4)**	**0.012**	**1 (2.9)**	**6 (20.0)**	**0.026**	**1 (2.2)**	**7 (36.8)**	**<0.001**	**4 (7.4)**	**12 (40.0)**	**<0.001**
Vagina symptoms															
Vaginal discharge	**51 (22.7)**	**60 (41.1)**	**<0.001**	**13 (14.4)**	**20 (29.9)**	**0.019**	12 (34.3)	13 (43.3)	0.455	**4 (8.7)**	**6 (31.6)**	**0.02**	4 (7.4)	3 (10.0)	0.68
Itchiness of vagina	**27 (12.0)**	**37 (25.3)**	**0.001**	**11 (12.2)**	**17 (25.4)**	**0.033**	6 (17.1)	9 (30.0)	0.22	4 (8.7)	5 (26.3)	0.061	4 (7.4)	3 (10.0)	0.68
Pain during intercourse	**20 (8.9)**	**30 (20.5)**	**0.001**	1 (1.1)	2 (3.0)	0.396	4 (11.4)	7 (23.3)	0.202	3 (6.5)	1 (5.3)	0.848	**2 (3.7)**	**5 (16.7)**	**0.039**
Climacteric symptoms															
Hot flashes of face or upper body	**50 (22.2)**	**73 (50.0)**	**<0.001**	**14 (15.6)**	**33 (49.3)**	**<0.001**	**7 (20.0)**	**19 (63.3)**	**<0.001**	22 (47.8)	10 (52.6)	0.681	7 (13.0)	8 (26.7)	0.116
Sweat easily	**123 (54.7)**	**104 (71.2)**	**0.001**	**44 (48.9)**	**48 (71.6)**	**0.004**	20 (57.1	20 (66.7)	0.431	31 (67.4)	15 (78.9)	0.352	28 (51.9)	21 (70.0)	0.122
Unable to fall asleep at night	**108 (48.0)**	**104 (71.2)**	**<0.001**	**47 (52.2)**	**49 (73.1)**	**0.008**	17 (48.6)	20 (66.7)	0.142	23 (50.0)	13 (68.4)	0.174	**21 (38.9)**	**22 (73.3)**	**0.002**
Fall asleep but often awake at night	**119 (52.9)**	**108 (74.0)**	**<0.001**	**37 (41.1)**	**48 (71.6)**	**<0.001**	21 (60.0)	24 (80.0)	0.082	33 (71.7)	12 (63.2)	0.495	**28 (51.9)**	**24 (80.0)**	**0.011**
Easily excitable, often irritable	**110 (48,9)**	**110 (75.3)**	**<0.001**	**59 (65.6)**	**56 (83.6)**	**0.012**	**18 (51.4)**	**23 (76.7)**	**0.036**	**19 (41.3)**	**13 (68.4)**	**0.047**	**14 (25.9)**	**18 (60.0)**	**0.002**
Always anxious	**111 (49.3)**	**112 (76.6)**	**<0.001**	**53 (58.9)**	**52 (77.6)**	**0.014**	**19 (54.3)**	**25 (83.3)**	**0.013**	23 (50.0)	13 (68.4)	0.174	**16 (29.6)**	**22 (73.3)**	**<0.001**
Worry about minor things	**117 (52.0)**	**115 (78.8)**	**<0.001**	**52 (57.8)**	**54 (80.6)**	**0.003**	21 (60.0)	24 (80.0)	0.082	25 (54.3)	13 (68.4)	0.295	**19 (35.2)**	**24 (80.0)**	**<0.001**
Worry and often become depressed	**102 (45.3)**	**99 (67.8)**	**<0.001**	50 (55.6)	47 (70.1)	0.063	17 (48.6)	20 (66.7)	0.142	19 (41.3)	12 (63.2)	0.109	**16 (29.6)**	**20 (66.7)**	**0.001**
Lack of energy, easily tired	**104 (46.2)**	**102 (69.9)**	**<0.001**	**51 (56.7)**	**53 (79.1)**	**0.003**	20 (57.1	22 (73.3)	0.174	20 (43.5)	12 (63.2)	0.149	**13 (24.1)**	**15 (50.0)**	**0.016**
Tired feeling of eyes	**166 (73.8)**	**132 (90.4)**	**<0.001**	64 (71.1)	55 (82.1)	0.112	**25 (71.4)**	**30 (100.0)**	**0.001**	37 (80.4)	18 (94.7)	0.146	**40 (74.1)**	**29 (96.7)**	**0.01**
Forgetful	**119 (52.9)**	**111 (76.0)**	**<0.001**	**42 (46.7)**	**48 (71.6)**	**0.002**	**18 (51.4)**	**25 (83.3)**	**0.007**	28 (60.9)	12 (63.2)	0.863	**31 (57.4)**	**26 (86.7)**	**0.006**
Dizziness	**57 (25.3)**	**75 (51.4)**	**<0.001**	33 (36.7)	31 (46.3)	0.226	**7 (20.0)**	**17 (56.7)**	**0.002**	**7 (15.2)**	**10 (52.6)**	**0.002**	**10 (18.5)**	**17 (56.7)**	**<0.001**
Heart pounds quickly	**41 (18.2)**	**69 (47.3)**	**<0.001**	**19 (21.1)**	**27 (40.3)**	**0.009**	**5 (14.3)**	**18 (60.0)**	**<0.001**	10 (21.7)	7 (36.8)	0.208	**7 (13.0)**	**17 (56.7)**	**<0.001**
Tight feeling of chest	**31 (13.8)**	**40 (27.4)**	**0.001**	17 (18.9)	18 (26.9)	0.235	**3 (8.6)**	**9 (30.0)**	**0.026**	6 (13.0)	3 (15.8)	0.771	**5 (9.3)**	**10 (33.3)**	**0.006**
Headaches	**90 (40.0)**	**86 (58.9)**	**<0.001**	51 (56.7)	47 (70.1)	0.084	11 (31.4)	15 (50.0)	0.128	**16 (34.8)**	**12 (63.2)**	**0.036**	12 (22.2)	12 (40.0)	0.084
Shoulder or neck stiffness	**165 (73.3)**	**134 (91.8)**	**<0.001**	**70 (77.8)**	**63 (94.0)**	**0.005**	29 (82.9)	29 (96.7)	0.073	31 (67.4)	17 (89.5)	0.065	35 (64.8)	25 (83.3)	0.072
Back or low back pain	**130 (57.8)**	**114 (78.1)**	**<0.001**	**54 (60.0)**	**51 (76.1)**	**0.034**	**20 (57.1)**	**24 (80.0)**	**0.049**	27 (58.7)	15 (78.9)	0.12	**29 (53.7)**	**24 (80.0)**	**0.017**
Joint of hands and feet painful	**70 (31.1)**	**74 (50.7)**	**<0.001**	**14 (15.6)**	**22 (32.8)**	**0.011**	**10 (28.6)**	**20 (66.7)**	**0.002**	17 (37.0)	12 (63.2)	0.053	29 (53.7)	20 (66.7)	0.248
Coldness	**104 (46.2)**	**98 (67.1)**	**<0.001**	47 (52.2)	42 (62.7)	0.191	**16 (45.7)**	**23 (76.7)**	**0.011**	20 (43.5)	12 (63.2)	0.149	**21 (38.9)**	**21 (70.0)**	**0.006**
Numbness of hands and feet	**42 (18.7)**	**52 (35.6)**	**<0.001**	13 (14.4)	17 (25.4)	0.085	**4 (11.4)**	**12 (40.0)**	**0.008**	15 (32.6)	8 (42.1)	0.466	**10 (18.5)**	**15 (50.0)**	**0.002**
Recently sensitive to sound	**30 (13.3)**	**59 (40.4)**	**<0.001**	**12 (13.3)**	**27 (40.3)**	**<0.001**	**8 (22.9)**	**15 (50.0)**	**0.023**	**5 (10.9)**	**7 (36.8)**	**0.014**	**5 (9.3)**	**10 (33.3)**	**0.006**

N. of dryness: number of regions of dryness
TMJ: temporomandibular joint
Forgetful: difficulty remembering things or often forgetful
Headaches: heavy feeling of the head or frequent headache
Coldness: cold feeling of low back or hands and feet

exposure to soaps, detergents, chemicals or medications; genetics; diseases; hormone imbalances; and ageing [17]. The vagina, vulva, urethra and trigone of the bladder all contain oestrogen receptors and undergo atrophy when oestrogen levels decrease. The vulva and vaginal walls also become pale and thin and lose their elasticity, which results in decreased vaginal secretion [18]. As noted above, causes of dryness of the eyes, nose, mouth, skin and vagina differ. However, oestrogen receptors have been detected in the eyes [19], nose [20], mouth [9,21], skin [22] and vagina [23]. Therefore, the decrease in oestrogen may be related to dryness in these regions [24]. In addition, secretion from

Table 4: Multiple logistic regression analysis for oral dryness by age.

Age, years	Determine predictive value	Explanatory variables	β	Standard error	P-value	OR	95% CI		
Total	77.0	N. dryness regions	0.74	0.12	<0.001	2.09	1.65	–	2.67
		Difficulty of swallowing	1.25	0.46	0.006	3.49	1.42	–	8.55
		Hot flashes of face or upper body	0.61	0.27	0.027	1.83	1.07	–	3.13
		Recently sensitive to sound	1.14	0.30	<0.001	3.12	1.75	–	5.57
<45	75.2	N. dryness regions	0.67	0.21	0.001	1.96	1.30	–	2.95
		Hot flashes of face or upper body	1.38	0.45	0.002	3.97	1.66	–	9.50
		Nocturnal awaking	1.10	0.41	0.008	3.01	1.34	–	6.74
		Recently sensitive to sound	1.21	0.46	0.009	3.34	1.35	–	8.30
45–55	84.6	N. dryness regions	0.84	0.27	0.002	2.32	1.37	–	3.92
		Heart pounds quickly	1.75	0.69	0.011	5.78	1.50	–	22.28
56–64	75.9	Menopause years	0.22	0.10	0.022	1.25	1.03	–	1.51
		N. dryness regions	0.95	0.30	0.001	2.59	1.44	–	4.66
≥65	80.0	N. dryness regions	0.74	0.31	0.016	2.09	1.15	–	3.81
		Gum bleeding	1.60	0.73	0.027	4.97	1.20	–	20.64
		Worry about minor things	1.50	0.68	0.029	4.46	1.17	–	17.08
		Heart pounds quickly	1.91	0.68	0.005	6.78	1.79	–	25.69

OR: odds ratio
CI: confidence interval
N. of dryness: number of regions of dryness

the lacrimal, nasal, and salivary glands is associated with muscarinic receptors, and may be influenced by the autonomic nervous system. It is therefore important to consider muscarinic receptors, as these reflect the involvement of the autonomic nervous system.

We found that factors associated with oral dryness included being 'always anxious', 'worry about minor things' and 'depression' in univariate analysis. It is possible that these symptoms indicate psychological stress. Because salivary secretion is regulated by the autonomic nervous system, this may also be related to oral dryness. In addition, some climacteric symptoms (e.g., hot flashes and sweating) are regarded as autonomic nervous symptoms. Therefore, dysfunction of the autonomic nervous system combined with a decrease in female hormones may cause dry feelings. However, as this survey was web-based, we could not evaluate objective indicators such as 17- βestradiol, autonomic nerve function and stress markers in saliva. Few reports have discussed oral dryness in relation to these objective indicators. It is therefore important to clarify these relationships in further studies.

In this survey, participants were divided into four age groups: <45, 45-55, 56-64 and ≥65 years. However, the number of people in each age group differed because of unequal grouping. The reasons for this grouping were that 45-55 years is considered to cover the menopause and those aged >65 years are regarded as older adults in Japan. We considered two hypotheses before starting this survey. First, oral dryness in those aged 45-55 years would relate more to climacteric symptoms compared with other age groups. Second, the prevalence of oral dryness would be higher in older people than in younger people. An earlier study revealed that more older adults feel oral dryness than young adults [25]. However, the present analysis indicated that the prevalence of oral dryness was higher in younger than older adults. The comprehensive survey of living conditions conducted by the Japan Ministry of Health, Labour and Welfare demonstrated that young adults (aged 20-29 years) felt psychological stress more than those aged over 60 years [26]. A recent survey in America and Canada showed that younger adults tended to feel psychological stress [27]. Oral dryness induced by psychological stress may therefore be present in large number of young adults. A further investigation of this issue that includes participants younger than 30 years of age is needed. In contrast, older adults may not feel dryness because of age-related changes in oral sensation or familiarity with a dry feeling. This may lead to inconsistencies between objective salivary secretion and subjective oral dryness. A huge epidemiological study on oral dryness, salivary flow, and psychological stress by age is needed in the future.

A limitation of this study was the presence of bias because participants were limited to Internet users. Previous face-to-face surveys reported the prevalence of oral dryness as 38.8% [28] and 37.8% [29]. These rates were similar to the prevalence reported in our results using a web-based survey. Although web-based surveys are increasingly used in the medical field [8,30], discussion regarding their features continues. A recent study cautioned that because potentially vulnerable patients tended to prefer paper-based questionnaires over web-based questionnaires, researchers must carefully weigh the pros and cons of survey administration modes to ensure representative samples and high-quality data [31]. A relevant cultural factor may be that women are ashamed to talk about menopausal and vaginal symptoms, especially in Japan. Therefore, a web-based survey may have advantages in that people can answer honestly without feeling shame. Another limitation was the lack of data about diet and nutrition. Ingestion of spicy foods or too much alcohol may lead to oral dryness. In addition, dehydration status may be directly related to oral dryness. Because this survey was performed in May, it is not the summer season in Japan, we assumed that there was little possibility that participants demonstrated dehydration. However, questions covering diet, nutrition, and liquid consumption should be included in the next survey.

Conclusion

This survey revealed that although factors associated with oral dryness differ by age, the number of dryness regions in the body is a common factor for all ages. The departments of treatment are divided according to specialty; for example, patients who complain about eye dryness visit the eye clinic, and those who have oral dryness go to the dental clinic. It is therefore important to ask patients who complain of dryness in a certain region of the body whether they also feel dryness in

other regions. Paying attention to factors associated with oral dryness will support early detection and improvement of dryness symptoms and may contribute to improved QOL.

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Ethics Approval

The Ethics Committee of the Niigata University Faculty of Dentistry approved the study protocol and waived the requirement for informed consent for this study (approval number 447).

Declaration of Competing Interest

None of the authors has anything to disclose.

Author's Contribution

Masayo Yasuda designed this study, analyzed the data, and wrote the first draft of the manuscript.

Kayoko Ito, the main author, designed this study, analyzed the data, and wrote the draft of the manuscript and was responsible for the manuscript.

Saori Funayama, Kiyoshi Takamatsu, Mariko Ogawa, and Makoto Inoue discussed the design, analyzed the data, and wrote the draft of the manuscript.

Kaname Nohno discussed the analysis of the data and wrote the draft of the manuscript.

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