Relationship between dietary factors and recurrent aphthous stomatitis: A cross-sectional study

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Abstract

Background: Recurrent aphthous stomatitis (RAS), a common oral mucosal disorder characterized by chronic, inflammatory, and ovoid ulcers, has a complex aetiology. The purpose of the study was to investigate the dietary factors influencing the prevalence of RAS.

Methods: A total of 754 participants aged 18 to 59 years in Nanjing were enrolled in this descriptive cross-sectional study. An anonymous questionnaire was adopted to investigate the distribution of RAS, dietary factors, self-reported trigger factors and therapeutic methods.

Results: Among all participants, the prevalence rate of RAS was 21.4%. Univariable analysis identified fruits, dairy products, vegetables and drinking water, but not fried foods, fermented foods, spicy foods, or eggs, as influencing factors of RAS. After adjusting for age and sex, multivariable regression analysis identified fruits (adjusted odds ratio [aOR] = .432, 95% confidence interval [CI] = [.219-.853], p = .015) and drinking water (aOR = 3.603, 95% CI = [1.280-10.147], p = .015) as protective factors of RAS.

Conclusion: RAS is prevalent among the 18- to 59-year-old Nanjing population. A lower intake of fruits and drinking water might be associated with a higher prevalence of RAS. These factors could be used as daily preventive measures for RAS.

Background

Recurrent aphthous stomatitis (RAS), or recurrent oral ulceration (ROU), one of the most common oral mucosal disorders, affects 2%~66% of the population according to worldwide epidemiological data.[1] Characterized by ovoid, small, multiple, and recurrent ulcers with circumscribed margins, yellow or grey floors, and erythematous haloes,[2] RAS might be caused by local trauma, food intake, vitamin and trace element deficiencies, stress, drugs, and hormonal changes.[3] In severe cases, RAS can result in severe pain, which can greatly impact the function of eating, speaking and swallowing.

Various factors have been proposed to elucidate the pathogenesis of RAS, including genetic factors, haematinic deficiencies, immune dysregulation, hormonal changes, stress, pernicious anaemia, cyclic neutropenia, and inflammatory bowel disease.[4–6] However, to date, the exact mechanism remains unknown, which greatly impedes the development of preventions against and treatments of RAS.

In the literature, an increased risk of RAS among individuals is linked to particular dietary habits.[3, 6, 7] In previous studies about dietary risk factors for RAS, some reported that the intake of fried food and spicy food could increase the prevalence of RAS.[7, 8] Other studies have suggested that several foods that commonly cause allergic reactions, for instance, milk, could lead to the occurrence of RAS.[9] Furthermore, it was shown that allergic reactions, including RAS, can be caused by both milk and grains.[9, 10] These aforementioned studies only involved a subset of special foods. Therefore, a systematic investigation of

potential dietary risk factors for RAS, especially research including the intake of fruits and drinking water, which are noticed clinically but rarely referenced in the literature, is necessary.

The aim of this cross-sectional survey was to collect data regarding the prevalence of RAS, dietary factors, self-reported trigger factors and therapeutic methods to examine the hypothesis that special dietary factors could increase or decrease the morbidity and severity of RAS. This work has the potential to encourage further study of the aetiology of and prevention measures against RAS in the clinic.

Material And Methods

Sample size, study design and participants

A sample size of approximately 700 people was determined with the following formula: (see Formula 1 in the Supplementary Files.)

in which N represents the sample size, U_α represents the Z-score for a given confidence interval ($\alpha = .05$, $U_\alpha = 1.96$), P_0 represents the estimated prevalence ($P_0 = 20\%$),[7] and D represents the permissible error ($D = .15 \times P_0$).

The cross-sectional study was conducted in Nanjing from June 2017 to September 2017 with a multistage random sampling method employed to randomly select 5 districts of Nanjing. Four neighbourhood communities were randomly chosen from each district. Forty civilians aged 18 to 59 years who had resided in Nanjing for at least 1 year were selected from each community. The exclusion criteria were mental/cognitive impairments, communication disabilities, and illiteracy.

Participants were invited to fill out an anonymous questionnaire during a face-to-face interview to collect relevant information, including demographic information, dietary factors, self-reported trigger factors and therapeutic methods. Dietary factors included daily intake of fruits, vegetables, dairy products, and drinking water, and the intake frequency of fried foods, fermented foods, spicy foods, high-temp foods (including spicy hotchpotch, hot soup, hot pot, hot tea), and eggs. The frequency of food intake was divided into 3 grades: often (once every two days), sometimes (weekly), and hardly. Eating eggs at least once per week was regarded as forming a habit of eating eggs for ease of interpretation. Participants who did not complete all questions on the questionnaire were excluded.

Case Definition

According to the criteria suggested by S. S. Natah,[3] we applied a set of diagnostic criteria (Table 1, Table 2) for RAS to distinguish it from other diseases. All criteria are based on clinical experience to be practical, and further studies are necessary before widespread use of these criteria can occur. Symptoms must meet all major criteria and at least one of the minor criteria to obtain a definite diagnosis of RAS.

Table 1

Major criteria for RAS

Major criteria	Description
1. Appearance	multiple, small, ovoid, recurrent ulcers with erythematous haloes, circumscribed margins, and yellow or grey floors.
2. Recurrence	Averagely one occurrence of RAS yearly at least and the recurrence does not affect the same site.
3. Mechanical hyperalgesia	A symptom of painful lesions and movement of lesion can exacerbate pain.
4. Self-limitation	The ulcer can heal spontaneously without treatment.

Table 2

Minor criteria for RAS

Minor criteria	Description
1. Family history of RAS	Presence of the RAS in at least one first-degree relative.
2. Location of ulcers	Non-keratinized oral mucosa.
3. Duration	Several days to two weeks.
4. Precipitating factors	Stress, local trauma and infections.
5. Smoking	Non-smoker.

Statistical analysis

The original data from the paper questionnaire were processed and transcribed to Excel and the Statistical Package for the Social Science 22.0 to set up a database of the results. All categorical variables are described by frequencies and percentages. Univariable analysis was performed to obtain a preliminary result and screen out variables with little evidence of association. Variables with a p value < .05 in the univariable analysis were included in multivariable regression analysis to evaluate the connection between the dietary factors and RAS. The multivariable logistic regression was adjusted for age and gender, and statistical significance was defined as $p < .05$.

Results

Participant characteristics

A total of 754 participants consisting of 336 males and 418 females were enrolled in this study, with an RAS prevalence of 21.4%. The demographics of the participants are summarized in Table 3. There was

no significant difference in gender ($p > .05$) or age ($p > .05$) among RAS or non-RAS participants according to univariable analysis.

Table 3
Demographics of the subjects

		N	RAS		OR	95%CI	P
			Yes (%)	No (%)			
Gender	Male	336	72 (45)	264 (45)	1.000		
	Female	418	89 (55)	329 (55)	0.992	0.699–1.408	0.964
Age	18–29	576	117 (73)	459 (77)	1.000		
	30–44	114	29 (18)	85 (14)	1.338	0.838–2.137	0.222
	45–59	64	15 (9)	49 (8)	1.201	0.651–2.217	0.558

The self-reported trigger factors and therapeutic methods of the RAS group (161, 21.4%) are summarized in Table 4. A total of 53.4%, 56.5%, 69.6%, 69.6%, and 78.9% of the RAS group self-reported stress, reduced immune function, irregular life schedule, and unhealthy diet as a trigger factor, respectively, and the distribution of trigger factors in the various age groups is shown in Fig. 1. Nearly half (89, 55.3%) of the participants were not undergoing treatment for RAS, while 29.2% and 15.5% of the RAS group chose conventional medicine or alternative treatments (ATs), respectively.

Associations Of Dietary Factors With Ras

The distribution of the prevalence of RAS in groups with different dietary habits is shown in Fig. 2, and Table 5 presents the preliminary results of the relationship between RAS and putative dietary factors from the univariable analysis, showing statistical correlations between RAS and the intake of fruits, dairy products, vegetables and drinking water ($p < .05$) (the odds of having RAS decreased with increasing intake of vegetables and are presented in Table 5 as a binary variable for ease of interpretation). Other variables, including fried foods, fermented foods, spicy foods, and eggs, showed no significant correlations ($p \geq .05$). The significant variables were all included in the multivariable logistic regression, which was adjusted for age and gender, as shown in Table 6 and Fig. 3. After adjustment for the confounders, the multivariable logistic regression revealed that the intake of fruit (adjusted odds ratio [aOR] = .432, 95% confidence interval [CI] = .219-.853, $p = .015$) and drinking water (aOR = 3.603, 95% CI = 1.280-10.147, $p = .015$) had a significant association with RAS. Specifically, people who ate less than 100 g of fruit per day and who drank less than 1 L of water were more likely to suffer from RAS.

Table 5

univariate analysis of the relationship between dietary factors and RAS

Table 4. Self-reported trigger factors and therapeutic methods in various age groups					
	n (%)			Percent	
	18–29 (N = 117)	30–45 (N = 29)	46–59 (N = 15)		
Self-reported trigger factors (multiple choice)					
Stress	64 (55)	14 (48)	8 (53)	53.4	
Reduced immune function	61 (52)	19 (66)	11 (73)	56.5	
Irregular life schedule	84 (72)	19 (66)	9 (60)	69.6	
Unhealthy diet	99 (85)	17 (59)	11 (73)	78.9	
Others or no	22 (19)	6 (21)	3 (20)	19.3	
Therapeutic methods					
Conventional medicines	30 (26)	10 (35)	7 (47)	29.2	
Alternative treatments	14 (12)	7 (24)	4 (27)	15.5	
No treatment	73 (62)	12 (41)	4 (27)	55.3	
Variables	**RAS (%)**	**Control (%)**	**OR**	**95%CI**	**P**
Fruits					
≤ 100 g	64 (40)	178 (30)	1.000		
100 ~ 200 g	78 (48)	299 (50)	0.726	0.497–1.060	0.097
200 ~ 300 g	13 (8)	90 (15)	0.402	0.210–0.768	0.006
> 300 g	6 (4)	26 (4)	0.642	0.253–1.631	0.351
Dairy products					
Hardly	28 (17)	71 (12)	1.000		
≤ 100 g	44 (27)	185 (31)	0.603	0.349–1.042	0.070
100 ~ 200 g	74 (46)	256 (43)	0.733	0.441–1.218	0.231

Table 4. Self-reported trigger factors and therapeutic methods in various age groups					
> 200 g	15 (9)	81 (14)	0.470	0.232–0.949	0.035
Vegetables					
≤ 100 g	29 (18)	132 (12)	1.000		
> 100 g	132 (82)	522 (88)	0.619	0.386–0.993	0.047
100 ~ 200 g	81 (50)	311 (52)	0.638		
200 ~ 300 g	45 (28)	181 (31)	0.609		
>300 g	6 (4)	30 (5)	0.490		
Drinking water					
> 2L	15 (9)	67 (11)	1.000		
1-2L	85 (53)	317 (53)	1.198	0.651–2.202	0.561
≤ 1L	50 (31)	198 (33)	1.128	0.595–2.139	0.712
Hardly	11 (7)	11 (2)	4.467	1.663–12.214	0.004
High-temp foods					
Hardly	70 (43)	273 (46)	1.000		
Sometimes	69 (43)	257 (43)	1.047	0.721–1.521	0.809
Often	22 (14)	63 (11)	1.362	0.784–2.365	0.273
Spicy foods					
Hardly	22 (14)	94 (16)	1.000		
Sometimes	87 (54)	354 (60)	1.050	0.624–1.766	0.854
Often	52 (32)	145 (24)	1.532	0.874–2.688	0.137
Fried foods					
Hardly	33 (20)	114 (19)	1.000		
Sometimes	102 (63)	397 (67)	0.888	0.569–1.384	0.599

Table 4. Self-reported trigger factors and therapeutic methods in various age groups					
Often	26 (16)	82 (14)	1.095	0.609–1.970	0.761
Fermented foods					
Hardly	61 (38)	214 (36)	1.000		
Sometimes	94 (58)	363 (61)	0.908	0.631–1.307	0.605
Often	6 (4)	16 (3)	1.316	0.494–3.507	0.583
Habit of eating eggs					
Yes	158 (98)	568 (96)	1.000		
No	3 (2)	25 (4)	2.318	0.691–7.777	0.173

Boldface values are statistically significant to $P < 0.05$.
Abbreviations: RAS, recurrent aphthous stomatitis; CI, confidence interval; OR, odds ratio.

Table 6

Multivariate logistic regression of the relationship between dietary factors and RAS

Variable	RAS(%)	Control (%)	Unadjusted OR (95% CI, P Value)	Adjusted OR (95% CI, P Value) [a]
Fruits				
≤ 100 g	64 (40)	178 (30)	1	1
100 ~ 200 g	78 (48)	299 (50)	0.756 (0.505–1.132, 0.175)	0.737 (0.489–1.111, 0.145)
200 ~ 300 g	13 (8)	90 (15)	**0.435 (0.222–0.852, 0.015)**	**0.432 (0.219–0.853, 0.015)**
> 300 g	6 (4)	26 (4)	0.755 (0.289–1.970, 0.566)	0.735 (0.276–1.960, 0.539)
Dairy products				
Hardly	28 (17)	71 (12)	1	1
≤ 100 g	44 (27)	185 (31)	0.682 (0.389–1.197, 0.183)	0.714 (0.402–1.266, 0.714)
100 ~ 200 g	74 (46)	256 (43)	0.922 (0.539–1.577, 0.765)	1.005 (0.570–1.773, 0.985)
> 200 g	15 (9)	81 (14)	0.573 (0.276–1.187, 0.134)	0.635 (0.296–1.364, 0.245)
Vegetables				
≤ 100 g	29 (18)	132 (12)	1	1
> 100 g	132 (82)	522 (88)	0.697 (0.421–1.152, 0.159)	0.682 (0412.-1.130, 0.137)
Drinking water				
> 2L	15 (9)	67 (11)	1	1
1-2L	85 (53)	317 (53)	1.219 (0.659–2.256, 0.529)	1.216 (0654.-2.263, 0.536)
≤ 1L	50 (31)	198 (33)	1.046 (0.546–2.004, 0.893)	1.051 (0.540–2.047, 0.884)
No	11 (7)	11 (2)	**3.607 (1.294–10.053, 0.014)**	**3.603 (1.280.-10.147, 0.015)**

[a]Adjusted for age, gender.
Boldface values are statistically significant to $P < 0.05$.
Abbreviations: RAS, recurrent aphthous stomatitis; CI, confidence interval; OR, odds ratio.

Discussion

RAS is a chronic, inflammatory disease characterized by painful, ovoid ulcers and is observed worldwide but is rarely associated with systemic diseases.[11]

In this cross-sectional study, we explored the distribution of RAS, dietary factors, self-reported trigger factors and therapeutic methods among a study population from Nanjing and reported a prevalence of 21.4% in accordance with the literature. In Iran, the prevalence of RAS is 25.2% (10,291 respondents), in Brazil, 24.9% (2,427 respondents), and in Turkey, 22.8% (11,360 respondents).[12–14]

In this study, RAS was associated with fruits, vegetables, dairy products and drinking water intake through univariable analysis ($p < .05$). Other variables, including fried foods, fermented foods, spicy foods, eggs, gender and age, showed no statistically significant associations ($p \geq .05$). Previous studies have shown that there is a significant association between vegetables, dairy products and RAS.[8, 9, 15] However, in the present study, there was no significant association of these factors with RAS in the multivariable logistic regression, although a trend was found. This is likely due to the limited sample size. Further large-scale studies are necessary to verify our results. Dairy products might cause RAS due to milk, which has been reported as an allergic agent of RAS,[9] causing adverse reactions in certain individuals. Vegetables might prevent RAS by increasing the serum levels of Zn and Se, which are reported to be low in RAS patients and are highly associated with immunity and oxidative stress.[15]

Another finding of our study was that multivariable logistic regression demonstrated a strong association between fruit intake and RAS. Although clinicians usually instruct patients affected with RAS to avoid acidic and spicy foods, it has been reported that local lemon salt (citric acid) is effective in treating chronic wound infections by significantly reducing infectious agents and boosting fibroblastic growth to hasten wound healing.[16, 17] Furthermore, pomegranate has been reported to have immunomodulatory, strong antioxidant, and antibacterial characteristics, and pomegranate extract has been reported to offer protection against aspirin- and ethanol-induced gastric ulceration.[18] As discussed above, sufficient fruit intake might prevent RAS through antimicrobial effects, immunoregulation and immunoregulatory effects.

Multivariable logistic regression also revealed that the consumption of drinking water might directly or indirectly affect the development of RAS. It is noteworthy that RAS was first found to be associated with drinking water in this study. Cardiovascular disease and RAS share common risk factors, such as hypertension and hyperlipidemia.[15, 19] Insufficient water intake increases the plasma salt level and osmolality, which are known to be critical to health. Extracellular osmolality, affected by drinking water intake, is reported to promote the expression of the AQP5 gene, which facilitates the bidirectional movement of water across membranes depending on the osmotic gradient and hydrostatic pressure. As discussed above, reduced water intake, a common phenomenon resulting from various factors, including decreased kidney function, social isolation, and cognitive disorders,[20] might promote the increase of plasma osmolality and lead to RAS.

Our study assessed the types of treatments used by patients with RAS to assess the level of patient awareness of the disease. Less than half (72, 44.7%) of the RAS group had ever received treatment for RAS, which was lower than that reported in another study,[7] and approximately one-third of those who were treating their RAS lesions were using ATs instead of conventional medicine, indicating a high prevalence of AT use, despite a lack of randomized controlled trials proving the benefit of ATs in treating RAS. These results indicated that patient education on the importance of RAS treatment is needed.

We acknowledge a bias towards a younger population that might result from a high percentage of students in the chosen neighbourhood communities. However, considering that no significant association was found between age and RAS in this study, this bias should not affect the generalizability of our results. Nevertheless, despite our attempts to choose districts representative of different demographic statuses, including participants solely from Nanjing poses some inevitable limitations on the generalizability and extrapolation of the results to other urban and rural areas.

Conclusion

The present study indicated that the intake of fruits and drinking water might be potential protective factors of RAS. A greater intake of fruits and drinking water might be valuable as daily preventive measures for RAS. These results could provide new insights into the prevention and treatment of RAS.

Abbreviations

RAS: recurrent aphthous stomatitis; ATs: alternative treatments; aOR: adjusted odds ratio; CI: confidence interval

Declarations

Acknowledgements

Not applicable.

Authors' contributions

WM Wang conceived and supervised this study. X Wang co-supervised, co-designed and co-conducted this study. KY Xu and CC Zhou designed the study, conducted the survey, conducted the statistical analysis, designed the framework of the manuscript, and drafted the manuscript. YY Wang and N Duan co-designed the study and conducted the survey. LC Zheng participated in the data processing and analysis. All the authors have read and approved the final manuscript.

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Availability of data and materials

The data supporting this study are available from the corresponding author on reasonable request.

Ethics approval and consent to participate

Informed consent was obtained from each participant, and the Ethics Committee of Nanjing Stomatological Hospital confirmed this form of consent and approved this survey (2014NL-002 (KS)). All participants joined voluntarily and were informed of their rights to withdraw from the survey at any time. The participants answered the questionnaires anonymously.

Consent for publication

Not applicable.

Declaration of conflicting interest

The authors declare no potential conflicts of interest with respect to the research, authorship, or publication of this article.

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Figures

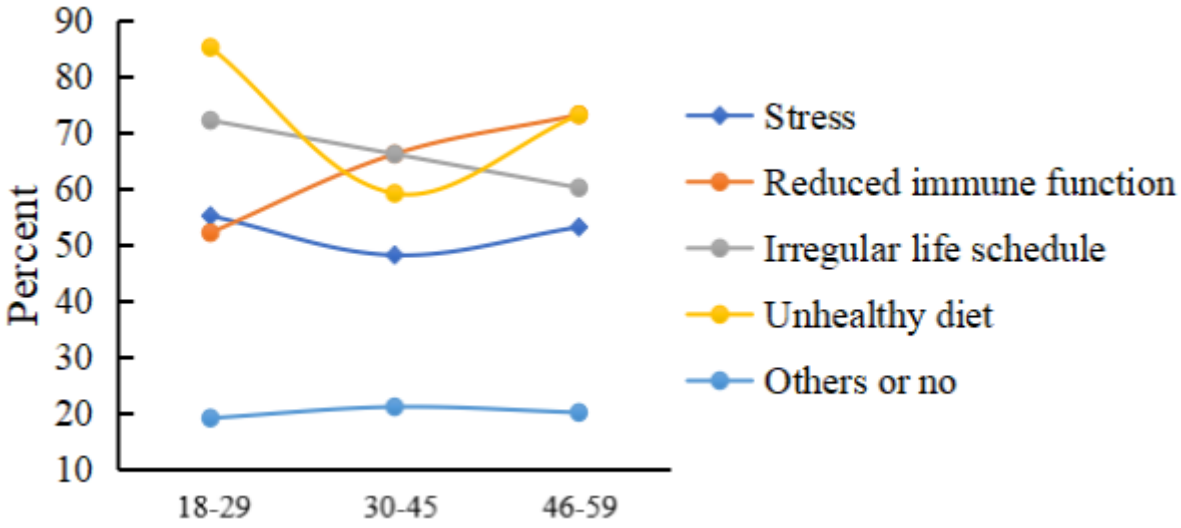

Figure 1

Distribution of trigger factors in the different age groups.

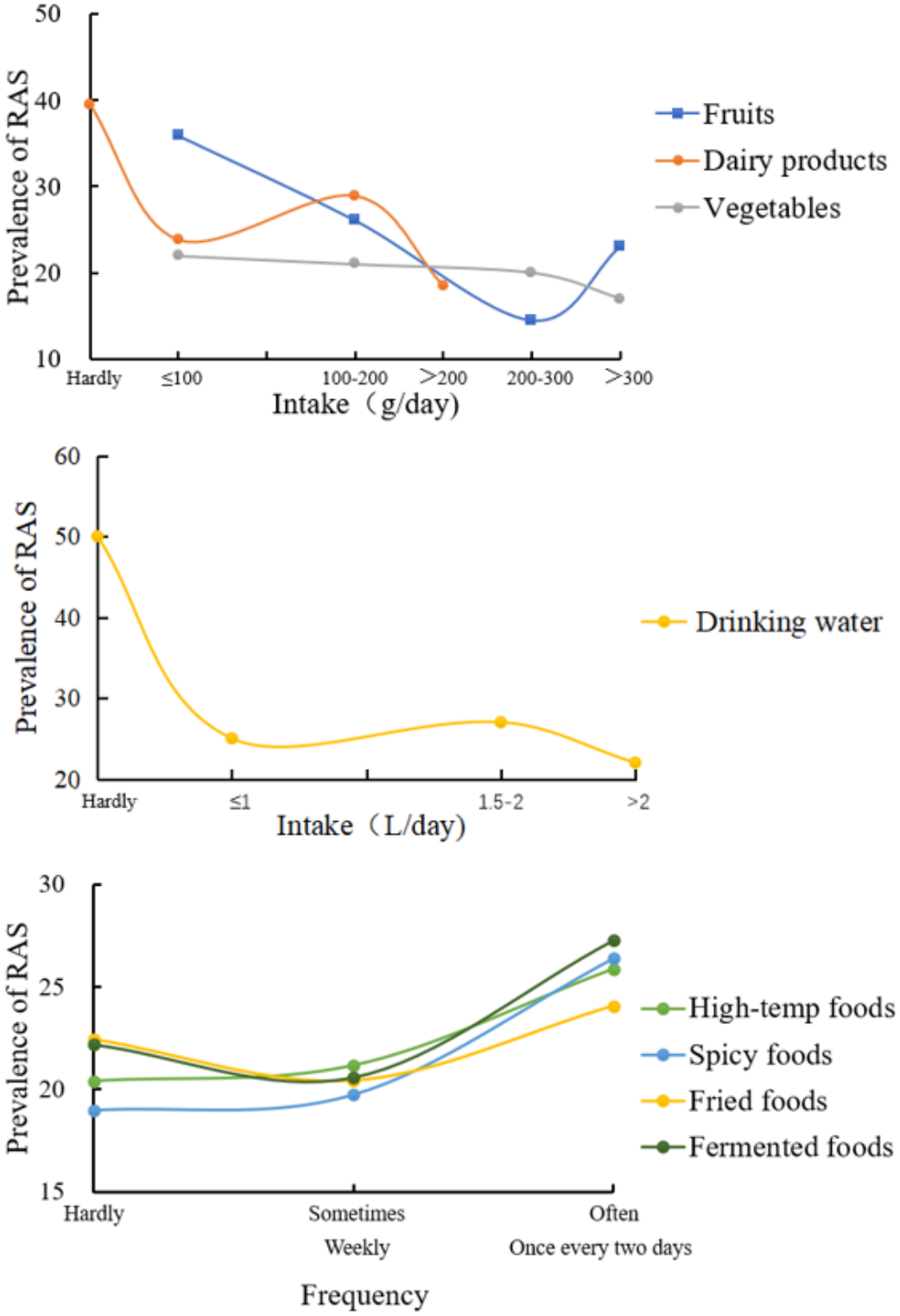

Figure 2

Distribution of the RAS rates in groups with different dietary habits, including fruits, dairy products, and vegetables (A), drinking water (B), and spicy foods, high-temp foods, fried foods, and fermented foods (C).

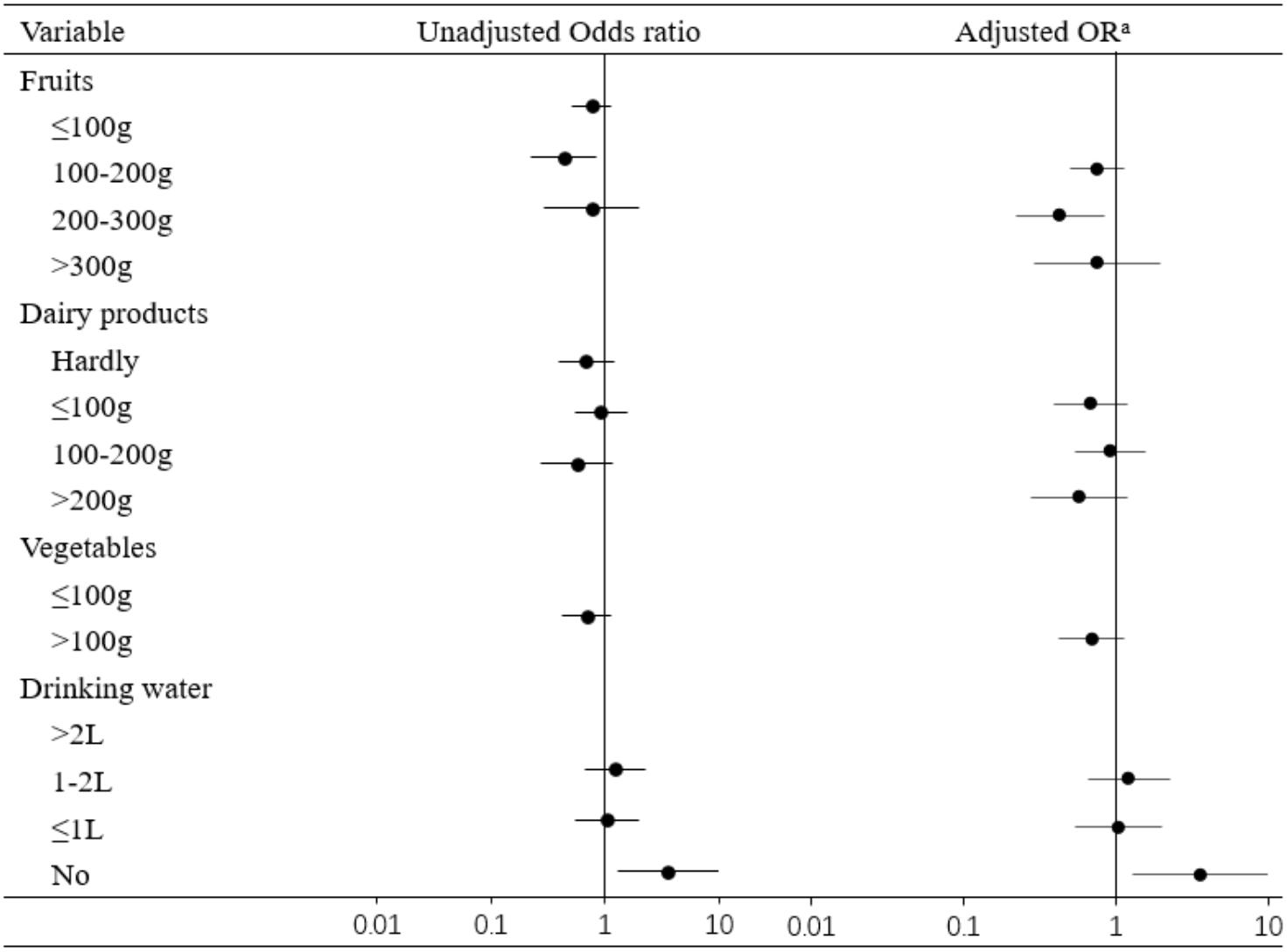

Figure 3

Multivariable logistic regression of the relationship between dietary factors and RAS. aAdjusted for age and gender.

Supplementary Files

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- Formula1.pdf