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Relationship of tooth loss to mild cognitive impairment among middle-aged Mongolians: Mon-Timeline study

Urangoo Ganbaatar [1], Oyuntuya Gantulga [1], Puntsagdulam Byambajav [2], Maralgua Och [3], Ganjargal Ganburged [4], Tsolmon Jadamba [3,5], Byambasuren Dagvajantsan [2]*, Oyuntugs Byambasukh [1]*

[1] Graduate School, Mongolian National University of Medical Sciences, Ulaanbaatar, Mongolia
[2] Department of Neurology, School of Medicine, Mongolian National University of Medical Sciences, Ulaanbaatar, Mongolia
[3] Timeline Research Center, Ulaanbaatar, Mongolia
[4] Department of Orthodontics, School of Dental medicine, Mongolian National University of Medical Sciences, Ulaanbaatar, Mongolia
[5] Brain and mind institute, Mongolian Academy of Sciences, Ulaanbaatar, Mongolia
* Correspondence: oyuntugs@mnums.edu.mn; Tel.: +976-99017063

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Abstract: Cognitive impairment is common in elderly people, so it is considered an ageing disorder. However, cognitive decline, including dementia, can also occur in middle-aged people. Cognitive impairment is associated with multiple risk factors. We hypothesised that tooth loss might also be a potential risk factor among Mongolians, as oral health problems are one of the significant health issues in Mongolia, especially in middle-aged people. In this cross-sectional study, we used the baseline data from the Mon-Timeline cohort study, including people older than 40 years of age (n=279). The amount of tooth loss was assessed by a trained researcher. Mild cognitive impairment (MCI) was defined as those participants scoring a total of ≤ 24 points based on the Mini-Mental State Examination (MMSE). Unadjusted analysis showed that having more tooth loss (>10) increased the risk of MCI by an odds ratio of 3.03 (1.49-6.17), as compared with having less tooth loss (≤10). Even after adjusting for covariates, the association remained significant, suggesting that tooth loss is associated with MCI risk, independent of age, education, and other socioeconomic factors. There was no significant interaction effect of age in the association between tooth loss and MMSE scores. In conclusion, tooth loss may play a role in developing cognitive decline, especially in the early onset of dementia. Further studies are needed to investigate whether early tooth loss at younger ages is associated with dementia, especially among middle-aged people.

Keywords: Tooth loss; mild cognitive impairment; MMSE; Mon-Timeline study;

1.0 INTRODUCTION

Cognitive impairment is one of the most common disorders in the general population that reduces the quality of life (Bárrios et al., 2013). Mild cognitive impairment (MCI) is defined as an ageing-related cognitive decline, which can also progress to illnesses

such as dementia (Mariani et al., 2007; Prince et al., 2013). It has been estimated that 50 million people have dementia, with an increase of nearly 10 million new cases every year (World Health Organization, 2019). This increase is mainly attributed to the rising number of those who have dementia in low- and middle-income countries, which are estimated to account for nearly 60% of all dementia cases (World Health Organization, 2019). In Mongolia, the prevalence of cognitive impairment, 39.7% of Mongolian adults over 60 years old had cognitive impairment in 2011 (Oyunkhand, 2011). The study used the same method to identify cognitive impairment (ICD 10, G31. 84), which is defined as cognitive impairment when Mini-Mental State Examination (MMSE) score 24 in our study (Folstein et al., 1975). Cognitive impairment is caused by multiple factors, including ageing, vascular diseases, and neurodegenerative diseases such as Alzheimer disease and other forms of dementia (Biessels et al., 2006; Sharp et al., 2011). Furthermore, many other risk factors for the development of cognitive impairment are reported in the literature (Beydoun et al., 2008; Fang et al., 2018; Munkhsukh et al., 2021; Namjil et al., 2021; Tonsekar et al., 2017). It is crucial to identify potential risk factors, especially for multiple countries and territories, to improve the prevention of dementia. Tooth loss is a risk factor for the development of cognitive impairment, especially in low- and middle-income countries (Fang et al., 2018; Tonsekar et al., 2017).

In Mongolia, oral health-related diseases are highly prevalent (Chinzorig et al., 2019; Jargaltsogt et al., 2018; Karvonen et al., 2003; Mongolian Government, 2006). The prevalence of dental caries, especially, is considerably higher in children. According to a study conducted in 2019, the prevalence of dental caries (ICD code K02.1-9) among children under 18 years of age is 89.3% (Chinzorig et al., 2019), showing that the prevalence of this disease has not significantly changed from 93.2% in 1993 (Jargaltsogt et al., 2018) and that the burden of dental caries has not changed in the last 20 years. Therefore, we hypothesised that tooth loss might be one of the potential risk factors for cognitive impairment among Mongolians, as oral health problems are one of the major health issues facing Mongolians. Although tooth loss may be associated with ageing, fewer teeth from a young age may be a risk factor for cognitive impairment. It is prevalent for people under the age of 40 to have 20-24 teeth (Tonsekar et al., 2017). However, Mongolians have already lost 6-7 teeth since 20 (Chinzorig et al., 2019; Jargaltsogt et al., 2018). This study explored the association between tooth loss and cognitive impairment within a representative data set of middle-aged people.

2.0 MATERIALS AND METHODS

2.1 Data source and study population

The Mon-Timeline is a multidisciplinary, prospective, population-based cohort study in Mongolia investigating various health problems among Mongolians, especially concerning oral and mental health. The sample size was calculated based on the prevalence of dental caries (P=89.3%) in the previous study (Chinzorig et al., 2019), assuming a 95% confidence interval (Z=1.96) with a 5% acceptable margin of error, which gave us a sample size of 1780 persons. A total of 1860 randomly selected Mongolians of rural and urban areas, including 18 clusters, participated in this study. In this cross-sectional study, we used the baseline data from the Mon-Timeline cohort, including people older than 40 years of age (n=748). The exclusion criterion was any missing data related to the primary determinant and outcome (n=124): oral health and cognitive examination.

Furthermore, participants with a history of head trauma, stroke, heart failure or renal failure were excluded (n=118). Another exclusion criterion was any psychiatric disorders such as depression diagnosed by a psychiatrist during the examination (n=58). The psychiatrist also asked about previous mental illnesses and checked the patient reports. Additionally, we asked how participants would assess their health status (poor, fair, good or excellent); those with their health status assessed as poor were excluded (n=157) based on a previously published method (Amaral et al., 2019) to rule out possible coexisting diseases. Ultimately, 279 participants were included in the current study.

The study was approved by the medical ethical committee of the Mongolian National University of Medical Sciences (METc 2020/3-05). According to the Helsinki declaration, all participants provided their written informed consent.

2.2 Variables and measurements

Independent and dependent variables: The amount of tooth loss was assessed by a trained researcher. Based on previous studies which categorised the tooth loss in relation to cognitive impairment (Saito et al., 2018; Tsai et al., 2020), the study participants were divided into two groups, according to the number of teeth lost: (1) Group 1 included participants with up to 10 teeth lost (<10), and (2) Group 2 included participants with ten and more teeth lost ($\geqslant$10). Cognitive function was

evaluated with the MMSE (Folstein et al., 1975). The MMSE consists of 11 items, including orientation (2), retention (1), attention and calculation (1), recall (1), language (5), and copying (1); with a total score of 30 points. MCI was defined as the participants scoring 24 points or above.

Covariates and other variables: The level of education was categorised as low, medium, and high. Participants were classified as married or cohabiting and single as a dichotomous variable. We made a group according to family income based on the distribution of the variable: low, medium, and high. We categorised all participants into groups of non-smokers and smokers according to smoking status. Daily fruit and vegetable intakes were evaluated using the Food Frequency Questionnaire (Ministry of Health Mongolia, 2013). Physical activity was assessed using the Global Physical Activity Questionnaire (Armstrong & Bull, 2006). The level of physical activity and intake of fruits and vegetables were categorised as sufficient and insufficient, separately. 'Participants' body weight (in kg) and height (in cm) were measured by well-trained assistants using a standardised protocol, and Body Mass Index (BMI; kg/m^2) was subsequently calculated.

2.3. Statistical analysis

The study characteristics were expressed as means with a standard deviation (S.D.) for normally distributed variables tested by histogram and z-scores and as numbers with percentages in cases of categorical data. ' 'Student's T-test and Pearson Chi-Square test were used to compare grouping variables. Estimated MMSE was calculated according to tooth loss and age groups using age-adjusted Analysis of Variance (ANOVA). Furthermore, a two-way ANOVA was used to compare the difference between means of MMSE according to groups for tooth loss age. The study population was categorised according to age (<60 and ⩾60 years of age) because cognitive decline, especially ageing related CI, is common for people ⩾60 years of age (World Health Organization, 2019). Spearman's correlation coefficient was calculated to evaluate associations of the amount of tooth loss and age with MMSE scores.

Binary logistic regression analysis was performed to evaluate the association between tooth loss and MCI. Odds ratio (OR) was reported with a 95% confidence interval (CI). Analysis was adjusted for age, which included age and square of age (age^2, because age may be linearly related to independent and dependent variables), education, marital status and family income, diet and physical activity. The determinants consisted of two categories of tooth loss (<10 and ⩾10), with <10 as the reference group for regression analysis. Furthermore, the interaction effect was tested with age in the association of tooth loss with outcome variables. Additionally, given that age may reflect the cognitive decline of ageing, Spearman's partial correlation coefficient was performed for the individual MMSE components. All statistical analyses were performed using IBM SPSS V.22.0 (Chicago, IL) and GraphPad Prism V.4.03 (San Diego, CA). A two-sided statistical significance was set at $p<0.05$ for all tests.

3.0 RESULTS

The number of people with tooth loss ⩾10 accounted for 45.5% (n=127) of the total population. People with tooth loss ⩾10 were older (**Table 1**) and more likely to have lower MMSE scores (**Table 2**). According to gender, socioeconomic factors, lifestyle characteristics, and BMI, there were no significant differences between people with and without tooth loss of ⩾10.

MMSE scores differed statistically depending on the amount of tooth loss and age. Although the lower MMSE scores observed in tooth loss ⩾10 groups within both age groups were highlighted, this was especially clear in the older age group (**Table 2**). These differences were significant when tested using a two-way ANOVA: mean MMSE was significantly lower in the tooth loss ⩾ 10 and ⩾60-year group when compared with other groups. Furthermore, age-adjusted MMSE scores were significantly different throughout tooth loss groups: 27.5 and 24.3 for people with tooth loss <10 and ⩾10, respectively ($p<0.001$).

' 'Spearman's correlation analysis yielded that the amount of tooth loss was inversely correlated with MMSE scores ($r=-0.191$, $p<0.0001$). Furthermore, age was significantly correlated to MMSE scores ($r=-0.306$, $p<0.0001$) but positively correlated to the number of teeth loss ($r=0.168$, $p<0.0001$).

People with MCI (MMSE⩾24) accounted for 20.1% (n=56) of the total population. The higher presence of MCI was observed in tooth loss ⩾10 groups within both age groups, especially in the older age group (**Figure 1**). The prevalence of MCI was 9.2% (n=11) and 18.2% (n=6) in tooth loss < 10 groups while it was 25.0% (n=23) and 45.2% (n=16) in tooth loss ⩾10 groups in people aged <60 and ⩾60 years of age respectively.

Logistic regression analysis showed that having more tooth loss (⩾10) increased the risk of MCI by an OR of

Table 1: General characteristics of the study population.

Characteristics	**Tooth loss (<10)** (n=152)	**Tooth loss (≥10)** (n=127)	***P*-value**
Age (year)	53.8 ± 9.7	55.4 ± 7.6	**0.004**
Age category			
<60 (n=211)	119 (78.3)	92 (72.4)	0.150
≥60 (n=68)	33 (21.7)	35 (27.6)	
Male gender, n (%)	46 (23.8)	25 (29.1)	0.217
Education: low level, n (%)	46 (23.8)	25 (29.1)	0.556
Married or cohabitant, n (%)	26 (13.5)	18 (20.9)	0.082
Family income level: Low, n (%)	68 (35.2)	34 (39.5)	0.581
Current smokers, n (%)	28 (14.5%)	19 (22.1%)	0.291
Alcohol use, n (%)	48 (24.9)	29 (33.7)	0.084
Fruit and vegetables use: Insufficient, n (%)	69 (35.8)	27 (31.4)	0.285
Physically inactive, n (%)	29 (15.1)	13 (15.3)	0.550
Body mass index (kg/m^2)	29.97 ± 5.12	29.31 ± 5.51	0.404

Data are presented as mean ± S.D. and number (percentages, %).

Table 2: Association between tooth loss and mean of MMSE scores by age

Category	**Mean ± SD**			**Age-adjusted mean ± S.E.**
	Total (n=279)	**< 60 years (n=211)**	**≥ 60 years (n=68)**	**Total**
Tooth loss < 10 (n=152)	27.4 ± 3.4	28.0 ± 3.0 (n=119)	26.1 ± 3.1 (n=92)	27.5 ± 0.3
Tooth loss ≥ 10 (n=127)	25.7 ± 4.2	27.0 ± 4.3 (n=33)	22.5 ± 4.8 (n=35)	24.3 ± 0.4
P-value*	<0.0001	0.002	0.001	-
P-value**	-	<0.0001		<0.0001
Age x tooth loss interaction P-value = 0.045				

* Student-T-test, ** Two-way ANOVA

Table 3: Association of tooth loss and mild cognitive impairment.

Models	**Risk of Mild cognitive impairment**			
	< 60 years		**≥ 60 years**	
	OR (95% CI)	*P*-value	OR (95% CI)	*P*-value
Unadjusted	3.27 (1.50-7.14)	**0.003**	3.79 (1.25-11.46)	**0.018**
Adjusted for age*	2.81 (1.25-6.30)	**0.012**	4.86 (1.39-16.90)	**0.013**
Adjusted for age*, gender and education	2.82 (1.23-6.44)	**0.014**	5.34 (1.40-20.34)	**0.014**
Adjusted for age*, gender and SES factors	2.74 (1.19-6.28)	**0.017**	8.61 (1.93-38.44)	**0.005**

Data are presented as OR with CI. * Age and square of age. SES, Socioeconomic status factors which includes education, marital status and family income.

Table 4: Correlations of tooth loss and age with individual components of MMSE

Total MMSE and domain scores	Tooth loss	Age	Tooth loss (age-adjusted)
Orientation to time	**-0.180****	-0.038	**-0.217****
Orientation to place	-0.112	-0.079	-0.168
Retention	-0.115	**-0.143***	-0.123
Calculation and attention	**-0.169***	**-0.223****	**-0.158***
Recall	-0.111	**-0.308*****	-0.118
Language expression /naming/	**-0.150***	-0.120	**-0.168***
Language expression /repetition/	**-0.183****	**-0.150***	**-0.170***
Language comprehension /verbal/	**-0.162***	**-0.131***	**-0.139***
Language comprehension /written/	**-0.146***	-0.022	**-0.187****
Language expression /sentence writing /	**-0.182****	-0.086	**-0.154***
Copying	**-0.213****	**-0.235*****	**-0.180****
Total MMSE score	**-0.191****	**-0.306****	**-0.234*****

Data is presented as Spearman's correlation coefficients. *p <0.05, **p<0.01, ***p<0.001

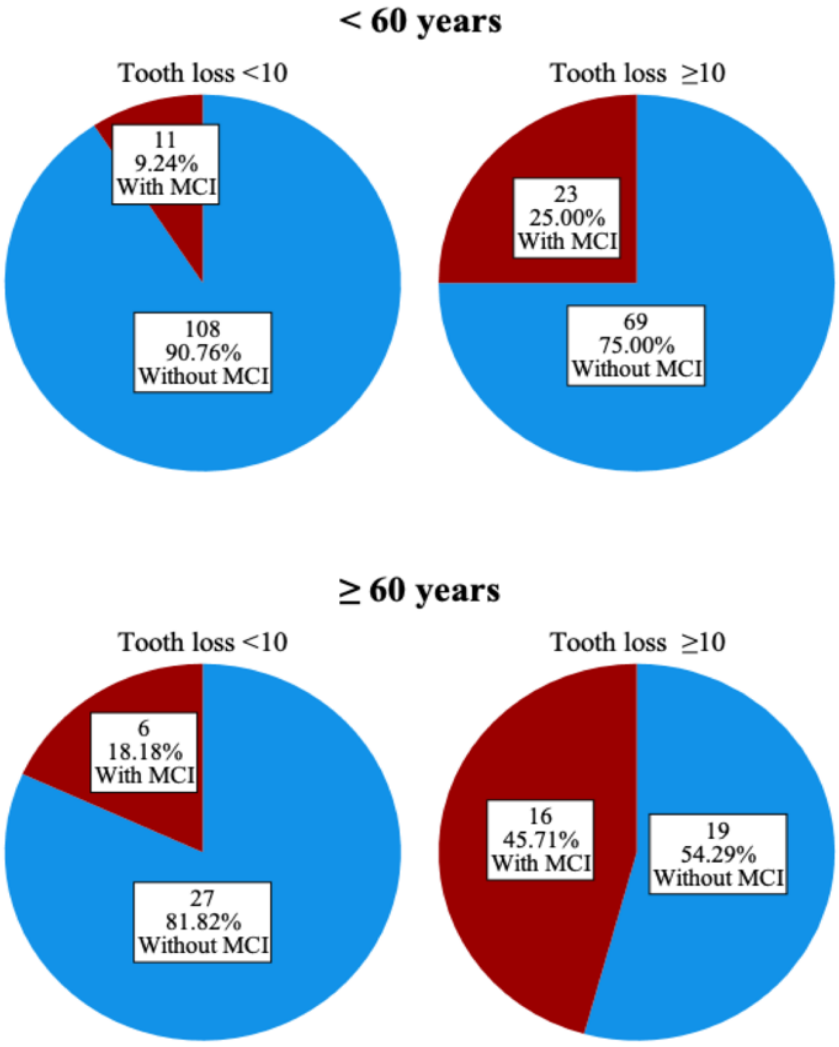

Figure 1: The presence of MCI, according to age and tooth loss group.

3.27 (1.50-7.14) and 3.79 (1.25-11.46) for people aged <60 years and ≥ 60 years, respectively, as compared with having less tooth loss (<10). This association remained significant after adjusting for age in both age groups (**Table 3**). However, the OR increased in the older age group while it decreased in the younger age group, suggesting that tooth loss, rather than age, may play a role in developing MCI in middle-aged people. Moreover, the association remained significant after further adjustments; thereby, suggesting that tooth loss is associated with MCI risk, independent of gender, education, marital status and family income, diet and physical activity.

In an additional analysis, we compared tooth loss and age with individual MMSE domain scores, separately, using Spearman's correlation to test the independent association of tooth loss with cognitive impairment. Furthermore, the correlation between tooth loss and MMSE (before adjusted for age r=-0.191 and p<0.01) remained significant and unchanged after adjusting for age (r=-0.234 and p<0.001, **Table 4**). The amount of tooth loss was more associated with orientation and language expression domains, while age was associated with retention and recall domains (r=-0.111, p=0.213 for tooth loss and r=-0.308, p<0.001 for age); thereby, suggesting that tooth loss might be associated with MCI via different pathways (**Table 4**).

4.0 DISCUSSION

This study found that multiple tooth loss is significantly associated with an increased risk of cognitive decline independent of age. Moreover, the association between tooth loss and the presence of MCI was found to be independent of gender and socioeconomic and lifestyle factors, such as education, marital status, family income, smoking, alcohol use, diet and physical activity.

In accordance with our results, previous studies have found an independent association between the number of teeth and cognitive function (Fang et al., 2018; Tonsekar et al., 2017). For instance, a Japanese 4-year follow-up study including 140 older adults who were evaluated with MMSE (MMSE⩾24) found that cognitive impairment (MMSE≤24) was more developed in participants with 0-9 teeth lost than those with ⩾10 teeth lost (Saito et al., 2018). A Taiwanese population-based (n=43026) retrospective study found that patients with more teeth extracted had a greater risk of dementia (Tsai et al., 2020). Both tooth loss and cognitive function are caused and influenced by multiple factors, such as socioeconomic factors and periodontal diseases (Ismail et al., 2019; Reyes-Ortiz et al., 2013; Tonsekar et al., 2017). Therefore, studies tested the association between tooth loss and cognition impairment with various confounding variables. In most of the studies, the association yielded significant results; but in a few studies, the association was mediated by age and socioeconomic factors (Ismail et al., 2019; Matthews et al., 2011). In our study, the association was significant after adjustment for various factors, such as education level, family income, marital status, smoking, alcohol use, diet and physical activity. The significant association between tooth loss and cognitive impairment has been proved by studies that explored various mechanisms in the pathogenesis of oral health-related cognitive impairment (Aida et al., 2006; Kornman et al., 1997; McGeer & McGeer, 2001; Tonsekar et al., 2017). Studies concluded that the principal exploration involves masticatory dysfunction, which may occur due to tooth loss; thereby, causing decreases in the maximum bite force and occlusal contact area (Lexomboon et al., 2012; Tonsekar et al., 2017).

Indeed, cognitive decline is common in elderly people and is therefore largely considered an ageing disorder (Mariani et al., 2007; Prince et al., 2013; World Health Organization, 2019). However, cognitive decline, including dementia, can also occur in middle-aged people (World Health Organization, 2019). Especially in developing countries, the prevalence of early-onset dementia is increasing (World Health Organization, 2019). However, only limited studies have been conducted on middle-aged people. Our study included primarily middle-aged people and found a significant association between tooth loss and cognitive decline. In this study, the association was stronger in the older age group (≥60years), potentially explainable by the fact that cognitive decline is common in elderly people. Tooth loss also occurs more often in elderly people. However, there was no significant association between age and tooth loss in our study, as even middle-aged people were found to have a smaller number of teeth. In a stratified analysis, the association of tooth loss and MCI was significant in middle-aged people even after adjusting for age. Furthermore, when we tested the association of tooth loss with individual domain scores of MMSE compared to age. Tooth loss and age were differently associated with different domains of MMSE indicating that the development of cognitive decline may be different from age-induced cognitive decline due to tooth loss. Finally, we suggest that tooth loss may play a role in developing cognitive decline, especially for early-onset dementia. Further studies are needed to

investigate whether early tooth loss at younger ages is associated with dementia, especially in middle-aged people.

The above-mentioned tooth loss is a risk factor for the development of cognitive impairment, thereby suggesting the importance of the presence of teeth in cognitive abilities. This is the first study to explore the association of tooth loss with the presence of cognitive impairment in Mongolia, showing that having a smaller number of teeth may be a considerable risk factor for cognitive impairment. Unfortunately, a recent study showed that no significant improvements in dental care had been observed during the last 20 years (Chinzorig et al., 2019; Mongolian Government, 2006). Dental care service was firstly studied in Mongolia in 1993, which showed a high prevalence of dental caries (93.2%) (Jargaltsogt et al., 2018). The latest study showed that the prevalence of dental caries was 89.3% in 2019 (Chinzorig et al., 2019). Furthermore, this and other studies have shown that the risk of dental caries is even higher among Mongolian children (Chinzorig et al., 2019; Jargaltsogt et al., 2018; Karvonen et al., 2003; Mongolian Government, 2006). More than half of the children under 18 were found to have visited dental clinics because of toothache (Chinzorig et al., 2019). One of the causes for this poor oral health is urbanisation, whereby a traditional milk-based diet was changed to a milk-based deficient diet (Karvonen et al., 2003). This suggests that there might be a difference between urban and rural areas in the prevalence of dental caries. However, a recent study found no differences in dental caries prevalence among urban and rural areas (Chinzorig et al., 2019; Mongolian Government, 2006). While the high prevalence of caries was explained by poor knowledge of parents regarding oral hygiene care for their children, this has not been confirmed by recent studies. The population's brushing habits remain poor regardless of parental education and socioeconomic status (Chinzorig et al., 2019). Therefore, practical approaches to improve dental and oral hygiene need to be implemented nationwide to reduce the persistent high caries occurrence in Mongolia.

The main strength of our study is its use of a representative data set of middle-aged people. Nevertheless, there are some limitations to our research. Our study design is cross-sectional. It is, therefore, not possible to rule out reverse causality. In addition, cognitive decline is typical in elderly people; therefore, ageing-related tooth loss can be more prevalent in elderly people (Bárrios et al., 2013; Mariani et al., 2007; Prince et al., 2013). Although we adjusted for age, there still could be a possibility of residual confounding by age-related factors. Some studies found that ageing-related cognitive decline could cause poor oral health, resulting in fewer teeth (Henriksen et al., 2005). This indicates a possibility of reverse causality in the association between tooth loss and cognitive decline due to ageing. Accordingly, we aimed to explore the association between tooth loss and cognitive impairment within middle-aged people. Another limitation is that we could not fully control periodontal diseases, oral hygiene and causes of tooth loss, its duration and places. Finally, the observational nature of the study precludes us from concluding causality.

5.0 CONCLUSIONS

Multiple tooth loss is significantly associated with an increased risk of cognitive decline. Further studies are needed to investigate whether early tooth loss at younger ages is associated with dementia, especially in middle-aged Mongolian people. Furthermore, this study results suggest that it is crucial to improve the care for oral health for Mongolians.

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Conflicts of Interest: The authors declare no conflict of interest.

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