



# Eating Fast and Until Full Is Associated with Elevated Alanine Aminotransferase Activity in Japanese Schoolchildren: A Cross-Sectional Study

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Alanine aminotransferase (ALT) activity has been recognized as a marker for monitoring the risk of metabolic syndrome, diabetes and non-alcoholic fatty liver disease in children. Higher ALT activity was reported to be associated with eating fast in Japanese adults, but the association in children is unclear. Moreover, eating fast and eating until full are reported to be associated with being overweight. This study examined the association between elevated ALT and eating behaviors (eating fast and eating until full) among population-based schoolchildren (aged 9-10 years) in Ina Town, Saitama, Japan. Data for eating behaviors were obtained from a self-written questionnaire. Blood samples were drawn to measure ALT. Elevated ALT was defined as > 30 U/L in boys and > 19 U/L in girls. Logistic regression models and structural equation models were used to calculate the effect of eating behaviors on elevated ALT. Final data analysis was carried out for 1,870 boys and 1,739 girls. “Eating fast and eating until full” was significantly associated with elevated ALT in each sex. “Eating fast and not eating until full” was significantly associated with elevated ALT in boys, but after adjusting for exercise and body mass index, this association was not significant. In conclusion, “eating fast and eating until full” was associated with elevated ALT in schoolchildren. A sex difference in the association of “eating fast and not eating until full” with elevated ALT was observed. Modifying the behaviors of eating fast and eating until full is important for schoolchildren to prevent ALT elevation.

**Keywords:** cross-sectional study; eating fast; eating until full; elevated alanine aminotransferase activity; schoolchildren

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## Introduction

Alanine aminotransferase (ALT) activity has been recognized as a marker for monitoring the risk of metabolic syndrome, diabetes and non-alcoholic fatty liver disease among children (Di Bonito et al. 2009; Doi et al. 2007; Elizondo-Montemayor et al. 2014). For instance, Elizondo-Montemayor et al. (2014) showed that the prevalence of metabolic syndrome was strongly associated with elevated ALT (50% in the elevated ALT group and 24.1% in the normal ALT group). Therefore, preventing ALT elevation in children is important for lifelong health.

Mochizuki et al. (2013, 2014) showed that higher ALT activity is associated with eating fast, but not with  $\gamma$ -glutamyl transpeptidase or aspartate aminotransferase, among healthy Japanese men and women. Eating fast is an intervening eating behavior. Improvements in ALT are often associated with childhood growth (Strauss et al. 2000; Tazawa et al. 1997). Additionally, Maruyama et al. (2008) reported that “eating fast and eating until full” was associated with being overweight, and “eating fast and not eating until full” was not associated with being overweight among Japanese men and women. For children, investigating the combined impact of eating fast and eating until full is rea-

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sonable because eating fast and eating until full are both eating behaviors that can be improved. Therefore, it might be necessary to consider eating until full to examine the association between elevated ALT and eating fast. Recent Japanese epidemiologic studies have demonstrated that the incidence of obesity and type 2 diabetes was higher in individuals with self-reported faster eating than in those with self-reported slower eating (Otsuka et al. 2008; Sasaki et al. 2003). In particular, eating faster could stimulate insulin secretion in association with postprandial hyperglycemia to a greater degree than eating slower, and these factors enhance fatty acid synthesis in the liver and adipose tissues. Jenkins et al. (1990) compared the same amount of glucose solution ingested at one time versus several times, and suggested that the amount of glucose in the body did not change after ingestion, but that insulin levels rose in the group that ingested all at once. However, no studies have examined the association of eating fast and eating until full with ALT among children.

Accordingly, we have hypothesized that the association between adult eating behaviors and elevated ALT is also found in boys and girls. The aim of this study was to investigate the association between elevated ALT with the combination of eating fast and eating until full in population-based Japanese elementary schoolchildren.

## Material and Methods

### *Study participants*

The present study was a cross-sectional survey that used data collected from a health promotion program for primary schools in Ina Town, Saitama Prefecture, Japan, from 2000 to 2009. The program consisted of a questionnaire survey, anthropometric measurements and a blood test, reported elsewhere (Kanda et al. 1997).

Subjects were 3,801 fourth grade primary schoolchildren aged 9 or 10 years in Ina-town. Of 3,801 subjects, 3,776 agreed to participate in this study (participation rate: 99.3%). One hundred sixty-seven schoolchildren were excluded because of missing data. Thus, final data analysis was carried out for 1,870 boys and 1,739 girls (Fig. 1).

Informed consent was obtained from a parent or guardian of each subject prior to participation. This study was approved by the Medical Ethics Committee of Showa University School of Medicine (Approval No. 127) and all procedures were performed in compliance with relevant laws and institutional guidelines.

### *Data collection*

A self-written questionnaire was distributed to each subject by a teacher at the primary school. Thereafter, the subject completed the questionnaire and returned it to the teacher. Parental consent was collected via the school, with documents distributed in advance via the school. The questionnaire asked participants about the following information: eating speed, eating until full and exercise (daily, sometimes, or none). For eating speed, answers were given

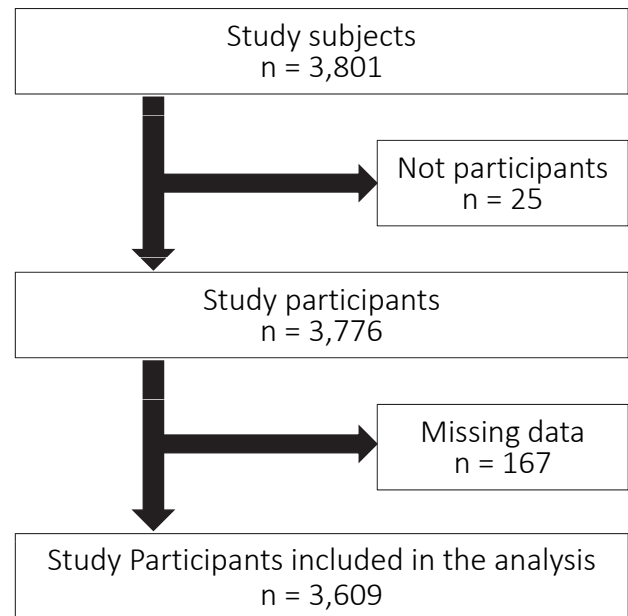


Fig. 1. Flow of study participants included in the analysis.

as “fast,” “medium,” or “slow” (Gerace and George 1996). For eating until full, answers were given as “yes” or “no” (Maruyama et al. 2008).

The height and weight of each participant were measured. Height was measured to the nearest 1 millimeter using a stadiometer, and weight was measured to the nearest 100 grams using a scale. Body mass index (BMI) was calculated as weight (kilograms) divided by height (centimeters) squared.

Blood samples were drawn from the study participants in the morning. ALT activity was measured using an automated analyzer (H7600-020; Hitachi High-Technologies Co., Ltd., Tokyo, Japan).

### *Statistical analysis*

In the statistical analysis, eating speed was divided into two categories: eating fast and not eating fast based on a previous study (Tanihara et al. 2011). Elevated ALT was defined as  $> 30$  (U/L) among boys, and  $> 19$  (U/L) among girls according to previous studies (Di Bonito et al. 2009; Park et al. 2013; Samani et al. 2011). In accordance with a previous study, the combination of eating fast and eating until full was divided into the following four categories: “not eating fast and not eating until full,” “eating fast and not eating until full,” “not eating fast and eating until full,” and “eating fast and eating until full” (Maruyama et al. 2008).

Statistical analyses were performed for each sex and eating speed. Data are presented as median (25<sup>th</sup>, 75<sup>th</sup> percentile) for continuous variables or n (%) for categorical variables.

We used the Wilcoxon rank sum test to compare continuous variables and the chi-square test to compare categorical

cal variables between two groups. We used the Kruskal-Wallis test to compare continuous variables or categorical variables between three groups. A logistic regression model was used to calculate the odds ratio (OR) for elevated ALT and the 95% confidence interval (CI). Exercise and BMI were included in the model as adjustments because these variables were reported to be related to elevated ALT (Mahady et al. 2017). We used structural equation modeling to determine the effect of BMI on eating speed, eating until full and ALT. All statistical analyses were conducted using JMP 15.0 (SAS Institute Inc. Cary, NC USA). *p* values less than 0.05 (two-tailed) were considered statistically significant.

## Results

Table 1 summarizes the characteristics of the present study participants according to sex. The median age was 9.0 years old. Approximately 17% of the participants ate fast. One-quarter of boys indicated that they eat fast, while

approximately 9% of girls reported eating fast. About 60% of boys and girls indicated that they eat until full. ALT levels were significantly higher among boys than among girls. The change of elevated ALT from 2000 to 2009 was statistically significant among boys and girls. Table 2 summarizes the characteristics of the present study participants according to eating speed. Neither BMI nor ALT was significantly different between “slow” and “medium”.

Characteristics of the study participants by ALT level are shown in Table 3 among boys and in Table 4 among girls. We found that those with elevated ALT tended to have higher proportions of eating fast among both boys ( $p < 0.001$ ) and girls ( $p = 0.007$ ). In contrast, the association between elevated ALT and eating until full was not statistically significant regardless of sex. The interaction of eating fast and eating until full for elevated ALT was not statistically significant among boys ( $p = 0.368$ ) or girls ( $p = 0.190$ ).

Table 5 shows the association of eating fast or eating until full with elevated ALT. In the crude model, eating fast

Table 1. Characteristics of study participants according to sex.

	Total (n = 3,609)	Boys (n = 1,870)	Girls (n = 1,739)
Age (years)	9.0 (9.0, 10.0)	9.0 (9.0, 10.0)	9.0 (9.0, 10.0)
Height (cm)	135.0 (131.0, 139.2)	135.1 (131.1, 139.0)	134.9 (130.8, 139.4)
Weight (kg)	30.1 (27.0, 34.6)	30.5 (27.2, 35.1)	29.8 (26.5, 34.0)
BMI (kg/m <sup>2</sup> )	16.5 (15.3, 18.2)	16.7 (15.5, 18.6)	16.3 (15.2, 17.9)
ALT (U/L)	13.0 (11.0, 15.0)	13.0 (11.0, 17.0)	12.0 (10.0, 14.0)
Exercise, n (%)			
Daily	1,872 (51.9)	1,152 (61.6)	720 (41.4)
Sometimes	1,006 (27.8)	452 (24.2)	554 (31.9)
None	731 (20.3)	266 (14.2)	465 (26.7)
Eating fast, n (%)			
Yes	621 (17.2)	468 (25.0)	153 (8.8)
No	2,988 (82.8)	1,402 (75.0)	1,586 (91.2)
Eating until full, n (%)			
Yes	2,149 (59.5)	1,111 (59.4)	1,038 (59.7)
No	1,460 (40.5)	759 (40.6)	701 (40.3)

Except where indicated n (%), values are median (25th, 75th percentile).

BMI, body mass index; ALT, alanine aminotransferase.

Table 2. Characteristics of study participants according to eating speed.

	Slow (n = 911)	Medium (n = 2,067)	Fast (n = 621)	<i>p</i> value*
<b>Boys (n = 1,870)</b>	(n = 369)	(n = 1,033)	(n = 468)	
BMI (kg/m <sup>2</sup> )	16.0 (15.0, 17.3)	16.5 (15.4, 18.3)	17.8 (16.3, 20.3)	< 0.001
Elevated ALT	15 (4.1)	41 (4.0)	46 (9.8)	< 0.001
<b>Girls (n = 1,739)</b>	(n = 552)	(n = 1,034)	(n = 153)	
BMI (kg/m <sup>2</sup> )	15.7 (14.8, 16.9)	16.5 (15.4, 18.2)	17.4 (16.2, 19.9)	< 0.001
Elevated ALT	34 (6.2)	77 (7.4)	20 (13.1)	0.016

Except where indicated n (%), values are median (25th, 75th percentile).

BMI, body mass index; ALT, alanine aminotransferase.

\*Kruskal-Wallis test or  $\chi^2$  test.

Table 3. Characteristics of boys according to category of elevated ALT.

	Non-elevated ALT (n = 1,768)	Elevated ALT (n = 102)	<i>p</i> value*
Age (years)	9.0 (9.0, 10.0)	9.0 (9.0, 10.0)	0.257
Height (cm)	135.0 (131.0, 138.9)	137.5 (133.9, 143.1)	< 0.001
Weight (kg)	30.2 (27.1, 34.3)	44.3 (36.6, 51.0)	< 0.001
BMI (kg/m <sup>2</sup> )	16.6 (15.4, 18.2)	22.7 (20.0, 25.7)	< 0.001
ALT (U/L)	13.0 (11.0, 16.0)	40.0 (33.0, 63.0)	< 0.001
Exercise, n (%)			< 0.001
Daily	1,107 (62.6)	45 (44.1)	
Sometimes	419 (23.7)	33 (32.4)	
None	242 (13.7)	24 (23.5)	
Eating fast, n (%)			< 0.001
Yes	422 (23.9)	46 (45.1)	
No	1,346 (76.1)	56 (54.9)	
Eating until full, n (%)			0.263
Yes	1,045 (59.1)	66 (64.7)	
No	723 (40.9)	36 (35.3)	

Except where indicated n (%), values are median (25th, 75th percentile).

BMI, body mass index; ALT, alanine aminotransferase.

\*Wilcoxon rank sum test or  $\chi^2$  test.

Table 4. Characteristics of girls according to category of elevated ALT.

	Non-elevated ALT (n = 1,608)	Elevated ALT (n = 131)	<i>p</i> value*
Age (years)	9.0 (9.0, 10.0)	9.0 (9.0, 10.0)	0.491
Height (cm)	134.8 (130.7, 139.3)	135.5 (131.9, 140.7)	0.146
Weight (kg)	29.5 (26.4, 33.6)	33.7 (29.9, 42.4)	< 0.001
BMI (kg/m <sup>2</sup> )	16.2 (15.2, 17.7)	18.6 (16.3, 22.2)	< 0.001
ALT (U/L)	12.0 (10.0, 14.0)	22.0 (20.0, 27.0)	< 0.001
Exercise, n (%)			0.008
Daily	679 (42.2)	41 (31.3)	
Sometimes	497 (30.9)	57 (43.5)	
None	432 (26.9)	33 (25.2)	
Eating fast, n (%)			0.007
Yes	133 (8.3)	20 (15.3)	
No	1,475 (91.7)	111 (84.7)	
Eating until full, n (%)			0.972
Yes	960 (59.7)	78 (59.5)	
No	648 (40.3)	53 (40.5)	

Except where indicated n (%), values are median (25th, 75th percentile).

BMI, body mass index; ALT, alanine aminotransferase.

\*Wilcoxon rank sum test or  $\chi^2$  test.

significantly increased the OR for elevated ALT among boys (OR: 2.62, 95% CI: 1.75-3.93) and girls (2.00, 1.20-3.32). After adjusting for exercise, eating fast also increased the OR among boys (2.89, 1.92-4.37) and girls (2.05, 1.23-3.42). The association of eating until full was not statistically significant in the crude or adjusted model for either sex.

Table 6 shows the crude and adjusted ORs of the combination of eating fast and eating until full for elevated ALT.

In the crude model among boys, significantly increased ORs for elevated ALT were observed in the “eating fast and not eating until full” group (3.33, 1.68-6.59) and the “eating fast and eating until full” group (3.10, 1.73-5.56). In the crude model among girls, a significantly increased OR for elevated ALT was found in the “eating fast and eating until full” group (2.28, 1.22-4.25). These results persisted even after adjusting for exercise (Model 1). However, after adjusting for exercise and BMI, ORs of the combination of

Table 5. Crude and adjusted odds ratios of eating fast or eating until full for elevated ALT.

		Total n	Elevated ALT* n (%)	Crude		Model 1**		Model 2***	
				OR	95% CI	OR	95% CI	OR	95% CI
Boys (n = 1,870)									
Eating fast									
	Yes	468	46 (9.8)	2.62	1.75-3.93	2.89	1.92-4.37	0.88	0.52-1.49
	No	1,402	56 (4.0)	1.00		1.00		1.00	
Eating until full									
	Yes	1,111	66 (5.9)	1.27	0.84-1.92	1.28	0.84-1.95	0.78	0.48-1.29
	No	759	36 (4.7)	1.00		1.00		1.00	
Girls (n = 1,739)									
Eating fast									
	Yes	153	20 (13.1)	2.00	1.20-3.32	2.05	1.23-3.42	1.37	0.79-2.38
	No	1,586	111 (7.0)	1.00		1.00		1.00	
Eating until full									
	Yes	1,038	78 (7.5)	0.99	0.69-1.43	0.98	0.68-1.41	1.01	0.69-1.48
	No	701	53 (7.6)	1.00		1.00		1.00	

ALT, alanine aminotransferase; OR, odds ratio; CI, confidence interval.

\*ALT > 30 U/L for boys and ALT > 19 U/L for girls.

\*\*Adjusted for exercise.

\*\*\*Adjusted for exercise and body mass index.

Table 6. Crude and adjusted odds ratios of combination of eating fast and eating until full for elevated ALT.

	Total n	Elevated ALT* n (%)	Crude		Model 1**		Model 2***	
			OR	95% CI	OR	95% CI	OR	95% CI
<b>Boys (n = 1,870)</b>								
Not eating fast and not eating until full	603	20 (3.3)	1.00		1.00		1.00	
Eating fast and not eating until full	156	16 (10.3)	3.33	1.68-6.59	3.76	1.88-7.50	1.22	0.53-2.80
Not eating fast and eating until full	799	36 (4.5)	1.38	0.79-2.40	1.39	0.79-2.44	0.94	0.50-1.75
Eating fast and eating until full	312	30 (9.6)	3.10	1.73-5.56	3.43	1.90-6.18	0.70	0.34-1.45
<b>Girls (n = 1,739)</b>								
Not eating fast and not eating until full	645	48 (7.4)	1.00		1.00		1.00	
Eating fast and not eating until full	56	5 (8.9)	1.22	0.46-3.20	1.23	0.47-3.25	0.93	0.34-2.55
Not eating fast and eating until full	941	63 (6.7)	0.89	0.60-1.32	0.88	0.60-1.30	0.93	0.62-1.40
Eating fast and eating until full	97	15 (15.4)	2.28	1.22-4.25	2.32	1.24-4.34	1.55	0.78-3.05

ALT, alanine aminotransferase; OR, odds ratio; CI, confidence interval.

\*ALT > 30 U/L for boys and ALT > 19 U/L for girls.

\*\*Adjusted for exercise.

\*\*\*Adjusted for exercise and body mass index.

eating fast and eating until full for elevated ALT were not significant among boys and girls (Model 2).

Fig. 2 shows the structural equation model testing for direct and indirect associations between eating behaviors (eating speed and eating until full) and ALT via BMI among boys and girls. The values on the path are the standardized coefficients. The fit index of this model among boys was  $\chi^2 = 18.76$ ,  $p < 0.001$ , goodness-of-fit index (GFI) = 0.995, adjusted goodness-of-fit index (AGFI) = 0.934, root mean square error of approximation (RMSEA) = 0.097. The fit

index of this model among girls was  $\chi^2 = 1.359$ ,  $p = 0.244$ , GFI = 0.999, AGFI = 0.999, RMSEA = 0.014. The models were shown to fit well for both boys and girls. Among boys, indirect associations between both eating behaviors (eating speed and eating until full) and ALT via BMI were significant. Among girls, indirect associations between eating speed and ALT via BMI were significant. However, direct associations between both eating behaviors (eating speed and eating until full) and ALT were not significant among boys or girls.

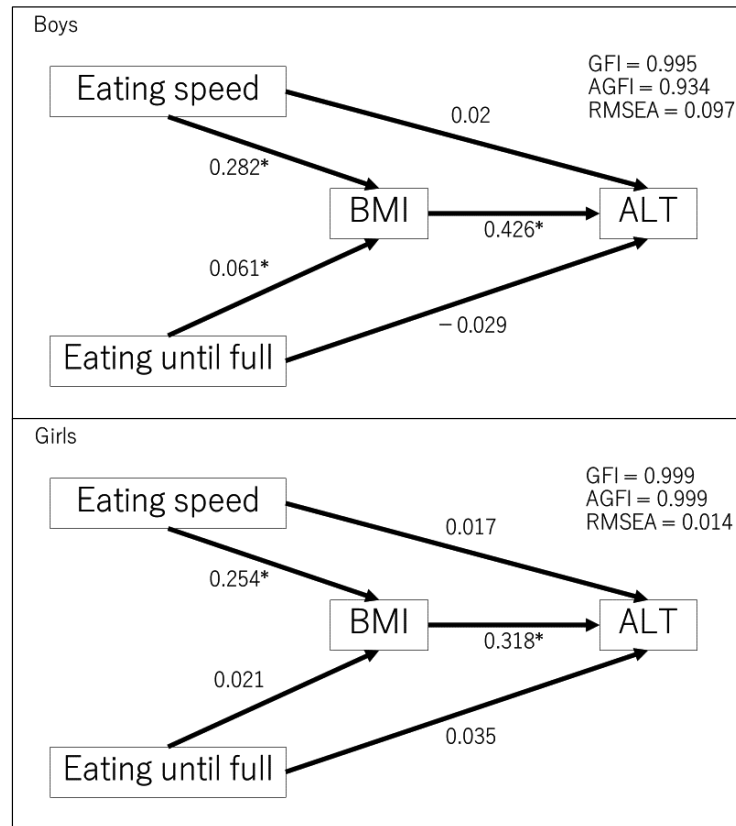


Fig. 2. Structural equation modeling showing the relationship between eating behaviors (eating speed and eating until full) and elevated ALT by sex.

Values in the model are standardization pass coefficients.

BMI, body mass index; ALT, alanine aminotransferase; GFI, goodness-of-fit index; AGFI, adjusted goodness-of-fit index; RMSEA, root mean square error of approximation.

\*Standardization pass coefficients significant at  $p < 0.05$ .

## Discussion

This study examined the association between eating fast and elevated ALT by considering eating until full among Japanese schoolchildren. The results showed that “eating fast and eating until full” was significantly associated with elevated ALT in both sexes. To our knowledge, this is the first study associating the combination of eating fast and eating until full with elevated ALT among schoolchildren in Japan.

In the present study, eating fast was significantly associated with elevated ALT, even after adjusting for exercise. Some previous studies showed a positive association between eating fast and BMI among Japanese (Sasaki et al. 2003; Yamane et al. 2014). In addition, Strauss et al. (2000) showed that children with overweight/obesity (defined as a BMI in the  $> 85^{\text{th}}$  percentile) were more likely to have elevated ALT compared with normal weight children. These studies suggested that eating fast led to an increase in BMI, which resulted in elevated ALT. In this pathway, BMI is an intermediate variable. Thus, the association between eating fast and elevated ALT disappears if BMI is adjusted for. In fact, the association disappeared after adjusting for BMI in

this study, which showed that the association was dependent on BMI. Mochizuki et al. (2013, 2014) reported that self-reported eating fast was associated with elevated ALT, but was dependent on BMI in Japanese men and women. This finding was consistent with our study results.

In our study, an association between “eating fast and eating until full” and elevated ALT was observed. The reason for this might be that eating fast and eating until full lead to overweight/obesity, which contributes to elevated ALT. Maruyama et al. (2008) showed that “eating fast and eating until full” was associated with being overweight among Japanese men and women. Moreover, Elizondo-Montemayor et al. (2014) showed that overweight and obesity were associated with elevated ALT among Mexican children. The results of these studies were also consistent with our study findings. Thus, modifying the behavior of “eating fast and eating until full” could be effective in preventing elevated ALT.

Sex differences in the associations of the combination of eating fast and eating until full with elevated ALT were found in this study; “eating fast and not eating until full” was significantly associated with elevated ALT in boys, but it was not significantly associated with elevated ALT in



girls. This result showed that the impact of “eating fast and not eating until full” on elevated ALT differed by sex. Therefore, it might be necessary to consider sex in the modification of eating behaviors such as eating fast and eating until full. Further studies will be needed to elucidate the biological mechanism of the sex difference because the mechanism is beyond our study scope.

This study has two strengths. Firstly, the participation rate was more than 90%. Secondly, ALT measurements were conducted among more than 3,000 population-based schoolchildren in Japan, and blood collection is not usually conducted in annual health examinations of schoolchildren. In contrast, the present study has several potential limitations. Firstly, our study was cross-sectional in design, so it is difficult to establish causal relationships. Secondly, this study employed self-reported data; therefore, it might not be objective. However, a previous study showed that self-reported eating fast aligned with laboratory-measured eating fast (Petty et al. 2013). Furthermore, total energy intake in the group that reported “eating until full” was higher than that in the group that reported “not eating until full” (Maruyama et al. 2008). Thirdly, participants in this study were from one town in Japan. Thus, it could be difficult to generalize our study findings to other populations. Fourthly, eating speed in our study was obtained from the question “How fast is your eating speed compared to others.” so it is not clear if the eating speed was different between school and home. Fifthly, because information about dietary patterns was not collected in this study, we could not investigate changes in dietary patterns from 2000 and 2009 on elevated ALT. Sixthly, there may be a lack of detection power because the number of schoolchildren in some categories was small. In particular, there were only five girls with elevated ALT in the “eating fast and not eating until full” category. Seventhly, no data of other confounders was related to ALT. Woo Baidal et al. (2018) demonstrated that early childhood vitamin E intake had lower odds of elevated mid-childhood ALT (Woo Baidal et al. 2018).

In conclusion, the present study showed that “eating fast and eating until full” was associated with elevated ALT in boys and girls. Moreover, “eating fast and not eating until full” was associated with elevated ALT in boys. This was a cross-sectional study, so a causal relationship cannot be determined. However, our study findings suggest the possibility that modifying eating speed could prevent elevated ALT among Japanese schoolchildren.

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### Author Contributions

A.M. and H.O. planned this study. R.N., R.Y. and M.A. contributed to improving this study in a meaningful way. A.M. drafted the manuscript. H.O., T.S. and R.N. performed data collection. T.S. supervised data collection. H.H. supported the draft of this manuscript and data collection. A.M. and H.O. contributed to the statistical analysis. A.K. made substantial contributions to the conception of this study and the revision of the manuscript. All authors read and approved the final manuscript.

### Conflict of Interest

The authors declare no conflict of interest concerning the present study. On the other hand, R.N. has received honoraria from Astellas Pharma Inc., Nippon Boehringer Ingelheim Co., Ltd., Eli Lilly Japan K.K., Kissei Pharmaceutical Co., Ltd., Medtronic Japan Co., Ltd., MSD, Novartis Pharma K.K., Novo Nordisk Pharma Ltd., Sanofi K.K., Sumitomo Dainippon Pharma Co., Ltd., Takeda Pharmaceutical Co., Ltd. R.N. has also received a grant from the Japan Diabetes Foundation.

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