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Prevalence of vitamin D insufficiency among children in southern china

A cross-sectional survey

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Abstract

Vitamin D deficiency is associated with numerous public health issues. Limited data are available for children in southern China, a region that receives abundant sunlight. We aimed to estimate the 25-hydroxyvitamin D (25(OH)D) levels in children in that area, and to determine seasonal variations in serum 25(OH)D levels. A total of 16,755 children aged 0 to 6 years, who visited the Guangdong Women and Children's Hospital for health examination between January 2016 and May 2017, were included in the present study. The serum 25(OH)D levels ranged from 10.5 to 307.4 nmol/L (mean ± standard deviation: 78.5 ± 26.3 nmol/L). The prevalence of vitamin D deficiency and insufficiency were 10.8% and 39.0%, respectively. The mean serum 25(OH)D level in spring (71.8 ± 24.9 nmol/L) was lower than that in other seasons. From January to April, we found a relatively high prevalence of vitamin D deficiency or insufficiency, both of which were also found to increase with age. Logistic regression analysis revealed that vitamin D deficiency and insufficiency were significantly associated with age and season. Deficiency and insufficiency of vitamin D are common among children in southern China, despite the area receiving sufficient sunlight.

Abbreviations: 25(OH)D = 25-hydroxyvitamin D, SD = standard deviation.

Keywords: 25-Hydroxyvitamin D, children, deficiency, public health

1. Introduction

It is a well-established fact that vitamin D influences calcium and phosphorus homeostasis, as well as bone health.[1] Increasing amounts of research on vitamin D metabolites in the serum reveal that the roles played by vitamin D have implications that reach beyond the health of skeletal tissue, and include the immune, nervous, and cardiovascular systems.[2–5] Low serum concentrations of vitamin D are associated with numerous adverse health issues, and the corresponding public health consequences are enormous.

Serum 25-hydroxyvitamin D (25(OH)D) is the vitamin D metabolite that is measured clinically to assess vitamin D status.[6] Despite disagreement surrounding the establishment of the minimal desirable serum concentration of 25(OH)D, with suggested cutoff levels ranging from 25 to >100 nmol/L,[7] the occurrence of vitamin D deficiency remains common worldwide, especially in children.[8] A study conducted in the state of Alaska, in the United States, and based on infants aged 6 to 23 months, found that 11% of children had 25(OH)D level <32.5 nmol/L and 20% of children had 25(OH)D level between 32.5 to 62.5 nmol/L.[9] The Canadian Health Measures Survey reported a prevalence of vitamin D insufficiency (<50 nmol/L) of 13% in children aged 6 to 11 years from April to October.[10] The Fourth Korea National Health and Nutrition Examination Survey found that 86.8% of males and 93.3% of females aged 10 years and older had a serum 25(OH)D level <75 nmol/L, demonstrating that vitamin D insufficiency or deficiency was very common among Koreans.[11] In addition, several studies have reported poor vitamin D status in children in China. A study in north China found that 45.2% of adolescent girls had 25(OH)D levels <12.5 nmol/L in the winter,[12] and 5 studies conducted in southeast China (Shanghai, Nanjing, Wenzhou, Wuxi, and Huzhou) found that vitamin D deficiency and insufficiency were prevalent among infants, preschool children, school children, and adolescents.[13–17]

Although inadequate vitamin D concentrations have been reported in different populations around the world, limited data are available on the vitamin D status among children in the southern regions of China, which receive abundant sunshine. This study aimed to describe the 25(OH)D status among children in southern China, and to determine the seasonal variations in serum 25(OH)D levels.

2. Materials and methods

2.1. Ethics statement

This study was approved by the Medical Research Ethics Board of Guangdong Women and Children's Hospital, and written informed consent was obtained from the parents of each child.

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The methods were carried out in accordance with the approved guidelines that conform to the Declaration of Helsinki.

2.2. Study design and participants

This large, hospital-based cross-sectional survey was conducted in Guangzhou district, which is located in South China (23°70'N latitude) and has a typical subtropical climate and receives plenty of sunshine. Children aged 0 to 6 years who visited the Department of Children's Health Care at Guangdong Women and Children Hospital for a health examination between January 2016 and May 2017 were included in the present study. Subjects were excluded if they were diagnosed with known skeletal disease, genetic syndromes, or malabsorptive disorders. Information on the age, sex, date of visit, and concentration of 25(OH) D were extracted from the hospital Laboratory Information System.

2.3. Vitamin D measurement

Vitamin D status was assessed through the determination of concentration of 25(OH)D, the major circulating form of vitamin D. Fasting venous blood samples (2 mL) were collected and transported on ice to the laboratory. A biochemical analysis was performed within 24 h and serum was stored at −80°C for future analysis. Serum 25(OH)D concentrations were measured through electrochemiluminescence immunoassay using the Abbott ARCHITECT i4000 instrument (Abbott Laboratories, Lake Bluff, IL). The inter-assay and intra-assay coefficients of variation were <10%, and the coefficient of variation for the precision of the assay from Abbott was 6.2%. Quality controls were included in each assay batch. Vitamin D status was categorized as follows: deficiency (25(OH)D < 50 nmol/L), insufficiency (50 nmol/L ≤ 25(OH)D < 75 nmol/L), and sufficiency (25(OH)D ≥ 75 nmol/L), according to the Endocrine Society's clinical practice guidelines.[18]

2.4. Statistical analysis

The seasons for blood sample collection were defined as: spring (March to May), summer (June to August), autumn (September to November), and winter (December to February).

The serum 25(OH)D levels were described using mean, standard deviations (SDs), medians, and interquartile ranges. Frequencies and percentages (%) were reported for categorical variables. Tests to determine differences in mean serum 25(OH)D levels, by sex, age, month, and season, were performed using analysis of variance. We used logistic regression to examine whether the prevalence of vitamin D insufficiency or deficiency differed by sex, age, month, and season, as a predictor. $P < .05$ was considered statistically significant. Analyses were performed using the SPSS statistical software package (V20, IBM Corp, Armonk, NY) and R software (V3.1.2, R Core Team (2014). R: A language and environment for statistical computing. R Foundation for Statistical Computing, Vienna, Austria. http://www.R-project.org).

3. Results

Data from 16,755 children, aged 0 to 6 years, were included in the analyses. The serum 25(OH)D levels ranged from 10.5 to 307.4 nmol/L (mean ± SD: 78.5 ± 26.3 nmol/L). The vitamin D statuses, stratified by the characteristics of the participants, are shown in Table 1. There were no significant differences between the male and female participants in terms of serum 25(OH)D level. Serum 25(OH)D concentrations varied with age, month, and season (Table 1; Fig. 1). Concentrations of serum 25(OH)D significantly decreased with age, and the serum 25(OH)D level in spring (71.8 ± 24.9 nmol/L) was lower than that observed in other seasons.

Overall, the prevalence of vitamin D deficiency, insufficiency, and sufficiency were 10.8%, 39.0%, and 50.3%, respectively. During certain months (from January to April), we found a relatively high prevalence of vitamin D deficiency or insufficiency. The prevalence of vitamin D deficiency was higher in spring (17.1%) than in summer (8.9%), autumn (5.6%), and winter (9.3%). The prevalence of vitamin D deficiency and insufficiency increased with age (Fig. 2). In addition, the logistic regression analysis revealed that vitamin D deficiency and insufficiency in children were significantly associated with age, month, and season (Table 2). Furthermore, the prevalence of deficiency or insufficiency (25(OH)D < 75 nmol/L) showed the same trends by month and season among the different age groups of children (Table 3).

4. Discussion

Although 25(OH)D levels are commonly used to define vitamin D status, there is no consensus on the cutoff levels for vitamin D deficiency and insufficiency. In the present study, we evaluated

Table 1

Serum 25(OH)D levels in children aged 0 to 6 years, stratified by participant characteristics.

		25-Hydroxyvitamin D levels, nmol/L		
Variables	N (%)	Mean ± SD	Median (IQR)	*P*
Sex				
Male	9671 (57.7)	78.2 ± 25.7	74.9 (61.2–92.0)	.093
Female	7084 (42.3)	78.9 ± 27.1	75.3 (61.0–93.3)	
Age, y				
0	6441 (38.4)	86.0 ± 27.3	83.0 (68.0–100.5)	<.001
1	4441 (26.5)	82.8 ± 25.4	79.7 (65.9–96.3)	
2	2060 (12.3)	76.4 ± 23.7	73.4 (61.2–87.7)	
3	1297 (7.7)	65.9 ± 19.2	65.2 (54.0–76.4)	
4	1066 (6.4)	62.1 ± 16.4	61.9 (51.1–72.8)	
5	793 (4.7)	57.7 ± 17.3	56.9 (47.6–67.7)	
6	657 (3.9)	58.5 ± 16.1	59.2 (47.9–68.7)	
Month of the year				
January	1234 (7.4)	75.2 ± 26.3	72.0 (57.8–90.0)	<.001
February	1229 (7.3)	71.7 ± 25.7	68.4 (53.5–86.2)	
March	1830 (10.9)	73.0 ± 23.5	70.4 (57.6–85.4)	
April	2018 (12.0)	70.8 ± 25.7	67.4 (54.2–83.9)	
May	2483 (14.8)	79.4 ± 28.3	76.1 (61.2–93.8)	
June	1187 (7.1)	82.5 ± 25.7	79.3 (65.0–96.4)	
July	1359 (8.1)	85.6 ± 26.2	80.6 (67.5–99.7)	
August	1283 (7.7)	80.6 ± 25.1	75.2 (63.8–93.1)	
September	985 (5.9)	85.3 ± 25.5	81.5 (68.6–99.2)	
October	1168 (7.0)	83.4 ± 24.6	80.1 (66.1–97.1)	
November	1002 (6.0)	80.6 ± 24.7	76.9 (64.1–95.0)	
December	977 (5.8)	82.3 ± 26.0	79.4 (64.2–96.0)	
Season				
Spring	6331 (37.8)	74.8 ± 26.4	71.7 (57.7–88.3)	<.001
Summer	3829 (22.9)	83.0 ± 25.7	78.4 (65.5–96.5)	
Autumn	3155 (18.8)	83.1 ± 25.0	79.7 (66.2–96.8)	
Winter	3440 (20.5)	76.0 ± 26.3	72.4 (58.3–90.8)	

Differences were tested using analysis of variance.
IQR = interquartile ranges, SD = standard deviation.

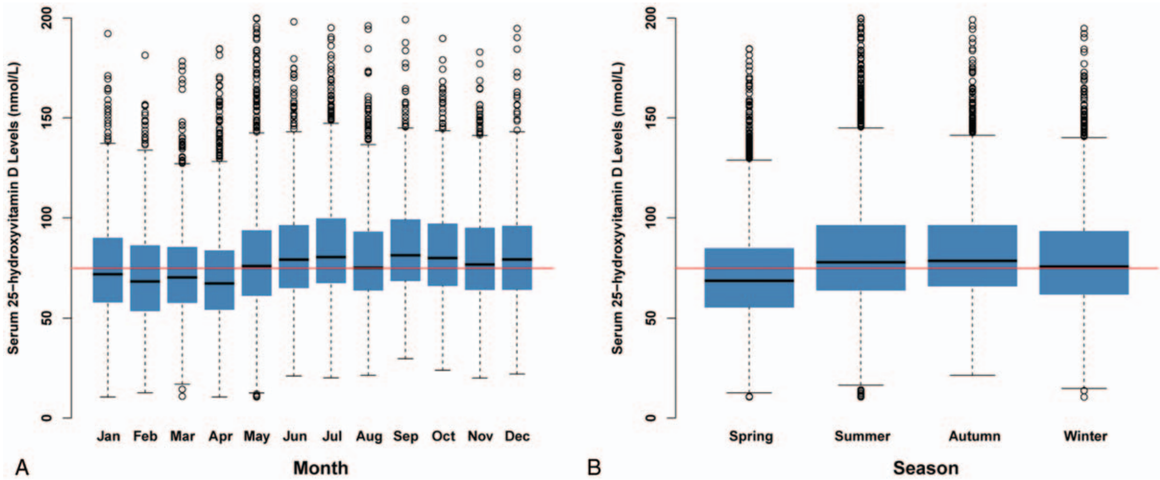

Figure 1. Variations in serum vitamin D levels by month (A) and season (B) in children aged 0 to 6 years. A sufficient level of 75 nmol/L is indicated by the red line.

vitamin D insufficiency on the basis of the conservative cutoff point suggested by the Endocrine Society. Our results showed that vitamin D insufficiency or deficiency is highly prevalent (49.8%) in southern Chinese children aged 0 to 6 years. The vitamin D levels were higher in infants than in children in the older age groups.

Vitamin D status is considered an important determinant of children's health. Vitamin D is either obtained through the diet or synthesized in the skin in response to the sun's ultraviolet B rays, and is metabolized in the liver to 25(OH)D, which plays an important role in bone and mineral metabolism. A deficiency of 25(OH)D is closely associated with osteomalacia and skeletal deformities in children.[6] The findings of the present study are in line with the current literature showing a high prevalence of vitamin D insufficiency or deficiency in young children. Various studies have reported on the prevalence of vitamin D deficiency in different parts of China. A study in Hangzhou reported that 33.6% and 5.4% of infants had serum 25(OH)D concentrations of <75 and 50 nmol/L, respectively; deficiencies were also found in adolescents, with the corresponding concentrations found in 89.6% and 46.4% of subjects, respectively.[19] In Wuxi, the prevalence of vitamin D deficiency (<50 nmol/L) was 16.1% among children aged 1 to 3 years. In Huzhou, 23.3% of children aged 0 to 18 years had a low vitamin D status (<75 nmol/L). In Beijing, 12.8% of children aged 12 to 35 months had a vitamin D deficiency,[20] and the prevalence of low 25(OH)D was 61% (<30 nmol/L) and 97% (<50 nmol/L) (mean 25(OH)D, 30 nmol/L) among adolescents.[21] The variations in the observed vitamin D status among studies could be attributed to differences in the study designs, the inclusion of different age groups, and the definition of insufficiency used, as well as the geographical differences.

A higher prevalence of vitamin D deficiency and insufficiency was observed in older children of the present study. These findings are in agreement with those of previously conducted studies that showed an association between lower levels of 25(OH)D and increasing age.[17,19,22,23] As serum vitamin D levels are determined by many factors, the cause of the age-related decline in 25(OH)D is multifactorial. Causes may include lack of vitamin D supplementation in older children, changes in diets and lifestyles, insufficient sun exposure, and spending less time on outdoor activities. A French study reported the lack of

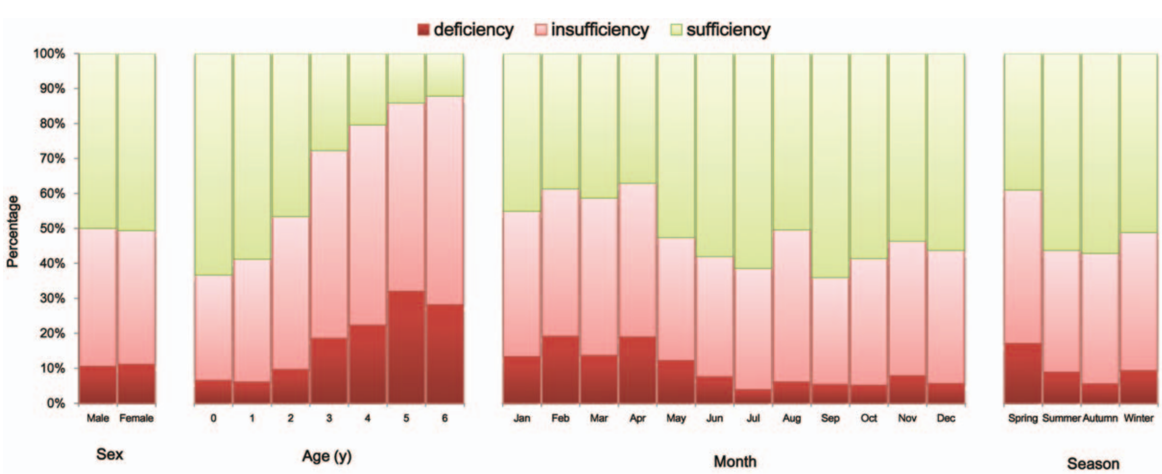

Figure 2. Percentage of vitamin D deficiency (25(OH)D < 50 nmol/L), insufficiency (50 nmol/L ≤ 25(OH)D < 75 nmol/L), and sufficiency (25(OH)D ≥ 75 nmol/L), stratified by sex, age, month, and season.

Table 2

Associations between sex, age, month, season, and vitamin D deficiency or insufficiency among children aged 0 to 6 years.

Variables	Total numbers	Deficiency (25(OH)D < 50 nmol/L) N (%)	OR (95% CI)	*P*	Deficiency/insufficiency (25(OH)D < 75 nmol/L) N (%)	OR (95% CI)	*P*
Sex							
Male	9671	1018 (10.5)	Ref.		4837 (50.0)	Ref.	
Female	7084	786 (11.1)	1.06 (0.96, 1.17)	.240	3497 (49.4)	0.97 (0.92, 1.04)	.405
Age, y							
0	6441	418 (6.5)	Ref.		2361 (36.7)	Ref.	
1	4441	269 (6.1)	0.93 (0.79, 1.09)	.362	1830 (41.2)	1.21 (1.12, 1.31)	<.001
2	2060	199 (9.7)	1.54 (1.29, 1.84)	<.001	1100 (53.4)	1.98 (1.79, 2.19)	<.001
3	1297	241 (18.6)	3.29 (2.77, 3.90)	<.001	937 (72.2)	4.50 (3.94, 5.13)	<.001
4	1066	238 (22.3)	4.14 (3.48, 4.93)	<.001	848 (79.5)	6.72 (5.74, 7.87)	<.001
5	793	254 (32.0)	6.79 (5.68, 8.12)	<.001	681 (85.9)	10.51 (8.55, 12.91)	<.001
6	657	185 (28.2)	5.65 (4.64, 6.88)	<.001	577 (87.8)	12.46 (9.81, 15.83)	<.001
Month of the year							
January	1234	165 (13.4)	Ref.		677 (54.9)	Ref.	
February	1229	235 (19.1)	1.53 (1.23, 1.90)	<.001	753 (61.3)	1.30 (1.11, 1.53)	.001
March	1830	250 (13.7)	1.03 (0.83, 1.27)	.818	1073 (58.6)	1.17 (1.01, 1.35)	.039
April	2018	383 (19.0)	1.52 (1.24, 1.85)	<.001	1269 (62.9)	1.39 (1.21, 1.61)	<.001
May	2483	303 (12.2)	0.90 (0.73, 1.10)	.312	1176 (47.4)	0.74 (0.65, 0.85)	<.001
June	1187	90 (7.6)	0.53 (0.41, 0.70)	<.001	498 (42.0)	0.59 (0.51, 0.70)	<.001
July	1359	53 (3.9)	0.26 (0.19, 0.36)	<.001	524 (38.6)	0.52 (0.44, 0.60)	<.001
August	1283	78 (6.1)	0.42 (0.32, 0.56)	<.001	636 (49.6)	0.81 (0.69, 0.95)	.008
September	985	53 (5.4)	0.37 (0.27, 0.51)	<.001	354 (35.9)	0.46 (0.39, 0.55)	<.001
October	1168	60 (5.1)	0.35 (0.26, 0.48)	<.001	483 (41.4)	0.58 (0.49, 0.68)	<.001
November	1002	79 (7.9)	0.55 (0.42, 0.74)	<.001	464 (46.3)	0.71 (0.60, 0.84)	<.001
December	977	55 (5.6)	0.39 (0.28, 0.53)	<.001	427 (43.7)	0.64 (0.54, 0.76)	<.001
Season							
Spring	6331	936 (14.8)	Ref.		3518 (55.6)	Ref.	
Summer	3829	221 (5.8)	0.35 (0.30, 0.41)	<.001	1658 (43.3)	0.61 (0.56, 0.66)	<.001
Autumn	3155	192 (6.1)	0.37 (0.32, 0.44)	<.001	1301 (41.2)	0.56 (0.51, 0.61)	<.001
Winter	3440	455 (13.2)	0.88 (0.78, 0.99)	.035	1857 (54.0)	0.94 (0.86, 1.02)	.132

CI = confidence interval, OR = odds ratio.

supplementation in older children; 53.4% of study participants did not have a prescription for vitamin D or had a prescription for supplementation below the recommended doses.[24] Although the Chinese Medical Association recommends that all children receive 400 IU vitamin D daily during the first 2 years of their lives, and that older children also receive vitamin D supplementation, the risk of vitamin D deficiency was found to increase with age in our study. This finding implies the development of an imbalance between nutritional intake and requirement with increasing age, and supplementation of 400 IU vitamin D daily may be ineffective in maintaining 25(OH)D levels at optimal concentrations (>75 nmol/L). The present study also revealed a

Table 3

Percentage of deficiency/insufficiency (25(OH)D < 75 nmol/L) among the different age groups, by month and season.

Variables	Age, y 0	1	2	3	4	5	6
Month of the year							
January	41.4	42.5	62.7	80.2	83.7	88.2	84.8
February	44.4	47.0	66.0	82.8	94.0	93.2	94.4
March	44.4	51.7	65.7	86.6	94.4	93.8	98.5
April	48.0	60.8	73.0	87.7	83.3	95.5	90.5
May	33.3	43.4	50.0	70.9	73.9	86.4	91.2
June	31.2	32.1	44.8	63.6	67.2	80.8	83.7
July	26.2	27.8	36.4	57.6	62.4	70.3	78.8
August	33.0	33.3	47.3	68.5	78.3	78.6	86.8
September	23.8	31.1	37.3	58.8	67.9	81.3	90.0
October	31.5	33.2	42.1	64.1	77.9	78.0	72.7
November	35.8	37.0	52.1	62.9	82.4	87.0	93.8
December	33.9	36.4	41.9	64.6	78.8	90.7	82.6
Season							
Spring	41.2	51.4	62.1	80.6	83.0	91.4	93.2
Summer	30.0	30.9	42.7	63.4	69.7	76.2	83.5
Autumn	30.6	33.6	43.5	62.3	76.2	82.4	84.0
Winter	40.1	41.9	57.9	77.7	87.4	90.8	88.6

relatively high prevalence of vitamin D deficiency or insufficiency in certain months. Seasonal changes in serum 25(OH)D levels may reflect the synthesis of whole-body irradiation.[25,26] There were significant variations in the prevalence of vitamin D deficiency during the 12 months of the year. The prevalence of vitamin D insufficiency or deficiency was higher from January to April than in the other months. This time period coincides with changes in relative humidity and the onset of a more humid period in Guangzhou; these factors may lead to inadequate sun exposure.

The present study evaluated the prevalence of vitamin D deficiency and insufficiency in children aged 0 to 6 years in South China. Nevertheless, the study had several limitations. First, this was a single-center study and the participant sample does not represent the general population. Second, detailed information on obesity status, lifestyle factors, and dietary composition (such as vitamin D supplementation) was not available. These factors might affect the vitamin D status of young children.[27,28] Third, we did not investigate the amount of sunlight to which every participant was exposed. Thus, we could not estimate how the degree of sun exposure differed among the participants, leading to seasonal variations.[29] Fourth, the current study lacked the gold-standard liquid chromatography–mass spectrometry measure of vitamin D. Serum 25(OH)D concentrations were measured by electrochemiluminescence immunoassay, which could be performed in a rapid, high throughput manner and offered excellent sensitivity; however, it was unable to distinguish between the various forms of vitamin D such as 25(OH)D_3 and 25(OH)D_2. Fifth, we did not assess the potential contribution of vitamin D axis gene polymorphisms, which could explain some of the observed differences. Furthermore, owing to the cross-sectional nature of the study, we cannot draw inferences regarding the key contributors to vitamin D deficiency, or the changes in vitamin D status over time.

5. Conclusions

Vitamin D deficiency and insufficiency are common among children in South China, despite the presence of sufficient sunlight in the region. Vitamin D status is worse in older children and in the winter.

Author contributions

Yong Guo and Jie-Ling Wu conceived and designed the study; Hai-Jin Ke, Ying Liu, Min Fu, Jing Ning, Li Yu, and Yu Xiao performed the experiments; Yong Guo, Di Che, Xiao-Yan Chen, and Yu-Hong Deng analyzed the data; Yong Guo and Jie-Ling Wu wrote the paper. All authors have seen and approved the final version of the manuscript.

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Project administration: Hai-Jin Ke.

Writing – original draft: Yong Guo, Jie-Ling Wu.

Writing – review and editing: Jie-Ling Wu.

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