



An exploration of clinical features and factors associated with pain frequency and pain intensity in children with growing pains: a cross-sectional study from Chongqing, China

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Abstract

Instruction: Growing pains are the most common cause of musculoskeletal pain in children, affecting both children's and caregivers' well-being. The lack of definitive diagnostic criteria complicates diagnosis and treatment.

Objectives: This study aims to outline the clinical features and identify factors associated with the frequency and intensity of growing pains in children in Chongqing, China.

Methods: A cross-sectional study was conducted in a children's hospital using its Internet hospital follow-up platform. Children initially diagnosed with growing pains between July and September 2022 were enrolled. Sociodemographics, pain locations, duration, frequency, intensity, and potentially related factors were collected.

Results: Eight hundred sixty-three children were enrolled (average age: 8.19 ± 3.24 years; 455 boys [52.72%]). Pain frequency was reported as quarterly (62.11%), monthly (24.80%), biweekly (1.74%), weekly (10.08%), and daily (1.27%). The prevalence of mild, moderate, and severe pain was 26.65%, 55.74%, and 17.61%, respectively. The knee was the most common pain location (63.85%), mostly encountered between 4 PM and 5 PM (20.51%). Multivariate analysis revealed that pain frequency negatively correlated with vitamin supplementation during pregnancy, positively correlated with underweight, bad temper, increased exercise, and cold lower extremities. Pain intensity positively correlated with irritability, increased exercise, and pain sensitivity but negatively correlated with age and vitamin supplementation during lactation.

Conclusion: Growing pains typically occur on a quarterly basis, predominantly affecting the knees during 4 PM to 5 PM. Factors in sociodemographics, maternal aspect, temperament, and exercise levels can influence pain frequency and intensity. Clinicians should consider these aspects when developing comprehensive strategies for pain management.

Keywords: Growing pains, Pediatrics, Clinical features, Pain frequency, Pain intensity, Cross-sectional study

1. Introduction

Growing pains is one of the most common causes of musculoskeletal pain in children,²⁵ its prevalence varies ranging from 2.6% to 36.9%,^{1,8,23} depending on different study populations, assessment methods, and definitions. Typically, growing pains affect children aged 3 to 12 years²⁵ and tend to occur during the evening or nighttime, with intensity that can

disrupt the child's sleep quality.³⁵ Intermittent episodes of growing pains can induce children's undesirable academic performance and diminished quality of life for caregivers.^{43,48} Therefore, enhancing the understanding of the interrelated determinants influencing pain frequency and intensity is of great importance. Mitigating the impact of growing pains is imperative for both children's and caregivers' well-being.

Sponsorships or competing interests that may be relevant to content are disclosed at the end of this article.

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Although the medical term “growing pains” was proposed by the French physician Duchanmp in the 1900s⁶ even now, it remains an enigma in medical research because of the inadequate understanding of its etiology and pathophysiological mechanisms. Growing pains is a diagnosis of exclusion, the absence of a clear definition,³⁵ normal radiography, and laboratory biomarkers²⁵ result in the diagnosis relying primarily on clinical manifestation. Therefore, detailed information on clinical features and factors linked to growing pains is pivotal. Such information not only enhances awareness among clinicians, patients, and caregivers about the impact of growing pains but also facilitates the identification of risk factors and aids in developing precise diagnostic criteria and treatment policies. However, far less attention has been directed towards the clinical features of growing pains and the association between pain frequency, pain intensity, and potential contributing factors, especially in Chinese children.

Consequently, this cross-sectional study aims to (1) explore the clinical features of children with growing pains, providing data on a sample of children with growing pains in Chongqing, China, and (2) identify factors associated with pain frequency and pain intensity, hoping to illuminate new targets for preventive and therapeutic interventions.

2. Methods

2.1. Study design and participants

This cross-sectional survey was conducted at a tertiary children's hospital in Chongqing between July and December 2022. The hospital is the National Children's Area Medical Center, ranks among the top 3 in the country, and serves patients from more than 30 provinces in southwest China. Children initially diagnosed with growing pains in general surgery clinic, orthopedic specialist clinic, orthopedic VIP clinic, and orthopedic night clinic between July and September 2022 (the peak period of summer outpatient visits) were enrolled. Children underwent thorough medical history assessments, physical examinations, and laboratory tests. Orthopedists made the diagnosis based on a comprehensive evaluation of the results.

The inclusion criteria were as follows: (a) Children who met the Peterson growing pains diagnosis criteria^{40,41}: (1) pain typically occurs late in the day or during the night and disappears in the morning; (2) pain is intermittent with some pain-free days and nights; (3) typical distribution of pain in the anterior part of the thigh, calf, and posterior part of the knees, and (4) usually in both legs; (5) pain localized in the areas outside the region of joints; (6) there is no limitation of mobility and no limping; (7) pain is not associated with local trauma, infection, tenderness, erythema, and swelling; and (8) the results of physical examination, laboratory tests, and roentgenograms are normal. (b) Children aged between 3 and 18 years. (c) Both children and caregivers were able to speak and understand. (d) Caregivers can fill out the questionnaire through mobile phones. The exclusion criteria were as follows: (a) children with serious diseases (eg, nephropathy, cardiovascular disease, cancer); (b) children or caregivers with impaired cognitive capability and judgment; and (c) caregivers unable to fill out the questionnaire through mobile phones.

The study was conducted following the Declaration of Helsinki and approved by the Institutional Review Board of the Children's Hospital of Chongqing Medical University (approval certificate number: 2022-302). All participants and caregivers gave their informed consent for inclusion before filling out the questionnaire.

2.2. Questionnaire content

A self-made questionnaire was designed, comprising 3 sections: sociodemographic factors, pain-related details, and potential associated factors. The questionnaire was developed by a research panel referring to the previous literature^{9,50} and underwent content validity evaluation by pain management specialists, pediatric orthopedics professors, psychologists, and statistics experts before implementation. The content validity was 0.86, falling within the acceptable range.

2.2.1. Sociodemographic information

The following sociodemographic information was collected: age, gender, weight, height, body mass index (BMI), ethnicity, educational level of caregivers, and monthly income. Participants' BMI classifications were determined according to the Chinese standard,²⁸ with categories including underweight (<5th percentile), normal (\geq 5th percentile, <85th percentile), overweight (\geq 85th percentile, <95th percentile), and obesity (\geq 95th percentile).

2.2.2. Pain-related information

Caregivers were requested to provide information regarding the occurrence of growing pains in children over the past 3 months, starting from the receipt of the questionnaire. This included details such as pain locations (ie, knee, calf, ankle, instep, sole, thigh, and others; bilateral or unilateral), pain intensity (with rating ranging from 0 = “no hurt” to 10 = “hurts worst” assessed by the Faces Pain Scale-Revised²⁴), pain type (pins and needles, sore pain, dull pain, itching, bursting pain, throbbing pain, numbness, vague), frequency of growing pains episodes, timing of pain onset most commonly, the average duration of pain, concomitant symptoms (cry, scream, sweat, cramp, vomit, weakness, asthenia), and negative impact because of the pain (reluctant to walk, difficulty sleeping, wake up at night).

2.2.3. Potential factors influencing pain frequency and pain intensity

2.2.3.1. Maternal aspect

Maternal aspect included delivery mode (vaginal or cesarean), feeding methods employed from 0 to 6 months after birth (breast feeding, formula feeding, mixed feeding), and whether the mother has vitamin supplementation during pregnancy (yes/no) and lactation (yes/no).

2.2.3.2. Psychological and behavioral problems

Caregivers were requested to provide information about the psychological and behavioral problems of participants over the past 6 months, starting from the receipt of the questionnaire. Psychological problems included irritability¹⁶ (has a low frustration tolerance and inappropriately throws tantrums), bad temper (has temper outbursts when does not get his/her way), and nervousness (having the feeling of anxiety about something or being afraid of something). Behavioral problems included picky eating⁵ (eating a limited amount of foods, rejecting novel foods, and having strong food preferences), pain sensitivity (a strong reaction to mild pain stimuli), inattention (lack of attention to something/somebody), and prosocial problems (unwilling to offer help to parents, teachers, and other children). Psychological and behavioral problems were assessed using a 5-point Likert scale (1 = “Never,” 2 = “Almost never,” 3 = “Sometimes,” 4 = “Often,”

5 = “Almost always”); participants were classified as having behavioral/psychological problems when caregivers chose “often” or “almost always.”

2.2.3.3. Special events

Special events included increased exercise and cold lower extremities. Increased exercise is defined as taking physical exercise for at least 60 minutes more than usual according to Physical activity guidelines for Chinese children and adolescents.⁵⁴ Cold lower extremities refer to children’s self-reported cooling experience of lower extremities.

2.3. Procedure

2.3.1. Participant selection

The medical records of eligible children were collected from the Big Data Center for Children’s Medical Care. Children with potential alternative diagnoses were excluded to maintain data accuracy.

2.3.2. Questionnaire distribution

The questionnaire link was sent to eligible children’s caregivers through the Internet hospital follow-up platform of the children’s hospital. Reminders were sent 7 days later to those who had not initially responded. Caregivers received questionnaire notifications through the WeChat Official Account of the Children’s Hospital of Chongqing Medical University (the most popular Chinese Internet social platform, the WeChat account is bound with the Internet hospital follow-up platform upon registration for making medical appointments). The questionnaire included instructions and detailed explanations for key variables to ensure consistent understanding among caregivers. Moreover, investigators’ contact information was attached, allowing caregivers to seek clarification or assistance if they encountered difficulties in understanding.

2.4. Statistical analysis

Data were processed using IBM SPSS Statistics (version 27.0). In the descriptive analysis, continuous variables were presented as mean \pm standard deviation (SD), whereas categorical variables were reported as percentages (n, %). Pain frequency was categorized as low frequency (≤ 1 time/month) and high frequency (> 1 time/month), whereas pain intensity was divided into mild (1–3 points), moderate (4–6 points), and severe (7–10 points) according to scale rating metric.²⁴ The χ^2 test was employed to examine the association between each variable and pain frequency or intensity, with statistically significant variables included in the subsequent regression analysis. Binary logistic regression was applied to analyze the association between pain frequency and related variables. A multivariable ordinal logistic regression model was used to explore the association between pain intensity and its related variables. The stepwise method was adopted for variable screening. Results were expressed as odds ratios (ORs) and 95% confidence intervals (CIs), with statistical significance defined as a P value of < 0.05 .

3. Results

As described in **Figure 1**, the questionnaire was distributed to 1,984 children between October and December 2022, 1,201 patients responded through the Internet follow-up platform, and

901 participants returned the questionnaire. After implementing quality control measures, 20 participants were excluded with incomplete sociodemographic information (refused to provide monthly income information), and 18 participants were eliminated with obvious logic errors, leaving a final of 863 participants.

3.1. Sociodemographic characteristics and clinical features of participants with growing pains

Table 1 summarizes the sociodemographic characteristics of participants and caregivers. The sample comprised 455 boys (52.72%) and 408 girls (47.28%), with a mean age of the children was 8.19 years (SD = 3.24; range = 3–16), with 6 year olds representing the largest group (17.73%). Overall, 39.52% of the children were classified as underweight, 44.84% as normal, and 15.64% as overweight/obesity. Among the caregivers, 816 (94.55%) were parents, and the remaining were next of kin.

Table 2 displays the clinical features of participants. Pain frequency was reported as quarterly (536, 62.11%), monthly (214, 24.80%), biweekly (15, 1.74%), weekly (87, 10.08%), and daily (11, 1.27%). The highest incidence of pain occurrence during the day was observed from 4 PM to 5 PM (177, 20.51%), followed by 8 PM to 9 PM (111, 12.86%) and 9 PM to 10 PM (103, 11.94%). Pain was predominantly located in the knee (551, 63.85%), followed by the calf (467, 54.11%) and ankle (223, 25.84%), although 514 participants (59.56%) reported bilateral pain. Concerning pain intensity, the mean pain score was 4.59 (SD = 2.20), and the prevalence of mild pain, moderate pain, and severe pain was 26.65%, 55.74%, and 17.61%, respectively. Regarding the pain type, 398 children (46.12%) described the sensation as a vague or unnamed feeling. When pain occurred, 374 children (43.34%) encountered difficulty sleeping, 371 children (42.99%) woke up in the night, 101 children (11.7%) had limb cramps, and 195 children (22.6%) were reluctant to walk.

In addition, the distributions of different clinical manifestations at each age are exhibited in **Figure 2**. **Figure 2A** shows the highest proportion of high frequency pain is 42.32% at age 3 years, followed by 23.11% at age 8 years, and 16.54% at age 10 years; **Figure 2B** shows the proportion of participants reporting mild pain rose steadily from 12.00% at age 4 years to 45.00% at age 14 years, while reported severe pain drop from 23.81% at age 3 years to 0% at age 16 years; in **Figure 2C**, the proportion of those who suffered pain in the late afternoon (4 PM to 6 PM) increased from 9.91% at age 3 years to 64.65% at age 14 years, then decline to 40.00% at age 16 years, and the proportion of those who suffered pain at night (6 PM to 10 PM) drop from 53.47% at age 3 years to 14.14% at age 14 years, then increased to 50.00% at age 16 years; in addition, the proportion of reporting the greatest pain intensity location other than lower limbs when growing pains occurs increased from 5.12% at age 3 years to 28.37% at age 15 years, before declining to 19.81% at age 16 years as exhibited in **Figure 2D**.

3.2. The comparison of pain frequency and pain intensity in participants with different features

Significant differences in pain frequency and pain intensity were observed across various variables, as revealed by the χ^2 test (**Table 3**). Factors related to pain frequency included age, BMI at the individual level of children; whether the mother has vitamin supplementation during pregnancy/lactation at the maternal level; irritability and bad temper in the psychological problems

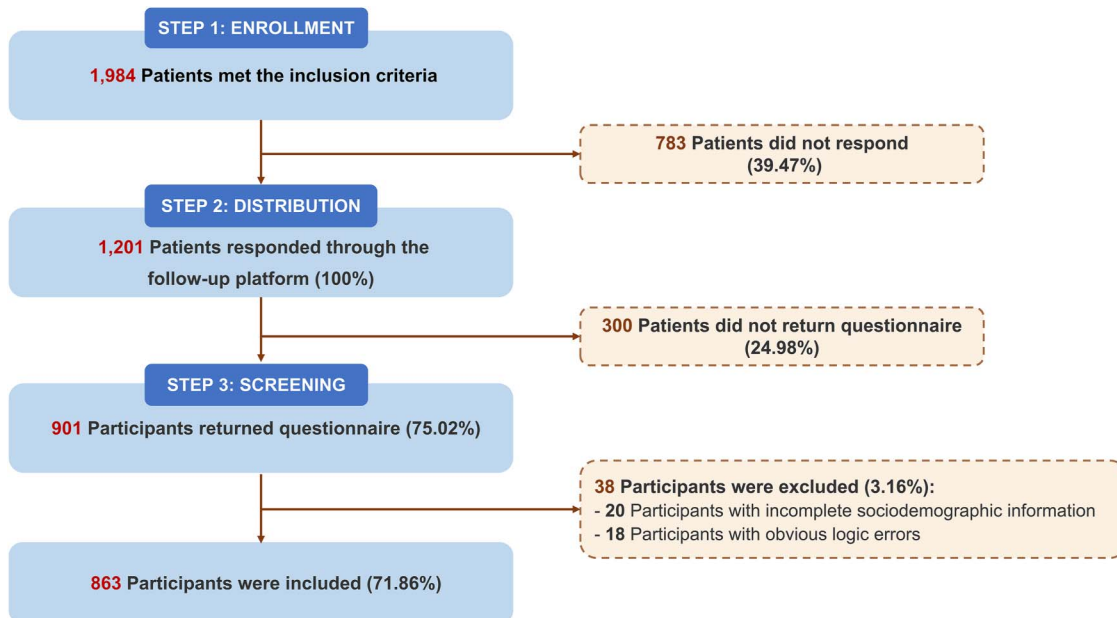


Figure 1. Flowchart of enrollment and exclusion of participants with growing pains.

aspect; and increased exercise and cold lower extremities in the special event aspect ($P < 0.05$).

Regarding pain intensity, related factors included age, BMI at the individual level of children; whether the mother has vitamin

supplementation during pregnancy/lactation at the maternal level; irritability, picky eating, and pain sensitivity in the psychological and behavioral problems aspect; and increased exercise and cold lower extremities in the special event aspect ($P < 0.05$).

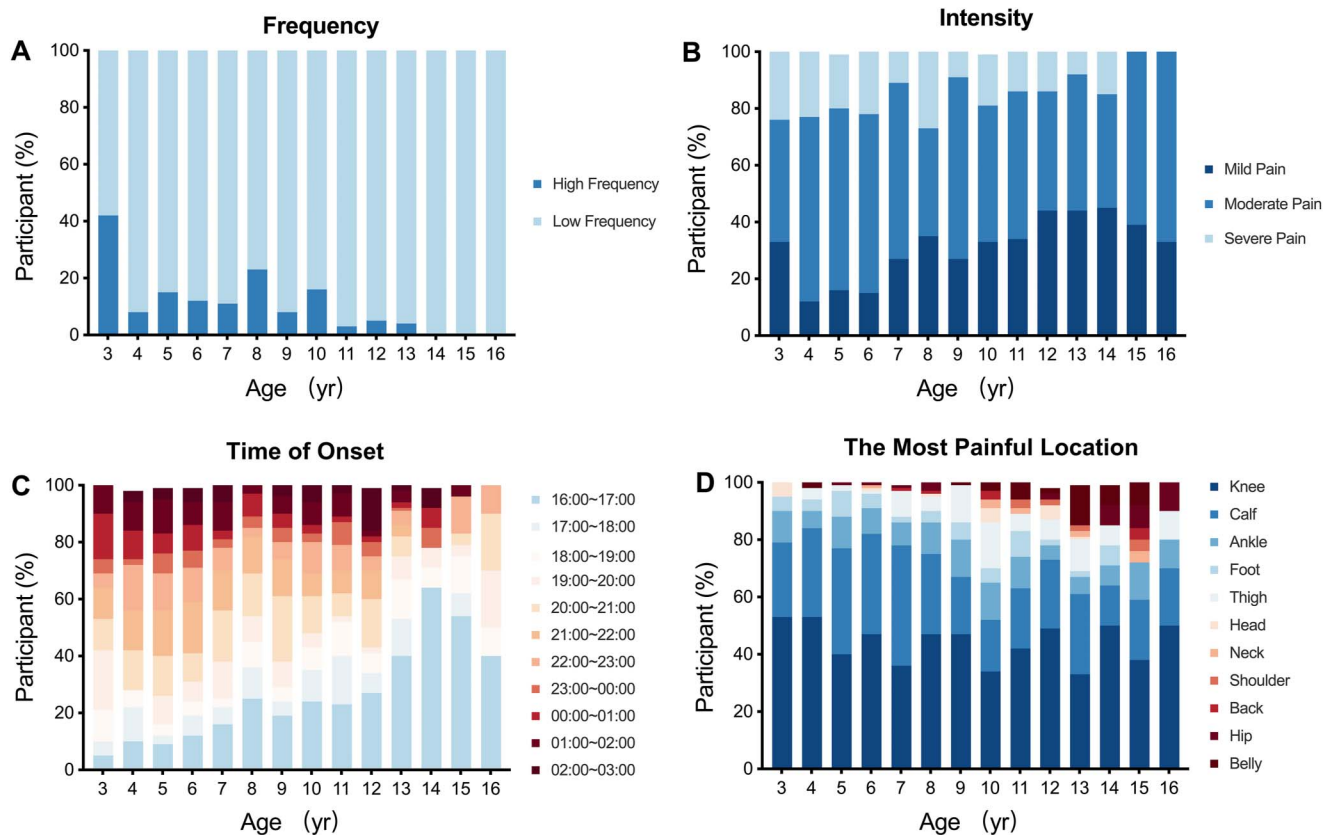


Figure 2. Stacked bar of clinical features of participants with growing pains at each age (n = 863). (A) Frequency, (B) intensity, (C) time of onset, and (D) the most painful location. The numbers on the x-axis indicate the age of participants from 3 to 16 years. The numbers on the y-axis indicate the proportion of participants in each clinical feature.

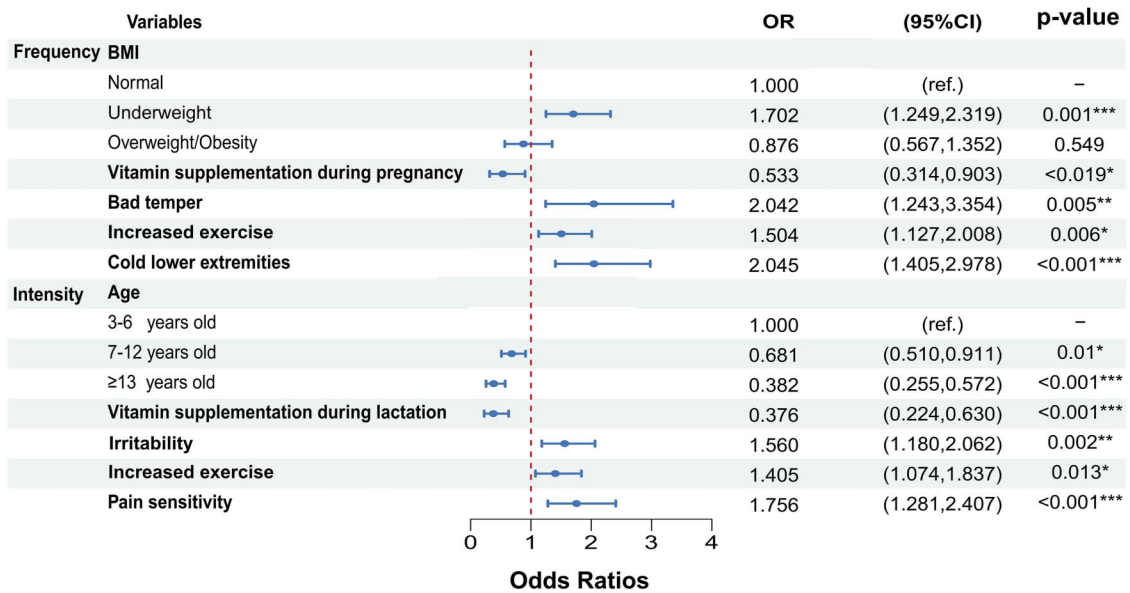


Figure 3. Forest plot depicting the association between variables and pain frequency, pain intensity. ORs and 95% CIs were computed by logistic regression analysis. Significant association, * $P < 0.05$, ** $P < 0.005$, *** $P < 0.001$. BMI, body mass index; CI, confidence interval; OR, odds ratio.

3.3. Results of regression analysis with regards to pain frequency and pain intensity

Factors associated with pain frequency and pain intensity are presented in **Figure 3**. Pain frequency was negatively associated

Table 1
Sociodemographic characteristics of participants and caregivers (n = 863).

Variables	N	%
Characteristics of participants		
Gender		
Male	455	52.72
Female	408	47.28
Age (y)		
3-6	320	37.08
7-12	410	47.51
≥13	133	15.41
BMI		
Underweight	341	39.52
Normal	387	44.84
Overweight/obesity	135	15.64
Ethnicity		
Ethnic Han	813	94.21
Ethnic minorities	50	5.79
Characteristics of caregivers		
Caregivers		
Parents	816	94.55
Next of kin	47	5.45
Monthly income*		
< 2000 CNY (< 281 USD)	139	16.11
2000~5000 CNY (281~702 USD)	304	35.23
5000~10,000 CNY (702~1405 USD)	275	31.86
> 10,000 CNY (> 1405 USD)	145	16.80
Educational level		
Primary school or below	74	8.57
Junior school	145	16.81
High school	116	13.44
College or higher	528	61.18
Employment		
Employed	794	92.00
Unemployed	69	8.00

* 1CNY = 0.1405 USD on 7 June 2023.
BMI, body mass index; CNY, China Yuan; USD, United States dollar.

with vitamin supplementation during pregnancy (OR [95% CI]): (0.533 [0.314–0.903]; $P < 0.019$). Underweight (1.702 [1.249–2.319]; $P = 0.001$), bad temper (2.042 [1.243–3.354]; $P = 0.005$), increased exercise (1.504 [1.127–2.008]; $P = 0.006$), and cold lower extremities (2.045 [1.405–2.978]; $P < 0.001$) were positively associated with pain frequency. However, age, vitamin supplementation during lactation, and irritability were not associated with pain frequency.

Pain intensity was significantly associated with several factors. Younger age was associated with a higher risk of pain intensity, participants aged 3 to 6 years exhibited the highest risk of reporting higher pain intensity, compared with participants aged 7 to 12 years (0.681 [0.510–0.911]; $P = 0.01$) and older than 13 years (0.382 [0.255–0.572]; $P < 0.001$). What’s more, vitamin supplementation during lactation (0.376 [0.224–0.630]; $P < 0.001$) indicated a lower risk of reporting higher pain intensity. Irritability (1.560 [1.180–2.062]; $P = 0.002$), increased exercise (1.405 [1.074–1.837]; $P = 0.013$), and pain sensitivity (1.756 [1.281–2.407]; $P < 0.001$) were associated with higher pain intensity. Body mass index, vitamin supplementation during pregnancy, picky eating, and cold lower extremities were not related to pain intensity.

4. Discussion

This study investigated the clinical features and identified factors related to pain frequency and pain intensity in 863 children with growing pains, using a questionnaire-based survey conducted through an internet follow-up platform. The findings provide further evidence that the clinical manifestations of growing pains are diverse. Body mass index, vitamin supplementation during pregnancy, bad temper, increased exercise, and cold lower extremities were associated with pain frequency. Age, vitamin supplementation during lactation, irritability, increased exercise, and pain sensitivity were related to pain intensity. To the best of our knowledge, this is the first study to report the clinical features and related factors of pain frequency and pain intensity in Chinese children with growing pains.

Table 2
Clinical features of participants with growing pains (n = 863).

Variables	N	%
Frequency		
Daily	11	1.27
Weekly	87	10.08
Biweekly	15	1.74
Monthly	214	24.80
Quarterly	536	62.11
Time of onset		
4 PM~5 PM	177	20.51
5 PM~6 PM	69	8.00
6 PM~7 PM	63	7.30
7 PM~8 PM	68	7.88
8 PM~9 PM	111	12.86
9 PM~10 PM	103	11.94
10 PM~11 PM	79	9.15
11 PM~12 PM	40	4.63
12 PM~1 AM	49	5.68
1 AM~2 AM	64	7.42
2 AM~3 AM	40	4.63
Pain location*		
Knee	551	63.85
Calf	467	54.11
Ankle	223	25.84
Instep	89	10.31
Sole	71	8.23
Thigh	159	18.42
Head	12	1.39
Neck	19	2.20
Shoulder	22	2.55
Back	22	2.55
Hip	30	3.48
Belly	42	4.87
Upper limb	43	4.98
No. of pain location(s)		
1	352	40.67
2	274	31.75
3	149	17.27
≥4	88	10.31
Pain limb		
Bilateral	514	59.56
Unilateral	349	40.44
Pain severity		
Mild pain	230	26.65
Moderate pain	481	55.74
Severe pain	152	17.61
Pain type*		
Pins and needles	109	12.63
Sore pain	195	22.60
Dull pain	262	30.35
Itching	15	1.74
Bursting pain	31	3.59
Throbbing pain	74	8.57
Numbness	75	8.69
Vague	398	46.12
Duration		
0–30 min	567	65.70
30–60 min	151	17.49
More than 60 min	145	16.81
Concomitant symptom*		
Cry	430	49.83
Scream	58	6.72
Sweat	78	9.04
Cramp	101	11.70
Vomit	5	0.58
Weakness	56	6.49
Asthenia	41	4.75
Negative impact*		
Reluctant to walk	195	22.59
Difficulty sleeping	374	43.34
Wake up at night	371	42.99

* Multiple-choice question.

4.1. Clinical features of growing pains

Approximately 62.11% of participants encounter growing pains quarterly, about one-third reporting pain at least once a month, which is more frequent than the results of Kaspiris and Zafiropoulou,²³ less frequent than Evans et al.,¹⁰ and Pavone et al.³⁹; this variance may be attributed to differences in population selection, age composition, and diagnostic criteria. Moreover, the study found that 55.74% of the participants reported moderate pain, which interfered with sleep (43.34%), and reluctant to walk (22.59%) also detected, which align with several previous studies.^{10,23,38,39}

As for the pain type, 46.12% of participants described it as vague and challenging to articulate in words. It may be related to the young age of children or the nature of the pain itself. Moreover, the results indicated that pain occurred not only in the evening or at night but in the late afternoon (28.51%), especially between 4 PM and 5 PM (Fig. 2C). This contradicts Türkdoğan et al.,⁴⁶ but in accordance with Hestbaek et al.,¹⁸ suggesting the importance of identifying the occurrence of growing pains at different times. The proportion of pain sites varies across studies, in line with previous studies,^{2,38} this study found knee (63.85%) was the commonest location of pain, followed by calf (54.11%) and ankle (25.84%). Conversely, several studies detected that pain primarily occurs in calf (41.7% to 91.4%)^{3,46,53} or “diffuse” (34.6%).¹⁸ The variation in race, age, and gender composition may resulted in this inconsistent result. Moreover, a cross-sectional study conducted in China observed that 29.1% (521/1789) of children with growing pains have asymmetric torsion of the lower limbs,³⁰ which can induce uneven pressure in the knee; it can aggregate by prolonged activities, overuse, and easily cause muscle fatigue, joint capsule relaxation, eventually leading to painful knee,⁵¹ and this might partly clarify the results of this study.

It is common for children with growing pains to report pain from more than one location.¹⁸ In this study, pain was reported in areas outside the lower extremities, such as head (1.39%), back (2.55%), hip (3.48%), belly (4.87%), upper arms (4.98%), and other regions. However, the proportion of pain occurring in these areas was smaller compared with findings in other studies.^{3,33,38} Furthermore, 118 participants (13.6%) reported the greatest pain locations other than lower limbs when growing pains occur, but it is not mentioned in Peterson diagnostic criteria. Although growing pains mainly present in lower limbs,^{25,35} sporadically in upper limbs,^{3,38} it can be accompanied by headaches and abdominal pain. However, the investigator inferred that it was a functional abdominal pain disorder⁴⁴ and headache induced by other causes, instead of a part of the growing pains phenotype. Therefore, it is imperative to recognize atypical clinical manifestations and differentiate growing pains from other diseases to avoid misdiagnosis in clinical practice.

4.2. Factors associated with pain frequency

Beyond the clinical features, this study identified that underweight children have a higher risk of suffering high-frequency pain compared with their normal counterparts. Friedland et al.¹⁴ have previously elucidated that children experiencing growing pains exhibit significantly lower bone mineral density (BMD) compared with healthy counterparts. Considering the well-established positive correlation between BMI and BMD,³⁷ it is postulated that among children with growing pains, those who are underweight may have an even more pronounced reduction in BMD compared with counterparts with a normal BMI. Consequently, underweight children with growing pains, characterized by

Table 3

Results of χ^2 test of related factors on pain frequency and pain intensity (n = 863).

Variables	Pain frequency		χ^2	P	Pain intensity			χ^2	P
	Low frequency	High frequency			Mild pain	Moderate pain	Severe pain		
Sociodemographic factors									
Age (y)									
3~6	176 (32.84)	144 (44.04)	11.122	<0.001***	56 (24.35)	199 (41.37)	65 (42.76)	35.916	<0.001***
7~12	274 (51.12)	136 (41.59)			117 (50.87)	217 (45.11)	76 (50.00)		
≥13	86 (16.04)	47 (14.37)			57 (24.78)	65 (13.51)	11 (7.24)		
Gender									
Male	291 (54.29)	164 (50.15)	1.395	0.238	126 (54.78)	249 (51.77)	80 (52.63)	0.568	0.753
Female	245 (45.71)	163 (49.85)			104 (45.22)	232 (48.23)	72 (47.37)		
BMI									
Underweight	183 (34.14)	158 (48.32)	17.388	<0.001***	69 (30.00)	212 (44.07)	60 (39.47)	13.201	0.010*
Normal	259 (48.32)	128 (39.14)			120 (52.17)	197 (40.96)	70 (46.05)		
Overweight/obesity	94 (17.54)	41 (12.54)			41 (17.83)	72 (14.97)	22 (14.47)		
Nation									
Ethnic Han	504 (94.03)	309 (94.50)	0.081	0.776	220 (95.65)	447 (92.93)	146 (96.05)	3.263	0.196
Ethnic minorities	32 (5.97)	18 (5.50)			10 (4.35)	34 (7.07)	6 (3.95)		
Maternal factors									
Mode of delivery									
Vaginal	266 (49.63)	170 (51.99)	0.453	0.501	117 (50.87)	233 (48.44)	86 (56.58)	3.075	0.215
Cesarean	270 (50.37)	157 (48.01)			113 (49.13)	248 (51.56)	66 (43.42)		
Feeding methods from 0-6 mo									
Breast feeding	327 (61.01)	206 (63.00)	2.335	0.311	140 (60.87)	296 (61.54)	97 (63.82)	5.418	0.247
Formula feeding	71 (13.25)	32 (9.79)			36 (15.65)	54 (11.23)	13 (8.55)		
Mixed feeding	138 (25.75)	89 (27.22)			54 (23.48)	131 (27.23)	42 (27.63)		
Caregivers									
Parents	510 (95.15)	306 (93.58)	0.974	0.324	216 (93.91)	457 (95.01)	143 (94.08)	0.445	0.801
Next of kin	26 (4.85)	21 (6.42)			14 (6.09)	24 (4.99)	9 (5.92)		
Whether the mother has vitamin supplementation during pregnancy									
Yes	507 (94.59)	292 (89.30)	8.287	<0.001***	226 (98.26)	441 (91.68)	132 (86.84)	18.662	<0.001***
No	56 (10.41)	33 (10.70)			4 (1.74)	51 (10.32)	19 (12.46)		
Whether the mother has vitamin supplementation during lactation									
Yes	507 (94.59)	295 (90.21)	5.919	0.015*	226 (98.26)	444 (92.31)	132 (86.84)	18.810	<0.001***
No	56 (10.41)	33 (10.79)			4 (1.74)	51 (10.69)	19 (12.54)		
Educational level									
High school or lower	200 (37.31)	135 (41.28)	1.348	0.246	92 (40.00)	184 (38.25)	59 (38.82)	0.200	0.905
College or higher	336 (62.69)	192 (58.72)			138 (60.00)	297 (61.75)	93 (61.18)		
Psychological and behavioral problems									
Irritability	167 (31.16)	127 (38.84)	5.335	0.021*	54 (23.48)	181 (37.63)	59 (38.82)	15.725	<0.001***
Bad temper	158 (29.48)	130 (39.76)			62 (26.96)	172 (35.76)	54 (35.53)		
Nervousness	67 (12.50)	47 (14.37)	0.622	0.430	32 (13.91)	61 (12.68)	21 (13.82)	0.265	0.876
Inattention	212 (39.55)	114 (34.86)			86 (37.39)	190 (39.50)	50 (32.89)		
Prosocial problems	17 (3.17)	19 (5.81)	3.538	0.060	7 (3.04)	21 (4.37)	8 (5.26)	1.231	0.540
Picky eating	153 (28.54)	106 (32.42)			56 (24.35)	163 (33.89)	40 (26.32)		
Pain sensitivity	116 (21.64)	86 (26.30)	2.458	0.117	33 (14.35)	120 (24.95)	49 (32.24)	17.776	<0.001***
Special events									
Increased exercise	242 (45.15)	183 (55.96)	9.502	<0.001***	88 (38.26)	248 (51.56)	89 (58.55)	17.402	<0.001***
Cold lower extremities	64 (11.94)	78 (23.85)			25 (10.87)	85 (17.67)	32 (21.05)		

Significant association, * $P < 0.05$, *** $P < 0.001$.

BMI, body mass index.

diminished BMD levels, may concurrently manifest a higher risk of reporting pain more frequently.

This investigation indicates that administering vitamins during pregnancy may be associated with a lower risk of suffering high-frequency growing pains. It is widely acknowledged that vitamins play a vital role in bone metabolism, contributing to improve BMD and bone mass, and

subsequently reducing the occurrence of growing pains.^{4,29} Javaid et al.²² found that maternal vitamin D supplementation during pregnancy was predicted to enhance greater childhood bone mass, providing a foundational basis for the hypothesis that maternal vitamin supplementation during pregnancy could lead to a subsequent reduction in the frequency of growing pains in children. Consequently, it is advisable to

follow the Chinese Dietary Guidelines for the Chinese population to routinely supply vitamins during pregnancy.⁴⁵

Bad temper is related to higher pain frequency according to the results, which is consistent with previous study.³⁶ It is widely recognized that the effect of pain and psychobehavioral problems are bidirectional for shared neuromechanism,^{19,52} and recurrent pain can result in maladaptive cognition and behaviors, increase psychological stress, and even exacerbate the pain itself.¹⁷ Acknowledging this, cognitive-behavioral therapy has been shown to effectively reduce pain intensity in children.^{7,13,27}

Moreover, take physical exercise for at least 60 minutes more than usual was recognized as a risk factor that may contribute to higher pain intensity, which conforms to previous studies.⁴² Researchers defined this phenomenon as the fatigue theory,³⁴ but few investigations evaluated this theory within the context of growing pains. Hence, an urgent imperative lies in conducting further trials that explore the correlation between physical exercise and growing pains. Cold exposure may cause musculoskeletal pain, which has been mentioned in several studies,^{11,12,15,26} a finding also supported by the results of this study. However, the mechanism behind cold-induced pain remains insufficiently established, and various explanations were suggested (eg, cold-induced vasospasm, reduced muscular blood flow induces ischemic nociceptive pain, ion channels).³¹ As such, self-reported cold lower extremities in children with growing pains deserve attention and further investigation.

4.3. Factors associated with pain intensity

The present data indicates that several factors were associated with pain intensity, some of which in the same aspect were linked to pain frequency as well. Younger age predicted a higher risk of suffering higher pain intensity. **Figure 2B** depicts the percentage of participants reporting severe pain diminished with increasing age. This may be partly explained by elder children possessing improved capacity³² and higher pain threshold, contributing to reporting lower pain intensity. Similar to our findings, a longitudinal study conducted in the United States revealed that children experiencing persistent growing pains exhibited notably lower pain thresholds compared with those whose pain resolved over a five-year period,⁴⁷ further supporting the relationship between pain intensity and age.

Aside from pain thresholds, pain sensitivity is also identified as an indicator of pain intensity, and children exhibiting higher pain sensitivity are more likely to report greater pain intensity. This study found that irritability was associated with an increased risk of higher pain intensity, corroborating previous articles highlighting the prevalence of psychological problems among children with growing pains.^{34,36,39} This study further affirms that irritability is a specific contributing factor. Researchers have demonstrated that physical exercise not only increases the frequency of growing pains but also increases the intensity.^{20,42} Hence, to develop strategies to mitigate pain intensity, elucidating the nature of the relationship between pain and physical exercise is the first step, so further trials focusing on physical exercise in children with growing pains are urgently needed.

As expected, vitamin supplementation during lactation is significantly related to lower pain intensity, and vitamin D supplementation can decrease the intensity of growing pains has been verified.^{21,49} But current research is constrained in examining the impact of vitamin D supplementation during lactation on growing pains. Similarly, for pain frequency, the causality of this significant association could not be addressed. Hence, planned longitudinal studies with high methodological

quality, large sample size, and long-term follow-up are imperative to elucidate whether maternal vitamin supplementation during pregnancy results in lower pain intensity of growing pains.

However, this study has several limitations as well. First, the information about the growing pains was retrospective, so bias may arise due to inaccurate recall. However, to mitigate recall bias, detailed information was collected regarding the circumstances when growing pains occurred. Second, although these children's hospital has an annual outpatient volume of 371,4470 nationwide, only a few patients in other provinces were included in this study, which limited the generalization of our findings at the national level. Nonetheless, the results can still offer reference to the children with growing pains in the Sichuan-Chongqing region to some extent. Third, no valid scale was used to assess children's psychobehavioral problems in this study, but the questionnaire was self-made based on the existing scale content, and experts were invited to evaluate the content validity, which was within an acceptable range. Fourth, investigators did not audit a proportion of patients to follow-up to ensure that an alternative diagnosis was not made at a later date, so misclassification may exist. However, growing pains is a diagnosis of exclusion, and orthopedics make a diagnosis after a comprehensive evaluation. In addition, eligible participants with potential alternative diagnoses were excluded during the selection, so misclassification has been avoided to the greatest extent possible under the existing conditions.

5. Conclusions

In summary, this study yielded 3 main findings. First, growing pains typically occur on a quarterly basis, predominantly affecting the knees and usually occur during 4 PM to 5 PM, with a moderate level of pain intensity. Second, pain frequency is negatively correlated with vitamin supplementation during pregnancy and positively correlated with underweight, bad temper, increased exercise, and cold lower extremities. Third, pain intensity positively correlated with irritability, increased exercise, and pain sensitivity but negatively correlated with age and vitamin supplementation during lactation. This study suggests that clinicians should be aware of multimorph manifestations of growing pains. By considering these related factors, healthcare professionals can formulate more targeted and effective pain management approaches to address each patient's unique needs, ultimately improving pain management and overall quality of life.

Disclosures

The authors have no conflict of interest to declare.

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References

- [1] Abu-Arafeh I, Russell G. Recurrent limb pain in schoolchildren. *Arch Dis Child* 1996;74:336–9.
- [2] Akal F, Batu ED, Sonmez HE, Karadağ Ş G, Demir F, Ayaz NA, Sözeri B. Diagnosing growing pains in children by using machine learning: a cross-sectional multicenter study. *Med Biol Eng Comput* 2022;60:3601–14.
- [3] Ali MA, Haque M, Islam MI, Rahman SA. Severity of growing pain in children and its association with vitamin D: a tertiary hospital study. *J Bangladesh Coll Physicians Surg* 2023;41:282–6.
- [4] Cao J, Cao Y, Wang Z. Relationship between serum 25-hydroxyvitamin D3 level and growth pain in children. *Hainan Med* 2020;31:1300–2.
- [5] Dovey TM, Staples PA, Gibson EL, Halford JC. Food neophobia and 'picky/fussy' eating in children: a review. *Appetite* 2008;50:181–93.
- [6] Duchamp R-G. *Maladies de la croissance*. Paris: Fain, 1823.
- [7] Enomoto K, Adachi T, Fujino H, Kugo M, Tatsumi S, Sasaki J. Comparison of the effectiveness of cognitive behavioral therapy for insomnia, cognitive behavioral therapy for pain, and hybrid cognitive behavioral therapy for insomnia and pain in individuals with comorbid insomnia and chronic pain: a systematic review and network meta-analysis. *Sleep Med Rev* 2022;66:101693.
- [8] Evans AM, Scutter SD. Prevalence of "growing pains" in young children. *J Pediatr* 2004;145:255–8.
- [9] Evans AM, Scutter SD. Development of a questionnaire for parental rating of leg pain in young children: internal validity and reliability testing following triangulation. *Foot* 2004;14:42–8.
- [10] Evans AM, Scutter SD, Lang LMG, Dansie BR. "Growing pains" in young children: a study of the profile, experiences and quality of life issues of four to six year old children with recurrent leg pain. *Foot* 2006;16:120–4.
- [11] Farbu EH, Höper AC, Reiherth E, Nilsson T, Skandfer M. Cold exposure and musculoskeletal conditions: a scoping review. *Front Physiol* 2022;13:934163.
- [12] Farbu EH, Skandfer M, Nielsen C, Brenn T, Stubhaug A, Höper AC. Working in a cold environment, feeling cold at work and chronic pain: a cross-sectional analysis of the Tromsø Study. *BMJ Open* 2019;9:e031248.
- [13] Fisher E, Law E, Dudeney J, Palermo TM, Stewart G, Eccleston C. Psychological therapies for the management of chronic and recurrent pain in children and adolescents. *Cochrane Database Syst Rev* 2018;9:Cd003968.
- [14] Friedland O, Hashkes PJ, Jaber L, Cohen HA, Eliakim A, Wolach B, Uziel Y. Decreased bone speed of sound in children with growing pains measured by quantitative ultrasound. *J Rheumatol* 2005;32:1354–7.
- [15] Ghani N, Tariq F, Javed H, Nisar N, Tahir A. Low-temperature health hazards among workers of cold storage facilities in Lahore, Pakistan. *Med Pr* 2020;71:1–7.
- [16] Glahn DC. Editorial: irritable imaging: interpreting null results in psychiatric neuroimaging. *J Am Acad Child Adolesc Psychiatry* 2023;62:130–2.
- [17] He Y, Guo X, May BH, Zhang AL, Liu Y, Lu C, Mao JJ, Xue CC, Zhang H. Clinical evidence for association of acupuncture and acupressure with improved cancer pain: a systematic review and meta-analysis. *JAMA Oncol* 2020;6:271–8.
- [18] Hestbaek L, Lucking A, Jensen ST. Growing pains in Danish preschool children: a descriptive study. *Sci Rep* 2024;14:3956.
- [19] Hooten WM. Chronic pain and mental health disorders: shared neural mechanisms, epidemiology, and treatment. *Mayo Clin Proc* 2016;91:955–70.
- [20] Horii M, Akagi R, Takahashi S, Watanabe S, Ogawa Y, Kimura S, Yamaguchi S, Ohtori S, Sasho T. Risk factors for the occurrence and protraction of patellar and patellar tendon pain in children and adolescents: a prospective cohort study of 3 years. *BMC Musculoskelet Disord* 2022;23:389.
- [21] Insaf AI. Growing pains in children and vitamin D deficiency, the impact of vit D treatment for resolution of symptoms. *J Hea Med Nurs* 2017;39:80–5.
- [22] Javaid MK, Crozier SR, Harvey NC, Gale CR, Dennison EM, Boucher BJ, Arden NK, Godfrey KM, Cooper C, Princess Anne Hospital Study Group. Maternal vitamin D status during pregnancy and childhood bone mass at age 9 years: a longitudinal study. *Lancet* 2006;367:36–43.
- [23] Kaspiris A, Zafiropoulou C. Growing pains in children: epidemiological analysis in a Mediterranean population. *Joint Bone Spine* 2009;76:486–90.
- [24] Le May S, Ballard A, Khadra C, Gouin S, Plint AC, Villeneuve E, Mâsse B, Tsze DS, Neto G, Drendel AL, Auclair MC, McGrath PJ, Ali S. Comparison of the psychometric properties of 3 pain scales used in the pediatric emergency department: visual analogue scale, Faces pain scale-revised, and colour analogue scale. *PAIN* 2018;159:1508–17.
- [25] Lehman PJ, Carl RL. Growing pains: when to be concerned. *Sports Health* 2017;9:132–8.
- [26] Lewis C, Stjernbrandt A, Wahlström J. The association between cold exposure and musculoskeletal disorders: a prospective population-based study. *Int Arch Occup Environ Health* 2023;96:565–75.
- [27] Li C, Hu P. Clinic research of cognitive-behavioral therapy on preschoolers with anxiety who need tooth therapy. *J Clin Stomatol* 2019;35:415–7.
- [28] Li H, Ji C, Zong X, Zhang Y. Body mass index growth curves for Chinese children and adolescents aged 0 to 18 years. *Chin J Pediatr* 2009;47:8.
- [29] Lin S, Chen Q, Shao Y, Qi J, Qian N, Lin W, Fan Y. Relationship among bone metabolic markers, bone mineral density and calcium, phosphorus, metal elements contents in bone tissue. *Chin J Osteoporos Bone Miner Res* 2017;10:513–8.
- [30] Liu H, Li X, Fang K, Wen J, Zeng M, Tang ZW, Li FL. Measurement and distribution of lower limb alignment in children with growing pains. *Chin J Pediatr Surger* 2014;35:944–8.
- [31] Lolignier S, Gkika D, Andersson D, Leipold E, Vetter I, Viana F, Noël J, Buserrolles J. New insight in cold pain: role of ion channels, modulation, and clinical perspectives. *J Neurosci* 2016;36:11435–9.
- [32] Lynch AM, Kashikar-Zuck S, Goldschneider KR, Jones BA. Sex and age differences in coping styles among children with chronic pain. *J Pain Symptom Manage* 2007;33:208–16.
- [33] Haque M, Kamrul L, Mohammed MI, Mohammad II, Manik KT, Shahana AR. Assessment of growing pain and its risk factors in school children. *Am J Clin Exp Med* 2016;4:151–5.
- [34] Naish JM, Apley J. "Growing pains": a clinical study of non-arthritis limb pains in children. *Arch Dis Child* 1951;26:134–40.
- [35] O'Keeffe M, Kamper SJ, Montgomery L, Williams A, Martiniuk A, Lucas B, Dario AB, Rathleff MS, Hestbaek L, Williams CM. Defining growing pains: a scoping review. *Pediatrics* 2022;150:e2021052578.
- [36] Oberklaid F, Amos D, Liu CY, Jarman F, Sanson A, Prior M. "Growing pains": clinical and behavioral correlates in a community sample. *J Dev Behav Pediatr* 1997;18:102–6.
- [37] Ouyang Y, Quan Y, Guo C, Xie S, Liu C, Huang X, Huang X, Chen Y, Xiao X, Ma N, Xie R. Saturation effect of body mass index on bone mineral density in adolescents of different ages: a population-based study. *Front Endocrinol (Lausanne)* 2022;13:922903.
- [38] Pathirana S, Champion D, Jaaniste T, Yee A, Chapman C. Somatosensory test responses in children with growing pains. *J Pain Res* 2011;4:393–400.
- [39] Pavone V, Lionetti E, Gargano V, Evola FR, Costarella L, Sessa G. Growing pains: a study of 30 cases and a review of the literature. *J Pediatr Orthop* 2011;31:606–9.
- [40] Peterson H. Growing pains. *Pediatr Clin North Am* 1986;33:1365–72.
- [41] Peterson HA. Leg aches. *Pediatr Clin North Am* 1977;24:731–6.
- [42] Picavet HSJ, Berentzen N, Scheuer N, Ostelo R, Brunekreef B, Smit HA, Wijga A. Musculoskeletal complaints while growing up from age 11 to age 14: the PIAMA birth cohort study. *PAIN* 2016;157:2826–33.
- [43] Ragnarsson S, Johansson K, Bergström E, Sjöberg G, Hurtig AK, Petersen S. Recurrent pain in school-aged children: a longitudinal study focusing on the relation to academic achievement. *PAIN* 2022;163:2245–53.
- [44] Thapar N, Benninga MA, Crowell MD, Di Lorenzo C, Mack I, Nurko S, Saps M, Shulman RJ, Szajewska H, van Tilburg MAL, Enck P. Paediatric functional abdominal pain disorders. *Nat Rev Dis Primers* 2020;6:89.
- [45] The Chinese Nutrition Society. The Chinese dietary guidelines. 2022. Available at <http://dg.cnsoc.org/article/04/hjgfcxa3Ra69sKbvqDEtbq.html>. Accessed August 2, 2023.
- [46] Türkdoğan D, Mahmudov R. Overlapping features of restless legs syndrome and growing pains in Turkish children and adolescents. *Brain Dev* 2022;44:372–9.

- [47] Uziel Y, Chapnick G, Jaber L, Nemet D, Hashkes P. Five-year outcome of children with "growing pains": correlations with pain threshold. *J Pediatr* 2010;156:838–40.
- [48] Uziel Y, Friedland O, Jaber L, Press J, Buskila D, Hashkes PJ. Living with children with growing pains: how does it affect the parents? *J Musculoskelet Pain* 2010;15:19–23.
- [49] Vehapoglu A, Turel O, Turkmen S, Inal BB, Aksoy T, Ozgurhan G, Ersoy M. Are growing pains related to vitamin D deficiency? Efficacy of vitamin D therapy for resolution of symptoms. *Med Princ Pract* 2015;24:332–8.
- [50] Wan G, Wei Z, He H, He M. Prevalence of emotional disorders in preschool children in Shenzhen. *Chin J Child Health Care* 2011;19:1077–9.
- [51] Xu J, Liu H. Current research on mechanism of growing pains. *J Clin Pediatr Surg* 2007:56–7, 64.
- [52] Yao C, Zhang Y, Lu P, Xiao B, Sun P, Tao J, Cheng Y, Kong L, Xu D, Fang M. Exploring the bidirectional relationship between pain and mental disorders: a comprehensive Mendelian randomization study. *J Headache Pain* 2023;24:82.
- [53] Yousuf HA, Quadir MEU. Risk factors and management of unexplained limb pain among growing children in a tertiary hospital. *J Armed Forces Med Coll Bangladesh* 2021;16:59–62.
- [54] Zhang Y, Ma S, Chen C, Liu S, Zhang C, Cao Z, Jiang F. Physical activity guidelines for Chinese children and adolescents. *Chin J Evid Based Pediatr* 2017;12:401–9.