Current Situation Analysis and Prospect of Precocious Puberty in Children at Home and Abroad Based on the Combination of Traditional Chinese and Western Medicine

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Abstract: *Objective*: To review the scientific research results of early puberty in children in the past decade, and to explore the current status, hot spots and frontiers of research in the field of early puberty in children. *Methods*: From January 1, 2014 to April 30, 2024, literature on early puberty in children was retrieved from CNKI database and Web of Science (WOS) core collection. CiteSpace6.3. R1 software was used for bibliometric analysis of authors, institutions and key words, and related visual maps were drawn. *Results*: A total of 1548 English literatures and 1113 Chinese literatures were included. The number of published papers in both Chinese and English showed an increasing trend. The authors of the high production in Chinese were Ye Jin and Yang Li, and the high production institutions were the pediatrics department of Hubei University of Chinese Medicine and Shuguang Hospital Affiliated to Shanghai University of Chinese Medicine. The authors are Latronico, Ana Claudia, and Universidade de Sao Paulo. Hot topics in Chinese and English studies include bone age, hormones, genetic inheritance, the correlation between precocious puberty and obesity and short stature. *Conclusion*: There is an increasing trend of research in the field of early puberty in children. The research on physical identification of children with precocious puberty and the dynamic detection of precocious puberty, height and obesity by Internet is worthy of continuous attention by domestic scholars.

Keywords: Precocious puberty; CiteSpace; Bone age; Growth and development; Sex hormones; Constitution of traditional Chinese medicine

1. Introduction

Precocious puberty (PP) is a pediatric endocrine condition characterized by the onset of menstruation before the age of ten years in girls and the development of secondary sexual features before the age of 7.5 years in boys [1]. According

to clinical epidemiological research, the incidence of premature puberty is rising year, and the developmental stage of children's puberty is progressively progressing globally [2]. In China, precocious puberty is also growing more common in youngsters, ranking as the second most common pediatric endocrine illness. Typically, females are more likely to have this condition than boys [3]. Children's sexual health services must be strengthened in accordance with the State Council's Program for the Development of Chinese Children [4]. Despite advancements in research, there remain issues and difficulties because of the intricacy of influencing components and variations in study methodologies. Thus, it is crucial to thoroughly examine the patterns and hotspots of early puberty in children both domestically and internationally.

2. Data and methods

2.1. Data sources and search methods

The SCI, SSCI, and WOS core databases provided the English data used in this investigation. This study obtained the full record of the retrieved data with the cited references, exported it in plain text format as the source of the data, and retrieved a total of 1548 documents. The search formula for the subject term search is as follows: ((((((TS = (Precocious Puberties)) OR TS = (Precocious Puberty)) OR TS = (Central Precocious Puberties)) OR TS = (Central Precocious Puberty)) AND DT = (Article)) AND LA = (English)) AND DOP = (2014-01-01/2024-04-30). A total of 1,578 academic papers were retrieved from the literature during the search period of January 1, 2014, to April 30, 2024. The Chinese data were obtained from the CNKI Journal Full Text Database, subject term search. The search formula used was: SU = (precocious puberty + precocious girls + central precocious puberty + idiopathic precocious puberty). Before the literature was exported, conferences and articles unrelated to childhood precocious puberty were manually excluded. In the end, 1117 documents were obtained and exported in Refworks citation format, serving as the data source. CiteSpace de-weighting was used to analyze the 1113 documents.

2.2. Data handling

The downloaded plain text file for this study is titled Download_*, and CiteSpace is used to locate, extract, and examine it.

2.3. Statistical methods

A literature visualization and analysis program called CiteSpace 6.3.R1 was utilized in this work to search for terms in the data. The trend of yearly publications in the literature was plotted using Excel.

3. Research status

3.1. Analysis of the amount of publications

There is a generally fluctuating, rising trend in the number of published studies on PP, both domestically and globally. China, in comparison with other countries, has a very small body of literature on the management of child health, but it is expanding. Due to the literature collection as of April 30, 2024, there is a decreasing trend in the number of publications in 2024. In 2022, there were 197 publications in the English-language literature, while in 2023, there were 155 publications in China. Trends in the number of articles issued are shown in **Figure 1**.
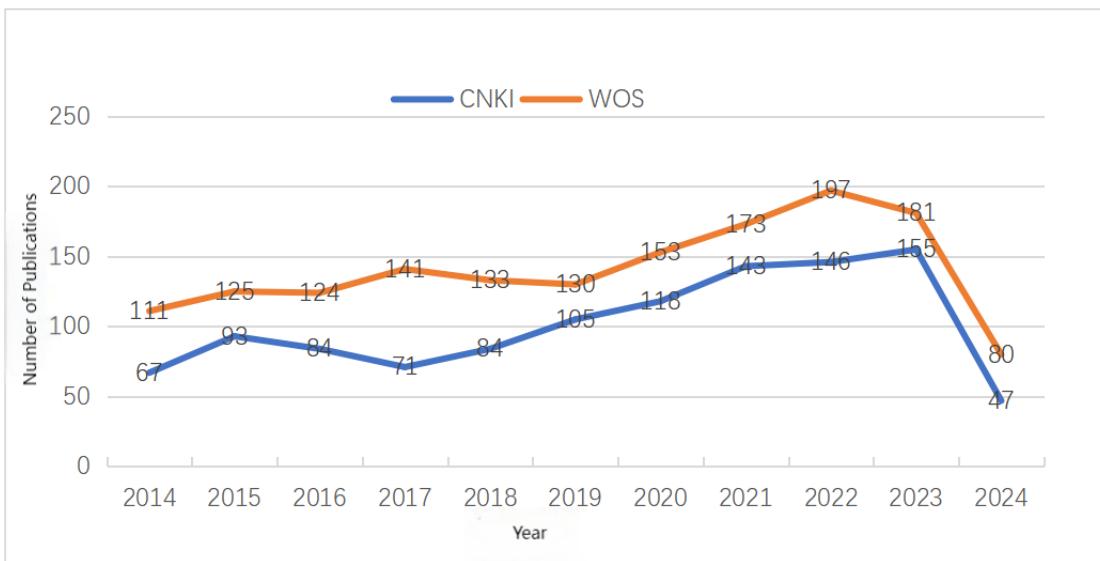
Figure 1. Number of domestic and international publications each year in the subject of child premature puberty.

3.2. Institution and author collaboration network

The data in **Table 1** and **Figure 2** demonstrates that the top 10 domestic organizations in terms of publications published 51 documents total, which accounts for 4.58% of the Chinese literature, while the top 10 foreign organizations in terms of publications published 370 documents total, accounting for 23.90% of the English literature. Ye Jin and Yang Li, who have the most publications, have each published eight articles. A core author group has not yet been formed, and the number of core authors who obtained three or more publications was 35 out of 162 total publications, or 27%. This suggests that the percentage of authors with higher publication volume is small and that there is not a strong bond between authors. This implies that there is a low percentage of authors with a high volume of publications, that there is not a strong bond among authors, and that there is no core group of authors. Of them, Yang Li's team at Jiangxi Children's Hospital's Department of Laboratory Medicine has published up to 44 articles. This team is the core for research on gene polymorphisms, the early development of precocious puberty girls' breasts, and the relationship between environmental endocrine disruptors and the clinical and regression of precocious puberty in children [5,6]. In the English literature, Ana Claudia Latronico has published the most, with 19 works. The group's primary focus is on Latronico, while Ana Claudia primarily studies the genetic mechanisms of genes and regulatory factors in children who experience early puberty [7,8]. There is a total of 28 core authors with ≥ 5 articles, accounting for 231 articles, or 28.1% of all articles. 28.1% of all articles, suggesting even more concentration on the part of English literary writers.

Table 1. Volume of publications by major domestic and international organizations

Number	Chinese		English	
	Organization Name	Number of posts	Organization Name	Number of posts
1	Hubei University of Chinese Medicine	8	Universidade de Sao Paulo	46
2	Department of Pediatrics, Shanghai University of Traditional Chinese Medicine Affiliated Shuguang Hospital	8	Harvard University	44
3	Heilongjiang University of Chinese Medicine	5	Universidade Estadual Paulista	41
4	Department of Laboratory Medicine Jiangxi Children's Hospital	5	Universite Paris Cite	40
5	Department of Pediatrics, Ruijin Hospital Affiliated to Shanghai Jiao Tong University School of Medicine	5	University of California System	38
6	The Children's Hospital of Fudan University	4	Assistance Publique Hopitaux Paris (APHP)	37
7	Shanghai Municipal Hospital of Traditional Chinese Medicine Affiliated to Shanghai University of Traditional Chinese Medicine	4	Shanghai Jiao Tong University	36
8	Department of Pediatrics, Yueyang Hospital of Integrated Traditional Chinese and Western Medicine, Affiliated to Shanghai University of Traditional Chinese Medicine	4	Institut National de la Sante et de la Recherche Medicale (Inserm)	36
9	Nanjing University of Chinese Medicine Affiliated Hospital	4	Harvard Medical School	32
10	Department of Pediatrics, Affiliated Hospital of Nanjing University of Chinese Medicine	4	Huazhong University of Science & Technology	20
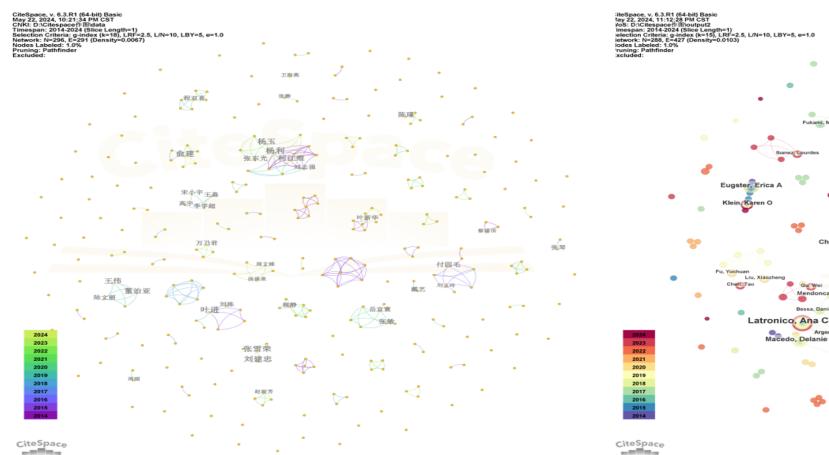
Figure 2. Graph of collaborative relationships between domestic and foreign authors.

The number of institutional publications can be used to determine the distribution of research power (**Figure 3**). The Universidade de São Paulo institution has the most publications out of the 270 research institutes in the English literature. Harvard University's main research group serves as the institution's focal point. The Department of Pediatrics at Shuguang Hospital, affiliated with Shanghai University of Traditional Chinese Medicine, is the main core research group in the Chinese literature. These organizations reflect a specific area of research that focuses on children's early puberty.

Figure 3. Graph of collaborative relationships between domestic and foreign institutions.

3.3. Keyword co-occurrence analysis

The higher the frequency of keyword occurrences, the more relevant they are in this research field in **Figure 4**. The top fifteen keywords (**Table 2**) in Chinese were precocious puberty, girls, children, sex hormones, puberty, precocious puberty, treprostinil, growth and development, vitamin D, risk factors, growth hormone, diagnosis, ovary, bone age, and leuprolide. The frequency threshold of keywords in the foreign literature were PP, central precocious puberty (CPP), children, girls, age, diagnosis, and treatment were among the top 15 keywords (**Table 2**), along with growth, final height, expression, menarche, mutations, body mass index, adult height, luteinizing hormone (LH), and sexual precocity.

One method to gauge an element's significance is by contemplating its centrality. An element is deemed highly important if its centrality is above 0.1. Keywords with a high frequency of occurrence do not always translate into high centrality in the keyword co-occurrence network, according to the investigation.
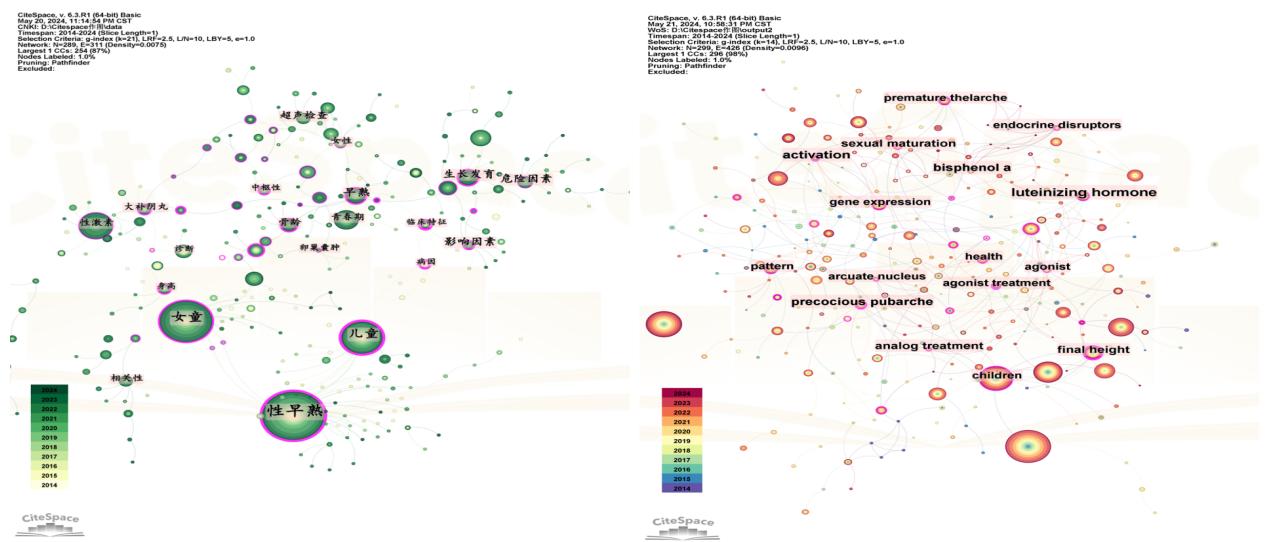
Figure 4. Keywords co-occurrence map of English and Chinese publications.

Table 2. Keywords, centrality, and frequency statistics on children's early puberty

Number	Chinese			English		
	Frequency	Centrality	Keyword	Frequency	Centrality	Keyword
1	313	0.56	precocious puberty	488	0.04	precocious puberty
2	231	0.36	girls	319	0	central precocious puberty
3	151	0.51	children	294	0.12	children
4	103	0.19	sex hormone	210	0.01	girls
5	58	0.04	adolescence	180	0.01	age
6	41	0.37	precocious	155	0.03	diagnosis
7	36	0.06	Triptorelin	149	0.03	growth
8	31	0.34	growth and development	96	0.28	final height
9	31	0.02	vitamin D	91	0.06	expression
10	30	0.14	risk factors	86	0.08	menarche
11	30	0.1	growth hormone	78	0.06	mutations
12	28	0.09	diagnose	75	0.11	body mass index
13	27	0.03	ovary	69	0.06	adult height
14	26	0.24	bone age	69	0.19	luteinizing hormone
15	26	0.11	Leuprorelin	65	0.05	sexual precocity

3.4. Keyword clustering analysis

By using cluster analysis, we can learn about the characteristics of research on precocious puberty in children at different times (**Figure 5**). In the Chinese literature, eleven clustering areas are displayed, and the associated clustering results can be broadly divided into three categories: clinical research, symptomatic research, and mechanism research. The clustering identity document (ID) numbers #1, #3, #6, and #8 primarily concentrate on "clinical research," while #5 represents multidisciplinary collaboration in the use of TCM to treat children. The youngsters can be treated with TCM using a multidisciplinary approach. In the foreign language literature, of the 11 clustering areas, #0, #1, #2, and #9 primarily represent "clinical research," #3 and #4 represent common symptoms, which are also pressing problems that need to be resolved, and #6, #7, #8, and #10 examine the disease's occurrence and treatment mechanism from the standpoint of biohormones and other factors.
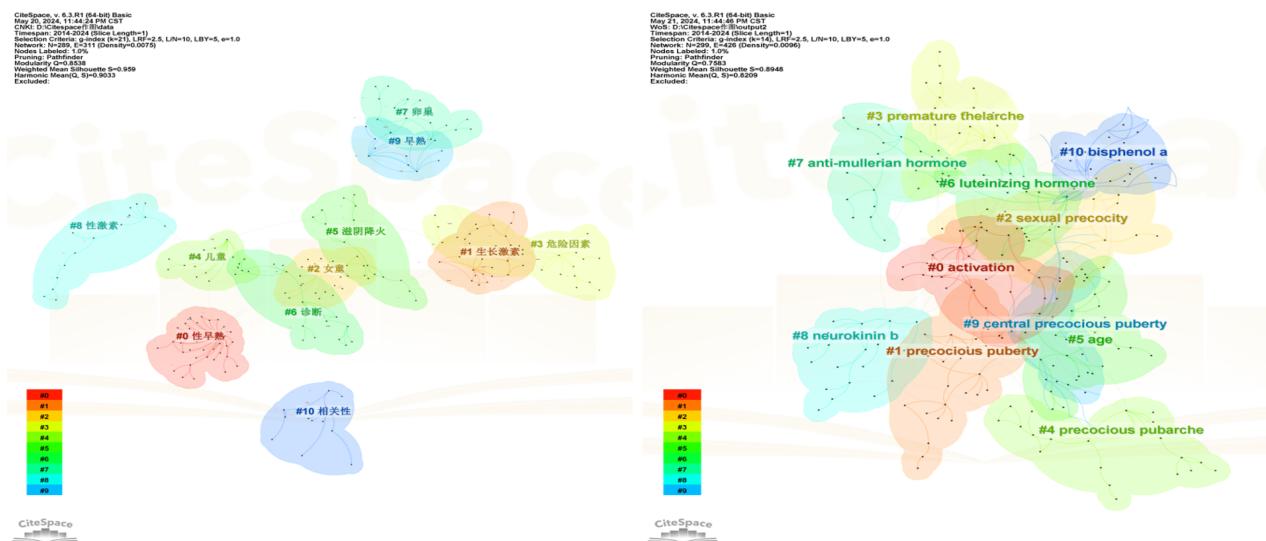

Figure 5. Keywords clustering map of English and Chinese publications.

3.5. Keyword emergence analysis

There were 25 emerging terms in each of the years 2014–2024 based on an analysis of keyword emergence in the field of premature puberty research conducted both domestically and internationally (**Figure 6**). The terms "sex hormone" (5.85) and "vitamin D" (3.74), respectively, emerged with the greatest intensity in the Chinese literature. Hot terms like "depression" and "nourishing yin and reducing fire" emerged in this field of study at this time. The terms "bone age" (5.58), "overweight" (3.74), "bone marrow" (5.85), and "overweight" (5.85) were the most often occurring terms in the foreign language literature. "Too heavy" (4.73). Popular terms like "genome-wide association," "short stature," and "insulin resistance" emerged in this field of study during this time.

Top 25 Keywords with the Strongest Citation Bursts

Keywords	Year	Strength	Begin	End	2014 - 2024
treatment	2014	3.1	2014	2016	
infant	2014	2.27	2014	2015	
depression	2014	1.82	2014	2018	
diagnose	2014	3.22	2015	2017	
etiology	2015	2.72	2015	2016	
efficacy	2015	2.16	2015	2017	
differential diagnosis	2015	1.88	2015	2016	
Da-Bu-Yin-Wan	2015	1.98	2016	2018	
uterine volume	2016	1.96	2016	2017	
vitamin D	2017	3.74	2019	2020	
review	2019	3	2019	2020	
treatment outcomes	2019	2.11	2019	2021	
triptorelin	2014	1.55	2019	2021	
leptin	2020	2.02	2020	2021	
lipid metabolism	2020	1.74	2020	2021	
ultrasound	2014	1.82	2021	2022	
Zi Yin Jiang Huo	2021	1.64	2021	2022	
adiponectin	2021	1.64	2021	2022	
sex hormone	2014	5.85	2022	2024	
bone age index	2018	2.73	2022	2024	
diagnostic value	2022	2.58	2022	2024	
pelvic ultrasound	2018	2.3	2022	2024	
bone age	2014	1.95	2022	2024	
follicular size	2022	1.62	2022	2024	
adverse effects	2015	1.56	2022	2024	

Top 25 Keywords with the Strongest Citation Bursts

Keywords	Year	Strength	Begin	End	2014 - 2024
secretion	2014	4.47	2014	2015	
breast cancer	2014	4.03	2014	2015	
follicle stimulating hormone	2014	3.85	2014	2016	
body composition	2014	3.66	2014	2015	
adolescent girls	2014	3.25	2014	2015	
features	2014	3.25	2014	2015	
assays	2015	3.88	2015	2017	
missense mutation	2016	4.64	2016	2017	
gene	2014	3.75	2016	2017	
premature adrenarche	2016	3.61	2016	2017	
insulin resistance	2016	3.57	2016	2017	
genome wide association	2016	3.48	2016	2019	
imprinted gene mkrn3	2017	4.14	2017	2018	
adolescents	2014	3.69	2017	2018	
cyproterone acetate	2017	3.62	2017	2018	
in utero	2018	3.39	2018	2020	
mechanisms	2018	3.26	2018	2021	
bone mineral density	2015	4.5	2019	2020	
quality of life	2019	3.26	2019	2021	
short stature	2014	4.34	2020	2021	
estradiol	2016	3.65	2020	2021	
genetics	2020	3.46	2020	2021	
bone age	2021	5.58	2021	2022	
overweight	2021	4.73	2021	2024	
secular trends	2015	3.41	2022	2024	

Figure 6. Visualization graph of emergent words.

4. Discussion

4.1. Analysis of annual publication volume and author organization distribution

Based to the trend of annual publication growth, pertinent studies in the area of children's premature puberty is still intensifying, indicating that this area will continue to be a research hotspot in the years to come. Even though there exist a number of more visible author cooperation groups in this field, they are largely independent of one another and do not communicate or cooperate well enough, which suggests that research teams should improve their communication and cooperation in order to jointly advance the in-depth study of children's untimely puberty. Simultaneously, we can observe the disparity between the quantity of literature published domestically and internationally, with comparatively few high-yield creators and institutions and a little deficiency of domestic literature compared to foreign countries.

4.2. Keyword co-occurrence and cluster analysis

The clinical management of premature puberty and biological mechanism study are the primary areas of attention for research hotspots in China related to precocious puberty in children. The primary focus of clinical research is on risk factors, TCM evidence-based treatment, the efficacy and safety of medication therapy, and the foundation of diagnosis in both Chinese and Western medicine [9–11]. Gene regulation (such as the imprinted gene MKRN3), the neuroendocrine axis, the hypothalamic-pituitary-gonadal axis (HPGA) and the regulation of reproductive system development through the feedback of endocrine hormones like Kisspeptin neurokinin B, leptin,

testosterone, and other endocrine hormones are the main areas of focus for biological mechanism research [12–14]. In addition to studying related clinical symptomatic manifestations (e.g., precocious breasts, precocious pubic hair, menarche, etc.), diagnostic and therapeutic approaches (e.g., activation, agonist therapy, etc.), gene mutations, and genetic mechanisms of regulatory factors, foreign studies have become more varied, paying more attention to the body mass index and final height of children with precocious puberty.

4.3. Keyword emergence analysis

Research on early puberty in children has focused on bone age, pelvic ultrasonography, psychological state, and correlation with short height and overweight, according to an analysis of emerging phrases. Girls' uterine development is evaluated by pelvic ultrasonography, which is useful for clinical diagnosis. Research on early puberty in children has focused on bone age, pelvic ultrasonography, psychological state, and correlation with short height and overweight, according to an analysis of emerging phrases. Girls' uterine development is evaluated by pelvic ultrasonography, which is useful for clinical diagnosis [15]. According to an analysis, GnRHa, including treprostinil, leuprolide, and other medications, are the most commonly used by domestic researchers to treat PP. Some studies have found a correlation between vitamin D levels and the effects of GnRHa treatment [16]. Yet the exact mechanism by which vitamin D deficiency causes premature puberty in children is still unclear, and more research is required. Studies conducted abroad have focused more on how body composition, neurokinin B, LH, anti-Müllerian hormone (AMH), and bisphenol A affect the regulation of precocious puberty. A multifaceted viewpoint for the in-depth investigation of the pathophysiology of premature puberty is offered by the interaction mechanism of these regulators and their connection to PP.

5. Research hot spots and prospects

5.1. CPP

Pathogenesis of CPP:the precise processes underlying the early onset of HPGA function have been the subject of research, particularly the pulsatile secretion of GnRH and its regulatory mechanisms. Studies on the safety, effectiveness, and long-term follow-up outcomes of GnRHa therapy have gradually increased in recent years [10,17,18]. In order to improve therapy outcomes, researchers are investigating the best time and dose for GnRHa medication. The predictive value of the diagnosis of CPP in girls is improved when pelvic ultrasonography and bone age are combined. Other findings include the following: urine GnRH and urine LH testing may be an alternative to traditional serum LH testing; morning urine LH has a better predictive significance for the diagnosis of CPP; urine sampling is also more acceptable than continuous blood sampling; and so on [27]. However, there aren't enough high-caliber, multicenter, large-sample studies to confirm its accuracy and dependability. Future clinical research can further enhance and improve these noninvasive diagnostic methods.

5.2. TCM treatment

PP belongs to the category of "breast lump", "pre-menstrual period" and "early sprouting of heavenly decadence" in Chinese medicine. Children are the body of young yin and young yang, which makes it easy for the balance of yin and yang to be out of balance, and the deficiency of the kidney and the liver to be exuberant, leading to "early sprouting of the deca". In Chinese medicine, the diagnosis is mostly based on the Zang–fu organs, mainly involving the kidney, liver, and spleen [9]. The internal and external treatments of Chinese medicine can

significantly slow down the growth of children's bones and increase the expected height. Internal treatment mainly includes nourishing yin and supplementing the kidney (Zhi Bai Di Huang Pill, Da Tonic Yin Wan, etc.), detoxifying the liver and relieving depression (Chai Hu Shugan Powder, Danzhi Xiaoyao Pill, Longdan Xiegan Decotion as the representative formula), and resolving phlegm and dispersing knots (strengthening the spleen and dispersing dampness as the method), while external treatment includes auricular acupoints pressure and tuina method. The combination of internal and external treatments with TCM constitution treatment based on syndrome differentiation has achieved significant clinical efficacy and good safety [9,11].

Chinese medicine is not only gentle, non-invasive, and safe, but also focuses on the overall concept of TCM, which believes that different regions, the environment, and other factors can lead to differences in children's physique, and the different physique of an individual determines his or her susceptibility to certain diseases and tendency to certain TCM certificates [20,21]. As a result, patients should get therapy based on the various constitutions of the syndrome differentiation. TCM is currently making some strides in understanding the physical characteristics of children who experience early puberty. The fact that some kids still struggle to recognize and address them is still an issue, though. To provide a scientific foundation for the creation of a more individualized treatment plan, researchers can further examine the physical characteristics of children who experience early puberty in the future, particularly the identification of the Chinese medicine physique of children with Pingqi parts of the body [11]. TCM also focus on the guidance of living habits during the treatment process. Though there is a dearth of high-quality studies and clinical research evidence, TCM has some effectiveness in treating premature puberty. More multi-center randomized controlled studies will be carried out in the future to investigate the mechanism of action and confirm its safety and effectiveness.

5.3. Digital informatization

In the area of managing a child's sexual development, we may offer information more accurately and effectively by using the Internet or artificial intelligence (AI). For instance, using the online platform or AI assistant before the consultation to educate yourself on the child's sexual development symptoms, potential issues, and the causes and consequences of any tests or medications the doctor may prescribe later. Furthermore, it is possible to create a platform for health management that is more organized. For instance, WeChat groups are used for regular Q&A sessions; small programs are used for real-time dynamic monitoring of children's growth and development; and public figures are used to disseminate pertinent information, such as the signs of premature puberty, how it progresses, and how it affects children's height. Precocious puberty in children is influenced by a variety of circumstances, and our comprehensive, individualized health management service allows for intervention and life management to better support children's healthy development [22].

5.4. Adult height and obesity

The issues of height and obesity in adults are intimately linked to PP in childhood [23]. A child's height and bone growth are impacted by premature puberty, and girls may experience despair and low self-esteem as a result of these physical changes. Obesity and PP also interact to cause less-than-ideal height [24]. PP may make the obesity issue worse, and excessive adiposity in obese children raises the release of leptin from adipocytes, which may cause the HPGA to be activated too soon [25]. While the current treatment approaches are successful, they have significant drawbacks and adverse effects, thus future research into safer, more cost-effective, and more efficient medications or therapies is important.

5.5. Environmental factors

The findings of several domestic and international research show that environmental variables, particularly short-term exposure to air pollution, are linked to early puberty in children, particularly in females [26,27]. For instance, long-term exposure to BPA, significantly increases the risk of precocious puberty in children, particularly in the girl population [28]. The increased incidence of precocious puberty in children during the epidemic may be related to changes in children's lifestyles (e.g., decreased time spent outdoors, increased time spent on electronic screens, and changes in dietary habits), supporting the idea that the environment has an impact on precocious puberty [29].

5.6. Intestinal flora

Although the mechanism of the reciprocal changes in the sexually dimorphic nature of the human intestinal flora has not yet been accurately reported, sex hormone levels may be linked to the intestinal flora, which has been found to be influenced by sex hormone levels during puberty, even producing sex-specific flora [30]. It may also influence central nervous system components involved in the regulation of puberty [31]. Future research might investigate the role of gut flora in the pathophysiology of precocious puberty in order to potentially prevent and cure premature puberty, such as by the use of specialized probiotic treatment, as the precise mechanism by which gut microbiota affects HPGA is yet unclear.

5.7. Gene therapy

Early puberty has been linked to epigenetic changes and mutations in certain genes. Developmental issues have also been linked to EZH1 gene loss of function, and the synergistic effects of multiple mutated genes in the gene network can also affect the initiation of pubertal development [32,33]. The use of gene therapy in the treatment of premature puberty is growing more and more promising as gene monitoring technology advances. In the future, it may be used to precisely cure precocious puberty. For instance, repairing damaged genes, identifying gene targets, creating medications for gene therapy, etc.

6. Conclusion

Children who have precocious puberty have a complicated endocrine condition. Multidisciplinary collaboration, individualized comprehensive interventions, precision medicine, and the use of safe, noninvasive technologies are some of the traits of this field's research trends. Future research should examine the potential and safety of new technology in the study of precocious puberty, as well as the continuous developments in gene therapy and traditional Chinese medicine treatments.

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Disclosure statement

The authors declare no conflict of interest.

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