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Informing, Preparing, and Training are the Key to Overcoming Precocious Puberty in Children: A Lesson from the Experiences of Mothers

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Abstract

Background: Precocious puberty is associated with worries and challenges for affected children and their mothers as primary caregivers. The present study aimed to explore mothers› experiences of their children›s precocious puberty.

Methods: The data in this qualitative-descriptive phenomenological study were collected through semi-structured interviews. The mothers with female and male children who experienced puberty before age 8 or 9 were selected through purposive sampling in Tehran in 2023. Data saturation was achieved after interviewing 25 mothers. The collected data were analyzed using Colaizzi's seven-step method.

Results: The mothers' experiences of their child's precocious puberty were categorized into four main themes including "extreme surprise and confusion", "precocious puberty, a developmental period or a disease?", "mothers' self-imposed isolation", and "informing, preparing, and training parents as the key to overcoming precocious puberty".

Conclusion: Seeking assistance from doctors, nurses, midwives, and health counselors, reading related books, and using new information to understand puberty can enhance the patience and tolerance of mothers to help their children overcome the challenges associated with precocious puberty.

Keywords: Lived experiences, Mothers, Precocious puberty, Children

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Introduction

Puberty is defined as the period of full growth or development, encompassing biological, social, and cognitive changes in an individual (1). The standard age of puberty is from 8 to 13 years for girls and 9 to 14 years for boys (2-3). However, some children experience precocious puberty.

Precocious puberty happens when children's bodies turn into adults' bodies very quickly. It most often occurs before the age of 8 in girls and before the age of 9 in boys (3-4). There are two types of precocious puberty: (1) Central precocious puberty, which is the most common type. It resembles natural puberty but occurs early. In this case, the pituitary gland starts to produce hormones called gonadotropin. These hormones cause the testicles or ovaries to make other hormones like testosterone or estrogen. These sex hormones cause puberty changes such as breast growth in girls (3,5). (2) Peripheral precocious puberty, also known as pseudo-precocious puberty, is less common. Estrogen and testosterone cause some symptoms, but the brain and pituitary gland are not involved. It is usually a local problem in the ovaries, testicles, or adrenal glands (2,6,7). Precocious puberty can manifest in various signs and symptoms such as breast growth and the onset of menstruation in girls as well as the growth of the testicles, penis, and facial hair and a deeper voice in boys. Other symptoms may include the emergence of pubic or armpit hair, rapid growth, acne, and adult body odor (3,7-8).

Precocious puberty leads to several complications in children. One of these complications is short stature. Although children with precocious puberty may experience rapid initial growth and appear taller than their peers, their bones mature quickly, often resulting in earlier cessation of growth. Consequently, these children may end up shorter than average in adulthood. Social and emotional problems are other complications of precocious puberty among children with precocious puberty. Those who enter puberty significantly earlier than their peers may get upset by their physical changes, leading to

discomfort and potential impacts on self-esteem. This can increase the risk of depression and alcohol or substance abuse (1,6). Furthermore, as puberty ends, height growth stops. Due to accelerated skeletal maturation, untreated precocious puberty often limits a child's potential adult height (9). Although the growth spurt may make them initially taller than their peers, their growth may stop very soon, resulting in a shorter final height than expected (7). Precocious puberty can also be emotionally and socially challenging for children. For example, girls who experience precocious puberty may feel confused or embarrassed about experiencing menstruation or breast enlargement before their peers (1). This may be because they are treated differently as they look older than they are. It is even possible for children's emotions and behavior to change with precocious puberty (10). Girls may become moody and irritable. Boys can become more aggressive and develop sexual desires not fitting their age (11). The reactions of parents, especially mothers, as the main caregivers, can significantly affect the child's psychological conditions and moods. It is easy for mothers to worry about precocious puberty (12).

While mothers should take any symptoms seriously, they need to remember that symptoms that may seem like precocious puberty are often unrelated and they resolve by themselves. When treatment is necessary, it usually works well. Most children with symptoms of precocious puberty function well medically, psychologically, and socially (13). Precocious sexual maturity is a very important issue that preoccupies many parents, children, and therapists today and has been taken into consideration as one of the concerns of parents and children in the growing age (14).

Given the current social changes, technological developments, and the accessibility of films and websites for children, there is a growing need to address precocious puberty and its impacts. This study explored the real and lived experiences of mothers to more closely examine precocious puberty in children as an important issue affecting children's mental health and physical development. Accordingly, the present study aimed to explore the experiences of mothers of children with precocious puberty.

Methods

Using a qualitative and descriptive phenomenological approach, this study examined the lived experiences of mothers of children with precocious puberty to come up with a deep understanding of this phenomenon. The participants were mothers of 8-year-old girls and 9-year-old boys living in Tehran. Participants were selected through purposive sampling, which continued until the studied phenomenon was sufficiently explained and rich data were obtained. The inclusion criteria were: (1) mothers having children with precocious puberty and (2) precocious puberty being diagnosed by pediatricians or endocrinologists. Data were collected through semi-structured interviews. Sample interview questions included, "What was your experience with your child's early puberty?" and "Can you give an example?"

Before starting each interview, the researcher introduced herself and the subject in question. The interviewer held a master's degree in family counseling and worked as a school counselor for more than five years. The interviews were conducted in the counseling room at the school. The first interviewee was a mother whose daughter had experienced precocious puberty and had sought counseling for her child's communication problems with other students.

Participants completed an informed consent form before the interview, which was scheduled by appointment. After the end of each interview, the participants' contact numbers were taken to verify the reliability of the interviews or for follow-up purposes. Each interview lasted 45 to 60 minutes. The interviews were conducted from March 2023 to September 2023 in Tehran. At the end of each interview, the recorded interviews were transcribed for subsequent coding and analysis. The participants' demographic data are presented in Table 1. Once data saturation was reached, the findings were reviewed by three professors specializing in nursing, midwifery, and psychology to confirm the adequacy of the collected data.

The data from the interviews were analyzed using Colaizzi's seven-step content analysis method (15). The researcher listened to the recorded statements of the participants, transcribed the content of the interviews word by word on paper, and read them several times to understand the participants' feelings and experiences. Then, the significant statements related to the phenomenon in question were underlined. The themes underlying the significant statements reflecting the participants' ideas were extracted. The extracted themes were checked to ensure they were related to the participants' statements. The extracted themes were reviewed carefully and similar themes were placed in the same category. Thus, the themes formed thematic clusters. Then, the extracted categories were merged into more general categories. A thorough description of the phenomenon in question was developed. Finally, the data and findings were validated by asking the participants to review and confirm them. Furthermore, the findings were reviewed by three university professors experienced in phenomenological research, health and midwifery, nursing, and mental health counseling. Moreover, the credibility of the data was confirmed by engaging the participants in interpreting the findings and describing the procedures for data collection and analysis, allowing others to understand and assess the findings.

Results

The participants in the present study were 25 mothers of

Table 1. The mother's demographic information

Number	Age	Education	Occupation	Number of children	Birth order	Child gender	Puberty age
1	37	Bachelor's degree	Employee	2	First	Female	7 (Menarche age)
2	32	Bachelor's degree	Secretary	2	First	Male	9
3	33	Diploma	Housewife	1	First	Female	7 (Menarche age)
4	33	Associate's degree	Barber	2	Second	Male	9
5	30	Bachelor's degree	Housewife	1	First	Female	7 (Menarche age)
6	38	Master's degree	Employee	2	Second	Male	7
7	33	Diploma	Housewife	2	First	Male	8
8	35	Associate's degree	Housewife	3	Third	Male	8
9	30	Bachelor's degree	Employee	1	First	Female	7 (Menarche age)
10	33	Master's degree	Teacher	2	First	Female	8 (Menarche age)
11	29	Bachelor's degree	Kindergarten teacher	1	First	Female	7 (Menarche age)
12	31	Diploma	Hairdresser	2	First	Female	8 (Menarche age)
13	33	Master's degree	Employee	2	Second	Male	9
14	35	Bachelor's degree	Teacher	1	First	Male	9
15	29	Bachelor's degree	Legal consultant	1	First	Male	7
16	28	Bachelor's degree	Hairdresser	1	First	Female	8 (Menarche age)
17	30	Bachelor's degree	Housewife	1	First	Male	9-8
18	33	Bachelor's degree	Hairdresser	2	Second	Female	7 (Menarche age)
19	37	Master's degree	Employee	2	First	Male	7
20	27	Diploma	Housewife	1	First	Female	8 (Menarche age)
21	25	Bachelor's degree	Graphic designer	1	First	Male	7
22	33	Bachelor's degree	Teacher	2	Second	Male	7
23	29	Diploma	Hairdresser	1	First	Female	7 (Menarche age)
24	31	Bachelor's degree	Photographer	2	First	Male	8
25	28	Bachelor's degree	Pharmacy clerk	1	First	Female	7 (Menarche age)

Data analysis revealed four main themes, eight subthemes, and 31 primary categories. The main themes and subthemes are introduced first. Then, for each subtheme, primary categories are provided separately along with a sample of participants' quotes.

children with precocious puberty as detailed in Table 1. Table 2 presents the categories, themes, and subthemes derived from interviews conducted with mothers of children diagnosed with precocious puberty.

Theme 1: Extreme surprise and confusion

Data showed that mothers experienced extreme surprise and confusion, which stemmed from their sudden encounter with their child's precocious puberty and the confusion surrounding their maternal roles.

A. Confusion about maternal duties

Anxiety and fear

Participants reported significant anxiety regarding their child's condition. One mother expressed, "*I have two older daughters and I didn't know anything about early puberty. I was extremely anxious and worried about what I should do about this problem and I felt confused*" (Participant 24)

Unawareness of precocious puberty

Mothers conveyed feelings of confusion due to their lack of knowledge. A participant noted, "*Not knowing what to do about these problems was very annoying because I did not know exactly how to treat my daughter*" (Participant 1).

Feelings of inefficiency and powerlessness

Participants described feelings of inefficiency and inability to perform their maternal duties. A participant stated, "*My most important problem was that I really didn't know what to do and what not to do about this problem. Because my two older children were girls and they experienced their puberty at the normal age, I had no experience with it and this confused me*" (Participant 8).

Lifestyle changes

Participants stated that they were forced to change their living and career plans. A mother said, "*I had a lot of anxiety. I was constantly getting information about precocious puberty in girls, and I could not concentrate much on my work, and as school officials kept asking me to go to school about my daughter's issues, I had to take a leave from my workplace*" (Participant 21)

B. Mother's sudden encounter with the child's precocious

Table 2. The categories, themes, and subthemes extracted from interviews with Mothers of Precocious Puberty Children

Primary categories	Subthemes	Main themes
Anxiety and fear	Confusion about maternal duties	Extreme surprise and confusion
Unawareness of precocious puberty		
Feelings of inefficiency and powerlessness		
Lifestyle changes		
Fear of lasting psychosocial effects of puberty	Mother's sudden encounter with the child's precocious puberty	
Confusion in answering the child's sexual questions		
Ambiguity in understanding the boundary between childhood and adolescence		
Feeling ashamed of looking different	Child's psychological/physical reactions	Precocious puberty, a developmental period or a disease?
Disgust with face and body image		
Extreme aggression		
Peer ridicule	School/peer challenges	
Tendency to isolation and avoidance		
Bullying and disobedience		
School avoidance		
Academic failure		
Peer rejection		
Curiosity and frequent questions	Social stigma and unfair judgments	Mother's self-imposed isolation
People's fear of their child contracting a contagious or incurable disease		
Shameless judgments		
People's fear of the negative effects of precocious puberty on their children		
Blaming the mother for not doing her role as a mother	Isolation of mother and child	
Mother's avoidance of relatives		
Seeking help from the doctor and school counselor	Educating parents as a life-saving option	Informing, preparing, and training parents as the key to overcoming precocious puberty
Using the Internet and reading useful books		
The need to educate parents to understand adulthood		
Psychological and social support for the child	Support as the key to success	
Appeal to patience and tolerance		

puberty

Fear of lasting psychosocial effects of puberty

Mothers expressed surprise and confusion upon realizing their child's precocious puberty. A mother said, "*My son had suddenly gone out of his childhood state, and he did not understand what was happening to him. He became aggressive and had many conflicts with us"* (Participant 2).

Confusion in answering the child's sexual questions

Mothers reported that their children asked many sexual questions but they did not know how to answer them. A mother said, "*My most important problem was answering some of my daughter's questions that were mostly sexual questions because I was afraid that I would have a worse negative effect on her*" (Participant 12).

Ambiguity in understanding the boundary between childhood and adolescence

Mothers had difficulty understanding the boundary between childhood and adolescence. A mother said, "*My son's early physical development made him feel that he has grown up and should be in contact with adults and behave independently, and he was still dependent on the help from his father and me, and he could not do many things by himself*" (Participant 17).

Theme 2: Precocious puberty, a developmental period or a disease?

According to the participants' statements, precocious puberty involves a child's psychological/physical reactions and challenges with school and peers.

A. Child's psychological/physical reactions

Feeling ashamed of looking different

Mothers expressed concern that their children felt ashamed because of their rapid physical growth. A mother said, "*My daughter felt bad because her face became full of hair and her body was bigger than that of her peers. Her appearance had also changed, and she was constantly trying to be alone. She was very embarrassed because her appearance was different from her friends*" (Participant 5).

Disgust with face and body image

Participants reported that their children felt disgusted with their faces. A mother said, "*Because my son did not feel good about his appearance, he hated himself and looked exhausted. He did not interact with anyone and spent most of his time playing computer games*" (Participant 14).

Extreme aggression

The participants' statements indicated that they were surprised by the aggressiveness of their sons. A mother said, "*My son had become very bad-tempered and aggressive, and he no longer had the calm behavior he used to have. He was fighting with his older brother at home and with his classmates at school. He felt that he only had to show his anger to others*" (Participant 6).

Rapid mood swings

The participants reported that their children had many mood changes after puberty. A mother said, "*It was very stressful for us not to know the problems and challenges we were facing. His behavior changed quickly and caused us to lose our peace of mind and we had many changes in our lives*" (Participant 18).

Low self-confidence

Mothers reported that their child's self-esteem was negatively impacted. A mother shared, "*My daughter's extremely low self-confidence because of her appearance concerned us more than anything else. My daughter suffered psychological distress because of the changes in her appearance and her big body and appearance compared to the rest of her friends had reduced her self-confidence*" (Participant 9).

Menstruation: the peak period of change

Mothers who had a daughter considered their child's menstruation to be the peak of their child's psychological, emotional, and social challenges. A mother said, "*My daughter kept asking why this happened and thought she was sick and was very upset. Unfortunately, my worries were also transferred to her*" (Participant 12).

Rapid hormonal changes and appearance of skin acne

Participants reported that the emergence of facial acne and hormonal changes significantly affected their children. A mother said, "*The concerns that my daughter had about menstruation, and mental issues at this time were very critical. Her classmates looked different from her and she did not have a good sense of interaction with others*" (Participant 16).

B. School/peer challenges

Peer ridicule

Participants noted that ridicule from peers at school caused constant resentment for the child and the mother. A mother said, "*The sudden changes in my son's appearance, such as weight gain and growth of facial and body hair had created a bad feeling in him and also caused reactions from his teammates and other children in the family. For instance, they mocked him, which made him very irritable*" (Participant 25).

Tendency to isolation and avoidance

Mothers reported their children tended to isolate and avoid their peers. A participant said, "*She underwent early puberty before going to school. She was ridiculed by her friends and peers and they used to insult her. So, she decided to stop spending time with them*" (Participant 3).

Bullying and disobedience

Mothers believed that boys often engaged in bullying and disobedient behavior at school. A participant said, "*Because my son looked older in appearance, he became a bully and tried to bully other kids at school, and sometimes he started fighting them. His aggressive behavior caused complaints from teachers and mothers of other school children*" (Participant 7).

School avoidance

Participants stated that their children's unwillingness to attend school caused many problems. A participant explained, "*My daughter ran away from school and it caused me to constantly get into trouble with her teachers and school officials. So, I often had to go to school. I was also worried about her education and I didn't want to put too much pressure on her*" (Participant 23).

Academic failure

Participants noted that their children's academic failure had caused many problems. A mother remarked, " *The severe pain she endured every month was unbearable for a 7- or 8-year-old girl, and that's why every month when she was on her menses, she didn't go to school and so we had many problems and she had a poor performance in her first grade and we had to always hire a tutor to teach her*" (Participant 3).

Peer rejection

Participants expressed distress that their children had no friends at school. A mother said, "*My daughter did not receive good reactions from her peers and was very lonely during that period because she was experiencing things that were not understandable to the rest of her friends*" (Participant 16).

Theme 3: Mother's self-imposed isolation

Participants indicated that reactions and judgments of people around them, including relatives and the public, led to their deliberate and self-imposed isolation for

both themselves and their children. This self-imposed isolation was related to social stigma, unfair judgments, and feelings of loneliness.

A. Social stigma and unfair judgments

Curiosity and frequent questions

Mothers reported feeling overwhelmed by the judgments and frequent questions of other mothers at school and acquaintances. A participant stated, "*The sudden changes in my daughter were questionable for everyone, and they directly asked about her, which did not have a good impression on me and my daughter*" (Participant 9).

People's fear of their child contracting a contagious or incurable disease

The participants stated that people around them feared that their children might develop precocious puberty or get other diseases. A mother said, "*I didn't pay much attention to the reactions of others, because the things they said and how they reacted to my son's changes were very annoying. They treated my son as if he had an incurable disease*" (Participant 6).

Shameless judgments

A participant shared, "*At school, I tried not to talk to other mothers about my son's precocious puberty because their reactions did not have a good impression on me, and they made me feel as if my child were strange*" (Participant 11).

People's fear of the negative effects of precocious puberty on their children

Participants stated that people around them asked their children not to have contact with theirs. A mother stated, "*My son was harassed due to his physical and hormonal changes and the negative reactions of the people around him. Mothers no longer let their children be in contact with my child. They were afraid that my child's conditions would adversely affect their children*" (Participant 19).

B. Isolation of mother and child

Participants reported that they sought self-imposed isolation out of despair. Many mothers decided to cut off contact with others in their self-imposed isolation because people accused that mother of negligence in her role as a mother and the mother preferred to avoid interacting with others.

Blaming the mother for not doing her role as a mother

Participants reported that people around them started questioning their competence in performing their motherhood roles. A mother said, "*They were talking behind my back. They said that she was a careless mother and did not take care of her child, and that is why this problem happened to her child*" (Participant 22)

Mother's avoidance of relatives

Mothers explained that they avoided attending family gatherings, meetings, and parties to escape public negative judgments about themselves and their children. A mother said, "*My relatives and friends were very curious and did not like us to be at parties with them because of my son's precocious puberty, as they said that my son is mischievous and bullies, and we chose to have fewer interactions with them so as not to face protest about my son's behavior*" (Participant 21).

Theme 4: Informing, preparing, and training parents as the key to overcoming precocious puberty

Participants emphasized that providing information about precocious puberty is a way to overcome their own and their children's problems.

A: Educating parents as a life-saving option

Seeking help from the doctor and school counselor

Participants suggested that help from doctors and school counselors was effective in raising awareness of puberty problems and coping with them. A mother noted, "*The counselor's relaxation techniques and behavioral recommendations were very useful for us. We also saw a psychologist on the counselor's advice, who prescribed drugs for my son that improved his general condition*" (Participant 15).

Using the Internet and reading useful books

Mothers found it useful to read books about puberty and find useful information on the Internet to manage their children's precocious puberty. A mother said, "*I used to gather a lot of information from the Internet, or I consulted with the vice-principal of my child's school, who studied psychology. I checked many issues on the Internet and read several books in this field that were very helpful*" (Participant 5).

The need to educate parents to understand adulthood

Participants suggested that school health experts and nurses should hold training courses for parents from the very beginning and answer mothers' questions. "*My most important problem was that I did not know what to do in different critical situations and how to react so that my son would be less harmed and have fewer problems. The lack of information and experience bothered me a lot. There were no training courses either*" (Participant 7).

B: Support as the key to success

Psychological and social support for the child

Participants regarded support for their children as a vital issue. A mother stated, *"I think controlling the challenges and supporting children are the most important things that should be done, and the higher the awareness, the better the situation can be controlled" (Participant 4).*

Appeal to patience and tolerance

A mother remarked, "*Mothers should know that not everything is going to go well in this crisis and not try to put too much pressure on themselves and their children to reduce the problems and be patient so that the problems will alleviate with time. It is very important to be patient*" (Participant 10).

Discussion

This study explored mothers' experiences of children's precocious puberty. Most of the mothers did not have enough knowledge about puberty and did not what to do about precocious puberty due to the lack of knowledge and awareness. In line with these findings, Aghaee-Chaghooshi et al examined the challenges of puberty of girls with visual impairments and concluded that the lack of knowledge and information before puberty had confused them (16). The participants in the present study also reported that the lack of knowledge about precocious puberty led to extreme confusion and even surprise for them. The mothers stated that school officials did not make any arrangements for holding training courses by health educators or school counselors, and when the mothers discovered their children's precocious puberty they tried to seek help from a counselor or medical specialist.

The participants in this study also admitted that the judgments and misbehaviors of the people around them induced despair and depression in them due to the physical and behavioral changes of their children. Lee et al also showed that the guilt experienced by mothers who have children with precocious puberty is closely related to their stress and anxiety, and their feeling of guilt significantly decreases when they receive social support from others instead of rejection. Moreover, precocious puberty increases the risk of mental health and behavioral diseases for both children and mothers (17). The mothers in the present study pointed out that even though their children reached puberty, they behaved like children, which confused others, including parents, teachers, and peers. Accordingly, Mensah et al. suggested that precocious puberty may cause various problems, including the child's bones developing more like those of adults, while the child still lives in his/her childhood world (18). Indeed, when a child displays the symptoms of precocious puberty, he/she becomes almost similar to adults in terms of appearance and physicality, but mentally and intellectually, the child is not ready to face these unexpected changes (19). The participants in the present study stated that the lack of information about precocious puberty worsened their feelings of fear, anxiety, and helplessness in their motherly duties. Park et al identified four types of perceptions regarding precocious puberty among children including shyness-passive self-management, resentment-suppression, anxiety-fear, and adaptation-acceptance (20,21). Similarly, Maron admitted that the lack of knowledge and information among parents, especially mothers, can complicate the situation. When mothers do not have the necessary information and preparations for their children's early puberty, they may engage in behaviors that worsen the problems (19).

Another issue that was highlighted by the participants was their role pressure as the mother with a precocious child. Analysis of the mothers' experiences indicated that a mother whose child reaches puberty earlier than other children endures a kind of social stigma that causes them to experience more difficult conditions. Participants also reported that due to the precocious puberty of their child, they faced a social deterrence, leading to severe isolation of mother and child. Indeed, because early puberty for children is considered an unusual process during development, a child with this problem may be considered a sick child by others, and its effects also involve the mother and cause more problems for them. Studies have shown a direct relationship between obesity and high body mass in children and their early puberty (22-23). The participants in this study reported that the people around them mocked and ridiculed their children because of obesity. The results of the present study indicated that since mothers did not have enough knowledge and information about their child's precocious puberty, they did not succeed in showing effective reactions at the onset of this crisis. Mothers stated that after they decided to get information about their child's changes from a reliable source, their mental and behavioral conditions improved and their problems decreased. Khodabakhshi-Koolaee et al. showed that training and therapy sessions with families have a significant effect on the parent-child relationship. The family is one of the social institutions that form the basis of human social life, and one of its most important functions is having children and raising children, the burden of which predominantly falls on mothers (11). Thus, raising awareness of families about many issues related to children and adolescents can contribute to preventing many childhood problems that have consequences even in a person's adulthood. Family conflicts in childhood are related to the earlier onset of menstruation, and girls who mature early reach adolescence with emotional and social problems. This is to argue that a tense and anxiety-producing family environment causing children to withdraw and isolate themselves, contributed to the development of precocious puberty and negatively affects the parent-child relationship. Thus, more training is required to resolve these conflicts (24,25).

Participants also suggested that if a mother considers the possibility of precocious puberty for her child and prepares accordingly, she can more easily navigate this stage. An analysis of the mothers' experiences showed that going through precocious puberty requires patience

and mothers should be able to better support their children by maintaining their calmness and patience. The present study focused exclusively on mothers' experiences of their children's precocious puberty. However, fathers and siblings may also have unique and valuable insights regarding this issue. Thus, future studies need to examine the experiences of fathers and siblings about children's precocious puberty. Moreover, the participants in this study were mothers who lived in Tehran and mostly had a diploma or higher education. The findings from this study cannot be generalized to people in small towns, villages, and less developed areas where religious conservatism is more intense and stronger.

Conclusion

Participants in the present study stated that if a mother considers the possibility of precocious puberty for her child and makes the necessary preparations in advance, she and her child can navigate this developmental stage more effectively.

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Authors' Contribution

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Competing Interests

The authors declared no conflict of interest.

Ethical Approval

The protocol for this study was approved by Ethics Committee of Shahid Beheshti University under the code the IR.SBU.REC.1402.083.

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