The Study of Delayed Puberty in Females Referred to pediatric endocrine clinic for 5 years (from 78/12/29 to 82/12/1)

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بررسی علل تاخیر بلوغ در دختران مراجعه کننده به درمانگاه غدد کودکان دانشگاه علوم پزشکی مشهد

خلاصه

هدف : هدف مطالعه بررسی علل تاخیر بلوغ در دختران مراجعه کننده به درمانگاه غدد کودکان در طی یک مطالعه ٥ ساله از سال ۷۸ تا ۸۲ .

روش کار : این مطالعه به صورت گذشته نگر و آینده نگر انجام شد جمعیت مورد مطالعه ۳۱ دختر بودند که با تاخیر بلوغ به درمانگاه غدد کودکان مراجعه کرده بودند اطلاعات با سابقه، معاینه جسمی و پرسش از بیماران تکمیل شد و نتایج با نرم Exell , Spss مورد تجزیه و تحلیل قرار گرفت.

نتایج : دراین مطالعه ۳۱ دختر با تاخیر بلوغ مورد ارزیابی قرار گرفتند. متوسط سن بیماران ۱/٤٦±۱٤/۹۳ سال بود و متوسط سن استخوانی بیماران ۱/٥±۱۰ سال و متوسط وزن بیماران ۸/۳±۳۱ کیلوگرم بود. انحراف معیار قد و وزن برای سن به ترتیب ۳/۸۳و ۲/٦۸ بود. میزان استرادیول سرم در تمام بیماران پائین تر از طبیعی بود. در این بررسی ۲۷٪ موارد علل تاخیر بلوغ نوع سرشتی بود. تالاسمی ماژور در۱۳٪ موارد، کم کاری تیروئید (هیپوتیروئیدی) ۱۰٪ و سندرم ترنر در ۲۳٪ موارد مشاهده شد.

نتیجه گیری : تاخیر بلوغ سرشتی و سندروم ترنر شایع ترین علل تاخیر بلوغ بودند، اگر چه تالاسمی ماژور نیز در مقایسه با سایر بررسی ها شایع تر بود. توجه به علائم بلوغ در دخترانی که در زمان بلوغ به پزشک مراجعه می کنند، منجر به تشخیص زودرس تر تاخیر بلوغ خواهد شد. هم چنین انجام کاریوتیپ در تمام دخترانی که با کوتاهی قد و تاخیر بلوغ مراجعه می کنند، پیشنهاد می شود.

کلمات کلیدی : هیپوگونادیسم، سوء تغذیه، تاخیر بلوغ سرشتی، بیماریهای سیستمیک.

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Background :

Puberty is the acquisition of secondary sexual characteristics associated with growth spurt and resulting in the attainment of reproductive function . (1) Delayed puberty can be defined as the lack of pubertal development at an age of 2SD above the mean, which corresponds to an age of approximately 14 years for males and 13 years for females.(2,3)

Aim: We performed a retrospective and prospective study of clinical and laboratory data from female adolescents (< or = 18 yr of age) with delayed puberty who had been seen in our clinic between 78/12/29 and 82/12/1 (n = 31 subjects)

Method & Materials :

This study was done both retrospectively and prospectively in a descriptive-analytic manner. Data obtained from retrospective review of patients included chronological age (CA), bone age (BA), weight (WT), height (HT) and body mass index (BMI), Tanner stage, as well as levels of FSH, LH, Estradiol. In addition diagnostic evaluation for underlying disorders were reviewed.

Medical histories of concurrent disorders were examined, and parental height and family history of pubertal delay were obtained. Karyotype was down in some patients for assessment of Turner syndrome (not in all patients) data was displayed as the mean ±SD.Statistical analysis was performed with SPSS-excel.

Results:

Our case series consisted of 31 girls with mean age 14.93±1.46yr .

Mean height of patients was 136±13cm, and the mean weight was 31±8.3kg.

The comparison of WT and HT of patients with standard growth charts (NCHS) were in the 3rd percentile. Z score of WT to age was -2.7 and Z score of HT to age was -3.8 and mean bone age was 10±1.5years. BMI I was calculated in all patients and the results as below: mean wasting was 0.59 and mean stunting was 0.83. The estradiol level in all patients was low for chronological age with mean level 9pg/ml.

The etiologies of delayed puberty were divided into two groups according to LH, FSH levels.(Table1-graph1)

First group: hypogonadotropic hypogonadism with low level of LH (1miu/ml±0.75 miu/ml) and FSH (3miu/ml± 2.5miu/ml)

Second group: hypergonadotropic hypogonadism or gonadal failure with high level of FSH and LH.

In hypogonadotropic hypogonadism the causes were: constitutional delayed puberty, systemic disease and rare syndrome.

67.7%(21) of patients were in hypogonadotropic group with prepubertal level of gonadotropins

in this group: Constitutional delayed puberty in 8 patients (26%), major thalassaemia in 4 patients (13%), hypothyroidism in 3 patients (10%), 2 patients (6.4%) had epilepsy and one patient had cleido cranial dysostosis and 3 patients were not diagnosied (9%).

In hypergonadotropic hypogonadism group we evaluated 10 patients (32.3%). Of them 7 patient had Turner syndrome with 45X karyotype (23%), 2 patients with gonodal dysgenesis (6%) and one with fancony syndrome (3%).

Discussion:

Despite clinical importance of delayed puberty, the understanding of this condition is hampered by the lack of studies evaluating etiologies and predisposing factors among case series .

We have performed an extensive review of female adolescents with delayed puberty.

In this study we evaluated 31 girls with delayed puberty for five years .

Total number of females who referred for delayed puberty in other investigation is also low (4,5,6,7,8,9)

In a large case series study in Boston-Massachusetts of America in 1999 delayed puberty in females was 74 in spit of male 158.(5)

WT and HT of our patients in comparison with NCHS curve was in the 3rd percentile, suggesting that our patients have some degree of malnutrition.

Malnutrition is one of the important causes of delayed puberty and menarche, in both animals and humans,(10,11) the age of puberty appears to be related more to body weight than to chronological age (12).

BMI or body mass index also is a good criteria for assessment of malnutrition. In our patients 12 had abnormal BMI due to malnutrition (graph 2)

Bone age was delayed in all of our patients when compared with age, supported that they have greater growth deficiency.

In another study delayed bone age in girls was greater than in boys suggesting that girls may have been more severely affected than boys (5).

The most common cause of delayed puberty in our patients was constitutional delay of growth and maturation (CD) which affected 27% of our subjects.

Constitutional delay of growth and maturation is the most common cause of delayed puberty in males and females. (4,5,6,9,13,14,15,16,17,18,19,20).

Short stature and lack of sexual development may lead to emotional and social difficulties and in some patients their consequences can persist when normal height and full sexual maturation are attained (20). On the other hand a delay in the tempo of pubertal maturation may interfere with the normal bone accretion occurring during puberty, later causing osteoporosis (20,21,22,23,24,25).

Such findings suggest that treatment in constitutional delayed puberty may be necessary (1,18,23,26,27).

Turner syndrome and other gonadal dysgenesis is one of the important causes of delayed puberty or short stature in females. In our study the incidence of this syndrome was 23%.

Karyotype in any female with unexplained short stature or delayed puberty must be considered (28). In some countries diagnosis of Turner syndrome is made perinatal or in mid childhood, thus these patients donot present with delayed puberty.

The incidence of delayed puberty associated with chronic illness is unknown; however it is clinical importance relevantly due to the larger percentage of patients with chronic disorders surviving until the age of puberty.(5).

Virtually every child with any chronic disease could present with delayed puberty due to recurrent infections, immunodeficiency, gastrointestinal disease, eating disorders, renal disturbances, respiratory illness, chronic anemia, exercise, etc (1,5,29).

Pubertal delay associated with chronic illness is accompanied with a delay in growth and pubertal growth spurt.

The degree in which growth and pubertal development are affected in chronic illness depends on the type of disease and individual factors, as well as on the age at illness onset, its duration and severity, the earlier its onset and the longer and more severe the illness, the greater the repercussions on growth and pubertal development (1,10,29,30,31)

In our study major thalassaemia was the most important systemic disease with delayed puberty (10%).

Despite regular blood transfusion and desferrioxamine treatment, growth impairment and pubertal delay are commonly seen in children and adolescents with major thalassaemia, this problem has been investigated in many studies (1,5,31,32,33,34,35).

Delay in development of secondary sexual characteristics appears to be secondary to chronic anemia, iron overload, and the toxic effects of desferrioxamine, development of other endocrinopathies and under nutrition.

Hypothyroidism is the common cause of delayed puberty in both males and females, since thyroid hormones are essential for normal growth, sexual development and reproductive function. Hypothyroidism is the most endocrinopathy that cause delayed puberty in both males and females.

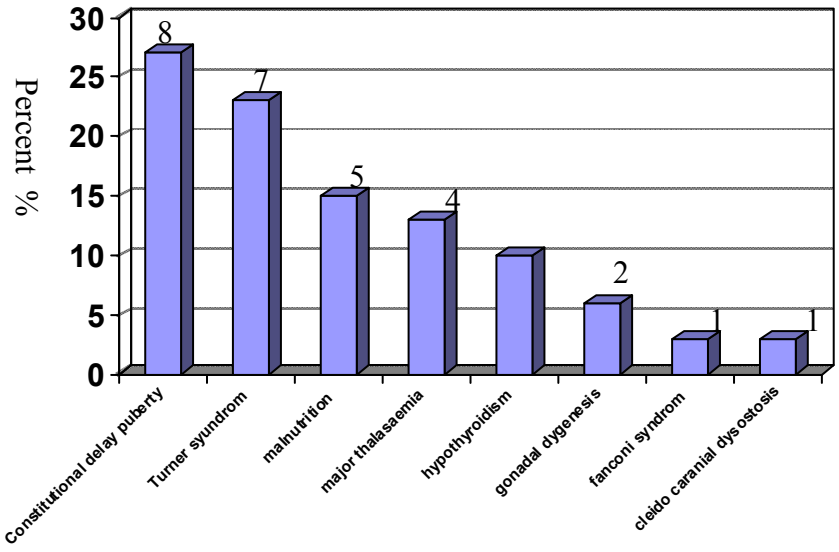
With the recognition and treatment of the disease growth impairment must be solved (26,37,38). 10% of our patients had delayed puberty due to hypothyroidism.

This incidence is very important and reflects in every child with delayed puberty thyroid function test must be evaluated.

In summery our data indicates that although C.D is the most common cause of delayed puberty, a thorough evaluation for underlying illnesses and familial predisposition is certainly warranted.

Table 1 : Causes of delayed puberty in Females

8	Constitutional delayed puberty
7	Turner Syndrome
2	Gonadal digenesis
1	Fanconi Syndrom
3	Hypothyroidism
4	Major thalasaemia
5	Malnutrition
1	Cleido cranial dysostosis
31	Total



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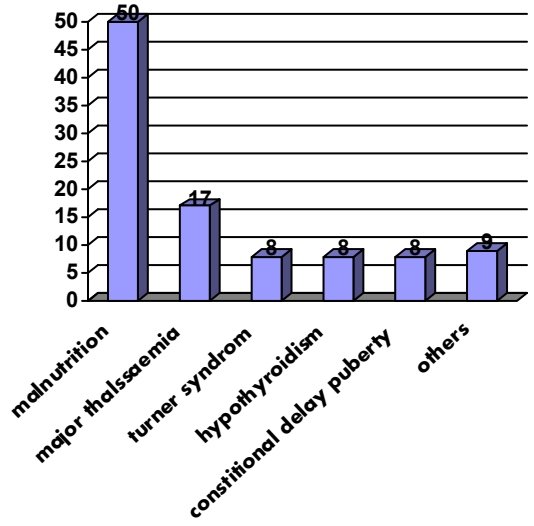
raph1: Causes of delay puberty in Females referred to pediatric clinic (percent)



Graph 2 : Dislribution of cause of delay puberty in female according to B.M.I < 5 th

Abstract

Purpose : The study of causes of delayed puberty in female referred to pediatric endocrine ward of university centers of Mashhad University of Medical Sciences from 1374 to 1382.

Method : This study was done both retrospectively and prospectively in a descriptive analytic manner. The studied population were 31 girls with delayed puberty referred to endocrinology pediatric clinic. The data was collected through history, physical examination, completing questionnaires, and was compared by T Test student Statistical analysis performed with SPSS-excel.

Result : On the whole, 31 girls with delayed puberty were studied. The mean age of the patients was 14.93±1.46 yr. Average bone age and weight was 10±1.5yr and 31±8.3 k gr respectively. Z score of Height and weight for Age was -3.83 an -2.68 respectively.

Serum estradiol level in all patients was less than normal. Delayed puberty in 27% was constitutional, 23% had Turner syndrome. Major thalassemia was the cause in 13% of the cases. The prevalence of hypothyroidism in the population was 10% other systemic diseases such as, fancony syndrome etc were the less common causes of delayed puberty.

Conclusion : Constitutional delayed puberty (27%) and Turner syndrome (23%) were the most common causes of hypogonadism and delayed puberty which concurs with other studies. The prevalence of major thalassemia (13%) is more than other studies which needs further studies. Attention to signs of puberty in the girls referring to physician at the time of puberty, leads to early diagnosis of delayed puberty in the patients. And also karyotype study is recommended in all girls with short stature and growth retardation.

Key Word : Hypogonadism, Mal nutrition, Constitutional delay puberty, Systemic disease.

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