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Diseases associated with growth hormone deficiency and short stature in Maternity and Child Teaching Hospital in Al-Diwaniyah Province, Iraq

[1] Dr. Qahtan Khayoon Hammood Alyasiry, [2] Dr. Moayed Mahdi Hussain, [3] Dr. Jomah Nasir Al-Obaidi

Abstract

Background: *One of the principal health parameters in children are growth and stature progress. One of frequent health issues in every day pediatric practice is the problem of short stature. The interplay among a multitude of processes and events determine the stature and growth in children including functioning endocrine system, genetic predisposition, effects of chronic diseases, nutritional status and level of physical activity. There is little if any information about the prevalence and nature of short stature in Al-Diwaniyah province, mid-Euphrates region of Iraq.*

Aim of the study: *the current study was aiming at highlighting the commonest causes and patterns of short stature in this province.*

Patients and methods: *Assessment of children height was done with standing position against wall-mounted, without foot ware, heels and back touching the wall, the child looking straight ahead, gentle but firm pressure upwards applied to the mastoid underneath with assessment of upper segment (US)/ lower segment (LS) ratio. Assessment of father and mother height was also carried out.*

Results: *The most frequent cause was mall for gestational age which was seen in 38 (27.9) cases, followed by chronic medical illness in 28 (20.6 %) cases and celiac disease in 26 (19.1 %) cases. Other causes included hypothyroidism in 17 (12.5 %), Genetic (isolated GH deficiency) in 13 (9.6 %), Congenital adrenal hyperplasia in 8 (5.9 %), Turner syndrome in 8 (5.9 % and Prader Willi syndrome in 2 (1.5 %). Chronic medical illnesses included: bronchial asthma, epilepsy, chronic constipation, recurrent UTI, chronic diarrhea, sickle cell anemia and thalassemia.*

Conclusion: *Small for gestational age, chronic medical illness and celiac disease were the principal causes of short stature in Al-Diwaniyah province.*

Key words: *growth hormone deficiency, short stature, Al-Diwaniyah Province, Iraq*

Introduction

One of the principal health parameters in children are growth and stature progress. One of frequent health issues in every day pediatric practice is the problem of short stature (Maghnie *et al*., 2018; Hussein *et al*, 2017; Al-Jurayyan *et al*., 2012). The interplay among a multitude of processes and events determine the stature and growth in children including

[1] *Consultant of pediatric University of Al-qadisiyah. qahtan.al_yasiry@qu.edu.iq*
[2] *Pediatrician/ Al-Diwaniyah Maternity and Children Teaching Hospital/ Al-Diwaniyah Province/ Iraq , Email of corresponding author. moayedalshimry@yahoo.com*
[3] *Consultant of pediatric_ jemjemy26@gmail.com*

functioning endocrine system, genetic predisposition, effects of chronic diseases, nutritional status and level of physical activity (Al-Jurayyan *et al*., 2012). Growth defect and subsequent retardation in stature may follow a disturbance in one or more of the above mentioned elements (Van Den Brande and Rappaport, 1993). Short stature is defined as "a height of less than 3rd percentile or 2 standard deviations below the mean height for age and sex in the same ethnic group" (Christesen *et al*., 2016; Rosenbloom, 2009). For that reason, short stature may be a natural outcome in constitutional growth delay and familial short stature to a pathological entity such as systemic disorders or endocrine abnormality (Al-Jurayyan *et al*., 2012). The natural subtype is the most frequent, and can be predicted by standard history and physical examination in addition to simple radiograph of skeleton for bone age assessment (Wit *et al*., 2008; Lee, 2006; Miller and Zimmerman, 2004). Constitutional growth delay is observed in 15% of children and has the potential to manifest at different phases of their maturation. It's essentail to consider that growth rate is variable accordingly. Between three to six months to two to three years of age, the anticipation is that a number of children will cross percentiles in their weight and growth charts with no real concerns for retardation in growth. This trend will often return to a standard velocity following this period. Following 4 years of age, there is steady constant growth. The discovery of growth retardation is often made at time of puberty as children start to divert from the curve, often as a result of late onset puberty which mirrors the delay in bone age (Rohani *et al*., 2018; Hussein *et al*., 2017).

There is little if any information about the prevalence and nature of short stature in Al-Diwaniyah province, mid-Euphrates region of Iraq; therefore, the current study was aiming at highlighting the commonest causes and patterns of short stature in this province.

Patients and methods

The study was a cross sectional one and included 136 children with an age range of 5 to 15 years. The study was carried out at Al-Diwaniyah Maternity and Children Hospital at AL-Diwaniyah Province, mid-Euphrates region of Iraq. The study has started on March 2019 and ended on April 2020.

Children assessment included full history and thorough physical examination. Children included within 5 to 15 years of age and information about gender was obtained. Assessment of children height was done with standing position against wall-mounted, without foot ware, heels and back touching the wall, the child looking straight ahead, gentle but firm pressure upwards applied to the mastoid underneath with assessment of upper segment (US)/ lower segment (LS) ratio. Assessment of father and mother height was also carried out. Standard child estimate was done according to following equations:

- Height (female) = height of father-13) + (height of mother /2)
- Height (male) = height of father+13) + (height of father /2)

Growth chart was used to assess normality of measured children height.

The following investigations were performed: estimation of bone age, growth hormone (GH) assessment (baseline, after clonidine stimulation, and estimation of insulin like growth factor "IGF"), Thyroid function test (T_3, T_4, and TSH), screening for celiac disease (anti-tissue transglutaminase "tTG" and ant-gliadin antibodies).

The study was approved by ethical approval committee and a verbal consent was obtained from parents of every child enrolled in the current study in addition to a formal agreement by the Directorate of Health of Al-Diwaniyah Province, the formal representative of Iraqi Ministry of Health.

Statistical description was done using statistical package for social science (SPSS, IBM, Chicago, USA, version 23). Categorical variables were expressed as number and percentage, whereas, quantitative variables were expressed as mean, standard deviation and range.

Results

The current study included 136 children with and age range of 5 to 15 years and a mean age of 9.41±23.26 years. The study included 82 (60.3 %) males and 54 (39.7 %) females, as shown in table 1. The frequency distribution of patients according to cause of short stature is shown in table 2. The most frequent cause was mall for gestational age which was seen in 38 (27.9) cases, followed by chronic medical illness in 28 (20.6 %) cases and celiac disease in 26 (19.1 %) cases. Other causes included hypothyroidism in 17 (12.5 %), Genetic (isolated GH deficiency) in 13 (9.6 %), Congenital adrenal hyperplasia in 8 (5.9 %), Turner syndrome in 8 (5.9 % and Prader Willi syndrome in 2 (1.5 %). Chronic medical illnesses included: bronchial asthma, epilepsy, chronic constipation, recurrent UTI, chronic diarrhea, sickle cell anemia and thalassemia.

Table 1: frequency distribution of children enrolled in the current study according to age and gender

Characteristic	**Result**
Gender	
Male, *n* (%)	82 (60.3 %)
Female, *n* (%)	54 (39.7 %)
Age (years)	
Mean ±SD	9.41±23.26
Range	5-15"
5-10, *n* (%)	84 (61.8 %)
11-15, *n* (%)	52 (38.2 %)

n: number of cases; **SD**: standard deviation

Table 2: Causes of short stature

Cause	***n***	**%**
Small for gestational age	38	27.9
Chronic medical illness	28	20.6
Celiac disease	26	19.1
Hypothyroidism	17	12.5
Genetic (isolated GH deficiency)	13	9.6
Congenital adrenal hyperplasia	8	5.9
Turner syndrome	4	2.9
Prader Willi syndrome	2	1.5

***n*:** number of cases

Discussion

One of the important aspects in children care is the assessment of longitudinal growth. The recognition of short stature can be promptly done only with adequate measurements of growth and thorough growth chart analysis. As mentioned before, "short stature is defined as a standing height more than 2 standard deviation below the mean for sex and age (or below 3rd percentile)" (Christesen *et al*., 2016; Rosenbloom, 2009). Despite the long list of causes implicated in growth retardation and short stature, they can be categorized into three principal categories: genetic causes, chronic disorders and endocrine abnormalities (Al-Jurayyan *et al*., 2012). Among genetic causes, constitutional delay of growth and development and familial short stature are included. The list of chronic illnesses is relatively long and it includes under nutrition. Endocrine causes are well recognized etiologies of short stature such as abnormalities in growth hormone (GH) production, hypothyroidism and congenital adrenal hyperplasia (Al-Jurayyan *et al*., 2012). In developed countries,

the most prevalent cause of short stature is genetic in origin (Al-Jurayyan *et al*., 2012). Genetic causes are also seen in developing countries and have been shown to causes approximately (51.8 %) of short stature cases in one nearby country (Al-Jurayyan *et al*., 2012). In the current study, genetic causes were seen in 13 (9.6 %). The principal features of familial short stature are normal growth velocity, a bone age appropriate for chronologic age and the predicted height is in line with exact child height. On the other hand, constitutional growth retardation is typified by normal growth velocity, retarded bone age, and predicted adult height in line with the familial pattern. Late puberty and constitutional growth delay are typically seen in a first degree or second degree relative of children with constitutional growth delay (Moayeri and Aghighi, 2004; Zargar, *et al*., 1998).

Endocrine illnesses such as congenital adrenal hyperplasia, hypothyroidism, uncontrolled type 1 diabetes mellitus and growth hormone deficiency have the potential to cause growth retardation. For that reason identification of the exact cause of short stature is the primary step in treating such presentation in children. In the current study, hypothyroidism was seen in 17 (12.5 %) and Congenital adrenal hyperplasia was seen in 8 (5.9 %). Chromosomal study is indicated in any short stature child as the condition is frequently associated with a number of genetic disorders such as skeletal dysplasia and Turner syndrome (Clement-Jones *et al*., 2000; Rao *et al*., 1997; Yamamoto, 1997 Al Jurayyan *et al*., 1995). In the current study, Turner syndrome was seen in 4 (2.9 %) and Prader Willi syndrome was seen in 2 (1.5 %). One of important causes of short stature in intrauterine growth retardation (IUGR), particularly, if affected children did not catch up by two years (Coutant *et al*., 1998). In the present study, small for gestational age was the main cause of short stature as it was observed in 38 (27.9 %). Celiac disease was a major cause of growth retardation in children in our province and this finding is in agreement with the findings of previous authors in nearby countries (Al-Jurayyan *et al*., 2012; Assiri, 2010).

A prospective study was carried out by Hussein *et al*. in 2017 has shown that "26% were the result of endocrine disorders; 11.8% ad GH deficiency, of which 63.6% had normal GH variants, 15.8% had constitutional growth delay, while a combination of both was present in about 5%"

So far, it can be concluded from current observation that Small for gestational age, chronic medical illness and celiac disease were the principal causes of short stature in Al-Diwaniyah province.

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