

Stature–weight growth delays: Clinical and etiological aspects

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ABSTRACT

Background: Stature–weight growth delay (SWGDD) is a frequent motivation of consultation. It could be a consequence of a known chronic affection, congenital or acquired affection. The purpose of this study is to describe epidemiological, clinical, paraclinical, and etiological aspects of SWGDD. **Patients and Methods:** This retrospective study included 103 patients presenting a growth delay with an average age of 14.44 years and ranging between 5 and 21 years. Male predominance was noticed in 68.93% of cases. Patients showed a stature lower to -2 standard deviation (SD) for corresponding age compared to Sempe and Pedron reference. Patients were hospitalized in Endocrinology and Metabolic Diseases Department of the University Hospital of Fez, Fez, Morocco. **Results:** Patient's history included a perinatal suffering in 6.7% of cases, a chronic pathology follow-up in 17.6% of cases, and psychomotor development disorder in 10.6% of cases. The average weight was -2.37 SD with extremes varying from -4 to -0.5 SD. The stature values varied between -4.5 and -2 SD for the given age, with an average of -3.12 SD. A severe stature delay (< -3 SD) was recorded in 39.6% of cases and the targeted average size was -2.44 SD with extremes varying from -4 to -1.5 SD. Growth delay etiologies were dominated by a deficit in growth hormones (GHs) in 60% of cases. **Discussion and Conclusion:** Dynamic tests objectified a total deficit and partial deficits in GH in 41.7 and 30% of patients, respectively. The hypothalamo–pituitary magnetic resonance imaging was pathological in 23.3% of patients and showed a syndrome of interruption of pituitary stem in seven patients, pituitary gland in three patients, a craniopharyngioma in two patients, prolactin microadenoma in one patient, and nonfunctional pituitary microadenoma in one patient. GH treatment was established in 16 children that were presenting a deficit in GH, and two girls presenting Turner syndrome, whereas etiological treatment was suggested in all remaining cases.

Keywords: Clinical, delays, etiological, growth, stature, weight

Introduction

Growth is a fundamental biological process valid for biological systems. It is expressed as increase of dimensions and size of the body of man. It is a well-known characteristic of the childhood and adolescence stages of life, which begins during the gestational phase. A given stature is normal when its value is

included between -2 and 2 standard deviations (SD) compared with the average range of studied age and gender of the child.^[1]

Accordingly, it is considered to be a delay of growth in any child with stature lower than mean (-2 SD). The systematic follow-up of the stature–weight growth is a key component of the supervision of children. This allows detecting any delay in growth that might be a consequence of known chronic affection, which could be improved by appropriate care. Thus, allowing to minimize stature delay impact.^[1] The care could cover stature–weight delay that might be due to congenital or acquired origins. Indeed, the early

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diagnosis allows detecting critical diseases and initiates appropriate treatments.^[1]

The purpose of this work is to study various clinical aspects of patients presenting a stature–weight growth delay (SWGd). The study reports the main exploration methods used and presents main etiological findings.

Patients and Methods

This retrospective study included 103 patients admitted in Endocrinology Diabetology and Metabolic Diseases Department of the University Hospital of Fez for exploration of SWGD. The study was carried out over a period of 6 years extending from January 2009 to October 2015.

The study included patients presenting a stature growth delay with a height size that was lower or equal to 2 SD for the corresponding age while considering the reference curve of Sempe and Pedron.^[2]

An investigating form allowed collecting data of demographics; patient's history, including the pregnancy evolution, neonatal pathologies, every chronic pathology, and family pathologies; the clinical examination data including weight (SD), stature (SD), targeted size (SD), and dysmorphic syndrome; paraclinical data, including basic biological assessment, hormones assessment, blood dynamic tests, and imaging assessment; and revealed etiologies, and indicated treatment.

Results

The study included 103 patients. The average age of our patients was 14.44 years, ranging from 5 to 21 years. Male predominance was significant with 68.93% of cases. The consanguinity and chronic pathologies were well demonstrated by patient's histories, with 19.4 and 17.65% of cases, respectively [Table 1].

The clinical examination data showed an average weight of -2.37 SD and ranging from -4 SD to -0.5 SD [Figure 1]. The stature demonstrated values ranging between -4.5 SD and -2 SD for corresponding age with an average of -3.12 SD. A severe stature delay of -3 SD was noticed in 39.6% of assessed cases. The average SDs of the stature of patients at their adulthood

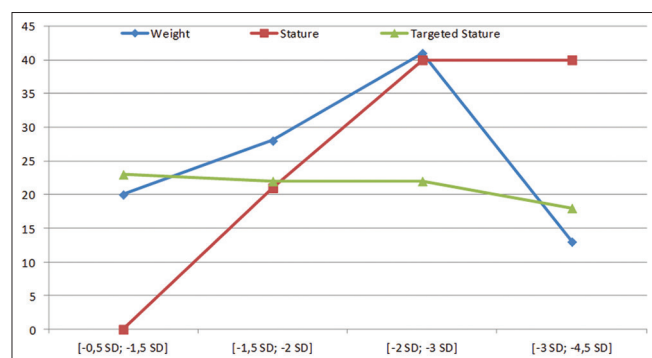


Figure 1: Presentation of the collected clinical data of patients

compared to their genetic size was -2.44 SD and was ranging from -4 SD to -1.5 SD.

The revealed dysmorphic signs were deficient morphotype of growth hormone (GH) in 51.4% of cases, a micropenis in 31% of cases, and a syndrome morphotype of Turner in 11.6% of cases. Delayed puberty was noticed in 27.4% of cases, 23.3% demonstrated puberty onset, whereas 5.8% of the patients were pubescent [Table 2].

The biological assessment of our patients demonstrated hypochromic microcytic anemia in 9.7% of studied cases; serological positive celiac disease in 5.8% of cases; biopsy jejune positive celiac disease in 14.5% of cases; normal renal function and phosphocalcic assessments in all patients; a peripheral hypothyroidism with high thyroid stimulating hormone and low LT4 in 4.8% of cases; and insulin-like growth factor-1 (IGF1) was inferior than its lower limit for each age in 40.7% of cases. Results of biological assessments are summarized in Table 3.

GH stimulation tests

Hypoglycemia insulin test was achieved in 64 patients, Glucagon–propranolol test was done in 26 patients, and Clonidine test was done in 20 patients; global deficit of GH was shown in 41.7% of our patients and partial deficit in 30% of cases [Figure 2].

Table 1: Pathological histories of studied patients

History	n	%
Pregnancy follow-up	71	68.93
Perinatal suffer	7	6.79
Psychomotor developmental disorder	11	10.67
Chronic pathology	18	17.65
Bon pathology	2	1.96
Consanguinity	20	19.4
Small familial stature	6	5.94

Table 2: Presentation of the signs dysmorphic symptoms revealed during clinical examinations

Clinical signs	n	%
Micropenis	32	31
Morphotype of GH deficits	53	51.4
Turner syndrome morphotype	12	11.6
Puberty delayed	28	27.4
Initiation of puberty	24	23.3
Pubescent	6	5.8

Table 3: Biological assessments achieved for each studied patients

Laboratory tests	n	%
Anemia hypochromic microcytic	10	9.7
Serologic tests for positive celiac disease	6	5.8
Jejunal biopsy for celiac disease	15	14.5
Normal renal function	103	100
Normal calcium and phosphate	103	100
Peripheral hypothyroidism	5	4.8
Low IGF1	42	40.7

Karyotyping was indicated for 40 patients, and was realized in 13 patients, whereas result was positive in six patients with diagnosis of Turner syndrome. X-ray measurements of the left hand and wrist were realized in all patients; image data were interpreted according to GREULICH and PYLE method. The average osseous age was 11.3 years, and the average difference between chronological age and osseous age (CA-OA) was 3.32 years. Magnetic resonance imaging was done in 60 patients, and demonstrated pathological diagnosis in 14 patients. The disorder findings were syndrome of interruption of pituitary tract in seven patients, atrophic pituitary gland in three patients, a craniopharyngioma in two patients, and pituitary microadenoma and prolactin in one patient.

Various etiologies were implicated as origin of the stature delay in child with predominance of GH deficits [Figure 3]. The difference between CA-OA is determined by involved etiology. CA-AO is very important in the hypothyroidism and Turner syndrome, with an average age of 9 and 5 years, respectively.

Celiac disease and GH deficit demonstrated difference superior to 2 years with an average of 4 and 3.1 years, respectively. Finally, CA-AO is lower in the puberty delay and the chronic diseases with an average of 2.67 and 2.17 years, respectively [Figure 4].

The treatment using GH was suggested in 16 children since presenting a deficit in GH, and two girls presenting a Turner syndrome. Unfortunately, other cases of GH deficit were indigent without strong medical care security, hence they were lost. Inappropriate etiologic treatment was initiated in other cases.

Discussion

Primary care medicine (PCM) is a major tool for early diagnosis and further treatment orientation of stature and weight growth. Indeed, most stature–weight delays are revealed during primary care of third benign diseases and disorders. The delay of growth is a frequent indication of PCM consultation. Various etiologies are involved and are mostly endocrine.^[3,4] The clinical analysis of patient’s data shows male dominance, which was reported by all authors.^[5-7] Louzada *et al.* and Moayeri *et al.* reported a series where the average age at the first consultation was ranging between 2 and 15 years, with an average of 8.6 years.^[2,8] In contrast, in our series average age was 14.44 years, ranging from 5 to 21 years with a clear male predominance in 68.93% of cases.

The growth delay is defined by a stature lower or equal to third percentile or to -2 SD below the average value of given age, gender, and population geo-ethnicity.^[1] The slowdown of growth speed (GS) is defined as a GS lower or equal to -2 SD, measured along 1 year, or equal or <1.5 SD measured along 2 years. The stature delay is severe whenever the measured size is lower or equal to -3 SD. The anthropometric data analysis reported by Strufaldi *et al.* at the first consultation revealed that 63% cases demonstrated -2 SD and 37% showed a stature delay^[2] according

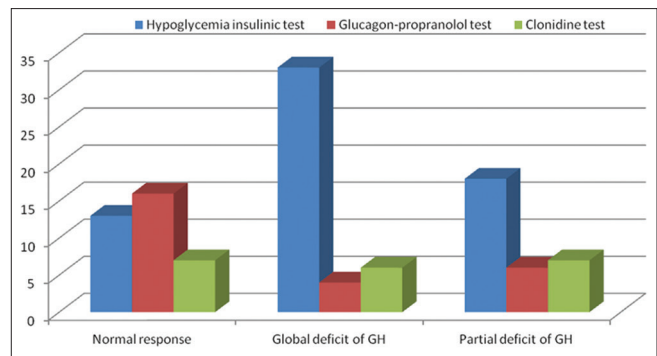


Figure 2: Results of growth hormones achieved in our patients

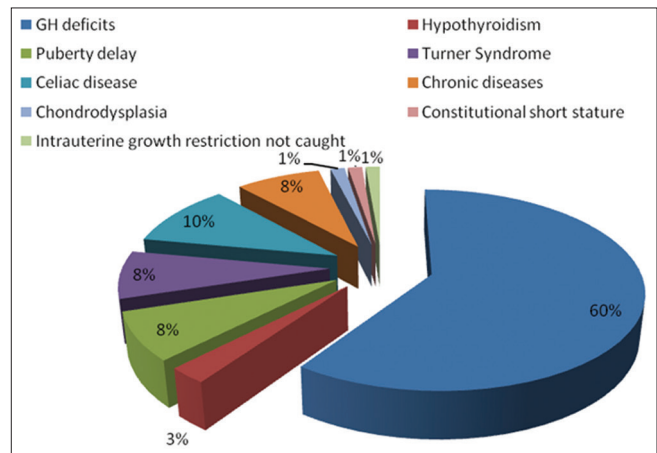


Figure 3: Presentation of RSP etiologies of our patients

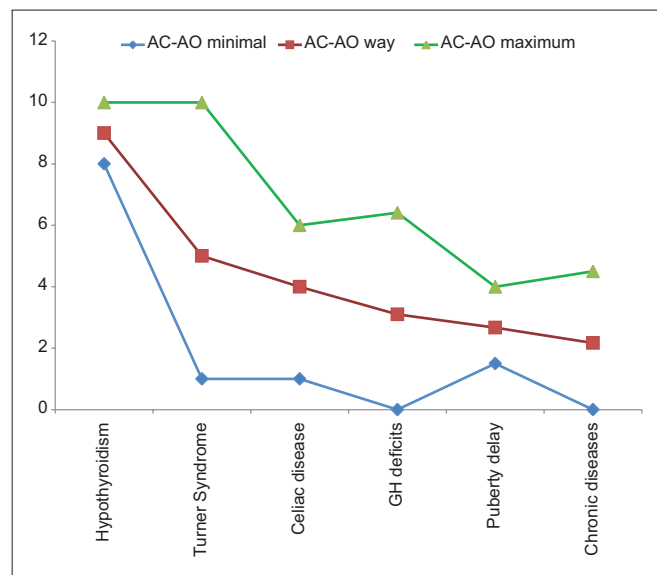


Figure 4: Difference between CA-AO according to RSP etiologies of our patients

to the stature referenced by Sempe and Pedron for the age.^[2] The anthropometric measurements of our study showed a stature varying between -4.5 SD and -2 SD for given age with an average of -3.12 SD. A severe stature delay of -3 SD was noticed in 39.6% of cases. The Moroccan population does not detain

any national reference curves, hence we compared with close Mediterranean basin that was reported by Sempe and Pedron. Hence, it could be probable that the accuracy of our comparison is not fully satisfied. Besides, the growth speed was not determined for our patients because they did not have their health record. Almost any chronic disease can cause short stature (renal disease, cardiac disease, coeliac disease, etc.). Common endocrinological causes of short stature include hypothyroidism, hypopituitarism, hypercortisolism, and classical Laron syndrome. All these are characterized by being overweight for height. Short stature may also be seen with severe intrauterine growth retardation (IUGR) or children born small for gestational age (SGA) and in large number of dysmorphic syndromes. Etiologies of SWGD are diverse. We have not distinguished any endocrine etiology such as chronic disease, severe IUGR, or children born SGA, and in large number of dysmorphic syndromes; and endocrine causes such as hypothyroidism, hypopituitarism, hypercortisolism, and classical Laron syndrome.

The endocrine pathology is involved in <10% of SWGD. The endocrine etiology diagnosis is crucial because to find out appropriate treatment that improves the stature prognosis.^{9,10} In our study, the endocrine etiologies of the SWGD are frequent. The isolated or secondary GH deficits constitute 60% of all etiologies. These observations could be explained by patients selection process achieved in our study, thus most patients were referred to our department for investigating a potential endocrine etiology and to eliminate other possible etiologies. Hence, the revealed frequency is higher compared to Mazouzi *et al.* and Moayeri *et al.* studies, including 50 and 34% of all etiologies, respectively.^{7,8}

Chronic diseases will slow the growth because of originating an increased basic metabolism and often in diseases such as anorexia, celiac disease, inflammatory diseases, renal disease, chronic lung disease, chronic encephalopathy, and heart disorders. According to some studies, the prevalence is varying from 5.9% reported by Rais *et al.* to 20.48%.^{6,11} Our series demonstrated 18.1% of chronic pathologies among all etiologies, including celiac disease, which constitute 10.3% of all etiologies of stature delay.

The genetic and malformative diseases are not frequent causes of stature delay; they are essentially dominated by Turner syndrome, which has to be evoked in context of any isolated apparent stature delay of females, thus Turner Syndrome represents 1/2500 at birth of females.¹² The genetic and malformative diseases are representing 7.8% of all etiologies.

Conclusion

PCM is a major tool for early diagnosis and for further treatment orientation of stature and weight growth. Thus PCM is mostly finding endocrine etiologies that are insignificant causes of abnormal human small body size. It is required to discard any clause

before initiating appropriate treatment. Stature and weight growth follow-up is essential and have to be systematic for every child. The dynamic and evolving aspect of stature and weight growth is very important; hence PCM must achieve measurements referenced within growth standards in the follow-up booklet and health file of children. This PCM assessment allows practitioner to detect without delay any abnormal growth, and therefore, helps in early detection of any critical diseases.

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Conflicts of interest

There are no conflicts of interest.

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