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# Short Stature in Children

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**ABSTRACT**

Short stature is a common problem in children. Short stature occurred due to many causes; these causes may be genetic, environmental or chronic diseases. Diagnosis of short stature could be achieved by two combined ways, physical examination, and laboratory tests. Treatment of short stature depends on the right diagnoses and the causative agent.

**Keywords: Short stature, Growth Hormone, children diseases.**

## INTRODUCTION

The general health of children can be monitored by growth which is an important parameter [(1)]. It is a continuous biologic process that depends on many factors including nutrition and hormone status [(2)]. Monitoring of growth in children is a part of preventive child health programs [(3)]. The monitoring of normal growth can be performed by growth charts [(4)]. Abnormal growth may refer to the presence of underlying disease in the apparently normal child**.** Early detection and diagnosis of short stature decrease the effect of any underlying health condition and optimizes final adult height [(5)]. Short stature (SS) is a problem in children globally [(2)] and especially in developing countries [(6)]. Short stature may be caused by many reasons related to the endocrine system, nutritional status, and genetic causes [(1)]. Short stature is considered as a sign of poor health in childhood [(3)]. It is unrecognized in early infancy that's why it is diagnosed at a late age which affects the improvement on health outcomes and stature [(7)].

## METHODS

Review articles and research articles between the year 1990 and 2016 were collected using different electronic databases such as PubMed and Google Scholar. Also, information was collected from Centers for Disease Control to identify the different definitions of short stature, its prevalence, its causes as well as management of short stature. Different keywords were used in the searching process, the title of each article was checked, and Articles which were not relevant have been rejected. Articles have been reviewed and collection of information has been done.

The study was approved by the Ethics Board of Tabuk University.

## DISCUSSION

### 1. Short stature definition and prevalence

The height of child results from the initial length at birth and the rate of growth over time [(5)].

Short stature is common in children, and it is a result of poor linear growth [(8)]. Short stature statistically is known as children who are shorter than 97% of their age and gender-matched peers [(9)]. Persons whose height is below the third percentile for age and sex, or more than two standard deviations below the mean are considered as suffering short stature [(4)]. Short stature can be defined by using velocity chart, if the growth velocity of a child is less than 25$^{th}$ percentile below the mean for that age, short stature will be considered. The height of the child can be interpreted by family's genetic potential for growth, in boys' mid-parental height = (father + mother +13)/2, while in girls= (father -13+ mother)/2]**.** The mid-parental height value is plotted as the adult height at 18 years and spread 6 cm on another side of the target height; the children height is considered to be normal when the height is with within this percentile [(10)]**.**The children whose height below the third percentile known as the lower limit of normal, most of them are healthy, however many of them will attain normal stature as adults [(11)], so the most common reason for referring to a pediatric endocrinologist is Short stature in childhood [(12)]. Most of the children whose height below the lower 2.5 percentile but with normal growth pattern is considered normal, however, those below 2.5 percentile an individual's \growth are thought to have a pathological condition keeping them from achieving their genetically determined height potential [(5)]. The first step to prevent short stature is to know its prevalence and its complications [(8)]. The prevalence of Short stature differs worldwide [(13)], the highest prevalence was reported in Bangladesh to be 73.6 % in 1991 [(14)]. Almost 2.2 million children under age 18 have heights below the third percentile in United States [(15)], although most of them are healthy, minor of them have pathologic etiology for short stature [(16)]**.** Australia was the lowest in prevalence where the percent of



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short stature was 0 % in 1995 [14]. In Saudi Arabia, it was found that in children and adolescents, short stature was intermediate at the international level [17]. In another study in Saudi Arabia by EL Mouzan et al. [18], they found that there was a higher prevalence of short stature in the Southwestern regions than that of the Northern or Central region.

## 2. Forms and Causes of short stature

Short stature can be normal variants or pathologic conditions; the normal form includes short familial stature and constitutional growth delay while pathological conditions include endocrine and systemic diseases [1]. Short stature may be caused by diseases which are systemic or endocrine or become a condition related to many syndromes [8]**.** Causes of short stature are various; three main causes of short stature **(figure1)** include chronic diseases such as undernutrition and its different causes, short genetic stature which in turn includes constitutional delay of growth and familial short stature and endocrine diseases including excessive secretion of androgens, hypothyroidism and growth hormone secretion abnormalities [1]**.**

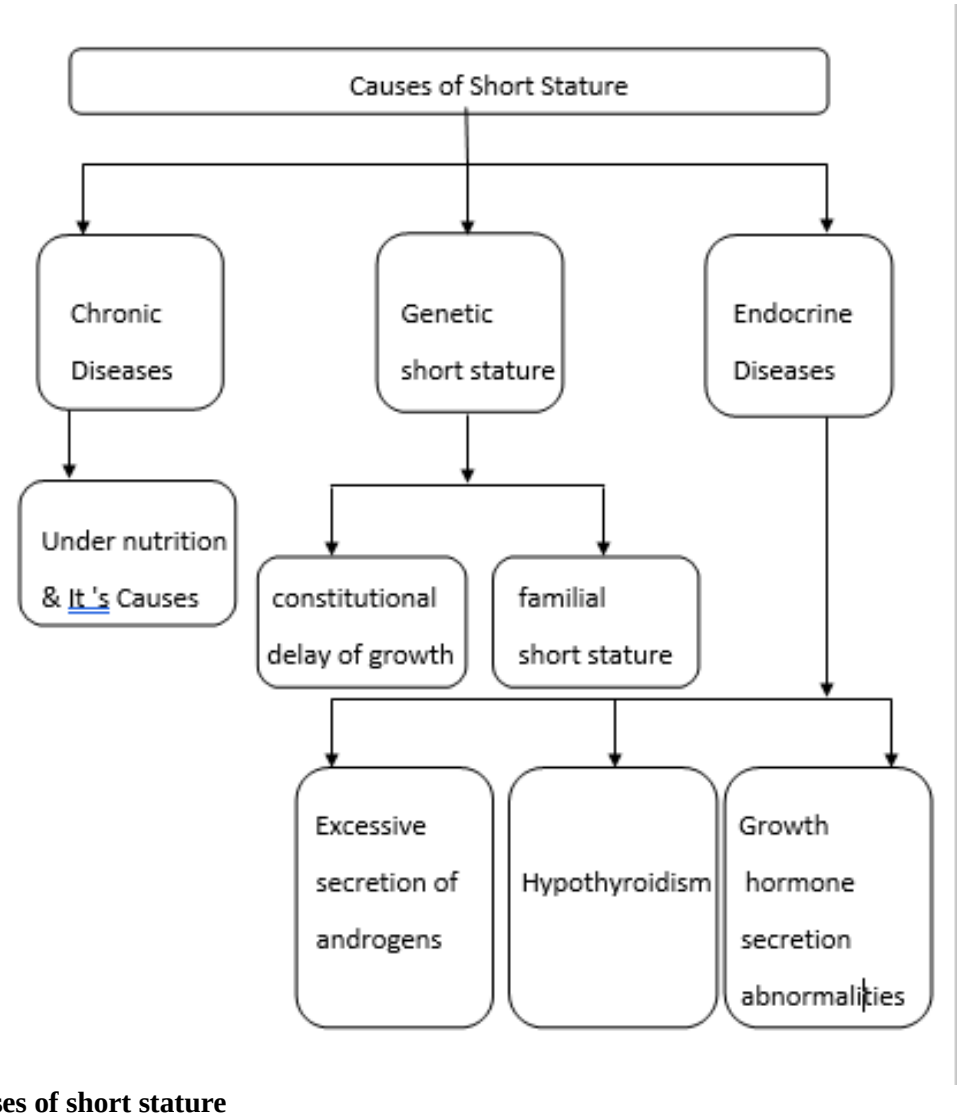


**Figure1: Causes of short stature**

Common causes of short stature can be expressed by mnemonics in 8 groups; endocrine, chromosomal, chronic diseases, iatrogenic, nutritional, skeletal, intrauterine and idiopathic [10]. Short stature of pathologic reasons represents 20 % of cases and including intrauterine, chromosomal, nutrition, skeletal disorders, chronic diseases, endocrinologic disorders [4]. Endocrine factors affect the normal growth in childhood stage [4], common endocrine causes of short stature include; hypothyroidism, Cushing's syndrome and growth hormone deficiency [18, 19]. Thyroid hormone which is an essential hormone for stimulation of growth may be defected or decreased in a case called hypothyroidism leading to short stature [4]. Hypothyroidism can occur in children at any stage of childhood**,** where bone age is delayed when compared with chronological age[11]**.**Growth hormone is essential for growth, it stimulates the production of somato medins,

which directly stimulate cartilage growth[4], excess levels of cortisol also can result in growth failure [11]. However endocrine diseases are rarely the cause of short stature [5]. Chromosomal disorders such as Turner syndrome are recognized by their physical stigmata. Turner syndrome which is present in one of 2000 female alive birth infants, accounts for one out of 60 cases of female short stature [4]. If a chronic disease in childhood is severe enough, they can lead to growth failure and short stature and they include; renal, and cardiac diseases, malignancy, cystic fibrosis and celiac disease [20].Celiac disease can result in short stature by causing malnourishment [4] especially in young children [21]. A very high prevalence of celiac disease in the Saudi Arabian community was shown with short stature being the only presenting symptoms [22]. Also, chronic diseases can disturb growth, where they are associated with low levels of insulin-like growth factor [4]. Other chronic diseases that cause short stature such as anemia and renal disease also were reported [4]. Iatrogenic causes include glucocorticoids; chemotherapy and radiotherapy also are other important causes of short stature [23]. Chronic undernutrition is an environmental factor which may cause an idiopathic short stature (ISS) in normal children [24]. In Saudi Arabia malnutrition which is a nutritional disorder is regionally varies, malnutrition in preschool children has been reported, this resulted in preventive programs for regions with high prevalence of malnutrition [25]. Malnutrition results from deficiency of specific nutrients including iron and zinc [4]. Severe intrauterine Growth Retardation also causes short stature [9]. The most cases diagnosed by physicians in developed countries have genetic short stature[1], this genetic cause includes constitutional growth delay and familial short stature which may reflects disorders of growth hormone secretion [4]. Child can inherit genetic short stature from their parents [5]. Genetic short stature represents almost half of child with short stature [10], however it was thought to be in higher percent reach to 80 % of children with short stature and they will be either with constitutional growth delay or familial short stature[4]. Normal growth velocity is seen in familial short stature in which a bone age appropriate for chronologic age [1]. Constitutional growth delay is more common in boys than in girls [11] and it is known as bone age is delayed relative to their actual age while growth is at a normal rate [26]. Theses genetic causes are considered to be idiopathic where there is no causative disorder can be identified for causing short stature [27].

## 3. Management of Short Stature

Short stature can be managed by 3 steps; growth monitoring and assessment, diagnosis and treatment. The growth assessment is important to identify short stature early and to predict it, while the diagnosis is necessary to confirm suspected cases to start treatment and finally is the treatment for short stature to eliminate its bad outcomes [16].

### 3.1 Growth monitoring

The pediatric endocrinologists determine which patient requires extensive evaluation or more conservative monitoring when these patients are seen for the first time [16]. Several factors influence linear growth and final stature of an individual, familial and genetic factors are among the most important factors influence the growth. The mid-parental height, which allows predictions of the child height [4]. The growth rate is the greatest in early infancy (with an average growth of 18 cm/year), slower in mid-childhood (with a growth range between 5 to 7.5 cm/y) while it accelerates at puberty, and then slow down and finally, growth ceases [4]. Growth velocity varies between different seasons, where it is accelerating in the spring and summer [28]. Growth assessment is very important in child care [1], where growth rate when evaluated routinely or an acute illness will provide the earliest identification of problems with growth [5], this can be performed by accurate measurements of growth and analysis of growth chart [1]. By reviewing 31 growth-monitoring studies, it was concluded that a single height screening might identify between 1:545 and 1:1793 new cases of potentially treatable conditions [29]. Monitoring normal growth patterns is determined by standard growth curve or growth charts which are the most useful method [4].The growth curves are used for evaluation of children less than 5 years old while for older children, growth charts are used [30]. Growth chart provides a picture of a child's growth pattern over time [31]. Current growth charts are derived from data collected in large population samples of normal healthy children [32]. However, many countries have developed growth reference charts specific to their populations [5], while serial measurements plotted on the curve give a clear picture of a child's rate of growth and stature [11]. Data obtained over time are plotted to allow the physician to determine whether the child is of normal stature and growing in normal rate or not [4]. Abnormal growth is appeared by a deviation from the percentile curve that the child followed, if the child is short stature, his height will be less than the third percentile for age, sex, and ethnic group [4], however the child's stature can be in the normal range while there is a failure of growth [11], so

growth rate should not be assessed alone but in combination with attained height. Growth deceleration is known as a growth velocity that is below the 5th percentile for age and gender [(5)]. The child is considered to be failed growth if he shows a length increment less than 10 cm between 12 and 24 months of age or less than 8 cm between six and 12 months of age. Between 2 and 5 years of age, the child should grow 6 cm/year at least until the start of adolescence [(11)].

### 3.2 Diagnosis of short stature

Diagnosis of short stature can be carried out by evaluation of short stature and physical examination as well as laboratory investigations [(11)].

#### 3.2.1 Short stature assessment

Evaluation of a child with short stature needs identification of medical family history, genetic growth potential data, a full physical analysis [(2)] including phenotypic characteristics, body proportions, and pubertal staging [(30)] and laboratory tests to exclude systemic disease and genetic conditions that related to short stature [(2)].The majority of children with short stature are diagnosed with idiopathic short stature due to the genetic factors [(12)]. Late onset of puberty-related to family history and the age at attainment of adult height show a slowed "tempo" of growth and development [(12)]. The child may have genetic or familial short stature if his parents are short [(5)]. It is important to assess the history of intrauterine growth restriction for the child because almost 15% of children with this condition suffer short stature throughout life [(35)]. In the female, it is helpful to identify Turner syndrome by history taking [(36)]. It is important to review the birth history of the child to find out abnormalities of fetal growth, nutritional status, medication use, psycho-social and cognitive development as well as perinatal complications [(30)]. The physical examination includes examining body abnormality appearance and proportions such as characteristics of genetic conditions like that seen in Turner syndrome, or that suggest hypothyroidism, poor weight gain and an increased ratio of the upper to lower body segment [(12)]. Severe hypothyroidism may cause increased BMI with continued weight gain, sallow complexion, and delayed relaxation of the deep tendon reflexes, chronic renal failure can cause ashen skin discoloration, edema, and pallor, while Cushing syndrome can cause obesity moon facies, violaceous striae, and cessation of linear growth, females with classic Turner syndrome with short stature are characterized by a webbed neck, shield-shaped chest, and a low posterior hairline; while those with mosaic Turner syndrome may have no stigmata [(31)]. Because malnutrition can cause short stature, it is important to determine causes of malnutrition such as chronic gastrointestinal illness which including inflammatory bowel disease, gluten enteropathy, causes of chronic diarrhea [(4)].

#### 3.2.2 Laboratory tests and investigations

For optimal treatment and management of short stature, it is crucial to identify the exact reason for short stature; this can be done by good diagnosis [(1)]. The diagnostic means required may differ between pediatric endocrinologists, however, this diagnostic approach is similar [(16)] as reported in a survey was done in 1995 where the responders stated that they were using a similar approach especially in laboratory investigations [(37)]. General tests are used to assess the major organ systems, such as the liver, kidneys, and gastrointestinal tract, while specific tests are performed for certain concern [(31)]. The general diagnosis can be assessed by performing endocrinal tests, biochemical investigations, specific investigation according to systemic disease exist such as karyotyping to rule out Turner syndrome [(10)]. Laboratory tests include erythrocyte sedimentation rate measurement to screen for chronic inflammation[(4)] and tissue trans-glutaminase antibodies for immune diseases detection [(12)], complete blood cell count to exclude diseases of blood that may lead to short stature such as anemia, leukemia or malabsorption, serum calcium and phosphorus and alkaline phosphatase evaluations to investigate the presence and absence of rickets, serum electrolytes, urea nitrogen and creatinine, as well as urine analysis, are required to investigate and exclude renal diseases, hypothyroidism which can lead to short stature and it can be investigated by serum-free thyroxine measurement, increased glucocorticoid can be assessed by 24-hour free cortisol testing or an overnight exam-ethasone suppression test, also growth hormone level is measured in children who have no obvious reason for short stature and those with abnormal growth velocity, normal body proportions, normal screening test results and delayed skeletal maturation [(4)]. Chromosomal analysis is used to rule out Turner syndrome in females, while in case of celiac disease identification; appropriate intestinal biopsy should be performed [(36)].

### 3.3 Treatment of short stature

Treatment of short stature depends on the underlying cause [(11).] It is important to identify constitutional or familial short stature to reassure the parents. These both cases possibly subtle

disorders of growth hormone secretion, although they are considered as normal variants due to genetic inheritance, children with constitutional growth delay or familial short stature has no serious underlying disorder [(4).] In children with constitutional growth delay, their adult height will be normal without intervention, but not with those of familial short stature [(11).] For most children with familial short stature, observation is a reasonable strategy to follow [(12)]. Hypothyroidism is treated by thyroid hormone replacement [(4),] and then they show normal stature once treatment is begun [(11).] If malnutrition is the cause then child should be treated by specific nutritional therapy [(4)]. Children with growth hormone deficiency are treated with growth hormone [(10)]. Recombinant human growth hormone (rhGH) is used in the treatment of children with short stature who are admitted to a pediatric endocrinologist for the evaluation of growth failure, however, there is no clinical characteristics are known for those who are evaluated for growth failure but do not receive rhGH treatment [(16)]. Previously, allergy side effects and antibody production were the complications of the first generation of biosynthetic growth hormone, but this problem has been resolved by the highly purified recombinant growth hormone [(4).] Growth hormone is not useful in case of Turner Syndrome [(11).] Growth hormone has shown effectiveness in increasing the growth rate and mean adult height by 1.2 to 2.8 inch or approximately 0.4 inch. (1.0 cm) per year [(30,38,39)]. The dose of growth hormone0.2 to 0.375 mg /kilogram of body weight per week and the treatment is continuing until completion of growth or reaching the normal value [(12).] In case of chronic diseases were found to be responsible for short stature, then medication of these diseases is required, however, the medication itself used to treat chronic disease may interfere with growth such as corticosteroids. If these diseases are resolved, an improvement will be noticed in growth [(11)].

### 4. Adverse effects of short stature and treatment outcome

Short stature is related to disorders of the cardiovascular system; also it adversely affects the health of female and survival of her offspring and is linked to impaired host immunity [(13)]. Treating diseases and hormonal abnormalities related to short stature will affect positively on the person, not only on growth but also on physical characteristics. Treatment for inflammatory bowel disease, cystic fibrosis, chronic renal failure and poorly controlled diabetes mellitus will result in good health and normalizing growth. Treatment of hypothyroidism result in improved energy and bowel function, in case of treating growth hormone deficiency or endogenous Cushing syndrome lead to get better muscle function and bone density [(5)].

## CONCLUSION

Short stature is common in children especially those in developing countries. The best management of short stature depends on three strategies, starting by monitoring the growth of children for early detection of any growth problem, then diagnosis to confirm cases and determine the exact cause of short stature to achieve the goal of treatment.

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