Review Article

Short stature — clinical approach to diagnosis : a 2018 perspective

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Concern for linear growth or short stature is unequivocally the most common pediatric endocrine problem. Growth in children is complex and predictable at same time. It is easy to detect any deviation from normal growth in children, but at the same time reaching an etiological diagnosis for same may be quite challenging and a daunting task. Nonetheless, reaching a diagnosis and institution of prompt treatment can be equally rewarding. Chronic systemic diseases are the most common cause for short stature in India, but endocrine diseases are being increasingly diagnosed. A systematic, but practical, approach is required to ascertain the cause of growth retardation in children.

[*J Indian Med Assoc* 2018; **116:** 56-62]

Key words **: Short Stature, Growth Stature Deficiency, Evaluation.**

Growth is a fundamental and inherent indicator of child hood and adolescence health. Even though the process of growth is multifactorial and complex, children usually grow in a remarkably predictable manner. Deviation from such a normal pattern of growth can be the first manifestation of a wide variety of disease processes, including endocrine and non-endocrine disorders and virtually involving any organ system of the body[1]. Growth retardation not only affect physical appearance of child but also lead to poor health related quality of life score and also various parents reported psychosocial problems. Treatment of children with short stature lead to better health related quality of life score[2]. Short stature or growth retardation is regarded as relatively early sign of poor health[3]. Hence monitoring of growth becomes utmost important and it is relevant to answer 3 simple questions while evaluating a child with short stature.

(1) Is child short?

(2) Is it physiological or pathological growth retardation?

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(3) What is a probable etiology?

This article intends to give practical clinical pathways to evaluate any child suspected to have short stature.

Materials and Methods

PubMed, Medline, and Embase search for articles published to April 2018, using the terms "short stature" [MeSH Terms] OR "short height" [All Fields] OR "growth hormone" [All Fields]. The references of the articles obtained from this search were also reviewed. The search was not limited to English language literature.

Results

Normal Growth Physiology :

Linear growth in human beings can be divided into four phases: 4 intrauterine, infantile, prepubertal and pubertal. Male and female siblings usually differ by 13 cm in final growth. This difference is contributed by late onset of puberty[5] and more height gained in pubertal growth spurt in males[6].

In nine months of intrauterine growth, a child grows by 50 cm, making it the fastest phase of growth in human lifespan. Growth in intrauterine life is affected largely by maternal factors and to a lesser extent by genetic make-up of child. These factors include maternal nutrition, placental size and function[8], maternal smoking, maternal age, birth order and genetic structure of child[7]. Presence of any of these factors can result in short-for-gestational-age babies. Endocrine factors do not seem to affect growth tremendously in this phase. First trimester growth is predominantly affected by genetic make up of child whereas subsequent growth is determined by both maternal as well as hormonal factors of fetus including pregnancy-associated plasma protein A (PPAPA),insulin like growth factor 2

(IGF2) and insulin like growth factor 1 (IGF1)[8]. First trimester growth is predominantly related to organogenesis. Second trimester is the fastest growing phase in any one`s life where fetus gains maximum length whereas 3rd trimester results in acquisition of body weight.

Infantile growth is again significantly contributed by nutritional status[9]. Presence of normal levels of growth hormone and thyroid hormone is permissive and essential for this phase of growth. Role of sex steroids during mini-puberty on linear growth has not been well studied and probably play a minor role only. Children typically grow by 25 cm in first year of life and 12 cm in second year.A child achieves a predictable channel (percentile) of growth by end of infancy[9] and follows the same channel during childhood to achieve genetically determined target height. After first two years of life, growth is usually 6-7 cm per year[10]. This childhood, also known as pre-pubertal, growth phase is predominantly due to growth hormone[11] and thyroxin[12,13] has a permissive role. Nutritional status can affect growth in this phase by hypothalamic suppression, by inducing secondary growth hormone resistance in case of malnutrition or by affecting timing of onset of puberty in case of obesity.

Pubertal growth spurt is driven by sex steroids by either direct action on epiphysis[12] or indirectly by increasing IGF 1 production locally at growth plate[14,15]. Presence of normal growth hormone is essential in this phase also. Any disease condition affecting either gonadal axis or growth hormone axis would also impair pubertal growth spurt. Child with low sex steroid would still continue to grow at pre-pubertal phase, while child with deficient growth hormone would typically have growth rate lower than six centimeter per year. Height gained during pubertal growth spurt is usually 20-30 centimeter. Onset of pubertal growth spurt correlates more closely with bone age than either chronologic age or height age. Females have growth spurt at bone age of 12 years and males have it at 13 years bone age[16].

Terminologies :

It is essential to know about exact meaning of different terminologies used during work up of a case of short stature. This is of paramount importance in case the patient follows up with another clinician. Common terms used are described in Table 1.

When to Evaluate :

Children, usually, follow centile curves on their growth chart according to mean parental height. Any child should be evaluated for growth retardation if he is deviating significantly from his/her growth curve observed over a period of time. This can be done by using either centiles or standard deviation scores (SDS). SDS is calculated as difference in observed minus expected height of patient and divided by standard deviation (SD) of population mean[17]. Specific cut-offs, for evaluation, have been used in different national programs, but they are for guidance only and each patient is to be evaluated individually.

There are few guidelines regarding when to start diagnostic work up of children with short stature. Oldest of them is Finish guideline[17] which was based on longitudinal studies of normal children. This guideline suggests the cutoff limits for height of child based on height and target height SDS of ±2.3. Other guidelines, from UK34 and Dutch,18 were based on consensus meeting. UK guidelines, alsoknown as Coventry consensus, stress on single measurement of height at school entry at 5 year of age. Evaluation of short stature is recommended if child's height is < 0.4 centile of corresponding UK normative data. However, it does not consider MPH, Growth velocity, and child who are short stature at or below 5 years of age.

Dutch guidelines[19], which were published in 1998, included three referral criteria: height SDS, change in height SDS, and difference between height SDS and target height SDS. In another guideline[20] published in 2008, children less than 3 years of age need to be evaluated are with extremely low or repetitive low height SDS. For children between 3 to 10 years, short for target height rule (height SDS minus target height SDS < 2) and height SDS < 2 should be the trigger for further evaluation.

Consensus Guidelines for diagnosis and therapy of GHD issued by GH research society[21] in 2000 also give criteria for immediate evaluation of children with suspected GHD, which includes : (a) Severe short stature, defined as a height more than 3 SDS below the mean. (b) Height more than 1.5 SDS below the mid- parental height. (c) Height more than 2 SDS below the mean and a height velocity over 1 year more than 1 SDS below the mean for chronological age, or a decrease in height SDS of more than 0.5 over 1 year in children over 2 year of age. (d) In the absence of short stature, a height velocity more than 2 SDS below the mean over 1

Table 1 — *Terminologies used in evaluation of a case of short stature*

Mid parental height (MPH) is mean of maternal and paternal height.
Target height is MPH plus 6.5 centimeter for male child and MPH minus 6.5 centimeter for female child.
Target height range has been defined variably in literature and is target height ± 8-10 centimeter. Target height range corresponds to two standard deviations from target height[28].
Bone age refers to maturation of bones as assessed by comparing x-ray of left hand (by convention) with reference x-rays/method e.g. Grulich and Pyle atlas or TW3 method. Correct estimation of bone age is most important step in evaluation of a case of short stature.
Height age is defined as age at which current height should correspond to 50th centile for that age.
Chronological age is defined as actual age of child as per his date of birth
Growth velocity is rate of linear growth and is expressed as growth over preceding one year. Minimum period required to assess growth velocity is six months because growth rate is not uniform over one year. Children may have period of saltation with excessive growth alternating with period of stasis with slow or even nil growth over 2-3 months. Seasonal variation should also be kept in mind while analyzing growth velocity; children may grow more during spring season[29].

year or more than 1.5 SDS sustained over 2 year.

However, each child needs to be treated individually based on various circumstances. In our country, we usually follow GH research society criteria. Table 2 summarizes the guidelines available in literature for screening of children for short stature.

Classification of Short Stature :

Short stature can be classified in two ways. One classification is based on relationship of height age, chronological age and bone age, which is more helpful in day to day practice whereas another isetiology based classification as suggested by European Society for Paediatric Endocrinology (ESPE)[22]. A child can be divided into one of three categories of short stature as intrinsic vs delayed vs attenuated growth which is predominantly decided by relationship between bone age (BA), height age (HA), chronological age (CA) and growth velocity. A child with CA=BA>HA with normal growth velocity would be classified as intrinsic shortness. A child with BA<CA with normal growth velocity will be divided two groups either delayed growth with normal growth velocity or attenuated growth with subnormal growth velocity[23]. Classifying a short child in one of these categories may narrow the spectrum of investigations required to reach an etiological diagnosis.

Another way to classify growth disorder can be adopted from ESPE classification of Paediatric Endocrine Diagnoses, where growth disorders are classified into 3 main groups[24].

(A) Primary growth disorders (conditions thought to be intrinsic to the growth plate) : This condition includes all condition associated with intrinsic shortness and includes genetic syndromes, short foe gestational age children and skeletal dysplasias.

(B) Secondary growth disorders (conditions that change the milieu of the growth plates): All other endocrine and systemic diseases are categorized as cause of secondary growth failure. They can present as delayed growth or as attenuated growth pattern. For example, a compensated systemic condition can lead to initial lag and followed by sustained growth at low-normal rate resulting in delayed pattern of growth. While, most of endocrine diseases present as attenuated growth failure.

(C) Idiopathic short stature (no recognizable cause is found): Idiopathic short stature (ISS) is subdivided into familial and non-familial short stature, and both can be further subcategorized into children with delayed and normal puberty.

Table 2 — *Summary of various guidelines for screening of children for short stature*

Guideline	Methodology	Recommendation for evaluation
Finnish[31]	Longitudinal	Height and target height SDS of -2.3
UK[34]	Consensus	Single measurement at 5 years of age. If height < 0.4 centile
Dutch[35]	Consensus	Based on height SDS, target height SDS and diff between both
Dutch (2008)[36]	Longitudinal	<3 year repetitive low height SDS 3-10 years < 2SDS
GH research society[37]	Consensus	• Height > 3 SDS below the mean • Height > 1.5 SDS below MPH • Decrease in Height velocity > 0.5 SDS over 1 year • Height velocity > 2 SDS below mean over 1 year

UK = United Kingdom, MPH = Mid parental height, GH = growth hormone

Evaluation of Short Stature :

The first step towards evaluation of these children is to determine whether the child is actually short for his parental height or not as almost 90 percent of children referred for evaluation of short stature may not be short and even children who are short almost 40 percent can be of normal variant[25].

The evaluation starts with a detailed clinical history (Table 3)[26]. A complete meticulous examination (Table 4) of child is of utmost importance in finding out etiology of short stature. Height should be ideally measured by same appropriately calibrated stadiometer each time to avoid instrumental variability in height. Child should stand on stadiometer in such a way that heel, buttock and occiput should touch the back of stadiometer and head should be positioned in Frankfurt plane. For children less than two years of age, infantometer should be used. Pubertal staging is essential part of examination. Sitting height should be measured in each child to calculate Upper segment (US) and lower Segment (LS). A disproportionate short stature can be due to different etiologies as mentioned in Table 5. Though difficult, certain features can help in differentiating between constitutional delay in growth and puberty, familial short stature and growth hormone deficiency (Table 6).

Growth charts: The most critical factor in evaluating the growth of a child is to determine the growth velocity. Serial plot of a height on the growth chart provides a valuable clue for identifying early growth retardation. However at least a period of 6 month is required to meaningfully determine growth velocity. Height determination in relation to age, sex, pubertal status, genetic potential, and population norm and in certain situations to syndrome specific growth curves (eg, Turner syndrome)[27] is indispensable. Deviation of growth from the appropriate disease related growth curve suggests the possibility of a second underlying cause, such as acquired autoimmune hypothyroidism in children with Down syndrome or Turner syndrome. There are various charts available for height plotting like CDC charts, KN Agarwal chart, WHO charts, Marwaha *et al* charts[28] and IAP charts[29] in our country. It is always confusing which charts to be used and plotting on two different charts can give different results[30]. IAP recommends to use WHO growth chart for children less than 5 year. For children between 5 to 18 years Revised IAP growth

Table 3 — *History in child with short stature*

History	Diagnosis
Maternal drug exposure (alcohol, phenytoin), maternal smoking,	Fetal alcohol syndrome, fetal hydantoin syndrome,
Maternal PIH, GDM, abruption placentae,	IUGR
Family h/o short stature	Familial short stature, CDGP
Neonatal hypoglycemia, prolonged neonatal jaundice, small size phallus	GHD, Hypothyroidism, Hypopituitarism
Recurrent respiratory complaints	Childhood asthma, cystic fibrosis, tuberculosis, Congenital Heart Disease
Chronic ear discharge	ASOM, CSOM, Turner Syndrome
Recurrent diarrhea, vomiting	Chronic gastrointestinal malabsorption syndrome, Celiac disease, Congenital adrenal hyperplasia
Blood transfusion	Malabsorption, PEM, thalassemia, sickle cell anemia, Celiac disease
Cyanosis, Dyspnea	Congenital Heart Disease
Recurrent jaundice, ascites	Chronic Liver Disease
Recurrent Urinary tract infection(UTI), ascites, oliguria, proteinuria	UTI, congenital urogenital system abnormality like vesicoureteric reflux, malformed kidney etc. Nephrotic syndrome
Salt craving, polyuria	Renal Tubular Acidosis
Bony deformity, h/s/o proximal muscle weakness, h/o dental abnormalities, h/o bone pain	Rickets and its various etiology
Head trauma, breach delivery, cranial irradiation, meningoencephalitis, visual difficulty, headache, Diabetes insipidus like features	GHD, panhypopituitarism, intracranial neoplasm like craniopharyngioma
Chronic steroid intake	Iatrogenic Cushing styndrome
Psychosocial history like binging, purging and altered body image	Anorexia Nervosa, Bulimia Nervosa

PIH = pregnancy induced hypertension, GDM = gestational diabetes mellitus, IUGR = Intrauterine growth retardation, CDGP = Constitutional delay in growth and puberty, GHD = growth hormone deficiency, ASOM = acute suppurative otitis media, CSOM = chronic suppurative otitis media, PEM = protein energy malnutrition

chart[31] or recent most published population specific charts should be used. However periodic update of these charts (at least every decade) are recommended to accommodate the changing socioeconomic scenario of population.

The first basic investigation in assessment of short child is to get X ray of left hand with wrist[31]and correct estimation of bone age by either Grulich and Pyle atlas or Tanners Whitehouse-3 (TW3) method. Counting the number of carpal bones is an inaccurate method for calculation of BA and should not be done. In infants less than 1 year, bone age may be estimated from radiographs of knee and ankle.

The initial baseline investigations have been elaborated in Table 7.CBC is done to look for evidence and type of anemia.Urine pH is must to look for evidence of renal tubular acidosis (RTA).Based on the analysis of 12 studies Van Rijn *et al*[32] concluded that in 2-8% of children presenting with only short stature (in the absence of typical gastrointestinal symptoms), celiac disease might be the underlying cause; whereas if we exclude other causes for short stature, this risk increases to 19-59%. Data from our country suggest prevalence of 11% celiac disease in children of short stature in institution based study with chronic diarrhea and anemia being significant predictor[33]. Hence all children with short stature should be evaluated for celiac disease. T4 and TSH34 should be done to rule out hypothyroidism. Girls with no other explanation for short stature should undergo karyotyping to exclude Turner syndrome, even in the absence of other features, as short stature may be the only presentation of Turner syndrome[35].

If no cause is identified on above investigation and there is strong suspicion of growth hormone deficiency (GHD),an IGF1[36,37] level should be done. A normal age and sex matched IGF 1 level essentially rules out GHD however few of mild GHD may be missed. A low IGF 1 level is very much in favor of GHD but it does not confirm the diagnosis of GHD[38]. However IGF 1 level estimation has its own problem as result need to be correlated with age and sex matched normative data, which is not available for most of countries, including India. Low IGF 1 level can also be seen in acquired GH resistance state like malnutrition[39], hypothyroidism[40], chronic inflammatory conditions, organ failure like hepatic[41] and renal failure[42].

Table 4 — *Examination findings in child with short stature*

Findings	Diagnosis
Evidence of malnutrition like dull lusterless hair, cheilitis, stomatitis, pallor, bitots spots, dry skin, loss of subcutaneous fat	PEM, malabsorption disorders
Dysmorphic features	Syndromic etiology
Hypertension	CHD like coarcation of aorta, CKD, cushing syndrome
Goiter, bradycardia, dry skin	Hypothyroidism
Rachitic changes likes wrist widening, rachitic rosary, frontal bossing, Harrison sulcus	Rickets
Heart murmurs	CHD
Wheeze, crepitation	Asthma, cystic fibrosis
Organomegaly	CLD, storage disorders, chronic infections
Overweight/ obese	Hypothyroidism, Cushing's syndrome, GHD, Pseudohypoparathyroidism
Hypotonia	Muscle disorder
Sign of neglect or abuse	Emotional deprivation
Disproportionate anthropometry, blue sclera	Skeletal dysplasia, `Osteogenesis imperfecta

PEM = protein energy malnutrition, CHD = Congenital heart disease, CKD = chronic kidney disease, CLD = Chronic liver disease, GHD = growth hormone deficiency

Table 5 — *Etiology of disproportionate short stature*

US>LS	LS>US
Achondroplasia	Spondyloepiphyseal dysplasia
Hypochondroplasia	Hemivertebrae
Chondro dysplasia punctate	Caries spine
Rickets	Mucopolysachroidosis
Osteogenesis imperfect	Mucolipidosis
Hypothyroidism	

US = Upper segment, LS = lower segment

Table 6 — *Differential features in CDGP versus Familial versus GHD*

Features	CDGP	Familial	GHD
Clinical	Short stature	Short stature	May have h/o hypoglycemia, midline defect, micropenis,
Endocrine	None	None	Other pituitary hormone deficiency
Bone age	Delayed	Normal	Delayed
Pubertal status	Delayed	Normal	Normal/delayed
Neuro-Imaging	Normal	Normal	Normal/Abnormal
Growth hormone stimulation test	Normal/ sometime abnormal	Normal	Abnormal

CDGP=Constitutional delay in growth and puberty, GHD=Growth hormone deficiency

Table 7 — *Investigations in evaluations of short stature*

Investigation	Diagnosis/clues towards diagnosis
Hemogram	Nutritional anemia, chronic anemia like thalassemia, sickle cell anemia, Celiac disease, chronic inflammatory disorders, chronic infections
Erythrocyte sedimentation rate	IBD, chronic infections
KFT	CKD
Electrolytes, urine PH	Renal tubular acidosis
Calcium, phosphate, ALP	Various etiology of Rickets
LFT	CLD
Urine routine and microscopy	Occult UTI, Renal tubular disorders
T4/TSH	Hypothyroidism
S IgA TTG	Celiac disease
X ray Skull	Craniopharyngioma, sellar mass
X ray Wrist with hand	Bone age, e/o rickets, skeletal dysplasia
Echocardiography	Congenital heart disease
Karyotype	Turner syndrome and other syndromic etiologies of short stature

IBD = inflammatory bowel disease, KFT = kidney function test,
CKD = chronic kidney disease, ALP = alkaline phosphatase,
LFT = liver function test, CLD = Chronic liver disease,
UTI = Urinary tract infection, TTG = tissue transglutaminase,

Children with poorly controlled T1DM also have low normal IGF1 but this rise to normal level once adequately treated[43]. The role of IGFBP3 in diagnosis of GHD is controversial in children more than 3 years of age however it is recommended in children less than 3 years of age[44]. IGFBP3 enjoys advantage of being GH dependent and has less variability with nutrition and age. Like IGF1, IGFBP3 level also does not have diurnal variation. IGFBP3 has good specificity and low level of IGFBP3 support diagnosis of GHD. However, in a study by Cianfarani *et al*, sensitivity of IGFBP3 was just 27 percent making it an imperfect tool in screening of GHD[44].

Growth Hormone Stimulation Test (GHST) :

Growth hormone stimulation testsare used as provocative testing tool for diagnosis of GHD. As, GH is predominantly secreted overnight in a pulsatile manner, with concentrations normally undetectable during the day, single random measurement of GH is of no value, except in neonates, in whom a random GH of <20 ng/ml is suggestive of GHD. Hence, a variety of GHST (Table 8), both physiological (such as sleep, exercise) and pharmacological (such as glucagon, insulin, arginine and clonidine) have been developed to determine an individual's capacity for GH secretion.Two or more provocative tests are to be done to confirm subnormal response, as 15-20% of normal children can have a subnormal response to single test[27]. However, single test would suffice for patients with defined central nervous system pathology, history of irradiation, multiple pituitary hormone deficiencies (MPHD) or a genetic defect known to be associated with GHD. The commonly used methods are clonidine stimulation test, insulin tolerance test (ITT) and glucagon stimulation test[45,46]. These tests are carried out in the morning after overnight fast using a standardized protocol. As child will require close observation for up to 2-3 hours after the test; a short admission is advisable for doing GHST. Severe/complete GHD is defined as peak GH value of <5 ng/ml after provocative testing and moderate/partial GHD as peak GH <10 ng/ml[47]. While interpreting results it should be kept in mind that higher BMI children can show poor response to stimulation test. Clonidine stimulation test is relatively safe and can be done easily in young children. Another test of glucagon stimulation is relatively safe and can be done safely in infant and young children but requires sampling for 3 hours. Overall clonidine stimulation test stands out as first test in children with suspected GHD except in very young children however recent study from Brazil based on Immunochemiluminescent assay (ICMA) has suggested as cut off of > or = 3 ng/ml to be normal[48].

Role of Sex Steroid Priming :

Sex steroid priming before GHST helps in differentiating between true GHD and CDGP. However over the years there has been debate over utility of priming, as some endocrinologists[49] believe that rise in GH post priming is just transient and levels can be insufficient for normal pubertal growth leading to under diagnosis of GHD in children. Advocates of priming[50] argue that it will increase specificity of GHST and will lead to decrease in false positive cases. ESPE[49] had recommended in 2010 that sex steroid priming should be restricted to boys with tanner stage 1 to 2 and age of >13.5-14 year and in girls with age >11.5-2s year with tanner stage 1-2. Rosenbloom[50] has argued this recommendation and suggested for sex steroid priming in all children of prepubertal and early pubertal age group. He particularly stressed upon priming for children during 4-5 year preceding normal timing of puberty. There are several protocols for priming. One protocol given by lazara and Philip is as follows: for girls, single daily dose of oral micronized Estradiol valerate 1 mg for children < 20 kg and 2 mg for children > 20 kg or ethinyl estradiol at the dose of 40 mcg/m2/day for 2-3 days preceding the GHST and for boys as 100 mg of depot testosterone 7- 10 days before testing. Whereas Williams text book1 suggests

giving 100 mg of depot testosterone 3 days before testing in boys and 5 mg of conjugated estrogens orally on the night before and the morning of the test, or 50 to 100 µg/day of ethinyl estradiol for 3 consecutive days before testing in girls.

MRI sella is indicated once diagnosis of GHD is made on provocative testing to rule out any associated developmental abnormalities such as optic nerve hypoplasia or dysgenesis of the corpus callosum and the identification of tumours in pituitary-hypothalamic area. Most common abnormal findings in MRI sella in GHD are presence of either an ectopic posterior pituitary gland or a hypoplastic anterior pituitary gland in association with a hypoplastic or absent pituitary stalk. However in most cases of GHD, MRI sella is normal. Once the diagnosis of GHD is made other pituitary hormone deficiency should be also looked for.

Table 8 — *Growth hormone stimulations test*

Agent	Mechanism	Procedure	Sampling	Remarks
Clonidine[65,66]	Probably acts through stimulation of GHRH	Clonidine tab 0.15 mg/m^2 orally	0, 30, 60, 90, 120 min	Watch for hypotension. Children becomes sleepy. Child should be preferably in lying down position during the test, observe subject for at least 2 hours after the test.
Glucagon[67-69]	Causes hyperglycemia leading to increase insulin release and secondary hypoglycemia	30 mcg/kg of SC or IM glucagon max up to 1 mg	- 30, 0, 30, 60, 90, 120, 150, 180	Can have nausea, cramps, delayed hypoglycemia
Insulin[66,67]	Hypoglycemia leading to increase GH response by decreasing SS and increasing alpha adrenergic response	0.10 – 0.15 U/kg IV	-30, 0, 15, 30, 45, 60, 90, 120	Hypoglycemia is a prerequisite for the test to be valid and for same blood glucose must drop by at least 50% from basal or < 40 mg/dl
Levodopa[69,76]	Increase GH secretion by dopaminergic and alpha adrenergic pathway	Oral, < 15 kg - 125 mg, 15 - 30 – 250 mg, > 30 kg- 500 mg	0, 30, 60, 90, 120	Side effects- nausea, vomiting, vertigo
GHRH-arginine test[70,77]	GHRH directly stimulates pituitary for GH secretion whereas arginine causes decrease in somatostatin leading to robust response of pituitary to combined test	1 mcg/kg IV GHRH at 0 min and 0.5g/kg of arginine from time 0 to 30 min (max 40 g)	0, 15, 30, 45, 60, 90, 120	GHRH not available in India

GHRH=growth hormone releasing hormone, GH=growth hormone, SC=subcutaneous, IM=intramuscular, SS=somatostatin

If despite extensive investigation including GHST, no etiology can be identifies then default diagnosis would be idiopathic short stature which is defined as height less than -2 SDS without evidence of any disease after thorough investigation.These children are GH sufficient and are of normal birth weight. These children will require long term follow up to look for growth velocity and appropriate management. Definition of idiopathic short stature also includes children with familial short stature and CDGP.

Summary :

Shortness of stature can lead to impaired quality of life. Importance of timely evaluation of stature cannot be overemphasized. Moreover, if diagnosed and treated late, potential gain in height despite treatment becomes low.

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