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A RETROSPECTIVE RESEARCH ON SHORT STATURE AND ITS ASSOCIATION WITH FAMILIAL, ENDOCRINE, CHROMOSOMAL DISORDERS AND CHRONIC DISEASES

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Abstract:

Objective:

Height below third centile is considered short stature. The factors responsible for short stature include familial, endocrine, chromosomal disorders and chronic diseases. The leading reason for short stature is considered idiopathic short stature. This study is conducted to identify various factors responsible for short stature complication in both adolescents and children.

Methods:

This study is retrospective in its design. It was carried out at Allied Hospital, Faisalabad (March, 2016 to February, 2017). Seventy healthy children/adolescents were selected in it. Evaluation of the subjects was executed clinically, radiologically, biochemically as per requirement. Biochemical testing encompasses testing of hormones and identification of endocrine causes. Analysis of data was carried out in SPSS.

Results:

Growth Hormone (GH) deficiency was noted in forty-eight subjects from total 70 patients being the rampant reason for short stature in the study at hand. Second commonest endocrine abnormality was Vitamin D deficiency in forty-four subjects (63%) out of total 70 patients. Other endocrine causes include pan-hypopituitarism, primary hypothyroidism and adrenal insufficiency. The weight for age was under third percentile in fifty-seven subjects (81%) having no connection with any other leading reason.

Conclusion:

Vitamin D deficiency and growth hormone are major reasons responsible for short stature.

Key Words: *Hypothyroidism, deficiency of growth hormone, Vitamin D deficiency.*

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INTRODUCTION:

Height below third centile is defined as short stature [1]. It has numerous reasons such as normal growth variants such as constitutional growth, familial short stature and puberty [2, 3]. Other caused of short stature include chronic systemic diseases (renal, pulmonary, coeliac and cardiac complications [4, 5]. It may have potential reason of endocrine disorders i.e. endogenous & exogenous Cushing syndrome, isolated deficiency of growth hormone, hypopituitarism, rickets, isolated hypothyroidism or osteomalacia, adrenal insufficiency [6 – 9], skeletal dysplasia's [12], chromosomal disorders (Turners syndrome) [11], and genetic (cystic fibrosis) [10]. Chemotherapy, radiotherapy, malnutrition and surgery are also potential reasons for short stature. [13]. CDGP and familial short stature are renowned jointly as 'Idiopathic short stature'. They are thought to be a leading reason for short stature mentioned in literature [14 – 17]. Child's genetics is used to determine final adult height. Parent's height range is acquired by child in familial short stature [18]. As far as CDGP is concerned, significant variations occur within axis of pituitary-gonad along with axis of growth hormone (IGF – I) which is responsible for skeletal maturation and delayed puberty spurt. It produces less height in comparison with expected adult height [19]. Despite this, it has been observed that CDGP children can possess familial short stature till 40% of the subjects [20]. Earlier detection of malnutrition or coeliac disease may permit the achievement of normal anticipated height. Timely detection and cure of hypothyroidism and idiopathic growth hormone deficiency can allow the height in normal range [21, 22]. Nutritional deficiency is common amongst Pakistani children [23]. Fifty-three percent children who are under age of five are stunted and 33% are underweight [24]. Ninety-four percent children are affected with Vitamin D deficiency that may decrease bone growth rate and skeletal mineralization [25].

METHODS:

This study was carried out at Allied Hospital, Faisalabad (March, 2016 to February, 2017). Relevant data of total seventy subjects was obtained. Inclusion criteria was; the subjects (labelled as short stature) who were having height under – II SD or under third centile for gender and age plotted on a chart (2000 CDC) [26]. Majority of subjects hailed from middle and upper class of the society. Evaluation of the subjects was executed clinically, biochemically and radiologically as per requirement. Complete physical examination and elaborated medical history was executed in clinical evaluation. Having gone through clinical evaluation, related biochemical profile (serum creatinine, blood urea, stool examination, complete blood count, liver function tests (LFT), urine, blood glucose, phosphorus and alkaline phosphatise, serum creatinine, fasting serum calcium, urinary pH and electrolytes) was acquired. Hormonal testing encompasses IGF-1 levels, Serum TSH, 8 am serum cortisol and free T4 assay. By using chemiluminescent micro particle immunoassay, Architect instrument was used for Vit-D levels. Growth Hormone deficiency was identified with level of serum IGF – I under normal sex and age range. On the grounds of values of FT4 and/or TSH, Hypothyroidism was identified. In selected cases, subsidiary tests i.e. FSH, anti-Tissue Transglutaminase antibodies, karyotyping, deficiency of growth hormone Insulin tolerance test and iron studies were carried out. Upon the manifestation of biochemical confirmation of pituitary hormone disorders, MRI pituitary without and with contrast executed. By employing Greulich and Pyle's Standards, X-ray hand was performed to evaluate the age of bone in all cases [27]. Entry of data was made. Analysis of data was carried out in SPSS. To measure the frequencies of different short stature cases, descriptive statistics were used. By using Fisher exact and Chi-square tests, contrast of categorical variables was executed (P-value < 0.05). Ethical standards were considered in the procedures.

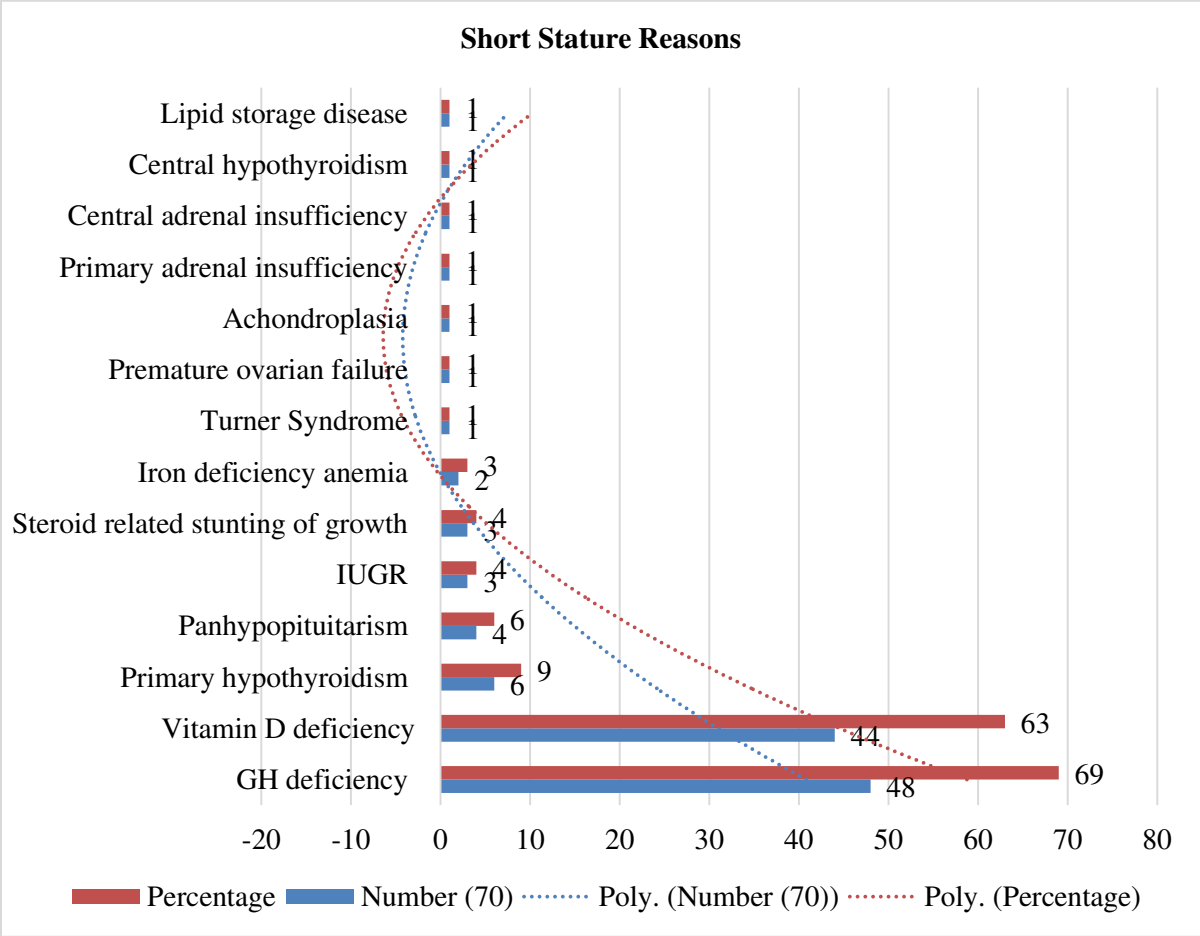
RESULTS:

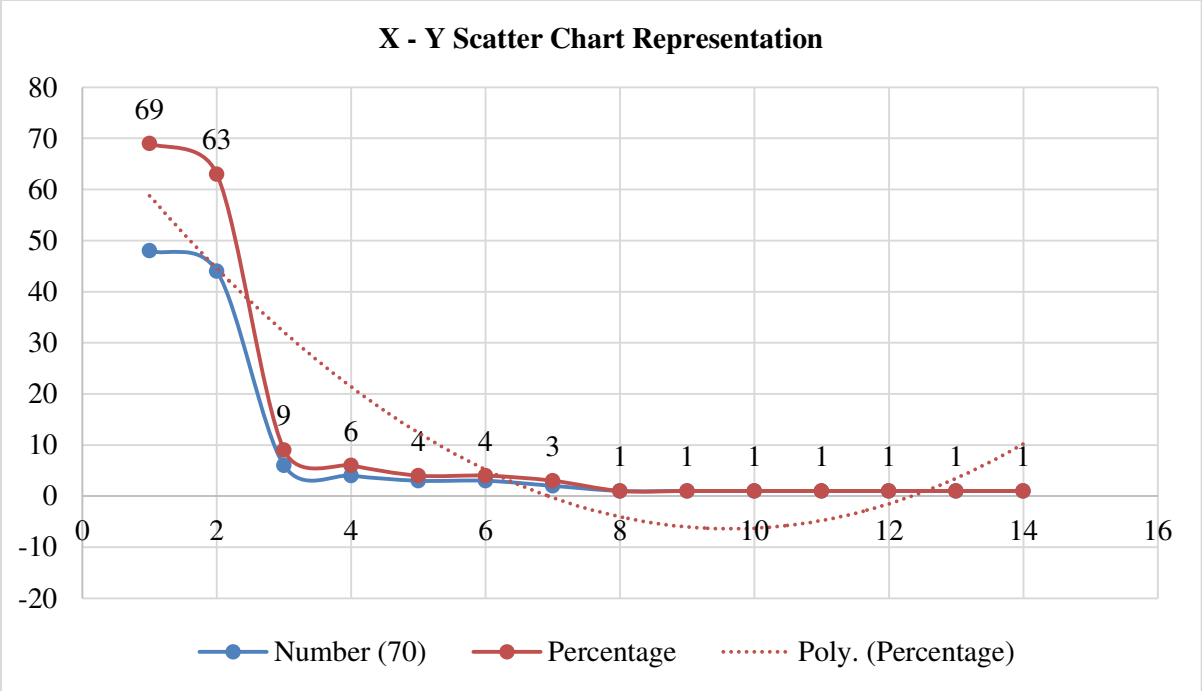
Analysis of seventy subjects having short stature was carried out. Eleven years was the median age which ranged from two to eighteen years. Thirty-eight subjects (54%) were male. In 57 cases (81%) the weight for age was under third percentile. Growth Hormone (GH) deficiency was noted in 48 / 70 subjects being the commonest cause for short stature in the study at hand as demonstrated in the given tabular data. Second commonest endocrine abnormality was Vitamin D deficiency in 44 / 70 subjects (63%). Four subjects (6%) showed Isolated Vitamin D deficiency which is attributed to combination of other endocrine abnormalities. Although the relationship was not good enough, GH deficiency was related to Vitamin D deficiency. Six cases (9%) displayed primary hypothyroidism. Short stature was caused in four cases (6%) by Pan hypopituitarism. Distribution of Vitamin D deficiency and Growth hormone deficiency was equal in both genders. Three cases (4%) had history of intrauterine growth retardation. History of steroid associated stunting of growth and asthma was recorded in three cases (4%). Two subjects were reported with high TIBC, low serum ferritin and iron deficiency anaemia as authenticated by microcytic

anaemia. One subject each was seen with rare causes i.e. premature ovarian failure, achondroplasia, lipid storage disease, Turner Syndrome, primary insufficient adrenal, central insufficient adrenal & central hypothyroidism. No noteworthy relationship was observed when cross tabulation of weight under the third centile was carried out against Vitamin D deficiency, Growth hormone deficiency, Primary Hypothyroidism and Pan-hypopituitarism.

Table: Short Stature Reasons

Condition	Number (70)	Percentage
GH deficiency	48	69
Vitamin D deficiency	44	63
Primary hypothyroidism	6	9
Pan hypopituitarism	4	6
IUGR	3	4
Steroid related stunting of growth	3	4
Iron deficiency anemia	2	3
Turner Syndrome	1	1
Premature ovarian failure	1	1
Achondroplasia	1	1
Primary adrenal insufficiency	1	1
Central adrenal insufficiency	1	1
Central hypothyroidism	1	1
Lipid storage disease	1	1





Majority of the cases displayed Vitamin D deficiency with other endocrine complications consequently the total of all such conditions was not analogous with the total strength of subjects.

DISCUSSION:

Despite vast research conducted on the topic at hand around the world, Pakistan still lacks that profundity. Growth Hormone (GH) deficiency was recorded in forty-eight subjects from total 70 patients being the commonest cause for short stature in our study. This trend seems incompatible with the global trend on the topic. Knoop et al. had indicated that 68% cases were either from familial short stature or CDGP [9]. When normal variants of growth constituted (52% – 85%) of short stature cases, other researches had come up with the same findings [16, 28 – 30]. This difference can be due to the fact that those studies were based on population which contrast to our specialist referral centre based study. Another reason can be the recruitment of the patients of those researches from tertiary health care centres in which significant number of cases were from poorer strata of society. On contrary, the study at hand recruited majority of subjects from upper strata of society. In earlier conducted researches, GH deficiency was noted the second commonest reason of short stature. Prevalence rate of (8% – 23%) was recorded in different studies based upon short stature [28, 29, 31]. The role of Vitamin D in growth and bone health is already recognised [32]. Its deficiency was reported globally [33, 34]. Vitamin D deficiency in Pakistan was recorded in 94% cases [25]. In this study, second commonest endocrine abnormality was Vitamin D deficiency in 44 / 70 subjects (63%). Four subjects (6%) showed Isolated Vitamin D deficiency which is attributed to combination of other endocrine abnormalities. Such results are poignant indicators of Vitamin D deficiency presence in Pakistan [35]. In linear growth and in the enlargement of bone in children, the role of Thyroid hormone cannot be overlooked. Lack of this hormone can result in stunted growth or maturation arrest [36]. Nine percent cases were presented with primary hypothyroidism in our study whereas the presence of central hypothyroidism was noted on one percent of the cases.

Sultan et al. in a Pakistani study has recorded 5.6% of hypothyroidism responsible for short stature causes [14]. Rabbani et al in a local study recorded percentage value of 17 of hypothyroidism responsible for short stature causes [15]. Short stature was caused in four cases (6%) by Pan hypopituitarism. On contrary, an Iranian study had indicated 3.5% of Pan-hypopituitarism causing short stature [31]. The weight under third centile in 81% in the study at hand is of vital significance since there was no detection of etiological factors when the subjects were hailed from upper/middle socio-economic class.

CONCLUSION:

Vitamin D deficiency and growth hormone are major reasons for short stature in Pakistani population. Timely detection of such implications can not only improve the life status but also prevent short stature cases to exacerbate further.

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