SHORT STATURE ETIOLOGICAL PROFILE AND ITS CORRELATION TO FSS AND CGD IN BOTH MALE AND FEMALE: A CROSS-SECTIONAL RESEARCH

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Abstract:
Objective: We aimed to determine etiological factors frequency in the patients having short stature.
Methods: Sample size of this research was 100 children studied at Mayo Hospital, Lahore (February 2016 to March 2017). Design of the research was cross-sectional descriptive. Forty-eight boys and fifty-two girls were selected in the research sample in the age bracket of 3 – 15 years with a mean age of (9.9 ± 3.4). All the children were reported for their short stature.
Results: Most common reasons for short stature were FSS and CGD which were reported in fifty-five percent of the total sample. Seventeen children were detected for non-endocrinal reasons considered as a single entity. Repeated etiological factors were FSS, CGD, GHD, Hypothyroidism and Celiac disease. Endocrinal causes and GHD cases were respectively 44% and 13%. Boys were dominant than girls with a proportion of 2.7 to 1 (P-value under 0.05).
Conclusion: Normal growth variants were considered as the most repeated cause short stature. Pathological reasons were more likely to be associated with the children having a height less than 0.4th percentile.
Keywords: FSS (Familial Short Stature), CGD (Constitutional Growth Delay), GHD (Growth Hormone Deficiency), Endocrinal and Short Stature.

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INTRODUCTION:
Development of a child in a normal way is the major concern in the childhood period. Abnormal and normal growth is to be differentiated [1]. Increase in the height in the first three years of age of a human is considered as the growth factor which decreases with the development of puberty in a progressive way [2]. In order to define growth an accurate measurement of head circumference, weight and height are measured in a precise way. Short stature is classified as abnormalities of primary growth, disorders of secondary growth and genetically short stature [3].

FSS and CGD are repeatedly observed as the cause behind the incidence of short stature in the early two years of a child [4, 5]. Any disease such as renal, cardiac and pulmonary causes the failure of growth. Younger children face the issues of Celiac disease [6]. Growth failure can be caused because of therapies such as glucocorticoids, surgery, chemotherapeutic drugs, nutritional deprivation and radiotherapy; whereas, nutritional deprivation includes reduced diet intake, enhanced expenditure of resting energy expenditure, malabsorption or restricted diet disorders [7]. Endocrinal issues such as hypothyroidism, hypopituitarism, hypercortisolism and classical Laron syndrome also cause growth issues such as short stature normally in the shape of overweight [8 – 13]. Short stature is also taken as idiopathic if there is identification is made about the causing abnormality. Various factors are involved in Pakistan in this regard such as GHD [14]. We aimed to determine etiological factors frequency in the patients having short stature.

METHODS:
A sample size of this research was 100 children studied at Mayo Hospital, Lahore (February 2016 to March 2017). Design of the research was cross-sectional descriptive. Forty-eight boys and fifty-two girls were selected in the research sample in the age bracket of 3 – 15 years with a mean age of (9.9 ± 3.4). All the children were reported for their short stature. Height was measured for the classification of short stature children. NCHS and CDC charts were considered for the measurement of height in centimetres. We included only those cases who had a proportionate short stature. Informed consent was taken from the parents. Both male and female children in the age group of 3 – 15 years with a short stature of (2 SD) were included in the research. Children height was not appropriate for the height of the parents. All cases with syndromes like Noonan, Prader-Willi, Russell Silver and malnutrition were not included in the sample population.

We also carried out a physical assessment and historical evaluation of the children. In the light of Tanner and Marshall Classification determination of puberty was made. Initial screening of blood CP, renal function test, ESR, Alk P, Ca, P, T3 & 4, TSH, stool test and radiographs (bone age) and urinalysis was carried out. Confirmation of GHD was made through the failure of the peak concentration of GH to reach a level of (10 ng / mL) with the help of the insulin tolerance test. Females were assessed through Chromosomal study and all other short stature reasons were not considered. Short stature is classified as abnormalities of primary growth, disorders of secondary growth and genetically short stature [3].

Growth was influenced by various growth variants which included non-endocrinal medical state which also influenced endocrine and growth disorders. Normal variants included delayed maturation of skeleton, delayed puberty, FSS and delayed growth spurt. FSS is taken as proportionate short stature which has a normal rate of growth and same chronic and skeletal age without any systemic abnormality. Celiac disease was diagnosed through anti-tissue transglutaminase “Ig A” screening with the help of histopathological assessment of the small gut biopsy. SPSS was used for the data entry and analysis.

RESULTS:
Most common reasons for short stature were FSS and CGD which were reported in fifty-five percent of the total sample. Seventeen children were detected for non-endocrinal reasons considered as a single entity. We included only those cases who had a proportionate short stature. Informed consent was taken from the parents. Both male and female children in the age group of 3 – 15 years with a short stature of (2 SD) were included in the research. Children height was not appropriate for the height of the parents. Repeated etiological factors were FSS, CGD, GHD, Hypothyroidism and Celiac disease. Endocrinal causes and GHD cases were respectively 44% and 13%. Boys were dominant than girls with a proportion of 2.7 to 1 (P-value under 0.05). Detailed analysis of the outcomes has been made in the given tabular data of Table – I and II. Outcomes have been analyzed with respect to gender distribution about the repeated short stature reasons (Table – I) and various studies etiological comparison (Table – II).
### Table I: Common causes of short stature.

<table>
<thead>
<tr>
<th>Etiology</th>
<th>Total</th>
<th>Male</th>
<th>Female</th>
</tr>
</thead>
<tbody>
<tr>
<td>A normal variant of growth</td>
<td>55</td>
<td>29</td>
<td>26</td>
</tr>
<tr>
<td>Hypothyroidism</td>
<td>15</td>
<td>3</td>
<td>12</td>
</tr>
<tr>
<td>Growth hormone deficiency</td>
<td>13</td>
<td>9</td>
<td>4</td>
</tr>
<tr>
<td>Celiac disease</td>
<td>8</td>
<td>4</td>
<td>4</td>
</tr>
<tr>
<td>Chronic renal failure</td>
<td>3</td>
<td>2</td>
<td>1</td>
</tr>
<tr>
<td>Turner's syndrome</td>
<td>3</td>
<td>0</td>
<td>3</td>
</tr>
<tr>
<td>Familial rickets</td>
<td>2</td>
<td>2</td>
<td>0</td>
</tr>
<tr>
<td>Chronic liver disease</td>
<td>1</td>
<td>0</td>
<td>1</td>
</tr>
</tbody>
</table>

### Table II: Comparison of aetiology of short stature with other studies

<table>
<thead>
<tr>
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</tr>
</thead>
<tbody>
<tr>
<td>Normal variant of growth</td>
<td>80.00</td>
<td>47.00</td>
<td>15.90</td>
<td>20.50</td>
<td>30.10</td>
</tr>
<tr>
<td>GHD</td>
<td>2.50</td>
<td>23.40</td>
<td>7.40</td>
<td>19.50</td>
<td>13.00</td>
</tr>
<tr>
<td>Turner Syndrome</td>
<td>1.50</td>
<td>4.50</td>
<td>7.40</td>
<td>7.40</td>
<td>3.00</td>
</tr>
<tr>
<td>Hypothyroidism</td>
<td>1.00</td>
<td>8.00</td>
<td>14.20</td>
<td>10.00</td>
<td>15.00</td>
</tr>
<tr>
<td>Chronic systemic diseases</td>
<td>10.00</td>
<td>4.00</td>
<td>12.40</td>
<td>8.50</td>
<td>17.00</td>
</tr>
</tbody>
</table>
DISCUSSION:
In the present research, common reasons for short stature were FSS (Familial Short Stature) and CGD (Constitutional Growth Delay) which were reported in fifty-five percent of the total sample which is comparable with local and global research studies [10, 13]. Sultan reported the incidence of CGD as 37.9% in his research as a most repeated entity [14]. Short stature is an important global issue frequently faced by paediatricians in the clinical practice. Three
percent of the total population falls in this category as per the definition of short stature. Genetic height cannot be gained in case of delayed treatment and diagnosis. Above 65% of the short stature, children are of normal variant [15]. No medical treatment is required for these normal variants, they only need proper monitoring of the growth. Short stature is also presented and caused by various serious treatable diseases. To gain normal height we need to cater a timely treatment and recognition of the pathological processes. All over the world ample literature is available on the topic but there is a scarcity of literature is evident in Pakistan.

It has been learnt through epidemiologic data that boys are twice prone to the growth of variants than girls. Delayed sexual development in males is concern reflected by the comparison made with the peers [16]. Endocrinal reasons were observed in 28% of the children with short stature in our research and 17% cases were attributed to non-endocrinal reasons. All the authors have reported GHD as the repeated endocrinal cause of short stature at the tertiary level of healthcare. Comparisons revealed five percent of endocrinal involvement in the general public [11]. Our GHD outcomes were 13% which is almost double as reported by Bhadda as 7.4% [7]. Zargar reported 22.8% and 23.4% GHD in the Iranian population [13]. Girls were reported as more prone to GHD which is not comparable with the outcomes various other authors. This fact was not reported with a precise variation. A local research held in Multan reported GHD in 18 cases (10.7%), it is comparable with our outcomes. Endocrine cases commonly reported with short stature normal variant as an entity [17]. Celiac disease was reported as common most non-endocrinal reason observed in 8 / 100 cases (8%) which can be compared with numerous global studies. Normal growth variants were reported as a repeated short stature contributing factor in children. Males and females were reported for CGD and FSS as repeated causes of the short stature which is the same as reported in an Indian research [18].

CONCLUSION:
Endocrine disorders were not commonly observed in the majority of the short stature children. Growth retardation was very much marked in the pathologial short stature cases as the height was under 0.4th percentile according to the chart of NCHS than normal variants; whereas, almost 40% cases were reported a height under 0.4th percentile. There is no need for the growth hormone analysis for every short stature child. Without any risk, we can use monitoring of growth velocity as a sensitive measure for fifty percent of the short stature children under the 0.4th percentile height. Better assessment of the etiological profile can be made with the help of more research work on various centres across the country.

REFERENCES:
15. Sultan M, Afzal M, Qureshi SM, Aziz S,