Occlusal Characteristics of Individuals with Growth Hormone Deficiency, Idiopathic Short Stature, and Russell-Silver Syndrome

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ABSTRACT

Purpose: The purpose of this study was to assess the occlusal characteristics of individuals with growth hormone deficiency (GHD), idiopathic short stature (ISS), and Russell-Silver syndrome (RSS), and compare them to the means of a normal population.
Methods: Data about the stage of dentition, diastema, maxillary transverse deficiency, overjet, overbite, molar classification, and maxillary and mandibular crowding were obtained from orthodontic screening notes and standardized clinical exams of children with growth disorders seen at screening events. The prevalence of these occlusal characteristics was calculated and compared to the pooled mean of a normal population as determined by the National Health and Nutrition Examination Survey studies.
Results: Twenty RSS subjects and 16 subjects with GHD or ISS were studied. The RSS cohort presented statistically significant greater mean overbite as well as mandibular and maxillary crowding compared to the general population. Descriptive statistics were performed for the GHD and ISS group.
Conclusion: Occlusal abnormalities are prevalent in children with growth disorders. (J Dent Child 2015;82(3):135-40)

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The process of craniofacial growth and development is complex and can be affected by disturbances that interfere with somatic growth. Growth hormone deficiency (**GHD**), idiopathic short stature (**ISS**), and Russell-Silver syndrome (**RSS**) are conditions that present with a deficit in stature as a common feature. These conditions may also present with specific facial and dental characteristics.

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The prevalence of GHD is estimated to be from 1:4,000 to 1:9,000.[1-3] The diagnosis is based primarily on clinical assessment and auxology. Growth hormone (**GH**) level testing remains a controversial diagnostic tool due to variation in provocative agents, questionable validity, and reproducibility.[4] Routine GHD diagnosis is not based on genetic testing. However, numerous mutations leading to GHD have been identified, and it is likely that the use of genetic testing will become a more important tool in diagnosing GHD in the future.[4]

GH has direct effects on body structures and also functions as a regulating trophic hormone, which stimulates the production of insulin-like growth factor 1 (**IGF-1**), among other peripheral hormones.[3] IGF-1 is an important mediator of GH and is essential for normal growth and development. Growth is impaired when IGF-1 levels

are low, despite normal levels of GH, a condition that is known as primary IGF-1 deficiency (**IGFD**).[5]

Another condition associated with reduced growth is ISS, which is defined as stature that is at least two standard deviations below the norm, with normal body proportions and without evidence of nutritional deficiencies, endocrine abnormalities, or chronic systemic or psychiatric diseases.[6] ISS children's birth weight falls within the normal range, and they present normal levels of GH. Despite normal GH levels, GH therapy has been demonstrated to be beneficial.[7]

Many studies have analyzed the dental and skeletal development of GHD and ISS individuals, who demonstrate skeletal delay on hand and wrist films; this delay is variable in ISS but steady in GHD.[8-10] They also present with underdeveloped maxilla and mandible.[9,10] Evaluation of skull radiographs of GHD patients has shown underdevelopment of the facial bones and sinuses, but normal or nearly normal cranial vault dimensions when compared to healthy control subjects.[9] There appear to be no differences in cephalometric analysis between GHD and ISS.[10] Cephalometric analyses of short individuals with varying GH levels demonstrated that most facial structures are significantly reduced in size and the cranial bases, maxilla, and mandible present disproportionate growth. As a consequence, their faces are retrognathic and the posterior facial height is proportionally smaller than the anterior facial height, with an increased vertical inclination of the mandible.[11]

Dental developmental delay is commonly present in GHD and ISS patients,[8-10,12] with two studies finding no difference in dental delay between GHD and ISS individuals.[10,12] However, one study found mild dental delay in ISS patients but a significant dental delay in GHD patients.[8]

GHD and ISS patients present particular dental features, such as small-sized teeth and high prevalence of crowding.[9,11-13] There appear to be no differences in tooth sizes between GHD and ISS patients but both GHD and ISS patients appear to present smaller teeth than healthy individuals of normal stature.[9,12] One study found less than 40 percent of dental crowding greater than two millimeters in GHD and ISS patients and no significant difference in the amount of crowding between them.[11] Another study found that malocclusion was present in approximately 40 percent of GHD patients and in approximately 16 percent of ISS patients.[10] However, this study did not define the criteria used to determine the presence of malocclusion.

Medication therapy (i.e., GH supplementation) to improve growth in GHD and ISS may affect the development of the craniofacial structures.[9,13] It has been observed that treatment with anabolic drugs stimulated exfoliation of primary teeth and eruption of permanent teeth.[9] GH therapy appears to have no effect on dental age while enhancing bone age.[13] GHD patients not treated with GH present significantly smaller mandibular arch length and a higher prevalence of crowding than those treated with GH (37.5 percent versus 23.3 percent for the latter).[13] A significant tendency for the arch dimensions of ISS children treated with GH to increase over time has been observed.[14]

A reduction in facial convexity associated with GH therapy has also been observed. The profile changes were due to changes in the vectors of the mandible and mandibular anterior growth.[15] The positive correlation between the duration of GH treatment and the amount of forward mandibular growth and increase in SNB angle suggests that GH therapy may lead to a more favorable pattern of growth.

Silver et al.[16] first described two children with RSS, and Russell described five children with similar features.[17] The term Russell-Silver syndrome later became used to describe individuals who present intrauterine growth restriction, postnatal growth hormone deficiency, relative microcephaly, and triangular facial appearance with or without fifth finger clinodactyly and/or body asymmetry.[18,19]

The diagnosis of RSS is based on clinical features that are nonspecific, vary in severity, and are more pronounced early in life. Therefore, the frequency of RSS is not easily determined. Abnormalities in chromosomes 7 and 11 have been found in approximately half of those clinically diagnosed with RSS.[20] There is still a significant number of individuals who present the clinical features of the syndrome in which the molecular cause is unknown.[20]

RSS patients have typical facial characteristics. Their overall facial dimensions are smaller, their mandible and maxilla are steeply angled, and their posterior facial height is diminished in relation to their anterior facial height.[21] They also present unique dental characteristics, such as greater prevalence of increased overjet, overbite, and dental crowding,[21-24] dental anomalies (multiple missing teeth, discolored teeth of variable size, high arched palate, delayed dental eruption, microdontia)[22,23] and malocclusions.[22,25] Dental maturity was found to be within normal limits, and time of eruption was significantly delayed (1.1 years) for RSS patients.[21] One case report also described normal overjet, increased overbite, and severe transverse discrepancy of the mandible in relation to the maxilla.[22]

Since disorders that affect general growth may interfere with the normal growth and development of the craniofacial structures, individuals affected by such disorders may present unique orthodontic needs. The purpose of this study was to assess certain occlusal characteristics of GHD, ISS, and RSS patients in order to improve the understanding of the orthodontic needs of this population.

METHODS

This study was approved by the Institutional Review Board (IRB protocol no. 2013-0501) of the University of Illinois at Chicago, Chicago, Ill., USA. This was a convenience sample of consecutive participants in orthodontic screenings done during the annual Magic Foundation National North American convention from 2010 to 2013. The Magic Foundation is a nonprofit organization based in Oak Park, Ill., USA, that helps families of individuals diagnosed with medical conditions affecting growth. The organization provides support primarily through education, networking, and medical referrals. The convention is attended by families from all over the world, but primarily from North America.

This study had retrospective and prospective components. The retrospective component consisted of data about the dental occlusion obtained from orthodontic screening notes prepared by the orthodontic consultant from 2010 to 2012. The prospective component consisted of data about the dental occlusion collected by the orthodontic consultant and a cross-trained assistant orthodontist using a similar standardized clinical evaluation in 2013. No subjects were evaluated more than once, and no treatment was delivered; it was not possible to obtain radiographs or dental casts during the Magic Foundation convention. The control group used in this study was the sample of the U.S. population examined during the National Health and Nutrition Survey (NHANES).[26-28]

The following information was obtained from the screening notes and standardized exam:

- Medical diagnosis.
- Dentition stage: primary, mixed, or permanent.
- Maxillary transverse deficiency (MTD), as determined by the presence of lingual crossbite and/or history of orthodontic maxillary expansion.
- Overjet (OJ):
  - — within normal limits (zero to two mm);
  - — increased (greater than two mm);
  - — negative; and
  - — millimetric measurement in subjects who participated in the prospective standardized exam.
- Overbite (OB):
  - — within normal limits (zero to three mm);
  - — deep bite: greater than three mm;
  - — edge-to-edge;
  - — negative overbite (open bite); and
  - — millimetric measurement in subjects who participated in the prospective standardized exam.
- Crowding (of at least two mm) or spacing.
- Mandibular and maxillary alignment scores (MandAlign and MaxAlign) for subjects who participated in the prospective standardized exam.[29]
- Presence of midline diastemas in subjects who participated in the prospective standardized exam.
- Permanent molar classification (Class I, II, or III).
- History of orthodontic treatment obtained from subjects who participated in the prospective standardized exam.

The cutoffs for increased OJ and OB were consistent with limits chosen by other authors[21-24] and comparable to the NHANES values.[26-28]

Descriptive statistics were determined for all the occlusal characteristics studied. A one-sample *t*-test was performed to compare the mean of a certain occlusal characteristic of the studied sample to the pooled mean of the general population, as reported by the NHANES studies. Data analysis was performed using SPSS 20.0 software (IBM, Chicago, Ill., USA).

RESULTS

A total of 16 subjects reported GHD, IGFD, or ISS. From the charts available, eight subjects reported GHD, one subject reported IGFD, and one subject reported ISS. From the subjects examined prospectively, four reported GHD and two reported IGFD. For statistical purposes, IGFD was considered to be in the spectrum of GHD. The mean age of those subjects was 12 years, nine months (range: five years to 14 years, 11 months). From the prospective cohort, four subjects had had or were having orthodontic treatment. All of them reported crowding as one of the reasons for treatment, one subject reported increased OJ and late eruption, and two subjects reported MTD in addition to crowding.

A total of 20 subjects reported RSS: six from the charts available and 14 examined prospectively for this study. The mean age of these subjects was nine years, eight months (range: five years to 16 years, seven months). From the prospective cohort, three subjects reported having had orthodontic treatment: one subject for overbite, one for overbite and crowding, and one for

Table 1. Dentition Stage, Maxillary Transversal Deficiency (MTD) and Crowding Characteristics

Groups	N	Primary dentition	Mixed dentition	Permanent dentition	MTD	Crowding
GHD+ISS	16	1 (6%)	8 (50%)	6 (37%)	4 (25%)	9 (56%)
RSS	20	3 (15%)	11 (55%)	6 (30%)	2 (10%)	17 (85%)

Table 2. Overjet, Overbite and Molar Classification

Groups	N	Increased overjet	Deep overbite	Class II	Class III
GHD+ISS	16	6 (37%)	6 (37%)	5 (31%)	1 (6%)
RSS	20	10 (50%)	15 (75%)	8 (40%)	0 (0%)

crowding. A summary of the occlusal findings for all subjects is found in Tables 1 and 2.

Data about diastemas, OJ, OB, and crowding from RSS subjects obtained from the prospective cohort were analyzed separately for statistical comparison with the values published by the NHANES studies. [26-28]

One subject from the prospective cohort did not present permanent central incisors. Therefore, this subject was not included in the analysis of diastema, OJ, OB, and alignment scores. The mean age for the remaining prospective cohort (N=13) was 10 years, 11 months (range: seven years, one month to 16 years, seven months). The prevalence of diastema was determined from 11 subjects who were younger than 11 years old and presented both permanent maxillary incisors at examination. A summary of the occlusal findings is found in Table 3.

Table 3. Characteristics of the patients with Russell-Silver Syndrome with standard deviation and Control Groups

Groups	Diastema (8-11 yrs)	Overjet (mm)	Overbite (mm)	MaxAlign (mm)	MandAlign (mm)
RSS	36%	4.31±2.52	6.77±3.29	7.15±6.18	10.15±9.30
Control	19%	3.20	3.00	3.00	3.10

The mean OJ and OB of the RSS cohort was compared to the values of the general population, as determined by the NHANES III study.[26-28] In that study, the population was distributed by age group. The pooled mean of OJ and OB values from the age groups eight to 11 years and 12 to 17 years was used for comparison because the age range for the RSS cohort was from six years, nine months to 16 years, seven months. The mean OJ for the general population (eight to 17 years) was determined to be 3.2 mm (N=2,243).[26-28] One-sample *t*-test revealed no statistically significant mean difference ($P>.05$) between the mean OJ of the RSS cohort (4.3 mm) and the mean OJ of the general population. The mean OB for the general population (eight to 17 years) was determined to be three mm (N=2,266).[26-28] One-sample *t*-test revealed a statistically significant mean difference ($P<.05$) between the mean OB of the RSS cohort (6.7 mm) and the mean OB of the general population.

The mean anterior alignment scores of the RSS cohort were compared to the values of the general population, as determined by the NHANES III study.[26-28] The pooled mean of maxillary and mandibular alignment indices from the age groups eight to 11 years and 12 to 17 years was used for comparison. One-sample *t*-test revealed a statistically significant mean difference ($P<.05$) between the mean maxillary alignment score of the RSS cohort (7.1 mm) and that of the general population (three mm, N =2,275).[26-28] One-sample *t*-test also revealed a statistically significant mean difference ($P<.05$) between the mean mandibular alignment index (10.1 mm) and that of the general population (3.1 mm, N=2,301).[26-28] Descriptive statistics and the results of one-sample *t* tests are presented in Table 4.

Table 4. Characteristics of the patients with Russell-Silver Syndrome with standard deviation and One-Sample t-Test

Variables	N	Mean (mm)	SD (mm)	*P*-value	Mean Diff (mm)	CI (95%) (mm)
Overjet	13	4.31	2.52	0.140	1.10	-0.42 – 2.64
Overbite	13	6.77	3.29	0.001	3.79	1.78 – 5.76
MaxAlign	13	7.15	6.18	0.011	5.15	1.41 – 8.89
MandAlign	13	10.15	9.30	0.008	8.15	2.52 – 13.77

DISCUSSION

In the GHD and ISS sample, the prevalence of MTD was 25 percent, which is higher than the prevalence of crossbite in the U.S. population (8.5 percent for six- to 11-year-olds and 7.9 percent for 12- to 17-year-olds).[14] No previous studies of GHD or ISS examined this characteristic.

Crowding was present in 56 percent of the subjects in this group, slightly higher than but similar to Kjellberg et al.,[11] who found that 44 percent of GHD or ISS children presented dental crowding greater than two millimeters. Increased OJ and deep OB were both found in 37 percent of our subjects, which is higher than those reported by Kjellberg et al.[11] (14 percent increased OJ and five percent increased OB). Differences in methodology and definitions are likely the reason for such discrepancies. In our study, an OJ greater than two millimeters and OB greater than three mm were considered increased or deep. Kjellberg et al.[11] on the other hand, considered an OJ equal to or greater than six millimeters and an OB equal to or greater than five millimeters as increased.

The prevalence of Class II molar classification in our sample was 31 percent. That is similar to the prevalence of Class II molar classification in the general U.S. population, namely 35 percent for six- to 11-year-olds and 32 percent for 12- to 17-year-olds.[27,28] Kjellberg et al.[11] found a prevalence of Class II malocclusion of 29 percent in GHD and ISS sample, which was also similar to our findings.

In the RSS sample, the prevalence of MTD (10 percent) was slightly higher but similar to that of the U.S. population.[26] Brunelle et al.[26] found that 8.5 percent of eight- to 11-year-old children and 7.9 percent of 12- to 17-year-old adolescents presented with a posterior crossbite. Crowding was present in 85 percent of the subjects in this group. The prevalences of increased OJ and increased OB were 50 and 75 percent, respectively. Bergman et al.[21] also investigated the occlusal characteristics of 15 RSS subjects and found that 25 percent presented OJ equal to or greater than six millimeters and 31.3 percent presented OB equal to or greater than five millimeters. In our study, an OJ equal to or greater than two mm and an OB equal to or greater than three millimeters was considered increased. This explains our higher prevalence of increased OJ and OB.

The prevalence of Class II molar relation in RSS subjects was 40 percent, also similar to that of the U.S. population, which is 35 percent for six- to 11-year-old children and 32 percent for 12- to 17-year-old adolescents.[27,28] Bergman et al.[21] also showed no difference in the prevalence of Class II molar relation between their RSS and control groups. The prevalence of Class II malocclusion in their sample (25 percent) was lower than in our sample (40 percent).

Data analyses of our prospective cohort revealed that RSS patients present with increased OB, maxillary alignment scores, and mandibular alignment scores when compared to the U.S. population ($P<.05$). No statistically significant mean difference ($P>.05$) was found in mean OJ between RSS patients and the general population.

There was a prevalence of diastema of 36.3 percent, a value higher than the 19.3 percent found in the U.S. population for eight- to 11-year-old children.[26] Since crowding exists in the RSS population, a reduced prevalence of diastema would be expected. The high prevalence of diastema in this population could be due to the sample size or the delayed development of the dentition.[22] In addition to that, it is possible that thick maxillary midline frenum or delayed/ectopic eruption of maxillary canines could contribute to the higher prevalence of diastema.

The most prominent features of malocclusion found in RSS children were deep bite (often 100 percent or greater), and crowding. Deep bites of this magnitude can compromise the periodontal health of the palatal surface of the maxillary incisors and the labial surface of the mandibular incisors. Gingival stripping associated with deep bite was observed in some of the children. All subjects presented with at least two mm of crowding. The most severe case presented with 35 millimeters of crowding. Crowding was worse in the mandible than in the maxilla. Case reports have shown similar findings.[23,25]

Our sample size was limited by the availability of data from orthodontic screening notes and the standardized clinical exam. Moreover, the subjects were not separated by stages of dental development. Evaluation of findings on panoramic radiographs and cephalometric analyses would yield a more thorough analysis of the orthodontic needs of this population.

This study did not include a detailed examination of the subjects' medical records, nor did it attempt to evaluate the effect of GH therapy on dental and craniofacial development. Future studies could focus on performing a thorough review of medical records to evaluate the gestational history and birth weight of the subjects, since these factors can present consequences that interfere with normal craniofacial development. They could also evaluate the effects of GH therapy on the craniofacial structures and the possible consequences of GH overuse.

CONCLUSIONS

Based on the results of this study, the following conclusions can be made:

1. Occlusal abnormalities are prevalent in children with growth deficiencies.
2. The most prominent features of malocclusion found in children with RSS were deep bite, often 100 percent or greater than the general population, and crowding.

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