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**Original Article**

# Effect of Growth Hormone Injections in Children with Growth Hormone Deficiency

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## ABSTRACT

The most frequent reason of short stature is Idiopathic short stature (ISS). If this condition is left untreated, the person's final height will be below the normal height range. **Objective:** To determine the efficacy of growth hormone treatment in short-stature children with isolated growth hormone deficiency. **Methods:** This was a retrospective cross-sectional study conducted in the department of Pediatric Endocrinology, Children Hospital, PIMS after approval from ethical review board. Epidemiological characteristics and response to therapies were noted and frequencies and Means were calculated. SPSS version 22 was used for statistical analysis. **Results:** Out of 87 study participants, there were 47 males and 40 female patients. The mean age was 10.04 ± 1.89. The mean height and weight of study participants was 105.13 ± 16.98cm and 21.55 ± 7.63kg respectively. The mean isolated growth hormone value was noted as 5.40 ± 1.43. The majority of the study participants were consanguineous i.e., 77%. Almost 48.3% study participants had growth hormone deficiency. The mean growth hormone velocity at 6th and 12th month was 6.52 ± 2.08 and 7.89 ± 2.54 respectively. In the end majority of the participants (82.8%) showed improvement. At 6th and 12th month both time points the results depicts a statistically significant difference among both groups (Improved Vs. Consistent) (p-value < 0.001). **Conclusions:** Recombinant growth hormone (GH) is an effective treatment for patients with GH deficiency to improve their growth. It was concluded that the children with ISS showed improvement after receiving GH therapy.

## INTRODUCTION

Growth is a continuous biological process that is influenced by factors such as genetics, environment, diet, and hormones. Any of these components that are disturbed may have altered growth potential. A major issue with children in developing countries is short stature [1]. The most frequent reason of short stature is Idiopathic short stature (ISS). If this condition is left untreated, the person's final height will be below the normal height range. It is described as a type of symmetrical short stature whose etiology has not yet been identified [2]. Since more people have become aware of the potential for curable problems and the provision of diagnostic tools, short stature is now a more commonly studied pediatric endocrine problem. Every child needs to have their height and weight measured annually to determine their growth potential, as healthy growth in children is a key indicator of their overall health [3]. ISS is a type of short stature that affects children who have normal birth weights, normal body compositions, normal GH responses to stimulation tests, height standard deviations (SDs) that is consistent with mean parental SDs, and no known underlying reason. However, ISS children are a diverse group of children with a wide range of non-specific explanations for their small height. The ISS category includes kids who are genetically short-statured and who also have constitutional growth and puberty delays [4]. Decisions about the use of GH have an impact on more than 1 million children in the US who may be candidates for GH therapy [5]. The major and most frequent common cause of short height in developing countries is severe malnutrition. In Pakistan, children under the age of five have severely poor nutritional conditions; over 40% of them are underweight, which

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frequently has lifetime effects on skeletal development [6, 7]. The majority of possible pediatric candidates for GH are children with idiopathic short stature. Idiopathic short stature thus is an important threshold in the extension of the non-traditional use of GH, along with the debate over the boundary between disease and the limits of natural variation. The usefulness of GH in improvement in growth for children with idiopathic short stature is unclear despite multiple research [8-10]. Patients with GH deficiency are individuals whose peak growth hormone concentration, as determined by the growth hormone stimulation test, is less than 10 ng/ml. the GH deficiency patients are treated with recombinant growth hormone to increase their growth and height [11, 12]. According to FDA-approved criteria, children whose height estimates are less than 160 centimeters are candidates for treatment with recombinant growth hormone (rGH) [13]. The etiology of short stature is complicated, and there is variation in the results of ISS according to different regions and ethnicity as well as in the outcomes of growth hormone therapy. However, limited literature is available regarding the effectiveness of growth hormone treatment in Pakistani children or efficacy of growth hormone treatment having growth hormone deficiency. Therefore, the current study aims to determine the efficacy of growth hormone treatment in short stature children with isolated growth hormone deficiency.

## METHODS

In the department of Pediatric Endocrinology, Children Hospital, PIMS after the approval from ethical review board a retrospective cross-sectional study was conducted. Total 87 children were enrolled in current study by non-probability consecutive technique. All the children 2-12 years of age diagnosed with isolated growth hormone deficiency by growth hormone provocative test (Levo Dopa & insulin) were enrolled in the study after taking informed consent from the parents. The parents of children not willing to participate in the study, all syndromic patients, chronic idiopathic disease and multiple pituitary hormone deficiency were excluded from current study. Their epidemiological characteristics were noted on a Performa along with height and weight. Response to therapy was noted by seeing the growth velocity at 6 months and 12 months after GH replacement therapy. The frequencies and percentages were used to express all category and qualitative characteristics (such as gender). The mean standard deviation was used to express all continuous/quantitative data such as age, height, weight, SDs, mother and father height, gestational age, and lab results like as growth hormone levels. All p values less than 0.05 were considered significant. Statistical analysis was done utilizing the statistical analysis software SPSS version 22.

## RESULTS

Out of 87 study participants, there were 47 males and 40 female patients. The mean age was 10.04 + 1.89. The mean height and weight of study participants was 105.13 + 16.98cm and 21.55 + 7.63kg respectively. Mean gestational age was 36.29 + 1.93 weeks, whereas the birth height and weight were 48.37 + 4.29 and 2.40 + 0.30 respectively. The mean isolated growth hormone value was noted as 5.40 + 1.43 (Table 1).

| Variables | | Mean + SD Or Frequency (Percentage) |
|---|---|---|
| Gender | Male | 47 (54.0%) |
| | Female | 40 (46.0%) |
| Age | | 10.04 + 1.89 |
| Height (cm) | | 105.13 + 16.98 |
| Weight (kg) | | 21.55 + 7.63 |
| Gestational Age (weeks) | | 36.29 + 1.93 |
| Birth Height (inches) | | 48.37 + 4.29 |
| Birth Weight (kg) | | 2.40 + 0.30 |
| Isolated Growth Hormone value | | 5.40 + 1.43 |

**Table 1:** Demographic and Anthropometric measurements of Pediatric Patients

Table 2 depicts the family history and outcome of the study. The majority of the study participants were consanguineous i.e., 77%. Almost 48.3% study participants had growth hormone deficiency in their family members whereas 51.7% participants were not having any family member with growth hormone deficiency. The mean growth hormone velocity at 6th and 12th month was 6.52 + 2.08 and 7.89 + 2.54 respectively. In the end majority of the participants (82.8%) showed improvement.

| Variables | | Mean + SD Or Frequency (Percentage) |
|---|---|---|
| Consanguinity | Yes | 67 (77.0%) |
| | No | 20 (23.0%) |
| GH Deficiency in Family members | Yes | 42 (48.3%) |
| | No | 45 (51.7%) |
| Growth Velocity at 6 months | | 6.52 + 2.08 |
| Growth Velocity at 12 months | | 7.89 + 2.54 |
| Outcome | Improved | 72 (82.8%) |
| | Consistency | 15 (17.2%) |

**Table 2:** Family History and Outcome of Growth Hormone Therapy

Table 3 compares the mean scores of growth velocity at 6th and 12th month among participants with improvement and consistency. At both time points the results depicts a statistically significant difference among both groups (p-value < 0.001).

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| Growth Velocity | Group I Improved Mean+ SD | Group II Consistency Mean+ SD | t-score | p-value |
|---|---|---|---|---|
| Growth Velocity at 6 months | 7.18 + 1.61 | 3.34 + 0.45 | 9.108 | <0.001 |
| Growth Velocity at 12 months | 8.72 + 1.92 | 3.90 + 0.57 | 9.608 | <0.001 |

**Table 3:** Comparison of means scores regarding Growth Velocity among patients

## DISCUSSION

Subsequently, recombinant human growth hormone (rhGH) therapy was approved for the treatment of short stature caused by a number of diseases, including Turner syndrome, Noonan syndrome, Prader-Willi syndrome, short stature caused by gene deficiency, chronic renal failure, and idiopathic short stature (ISS), as well as in children who are small for gestational age (SGA). This treatment has been accessible since 1985 [14]. In current study it was reported that out of 87 study participants, there were 47 males and 40 female patients. The mean age was 10.04 $\pm$ 1.89. The mean height and weight of study participants was 105.13 $\pm$ 16.98cm and 21.55 $\pm$ 7.63kg respectively. These findings were comparable in another study, it was reported that total 169 cases were enrolled, and the age group with the highest cases was >5 to 11 years. The ratio of men to women who were present was 1.17:1[15]. The results of current study it was reported that the mean growth hormone velocity at $6^{th}$ and $12^{th}$ month was 6.52 $\pm$ 2.08 and 7.89 $\pm$ 2.54 respectively. In the end majority of the participants (82.8%) showed improvement. The majority of the study participants were consanguineous i.e., 77%. Almost 48.3% study participants had growth hormone deficiency in their family members whereas 51.7% participants were not having any family member with growth hormone deficiency. These findings were compared with literature. GH deficiency, which was seen in 48 out of 70 (69%) patients, was the most common cause of low stature in the Pakistani population [16]. According to a study conducted in Germany by Knoop *et al.*, familial or CDGP short height accounted for 68% of all cases of short stature [17]. A meta-analysis of data from 21 clinical trials found that children with ISS who received rhGH had significantly greater height gain at the end of the first year than the control group. At the end of the 2nd year. Additionally, this therapy increased eventual adult height. For male patients, the difference between the 2 groups was 5.3 cm, and for female patients, it was 4.7 cm [18]. The Results of another observational research conducted in Korea reported that patients with GHD and ISS had higher height standard deviation scores (SDS) than those without these conditions [19]. Another study was conducted to see how well patients with GHD and ISS grew after receiving GH therapy for two years. The authors also attempted to determine whether the effect of GH therapy varies based on the peak GH on the GH stimulation test. After receiving growth hormone treatment for two years, they reported no differences in height SDS and height velocity between GHD and ISS patients. Additionally, there was no significant different between GHD patients' responses to growth hormone therapy based on peak GH levels [20].

## CONCLUSIONS

Recombinant growth hormone is an effective treatment for patients with GH deficiency to improve their growth. It was found that the children with ISS showed improvement after GH therapy. In order to distinguish between special cases of short stature requiring early diagnosis and treatment and normal growth variants, it is essential to accurately understand the prevalence of the multiple causes of short stature in a given population.

### Conflicts of Interest

The authors declare no conflict of interest.

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