# Evaluation of persistent high IGF-1 levels in patients with Turner Syndrome despite optimum doses of Growth Hormone

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## INTRODUCTION:

- Growth hormone (GH) treatment is used to accelerate growth in patients with Turner syndrome (TS).
- During treatment, evaluation of IGF-1 is strongly recommended for efficacy and safety. Despite optimum GH doses, some patients have persistent high IGF-1 levels.

## AIM:

- In this study, we aimed to evaluate of anthropometric, clinical and biochemical features of TS cases with elevated IGF-1 and to investigate the presence of *IGF1R* gene polymorphism.

## MATERIAL/METHOD:

54 patients with TS (19 classic, 35 mosaic) using GH (45-50µg/kg/day) were evaluated retrospectively. At the onset, SDS of birth weight (BW), anthropometric measurements, target height, and bone age (BA); and at the first and fourth years of GH-treatment, SDS of anthropometric measurements and IGF-1; and growth velocity (GV) and BA of the patients were noted.

According to IGF-1 levels, the patients were divided into 5 groups:

**Group 1**: Patients with IGF-1-SDS in normal ranges on GH treatment

**Group 2:** Patients whose IGF-1 SDS were increased on treatment and returned to normal with 10-20% dose reduction;

**Group 3**: Patients whose IGF-1SDS remained high despite 10-20% dose reduction;

**Group 4:** Patients whose IGF-1 SDS returned to normal without any dose change;

**Group 5:** Patients whose IGF-1 SDS remained high without any dose change. Comparisons were made between groups covering patients on treatment with normal IGF-1 levels (Group 1), and with increased IGF-1 levels (Groups 2,3,4 and 5).

*IGF-1R* gene analysis was performed in cases where IGF-1 levels were increased at least once.

## RESULTS:

- The age of treatment onset was slightly higher in Group 1 compared to others (p=0.046).
- No statistical significance was observed in comparison of BW, height SDS, BA and IGF-1SDS at the onset of treatment between Group 1 and Groups 2,3,4,5.
- While the weight and BMI SDS were significantly higher in Groups 2-3-4-5 (p=0.03; p=0.04), GV was better in Group 1 (p=0.025).
- At 1st-year of treatment, weight SDS (p=0.001), BMI SDS (p=0.002); and at 4th year of treatment, weight SDS (p=0.002), and BMI SDS (p=0.002) were higher in Groups 2-3-4-5. GV in 1st-year (p=0.037) and 4th-year (p=0.038) were better in Groups 2-3-4-5.
- No *IGF-1R* genepolymorphism was detected in any of the patients in Groups 2-3-4-5.

**Table 1: Comparisons of clinical findings of Group 1 and Group 2+3+4+5 at onset of treatment, at 1st-year of treatment and 4th year of treatment**

| | Onset of the treatment | | | 1st-year of treatment | | | 4th-year of treatment | | |
|---|---|---|---|---|---|---|---|---|---|
| | **Group 1 Median (**Min-Max) Mean±SD | **Group 2+3+4+5 Median** (Min-Max) Mean±SD | **p** | **Group 1 Median** (Min-Max) Mean±SD | **Group 2+3+4+5 Median** (Min-Max) Mean±SD | **p** | **Group 1 Median** (Min-Max) Mean±SD | **Group 2+3+4+5 Median** (Min-Max) Mean±SD | **p** |
| **Height SDS** | -3.3 (-6.4 and -1.2) -3.29±1.47 (n=18) | -2.8 (-5.4 and -1.6) -2.9±0.8 (n=31) | 0.334 | -3.2 (-5.1 and -0.2) -2.87 ±1.49 (n=18) | -2.3 (-4.4 and -1.3) -2.4±0.72 (n=31) | 0.224 | -2.7 (-5.4 and -0.6) -2.87±1.43 (n=8) | -2.1 (-3.5 and -0.7) -1.97±0.84 (n=19) | 0.123 |
| **GV** | 4.44 (1.8 and 8.3) 4.48±1.92 (n=18) | 3.9 (0 and 7.8) 2.9±2.4 (n=31) | **0.025** | 7.4 (3.5 ve 11) 7.4±1.7 (n=18) | 8.4 (6.1 and 12.3) 8.5±1.53 (n=31) | **0.037** | 4.37 (1.4 and 8.6) 4.35±2.28 (n=8) | 5.80 (3.22 and 8.91) 5.75±1.29 (n=19) | **0.038** |
| **BMI SDS** | -0.1 (-2.4 and 1.9) -0.27±1.14 n=18) | 0.6 (-1.0 and 2.4) 0.8±1.03 (n=31) | **0.04** | -0.4 (-2.7 and 2.1) -0.40± 1.14 (n=18) | 0.4 (-1.0 and 1.7) 0.41± 1.02 (n=31) | **0.002** | -0.95 (-2.7 and 1.1) -0.98±1.20 (n=8) | 0.5 (-0.5 and 2.4) 0.64 ±0.85 (n=19) | **0.002** |
| **BA** | 8.0 (3.0 and 11) 8.11±1.97 (n=17) | 7.8 (2.5 and 12) 7.5±2.32 (n=30) | 0.259 | 10 (3.5 and 12.5) 9.46± 1.96 (n=17) | 8.8 (6.8 and 12.5) 9.3± 1.8 (n=24) | 0.414 | 12 (0 and 13.5) 10.68 ±4.37 (n=8) | 11 (7.8 and 13.5) 11.27 ± 1.6 (n=19) | 0.419 |
| **IGF1 SDS** | -0.65 (-1.7 and 1.8) -0.58±0.95 (n=16) | -0.6 (-2.0 and 2.3) 0.36±1.34 (n=22) | 0.293 | 0.7 (-1.6 and 2.0) 0.51± 1.08 (n=18) | 2.5 (-3.3 and 10) 2.9± 2.7 (n=29) | **0.000** | -0.4 (-0.8 and 0.6) -0.2 ±0.58 (n=5) | 2.7 (0.6 and 5.7) 2.74 ±1.6 (n=19) | **0.001** |

SD: Standard deviation, SDS: Standard deviation score, GV: Growth velocity, BMI: Body mass index, BA: Bone age

## CONCLUSION:

- On GH treatment, the weight and BMI-SDS and GV of patients whose IGF-1 levels were increased at least once were higher than in patients with normal IGF-1 levels.
- High IGF-1levels in these patients could not be explained by *IGF-1R* gene polymorphism.