



# Growth hormone-IGF-1 axis in 18 children with Kabuki syndrome

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## Introduction

Kabuki Syndrome (KS; OMIM 147920) is a congenital anomaly/intellectual disability syndrome caused by a mutation in the KMT2D or KDM6A gene. Children with KS have a spectrum of clinical features, but one of the key features in KS patients is postnatal growth deficiency. Niikawa et al. (1981) were the first to describe the natural growth in male-subjects. They showed that birth weight and length are generally within the normal range, while in the first year of life many patients show a decline in height (1). Growth hormone (GH) deficiency has been reported in KS but in the majority of children with KS no cause for small stature in KS has been found.



## Objectives

As part of our GH therapy research project in KS patients, we studied the growth hormone and IGF-I pattern in order to learn more about a possible mechanism involved in postnatal growth retardation in KS.

## Patients and Methods

Currently, we have assessed 18 KS children, of which male 44% (age range 3,3-10,3 and mean 6.7 years) with a proven mutation. Height was variable, with a mean height SDS of  $-2,26 \pm 1.58$ .

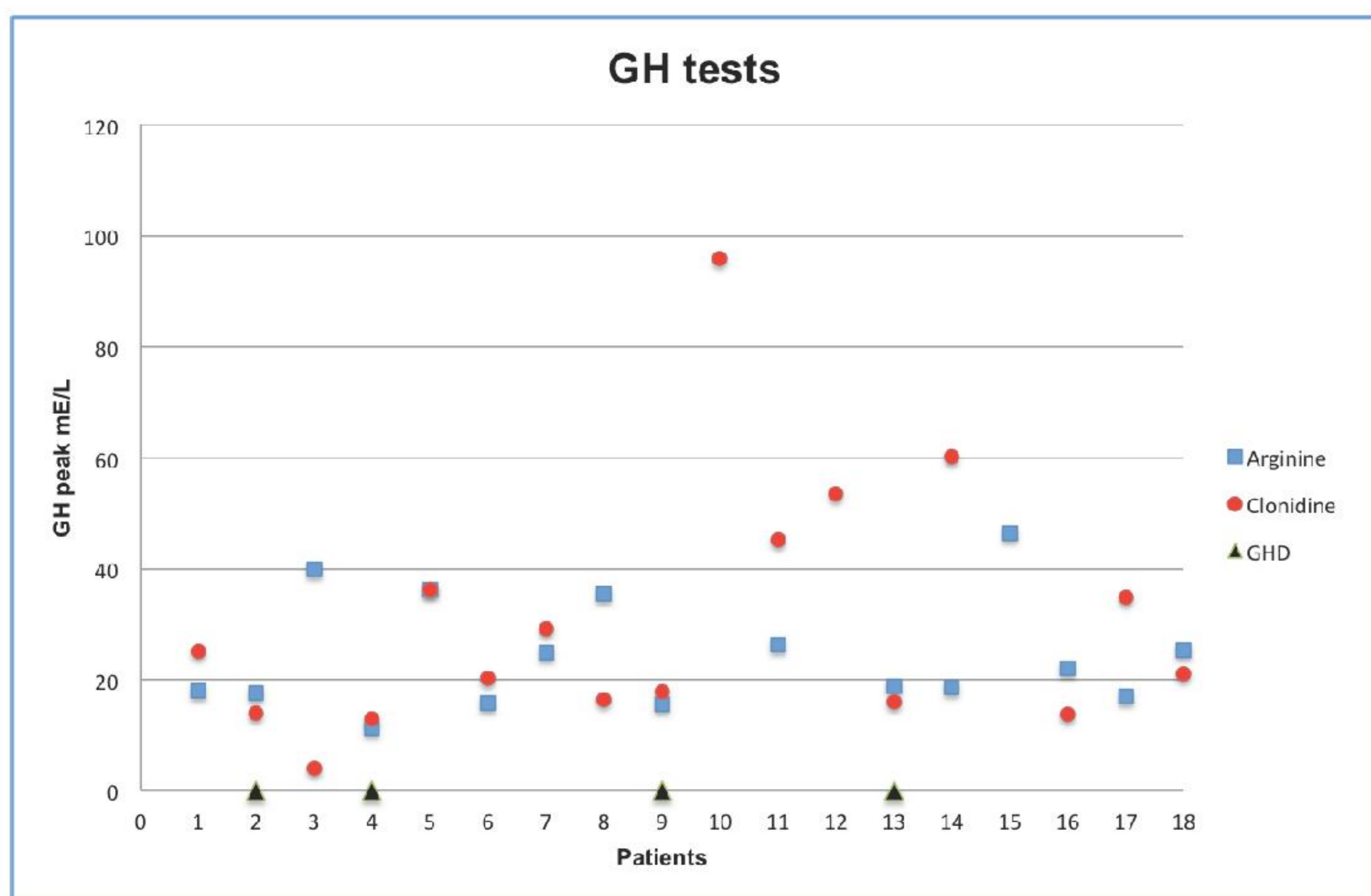
Both clonidine (CLO) and arginine (ARG) were used for stimulation. **Growth hormone deficiency (GHD)** was determined by a peak value under 20 mE/l in both tests. IGF-1 levels under -2 SDS were considered low (2).

## Results and Discussion

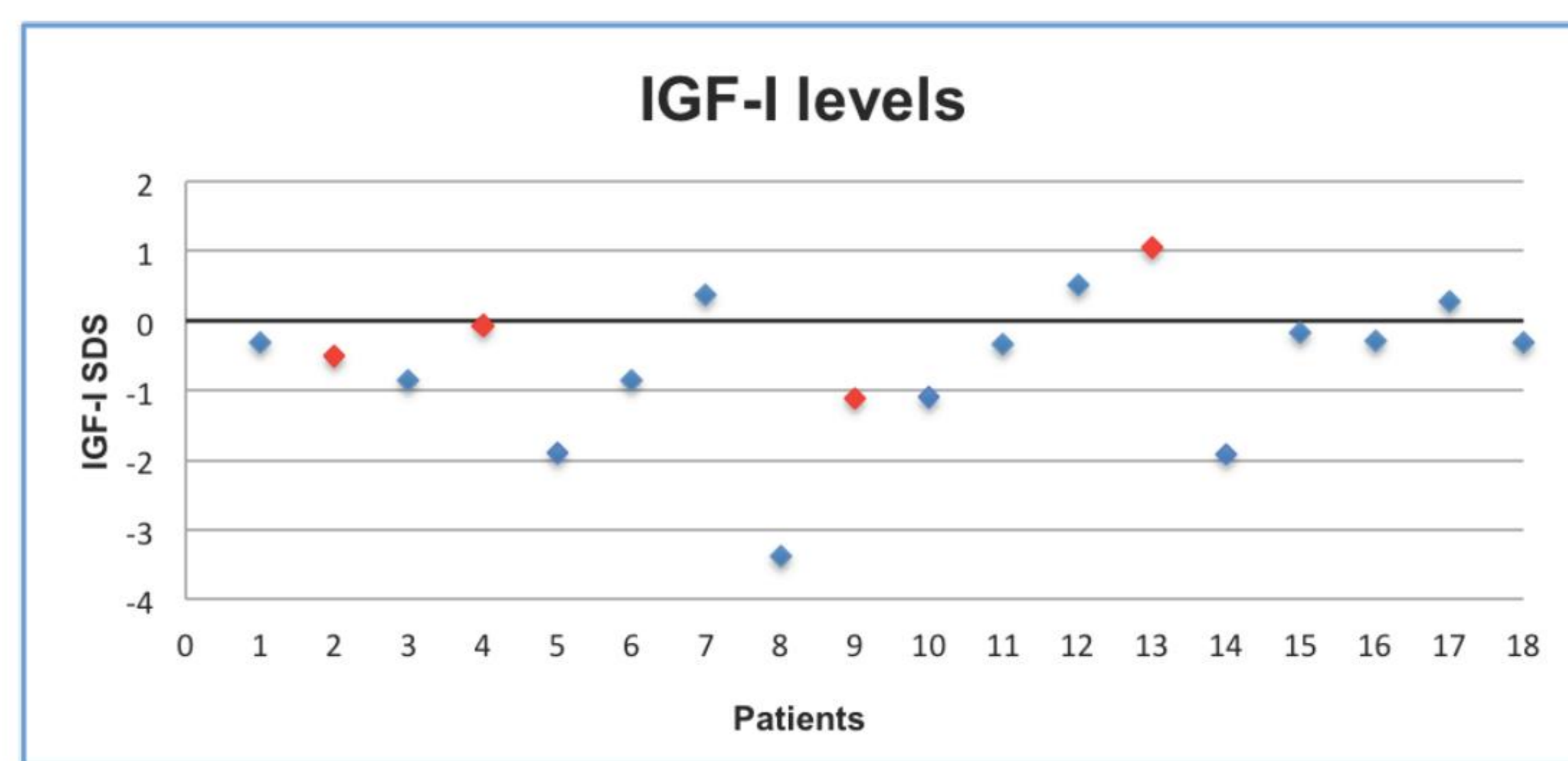
Clonidine and Arginine stimulation tests showed low GH peak levels in 7/18 (38,9%) and 8/16 (50%) children respectively. Combination of these tests showed a GH deficiency in 4/18 (22,2%) individuals. **See figure 1.**

Of all patients, only one had a IGF-1 below  $< -2$ . This patient did not fulfil the GHD criteria. **See figure 2.**

In most of the syndrome disorders, the cause of short stature is based at the cellular level. Growth failure as part of many syndromes may be due to a wide variety of mechanisms and in many of these syndromes, the underlying mechanisms are still unknown. Usually, there is no GH deficiency, but in some patients, a pathology in the GH/insulin-like growth factor-1 (GH/IGF-1) axis can be detected. The same is seen in our KS population.



**Fig 1.** Individual maximum GH peak response to CLO and ARG



**Fig 2.** Individual serum IGF-1 levels in SDS, GHD are indicated in red

## Conclusion

**Growth hormone deficiency was present in 4 of the 18 (22,2%) children.** Furthermore, the IGF-1 levels does not properly correspond with the GH test results. Apparently, growth hormone deficiency is not the only cause for small height in KS patients. In addition, in 2 children the GH tests showed a **tendency to growth hormone resistance**, although no one actually met the defined criteria. Further research is necessary to determine the underlying cause of growth retardation in the majority of KS patients.

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## References

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