

Development of Disease-Specific Growth Charts for Children with Alagille Syndrome: Results from The Gala Study Group

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Objectives and study: Variable degrees of growth retardation have been reported in children with Alagille syndrome (ALGS) yet these patients are routinely evaluated using standard growth charts. The aim was to develop disease-specific growth charts for ALGS utilizing modern statistical approaches.

Methods: Multicenter retrospective analysis of children with clinically and/or genetically confirmed ALGS. Anthropometric data were extracted from every clinic visit, and in-patient hospitalization until liver transplantation (LT), transfer to another centre, enrollment in a clinical trial, or death. Exclusion criteria: known history of prematurity (n = 179, 16.3%). The first available measurement in the following time intervals was used to create a balanced growth dataset: monthly for the first 2 years, every 3 months from 2-5 years and every 6 months thereafter. Generalized Additive Models for Location Scale and Shape (GAMLSS) were fitted using R to generate centile plots for weight and height relative to age and superimposed on the CDC growth charts to illustrate differences in growth patterns compared to typically developing children.

Results: Data from 1204 (42.3% female) children (9855 weights) with ALGS (82.6% had neonatal cholestasis, 25.4% LT and 8.1% died) were included for the modeling of the weight for age (WFA) growth charts and 1106 (42.6% female) children (8464 heights) with ALGS (81.9% had neonatal cholestasis, 25.4% LT and 8.1% died) for the modeling of the height for age (HFA) growth charts. WFA and HFA charts for boys (**Figure 1, black lines**) and girls (not shown) differ significantly from CDC growth charts (**Figure 1, red lines**).

Conclusions: Newly developed disease-specific growth charts for ALGS differ significantly from the CDC growth charts for typically developing children and provide a crucial tool for clinicians to evaluate growth in ALGS. Based on the ascertainment bias in GALA, these growth curves are most applicable to ALGS patients with cholestasis.

Figure 1

