

Impact of Pediatric Inflammatory Bowel Disease on Linear Growth: Data from a National Cohort Study in Saudi Arabia

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ABSTRACT

Background/Aim: Linear growth impairment (LGI) is one of the most important features peculiar to children with inflammatory bowel disease (IBD). The aim of this report is to define the impact of IBD on the linear growth of children in the Kingdom of Saudi Arabia (KSA). **Setting and Design:** Multicenter retrospective study. **Patients and Methods:** Data from a cohort of newly-diagnosed children with IBD from 2003 to 2012 were analyzed retrospectively. The diagnosis of IBD was confirmed in accordance with the published criteria. Length/height for age was measured at diagnosis. The World Health Organization (WHO) reference was used and LGI was defined by length/height for age < -2 standard deviation. Chi-square test was used to test the significance of estimates and a $P < 0.05$ was considered significant. **Results:** There were 374 children from 0.33 to 16 years of age, including 119 ulcerative colitis (UC) (32%), and 255 Crohn's disease (CD) (68%) patients. The prevalence of LGI was 26%, 28%, and 21% in IBD, CD, and UC, respectively. In children below 10 years, LGI was significantly more common in CD ($P = 0.010$), while in UC children, it was more common in older children ($P = 0.011$). **Conclusion:** This study demonstrates a prevalence of LGI consistent with that reported in the literature, but higher in CD children with early onset (< 10 years) and in older children with UC, underscoring the importance of monitoring growth in children with IBD in the Saudi population. Prospective studies are needed to define the impact of IBD on growth velocity, puberty, and final adult stature.

Key Words: Growth impairment, inflammatory bowel disease, Saudi children, short stature

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Inflammatory bowel disease (IBD) refers to two main clinical entities, ulcerative colitis (UC) and Crohn's disease (CD). Linear growth impairment (LGI) is also called growth failure, short stature, stunting in preschool children, and short stature in older children and adolescents. It is one of the most important features peculiar to children and adolescents, and maintenance of normal growth is considered one of the indicators of IBD control and success of therapy.^[1] Assessment of linear growth at diagnosis before any drug intervention

allows estimation of the impact of IBD on growth. Although less common in UC than in CD, the prevalence of LGI at diagnosis has been reported in some Western populations varying from 20 to 88%.^[2,3] Pediatric IBD is increasingly reported in the Kingdom of Saudi Arabia (KSA) with an intermediate incidence between Western and Southeast Asian populations.^[4] The lack of data from developing countries on the impact of IBD on growth prompted this report.

PATIENTS AND METHODS

Data from a cohort of newly-diagnosed children with IBD from 2003 to 2012 were analyzed retrospectively. The sample consisted of all children from birth to 16 years of age who were diagnosed in pediatric gastroenterology centers across the KSA. The diagnosis of IBD was confirmed in all cases in accordance with published criteria.^[5,6] Length for age (< 3 years of age) and height for age (> 3 years of age) were measured at

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diagnosis. The World Health Organization (WHO) standards and reference standard deviation (SD) charts were used as reference.^[7,8] The length and height for age at diagnosis for each patient were plotted on the corresponding chart. LGI was defined by length or height for age < -2 SD.^[7,8] Age stratification analysis was performed in accordance with Paris classification separating children < 10 years from older children.^[9] Chi-square test was used to test the significance of prevalence estimates and a $P < 0.05$ was considered significant.

This study is part of the characteristics of IBD in Saudi children, approved by the Institutional Review Board, College of Medicine, King Saud University (No. 10/2647/IRB).

RESULTS

There were 374 children from 0.33 to 16 years, including 119 UC (32%), and 255 CD (68%) cases. The prevalence of LGI at diagnosis is presented in Table 1, which shows the rates as 26%, 28%, and 21% in IBD, CD, and UC children, respectively. The prevalence of LGI in CD was higher than in UC (28% vs. 21%); the difference, however, was statistically not significant ($P = 0.137$). However, in children below 10 years, LGI was significantly more common in children with CD than in those with UC ($P = 0.010$). By contrast, in older children, LGI was significantly more common in children with UC than in those with CD ($P = 0.011$). Table 2 depicts gender-related variations in the prevalence of LGI and indicates no significant difference in the prevalence of LGI between male and female children with UC ($P = 0.436$), CD ($P = 0.918$), or IBD ($P = 0.598$).

DISCUSSION

The etiology of growth impairment in children and adolescents with IBD is multifactorial. Chronic malnutrition resulting from inadequate caloric intake as a result of

anorexia and abdominal pain, chronic inflammation, effect of proinflammatory cytokines, disturbed insulin-like growth factors, and drug therapy are the main contributing factors.^[10-15] The advantage of assessing growth at diagnosis is important as it excludes the effects of drugs such as steroids on growth, thereby reflecting the impact of the disease on growth. In this analysis, we chose to use the WHO reference for two reasons. The first was the unavailability of SD reference for Saudi children at the time of the study. The second reason is that using the WHO international reference facilitates comparison with other studies from other countries. However, taking into consideration the background prevalence of LGI in the general population defines more precisely the impact of IBD.

The 26% prevalence rate of LGI in IBD reported in this study is within the 15–40% reported in a Cochrane meta-analysis.^[16] However, even after subtracting the 11% prevalence of LGI in the Saudi preschool and school-age normal children,^[17,18] the adjusted prevalence of LGI of 15% (26-11) in Saudi children with IBD is still in the lower limit of the range.^[16] In addition, the 17% (28-11) adjusted prevalence of LGI in CD children is higher than the 9.5% reported in a population-based registry from northern France.^[19] Although not statistically significant ($P = 0.137$), the more common prevalence of LGI in CD than in UC in this report is in line with most studies from the West.^[20-23] This difference between CD and UC at diagnosis may be explained by the more widespread and longer duration of CD before diagnosis as reported in the literature.^[24,25]

In this study, age stratification revealed no significant difference in the prevalence of LGI in IBD children in either age group. However, LGI was significantly more common in young children with CD and older children with UC, a finding not documented in the literature. The relatively more widespread colonic inflammation in young children with CD reported in the literature^[25-27] may at least partially explain the greater impact of disease on the linear growth of younger children. Finally, there was no significant difference between males and females in any age group of either UC or CD.

In conclusion, this is the first study from a developing country that demonstrates the prevalence of LGI within the range reported in the literature. However, the higher impact of IBD on linear growth in CD children with early onset (< 10 years), as well as in older children with UC, a pattern rarely documented in the literature, underscores the importance of age stratification to identify the impact of IBD on linear growth. In addition, the result of this study is a reminder for physicians caring for children and adolescents with IBD to monitor the growth regularly and to manage any impairment early. Prospective studies are needed to define the impact of IBD on growth velocity, puberty, and final adult stature.

Table 1: Age-related prevalence of linear growth impairment

Age (years)	UC: No (%)	CD: No (%)	P value	IBD: No (%)
<10	8/67* (12)	17/55 (31)	0.010	25/122 (21)**
10-16	17/52* (33)	55/200 (28)	0.460	72/252 (29)**
All	25/119 (21)	72/255 (28)	0.137	97/374 (26)

UC=Ulcerative colitis, CD: Crohn disease; IBD: Inflammatory bowel disease.
* $P=0.011$, ** $P=0.122$

Table 2: Gender-related prevalence of linear growth impairment

Gender	UC: No (%)	CD: No (%)	IBD: No (%)
Males	16/68 (23.5)	43/151 (29)	59/219 (27)
Females	9/51 (17.6)	29/104 (28)	38/155 (25)
P value	0.436	0.918	0.598

UC: Ulcerative colitis; CD: Crohn disease; IBD: Inflammatory bowel disease

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