RESEARCH PAPER

Joint Involvement in Children with Celiac Disease

KAPIL GARG, PRIYANKA AGARWAL, R K GUPTA AND S SITARAMAN
From the Department of Pediatrics, SMS Medical college, Jaipur, India.

Correspondence to: Dr Kapil Garg, 5 JHA 22, Jawahar nagar, Jaipur 302 004, India. drkapilgarg@hotmail.com
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Objective: To determine early joint involvement as detected by ultrasonography in children with newly diagnosed celiac disease, and in children with celiac disease on gluten-free diet for more than 6 months. **Methods**: Cross-sectional comparative study evaluating joint abnormalities by ultrasonography. **Results**: Ultrasonography showed abnormalities in 19 out of 60 (31.7%) children with newly diagnosed celiac disease as compared to 2 (3.3%) out of 60 in those on a gluten-free diet for more than 6 months. **Conclusion**: Subclinical synovitis as detected by ultrasound is a frequent finding in newly diagnosed children with celiac disease.

Keywords: *Arthritis, Chronic diarrhea, Gluten-free diet, Synovitis, Ultrasonography.*

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Celiac disease (CD) is an immune mediated systemic disorder elicited by gluten and related prolamines in genetically susceptible individuals [1,2]. Together with the classical form, there are atypical forms presenting with predominating extra-intestinal clinical features [3,4]. Musculoskeletal manifestations of CD include arthalgia, myopathy and non-erosive arthritis, which may be clinically silent in earlier stages [5-7]. Musculoskeletal ultrasound has shown its superiority over conventional radiology to detect a wide set of early inflammatory and structural abnormalities in joints [8-11]. There is a paucity of studies evaluating early joint involvement by ultrasound in children affected by CD. The present study was undertaken to determine the proportion of cases with early joint involvement using ultrasonography in children with newly diagnosed CD, and in children with CD on gluten-free diet (GFD) for more than 6 months.

METHODS

This study included all children (age 2 to 18 years) diagnosed as CD as per the modified ESPGHAN criteria [2] from outpatient clinic or impatient services in SMS Medical College, Jaipur from May 2014 to April 2016.

We divided these children into two groups: group 1 constituted children newly diagnosed as CD and were on gluten-containing diet whereas group 2 constituted those already diagnosed with CD, and on GFD for more than 6 months. Children who had any connective tissue disorder, concomitant rheumatic fever or history of injury to joints in last two months were excluded from the study. Informed consent was obtained from parents of the enrolled children. The study was approved by the ethical committee of the institution.

All patients were evaluated by complete medical history, including history of musculoskeletal symptoms and other co-morbidities; and detailed physical exami-nation, including musculoskeletal assessment. Ultrasonographic assessment of bilateral hip, knee and ankle joints was performed, using a Hitachii Hivision Preirus machine, equipped with a 9–14 MHz linear array transducer, operating at 14 MHz frequency (gain 50%). Ultrasonography evaluation of joints was performed by a single radiologist experienced in pediatric musculo-skeletal Ultrasonography who was blinded to patient's laboratory and clinical features. The radiologist looked for joint effusion, synovial hypertrophy or power Doppler signal (evidences of synovitis) in the above mentioned joints.

Statistical analysis: Chi-square test was used to compare frequencies between two groups. $P<0.05$ was considered statistically significant.

RESULTS

A total of 120 children (mean (SD) age 6.7 (3.9)y; 63 males) were enrolled in the study. Group1 and Group 2 had 60 children each. No significant difference was observed between the two groups regarding the demographic profile and clinical presentation of CD (***Table* I**).

Ultrasonographic assessment showed presence of at least one abnormality in 19 (31.7%) CD patients in group 1 whereas only 2 (3.3%) of group 2 patients had USG abnormalities ($P< 0.001$).

TABLE I BASELINE CHARACTERISTICS OF STUDY PARTICIPANTS

	Group 1 (n=60)	*Group 2 (n=60)*	*P value*
Gender (M/F)	28/32	25/35	0.27
Age (y); mean (SD)	6.32 (3.7)	7.15 (3.9)	0.23
Clinical form of CD; n (%)			
Typical	45 (75%)	52 (86.7%)	0.16
Atypical	15 (25%)	8 (13.3%)	
Silent	0	0	
Arthralgia, *n* (%)	3 (5%)	0	0.242

CD: Celiac disease; Group 1: Newly diagnosis patients; Group 2: Patients on gluten-free diet for >6mo.

The most frequently involved joint was the knee where 11 children of group 1 had USG abnormalities. (***Table* II**). The finding in knee joint in group1 were: joint effusion in 7, synovial hypertrophy in 2, and joint effusion along with synovitis in 2 children. In group 2, both patient had joint effusion. Findings at hip joint included joint effusion in 3, synovial hypertrophy in one, and combined hypertrophy and effusion in one child. Two children in group 1 had evidence of joint effusion in ankle, and only one patient had multiple joint (hip and knee) involvement. Joint effusion was mild in all the cases.

Majority of the patients with ultrasonographic evidence of joint abnormalities were asymptomatic suggesting subclinical synovitis. Clinically only 3 (5%) patients of group 1 had joint pain and limitation of joint movement at presentation while none of group 2 patients had similar symptoms. The mean (SD) age of cases having arthralgia at the time of presentation was significantly higher than asymptomatic cases [11.7 (7.5) *vs* 6.0 (3.3) years; *P*=0.01].

DISCUSSION

In this study, ultrasonographic evidence of joint abnormalities were present in approximately one-third of children newly diagnosed with CD. This frequency was significantly higher than in children with CD on GFD for more than six months, suggesting that GFD may lead to improvement in joint abnormalities associated with CD. In our study joint effusion was the most common abnormality followed by synovial hypertrophy. Knee joint was the most frequently involved joint followed by hip and ankle.

Small sample size, lack of inclusion of healthy controls and cross-sectional nature of the study were few limitations of this study.

Adelizzi, *et al*. [12] first described the association of arthritis and CD following which there were many similar case reports [5,6]. Both arthritis and small bowel mucosal changes have been reported to improve with a gluten-free diet [13,14]. Lubrano, *et al.* [15] studied 200 adult patients with CD, and found that arthritis was present in 26% of patients. Lagnocco, *et al*. [8] in 2014, for the first time studied children with CD for joint involvement using ultrasonography. They found that 50% of their newly diagnosed CD children had abnormalities. The pattern of joint involvement was similar to our study.

TABLE II JOINT ULATRASONOGRAPHY FINDINGS IN CHILDREN WITH CELIAC DISEASE

	No. of patients (%)		*P value*
	Group 1 (n=60) n	*Group 2 (n=60) n*	
Any abnormality	19 (31.7)	2 (3.3)	<0.001
Joint effusion	13 (21.7)	2 (3.3)	0.006
Synovial hypertrophy	3 (5)	0	0.24
Joint effusion + Synovial hypertrophy	3 (5)	0	0.24
Frequency of Joint Involvements			
Knee	11 (18.3)	2 (3.3)	0.01
Hip	4 (6.7)	0	0.12
Ankle	3 (5)	0	0.24
Multiple Joints (Hip+Knee)	1 (1.7)	0	1.0

CD: Celiac disease; Group 1: Newly diagnosis patients; Group 2: Patients on gluten-free diet for >6mo.

Subclinical joint effusion seems to be a relatively frequent finding seen in newly-diagnosed CD patients. Ultrasonography should be considered as a useful imaging tool for identifying CD patients with joint changes that have not yet manifested clinically. Early diagnosis and treatment may prevent subclinical synovitis to manifest clinically in later life. These findings also suggest that GFD has the potential to improve joint manifestations seen in CD.

Contributors: KG: concept and design of study, drafted the manuscript; PA: collected and analysed the data; RKG: analysis of data and literature search; SS: intellectual input in final drafting and overall supervision.
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REFERENCES

1. Garg K, Gupta RK. What a practitioner needs to know about celiac disease? Indian J Pediatr. 2015;82:145-51.
2. Husby S, Koletzko S, Korponay-Szabó IR, Mearin ML, Phillips A, Shamir R, *et al*. European Society for Paediatric Gastroenterology, Hepatology, and Nutrition Guidelines for the diagnosis of celiac disease. J Pediatr Gastroenterol Nutr. 2012;54:136-60.

WHAT THIS STUDY ADDS?

- Subclinical synovitis, most commonly in knee joint, as detected by ultrasonography may be present in about one-third of newly diagnosed children with celiac disease.

3. Demir H, Yüce A, Koçak N, Özen H, Gürakan F. Celiac disease in Turkish children: Presentation of 104 cases. Pediatr Int. 2000;42:483-7.
4. Celiloðlu C, Karabiber H, Selimoðlu MA. Atypical presentations of celiac disease. Turkish J Pediatr. 2011;53:241-9.
5. Bourne JT, Kumar P, Huskisson EC, Mageed R, Unsworth DJ, Wojtulewskija. Arthritis and coeliac disease. Ann Rheum Dis. 1985;44:592-8.
6. Dawidowicz K, EA HK, Lahalle S, Qubaja M, Liote F. Unexplained polyarthralgia and celiac disease. Joint Bone Spine. 2008;75:325-8.
7. Hadjivassiliou M, Chattopadhyay AK, Grunewald RA , Jarratt JA, Kandler RH, Rao DG, *et al*. Myopathy associated with gluten sensitivity. Muscle Nerve. 2007;35:443-50.
8. Iagnocco A, Ceccareli F, Perricone C, Valesini G. The role of ultrasound in rheumatology. Semin Ultrasound CT MR. 2011;32:66-73. 29-350.
9. Tok F, Demirkaya E, Ozcakar L. Musculoskeletal ultrasound in pediatric rheumatology. Pediatric Rheumatol Online J. 2011;9:25.
10. Porta F, Radunovic G, Vlad V, Micu MC, Nestorova R, Petranova T, *et al*. The role of Doppler ultrasound in rheumatic diseases. Rheumatology (Oxford). 2012;51:976-82.
11. Ramos PC, Ceccarelli F, Jousse-Joulin S. Role of ultrasound in the assessment of juvenile idiopathic arthritis. Rheumatology (Oxford). 2012;51:vii10-2. 16
12. Adelizzi RA, Pecora AA, Chiesa JC. Celiac disease: Case report with an associated arthropathy. Am J Gastroenterol. 1982;77:481-5.
13. Chakravarty K, Scott DG. Oligoarthritis - A presenting feature of occult coeliac disease. Br J Rheumatol. 1992;31:349-50.
14. Borg AA, Dawes CH, Swan CH, Hothersall TE. Persistent monoarthritis and occult coeliac disease. P ostgrad Med J. 1994;70:51-63.
15. Lubrano E, Ciacci C, Ames PR, Mazzacca G, Oriente P, Scarpa R. The arthritis of coeliac disease: Prevalence and pattern in 200 adult patients. Br J Rheumatol. 1996;35:1314-8.