BRIEF COMMUNICATION

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Pediatric celiac disease diagnosis and adherence to the ESPGHAN 2012 and 2020 guidelines: a single centre experience

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Dear Sir,

The European Society for Paediatric Gastroenterology Hepatology and Nutrition (ESPGHAN) 2012 guidelines for celiac disease (CD) recommended a no-biopsy pathway (NBP) for symptomatic children who meet the so-called 'triple criteria'[1]:

- IgA anti-tissue transglutaminase antibody [TGA-IgA] titer ≥10-times upper-limit-of-normal [ULN] and are IgA sufficient.
- Positive IgA anti-endomysial antibody [EMA-IgA].
- Positive HLA-DQ2/DQ8 haplotype.

Biopsy based diagnosis remained mandatory for diagnosing all other children with suspected CD while remaining on gluten-containing diet[1]. Failure to follow ESPGHAN (2012) guidelines for CD diagnosis (across a range of results) was previously reported including two recently published studies from Southwest England[2,3].

The ESPGHAN guidelines for CD were revised in 2020 recommending that the NBP can be used in all children (symptomatic/asymptomatic) with[4]:

- TGA-IgA ≥10xULN.
- Positive EMA-IgA in a second serum sample.

Biopsy based pathway still remain mandatory for all other children with TGA-IgA is <10xULN.

The aim of this retrospective study (performed in January 2021) was to establish the level of adherence to established ESPGHAN (2012/2020) guidelines[1,4]. Potential cases (n=179) were identified from the laboratory database over an 8-year period (January 2013–December 2020). All patients investigated as per the ESPGHAN 2012 and 2020 guidelines were included in the study. However, children whose TGA-IgA had normalised in the interim period i.e. from the time of initial referral by their general practitioners (GPs) to when they were seen in the paediatric clinic, were excluded from the study (n=31). A further 17/179 children were excluded as they were not referred by their GPs and are currently being been assessed locally within the pediatric services.

FIGURE 1 details the study population managed following the ESPGHAN 2012 guidelines from January 2013 till December 2019; 113 of 118 children (aged <16 years) were diagnosed with CD. The NBP was utilised to diagnose CD in 57/118 (48.3%) and non-adherence to the established ESPGHAN criteria was noted in 20.3% cases (n=24). Five children were diagnosed with CD without biopsy (yet had TGA-IgA <10xULN) because parents were unhappy with gluten challenge despite the need for endoscopic assessment to adhere to ESPGHAN guidelines. Positive HLA-DQ2/

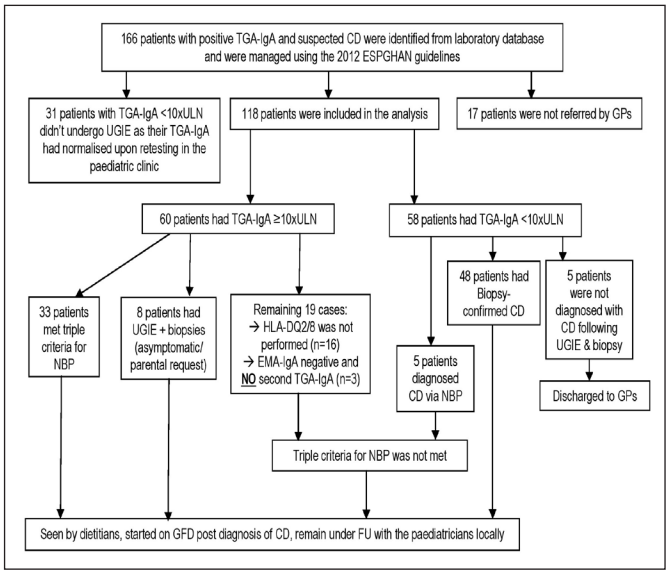

FIGURE 1. Diagnostic pathways used for children with suspected CD. CD: coeliac diseases; EMA-IgA: IgA-based anti-endomysial antibody; FU: follow-up; GFD: gluten-free diet; GPs: general practitioners; HLA: human leukocyte antigen; IgA: immunoglobulin A; NBP: no-biopsy pathway; TGA-IgA: IgA-based anti-tissue transglutaminase antibodies; UGIE: upper gastrointestinal endoscopy; ULN: upper limit of normal.

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DQ8 results (testing for which was requested inappropriately) in four of five patients likely contributed towards non-adherence to the guidelines. Seventeen patients (two with TGA-IgA >10xULN) were not referred by primary care until December 2020 and are being recalled and reassessed for CD.

In 2020, 13 children were diagnosed CD without biopsy: 11/13 met the revised 2020 ESPGHAN criteria for NBP[4]; two (with TGA-IgA <10xULN but >5xULN) were diagnosed using our regional interim COVID-19 NBP pathway.

Of the 126 children diagnosed with CD, there were 39 males and 87 females. The mean and median ages of the 126 children were 8.5 and 8.2 years respectively (range 0.8 year to 15.9 years). Out of 126 children, 106 were symptomatic: 82 had gastrointestinal symptoms (diarrhoea, constipation, abdominal pain, vomiting, faltering growth), fifteen had 15 extra intestinal manifestation (iron deficiency anaemia, tiredness, pubertal delay), and nine had mixed features. Twenty patients who were asymptomatic at diagnosis of CD belonged to high-risk groups: 12 had type 1 diabetes and eight had CD in a first-degree relative.

This study identified significant non-adherence to the 2012 ESPGHAN CD guidelines (n=24). However, some of these cases where non-adherence was noted will be admissible within the 2020 ESPGHAN revision of the CD guidelines[4], given the omission of HLA-DQ2/DQ8 typing (16/24 cases with TGA-IgA ≥10xULN had no HLA-DQ2/DQ8 performed). However, 5/24 cases who had TGA-IgA <10xULN would still require a biopsy diagnosis[4], with similar problems identified in two other English studies[2,3]. Due to the COVID-19 pandemic and limited endoscopy access, two symptomatic children with TGA-IgA <10xULN but >5xULN were diagnosed via NBP in 2020, a strategy suggested by a recently published Italian study[5].

Another issue identified: 17 of 179 (9.5%) children with positive TGA-IgA were not referred for confirmation of CD diagnosis by GPs. While a transient rise in titer is recognised after viral illnesses or in another condition e.g. cow's milk protein allergy, inflammatory bowel disease or other autoimmune conditions, it is quite possible that some were truly celiac and just not referred or may have been inappropriately diagnosed as CD in the primary care and commenced on gluten free diet (GFD). Similar issues were identified in two recently published studies from Southwest England where around 15% of children with a positive celiac serology were not initially referred[2,3], but following a recall, some were subsequently appropriately got diagnosed as CD (SPP personal communication).

Strict adherence to 2012 ESPGHAN guidelines was not seen in 24/118 (20.3%) cases. Considering CD is a life-long condition and GFD has significant challenges, we conclude that detailed understanding of, and tighter adherence to ESPGHAN 2020 guidelines is mandatory amongst general pediatricians involved in the diagnostic process in a non-specialist setting. Education events involving local pediatricians and GPs involved in referring/diagnosing CD are planned to update understanding, through dissemination of 2020 ESPGHAN guidelines, detailing challenging CD scenarios and emphasising the absolute need for referral to pediatricians or pediatric gastroenterologists to confirm a CD diagnosis.

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Authors' contribution

Tashtoush LB: data collection and analysis, prepared manuscript and literature review. Broad SR: project supervision and logistical support, data analysis, edited manuscript. Paul SP: project concept, supervision, edited manuscript and provided expert opinion. All the authors have approved the final manuscript.

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