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Towards a definition of refractory/therapy-resistant/intractable constipation in children: a cross-sectional, questionnaire-based, online survey

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ABSTRACT

Background The Rome criteria define childhood functional constipation but do not address refractory constipation. Attempts to define refractory constipation lack consensus. The interchangeable use of 'refractory' and 'intractable' or 'therapy-resistant' constipation and lack of understanding of the therapeutic ceilings before this diagnosis complicates the definition.

Aim To conduct an online cross-sectional study among medical professionals and researchers across a range of countries, to propose a consensus definition, terminology and duration of medically unresponsive constipation.

Method An expert-designed questionnaire was disseminated via Google Forms in a two-stage study over 2 months targeting paediatric gastroenterology professionals globally and Latin American clinicians with a translated version. The questionnaire had seven critical questions containing details needed to define medically unresponsive constipation. The study protocol was approved by the ethics review panel.

Results The survey involved 1079 participants: 87 from various countries in the first phase and 992 from Latin America in the second. There were 619 (57.3%) general paediatricians and 462 (43 %) paediatric gastroenterologists. The preferred term to indicate poorly responding constipation was 'therapy-resistant constipation' (47.8%), followed by 'refractory constipation' (43.6%). The majority of respondents (92.9%) agreed on considering a time frame for defining refractory constipation, with 37.7% suggesting 2–3 months. 467 (43.2%) recommended including failure despite maximum laxative therapy with two agents should be considered as previous therapy failure. Compliance with therapy was deemed essential for successful treatment by 91.1%, assessed through detailed history-taking (47.4%) or medical/pharmacy records (29.4%).

Conclusion Based on the professional views collected in this study, we propose the term 'therapy-resistant constipation' and it can be defined as constipation that is not responding to a maximum dose of at least two laxatives of different classes for a minimum of 3 months with good compliance in a secondary or tertiary care facility.

WHAT IS ALREADY KNOWN ON THIS TOPIC

⇒ None of the international diagnostic criteria iterations published by the Rome Foundation (Rome II–IV) provide criteria to diagnose therapy-resistant constipation. It is a priority for therapy-resistant constipation to have a single consensus definition to aid clinical and research practice.

WHAT THIS STUDY ADDS

⇒ The following definition was proposed based on the findings of this study. 'Therapy-resistant constipation' is defined as constipation that is not responding to a maximum dose of at least two laxatives of different classes for a minimum of 3 months with good compliance in a secondary or tertiary care facility.

HOW THIS STUDY MIGHT AFFECT RESEARCH, PRACTICE OR POLICY

⇒ This study highlights the complexities in defining refractory constipation in children among healthcare professionals. Future work is needed to consider, possibly refine and then incorporate this or an alternate definition into clinical and research practice.

INTRODUCTION

Functional constipation is a prevalent gastrointestinal clinical entity affecting children worldwide, with an estimated prevalence of 9.5%.¹ International guidelines outline the diagnostic workup and treatment of childhood constipation.^{2–4} Despite the best management practices and even in cases of full compliance, around one-third of children do not respond to standard treatments, progressing into adulthood with constipation.⁵ Persistent symptoms may lead to physiological and psychological consequences.^{6 7} Furthermore, some of these children undergo invasive investigations such as contrast studies and colonic biopsies, and a subset of them

are subjected to irreversible surgical interventions such as colonic resection.⁸

None of the international diagnostic criteria iterations published by the Rome Foundation (Rome II–IV) provide criteria to diagnose therapy-resistant constipation.^{9–11}

Due to the lack of a clear consensus clinical definition for this significant clinical problem, researchers have adopted many definitions which in turn describe a heterogeneous set of clinical paradigms. Common terms (refractory and intractable) may define different time durations for symptoms, and various requirements for previous therapeutic interventions but even within the use of the same term, studies vary in how they practically define it.^{12–16}

A recent meta-narrative systematic review also found only a few studies that gave explicit definitions at all.¹⁷ The lack of a clear definition substantially impacts research and, most importantly, clinical practice, leaving doubt as to the appropriateness of different therapies in different settings, the sequencing of treatments and the need for expert escalation.

It is a priority for therapy-resistant constipation to have a single consensus definition to aid clinical and research practice.¹⁷ The best way to reach such a consensus definition is by obtaining the view of practising clinicians.^{18 19}

Therefore, we sought to understand the perspectives of practising paediatricians, paediatric gastroenterologists and paediatric researchers on the definition of therapy-resistant constipation in children using an international cross-sectional study design.

METHODS

The questionnaire

This survey used a questionnaire designed and reviewed by four experts in paediatric disorders of gut–brain interactions: MAB and MT from the University of Amsterdam, the Netherlands, MG from the School of Medicine and Dentistry at the University of Central Lancashire, the UK and SR from the University of Colombo, Sri Lanka.

The questionnaire (online supplemental appendix 1) had seven critical questions designed to support the development of a definition for therapy-resistant constipation. The seven key areas include the capacity of the responder, the time frame of the duration of symptoms, core therapeutic items in therapy, the clinical setting of the diagnosis, compliance, how to assess the compliance and the term for poorly responding constipation. The selection of these items was based on an extensive literature review and a previous publication.¹⁷ Basic demographic details such as age, sex, country of origin were not collected as they were deemed unlikely to influence the thought process of diagnosing and management of therapy-resistant constipation. The initial questionnaire was piloted with 10 paediatricians, 2 of whom had a special interest in gastroenterology. Feedback from this pilot study, particularly concerning the clarity of the language used, was used to refine the final version of the

questionnaire. The final version was then converted into a Google Form.

Data collection and participants

The survey was conducted using Google Forms. We invited participants by email with one set of reminders to contribute their clinical knowledge and experience to establish a shared understanding that would eventually contribute to establishing a clear definition of therapy-resistant constipation in children.

The survey was conducted in two stages. The first stage targeted experts and clinicians who are directly involved in managing children with constipation specifically paediatricians and paediatric gastroenterologists practising in their respective countries. Additionally, researchers who have conducted and published studies on childhood constipation were also included in this stage. We also invited experts involved in the Rome V paediatric committees. These individuals are part of the Rome V group and are directly responsible for developing the Rome V criteria. All participants were recognised as expert clinicians and researchers in the field of paediatric gut–brain disorders. This stage of the survey was conducted in English.

The second stage involved paediatricians, paediatric gastroenterologists and researchers from several Latin American countries including Argentina, Chile, Dominican Republic, Bolivia, Colombia, Ecuador, Brazil, Costa Rica and El Salvador. These participants used a validated Latin-translated version of the same questionnaire. All participants were qualified paediatricians or paediatric gastroenterologists licenced to practice in their respective countries.

Participants were asked to read and consent to a series of statements before proceeding, with the questionnaire. The questionnaire consisted of seven questions, six of which were mandatory. Completing the survey took approximately 10–15 min, depending on the depth of responses. This survey was conducted approximately over 2 months. A single reminder was sent to participants who did not respond to the first email. Data were securely stored in password-encrypted files on University of Central Lancashire's protected servers.

Statistical methods

We used descriptive statistics to present the responses provided by the participants. Due to the notably higher response rate from Latin America in the second stage, we decided to analyse and compare the results from the Latin American group with those from the other participants using Fisher's non-parametric discrepancy test (online supplemental appendix 2). Our goal is to identify any significant differences between the two groups. Any systematic differences we find would be highlighted and discussed.

Patient and public involvement

It was not appropriate to include patients and public in this study as it was seeking professional stakeholder consensus on medical terminology.

RESULTS

Participants

In the first stage of the survey, 119 emails and reminders were sent to all at 2 weeks, leading to 87 participants who took part (73% response rate), with the majority (78.2%) being paediatric gastroenterologists, followed by paediatricians (24.1%) and researchers in the field (20.7%). In the second stage, there were 1750 email invitations sent and again 2-week reminders, with 992 participants taking part (56.7% response rate), with the majority being paediatricians (60.3%) and the remaining being paediatric gastroenterologists. In total, 1079 participants contributed to the survey across both stages.

Online supplemental appendix 2 compares results between the two groups, confirming the absence of significant differences.

Terminology

48% of responders preferred the term 'therapy resistant constipation', 43% 'refractory constipation', 7% 'intractable constipation' and 2% other terms.

Time frame for the diagnosis

A majority (92.9%) agreed that a specific time frame is necessary before diagnosing of therapy-resistant constipation. Among 1079 participants, 37.7% recommended a period of 2–3 months, 28.8% suggested less than 1 month, 17.3% proposed 4–6 months and 4.2% indicated a duration of more than 6 months.

Treatment before the diagnosis

The next question in the survey addressed whether previous therapy failure should be included in the definition of refractory constipation and how this should be defined. Most respondents (467, 43.2%) indicated that the definition should encompass failure despite maximum therapy using two laxatives. Additionally, 310 respondents (28.7%) suggested that it should include the need for different classes of treatments, such as enemas or pharmacological therapy. A smaller group of participants (113, 10.5%) believed that it should involve failure despite maximum laxative therapy with only one agent.

Clinical setting

Table 1 depicts the clinical setting for the diagnosis of therapy-resistant constipation. Most healthcare providers (58%) believe that the diagnosis should be made in secondary or tertiary care units.

Assessment of compliance for the therapy before the diagnosis

Most of the participants (91.1%) agreed that treatment compliance needs to be evaluated before diagnosing

Table 1 Level of clinical setting for the diagnosis of therapy-resistant constipation

Clinical setting	Number of respondents	Percentage
Primary/community	283	26
Secondary/hospital	280	26
Tertiary care/specialised unit	247	23
Secondary and/or tertiary only	269	25
Total	1079	100

therapy-resistant constipation. The respondents were also asked to select suggestions on how compliance should be assessed, with 47.4% suggesting history, 29.4% pharmacy and medical records and 11.6% other methods.

DISCUSSION

Constipation that is poorly responding to medical management is a challenging clinical problem in paediatric gastroenterology. Although it is known to occur in a significant proportion of children with constipation, this clinical entity has no clear definition. Since there are many therapeutic options, ranging from escalating medical interventions, sacral nerve modulation, temporary stomas, colonic washouts using cecostomy or appendicostomy tubes and permanent surgical resections, it is imperative to clearly define poorly responding constipation to prevent unnecessary interventions and complications.^{3 8 20 21} Our cross-sectional study attempts to create a clinically meaningful definition for constipation that is poorly responded to medical management.

Researchers have used different terms to define poorly resolving constipation.^{22 23} In determining the most suitable term for defining constipation as poorly responding to medical management, 'therapy-resistant constipation' emerged as the preferred choice. This suggests a preference for terms that imply ongoing therapeutic challenges rather than absolute treatment resistance. In contrast, the term 'refractory constipation' may convey a sense of obstinate resistance, while 'intractable constipation' implies an almost insurmountable barrier to successful treatment. The nuanced distinction between these terms is crucial for accurately communicating the nature of the condition to both healthcare professionals and patients, emphasising the dynamic and evolving nature of therapeutic interventions.

Participants overwhelmingly agreed that a time frame should be considered when defining therapy-resistant constipation, reflecting a common acknowledgement of the importance of treatment duration before assessing treatment failure. This consensus underscores the critical need to establish a standardised period during which treatments should be evaluated for efficacy, thereby ensuring that diagnosis of therapy-resistant constipation is based on thorough and consistent criteria. Interestingly, opinions were diverse regarding the specific time

Box 1 Proposed definition for therapy-resistant constipation

Therapy-resistant constipation is defined as constipation that is not responding to a maximum dose of at least two laxatives of different classes for a minimum of 3 months with good compliance in a secondary or tertiary care facility.

frame, with about one-third of the respondents (37.7%) suggesting 2–3 months, indicating variability in clinical practice and patient management approaches. The time used in the previous research varied from 3 months to 2 years.^{24–26} Establishing a universally accepted time frame could facilitate more uniform diagnostic criteria, improve patient outcomes and enhance the comparability of clinical research studies. Based on the findings, we recommend that patients receive at least 3 months of optimal treatment before making a diagnosis of therapy-resistant constipation.

Regarding previous therapy failure, many respondents (43.2%) advocated for defining therapy-resistant constipation as a failure despite maximum laxative therapy using two agents. This finding highlights a preference for rigorous therapeutic trials before classifying cases as therapy-resistant. It underscores the necessity of exhausting primary treatment options to ensure that the diagnosis of therapy-resistant constipation is both accurate and justified. Additionally, a substantial proportion of respondents emphasised the importance of including different classes of treatments—such as oral and or rectal laxatives, enemas or pharmacological therapies—in the definition. This further illustrates the complexity of treatment escalation in challenging cases beyond guidelines. A recent Cochrane review found there is no standard medical therapy for therapy-resistant constipation, and the modalities of treatment included varied widely from medical treatment to surgical interventions.²⁷ It is possible to include inadequate response to at least two therapeutic agents as the minimum therapeutic intervention before diagnosing therapy-resistant constipation.

The clinical setting for diagnosing refractory constipation emerged as another area of variability among participants. While approximately equal numbers favoured primary/community settings (26.3%) and secondary/hospital settings (26.0%), significant proportions also supported tertiary care/specialised units (22.9%) or a combined secondary/tertiary care approach (24.9%). This distribution suggests different opinions on the appropriate expertise and resources needed for accurate diagnosis and management. The nearly equal support for primary and secondary settings reflects the recognition that initial evaluation and management of constipation can often be effectively handled in these more accessible healthcare environments. However, the substantial support for tertiary care and specialised units underscores the complexity and severity of cases deemed therapy-resistant, which may require advanced diagnostic tools, specialised knowledge and multidisciplinary

approaches available in these settings. The preference for a combined secondary/tertiary care approach indicates an understanding that collaboration between different levels of care can provide a more comprehensive assessment and treatment plan. Based on the findings, diagnosing therapy-resistant constipation at least at secondary, tertiary care centres or specialised units is preferable.

Consideration of compliance with therapy garnered overwhelming support (91.1%) among participants as a crucial factor in defining refractory constipation. The preferred methods for assessing compliance varied, with a majority (47.4%) favouring detailed history-taking. This preference indicates the importance of patient-reported outcomes and treatment adherence in clinical assessment. By prioritising thorough history-taking, healthcare providers can gain valuable insights into patients' adherence to prescribed therapies, identify potential barriers to compliance and tailor treatment plans accordingly.

Our study has several strengths. We developed a questionnaire involving experts in the field highlighting all the necessary criteria to diagnose therapy-resistant constipation. In the first stage of the survey, we included experts in the field of neurogastroenterology, including the Rome committee members who are well versed in handling children with poorly responding constipation. In addition, we have included a large number of paediatric gastroenterologists and general paediatricians who are involved in the day-to-day management of both simple and therapy-resistant constipation. Obtaining their opinion regarding how to define this complex problem provides us with a better perspective. However, the majority of our sample is skewed towards Latin America. While this indeed is a potential limitation, the geographical location of the participants should not significantly influence their definitions of a clinical problem like therapy-resistant constipation. This is supported by the lack of significant differences in responses from participants in Latin America compared with those from other regions of the world. In addition, we did not obtain individual data on the duration of practice of the clinicians and the researchers who took part in the study. This could have a marginal effect on how they define poorly responding constipation.

Another limitation of our study is that it only involved medical professionals, including paediatricians, paediatric gastroenterologists and researchers, in defining medically unresponsive constipation. We did not take into account the perspectives of children and their parents, who are directly affected by this condition. This omission may limit the applicability of the definition, as it may not fully capture the lived experiences and practical challenges faced by patients and their families. Additionally, we did not consider the years of experience of the expert participants when including them in the survey, which could also influence clinical opinions on medically resistant constipation. Future studies should validate this definition in a clinical setting by incorporating

feedback from both patients and their caregivers. This would enhance its relevance and accuracy in real-world applications.

This survey highlights the complexity and variability in defining refractory constipation in children among healthcare professionals. The findings underscore the need for standardised diagnostic criteria for treatment duration, therapeutic trials, clinical setting, compliance assessment and terminology. Future efforts should focus on consensus-building initiatives to enhance diagnostic precision and optimise management strategies for this challenging paediatric condition. Considering all the findings, we may be able to suggest a definition for therapy-resistant constipation (box 1).

CONCLUSION

This study highlights the complexities in defining refractory constipation in children among healthcare professionals. Based on the international professional views collected in this study, the term 'therapy-resistant constipation' and its associated definitions have been identified. Future work is needed to consider, possibly refine and then incorporate this or an alternate definition into clinical and research practice.

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