Research Study on Classical Galactosaemia

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Galactosaemia is a life-threatening inherited metabolic disorder (IMD) of carbohydrate metabolism, where the body's ability to metabolise the monosaccharide, galactose, is impaired.[1] The disruption occurs in the Leloir pathway when any of the four enzymes involved in galactose metabolism are affected: galactokinase (GALK), uridine diphosphate galactose 4'-epimerase (GALE), galactose-1-phosphate uridyl transferase (GALT), or galactose mutarotase (GALM).[1-6] Classical galactosaemia (CG) (or type I galactosaemia, OMIM 230400),[7] caused by a deficiency in the GALT enzyme (EC 2.7.7.12),[1, 8] is the most common and severe type.[1] It is characterised by neonatal onset of symptoms following galactose ingestion, including: faltering growth, feeding difficulties, liver disease, *Escherichia coli* sepsis, encephalopathy and cataracts.[1, 9-11] Later complications involve cognitive deficits, learning disabilities, speech impairment, abnormal growth and infertility in females.[1, 2, 10] Despite early and stringent dietary elimination of galactose, these chronic complications are unavoidable, possibly owing to exaggerated endogenous galactose production in individuals with galactosaemia, among other factors.[1, 2, 12]

Globally, GALT-deficient galactosaemia occurrence is 1 in 62,000 live births, varying across regions.[13] In Europe, incidence ranges between 1 in 19,000 to 1 in 44,000,[12] with highest rates among consanguineous communities like the Republic of Ireland's Traveller population (1 in 480).[1, 2, 11] The United Kingdom (UK) has an estimated incidence of 1 in 38,621 live births.[1, 14] Despite a higher incidence of CG in the UK compared with that globally, only 12 to 18 children[1, 15, 16] are born with the condition annually in the UK – highlighting its rarity and the isolation families may experience following diagnosis.

Newborn screening

Newborn blood spot (NBS) screening programmes have been implemented in most developed countries, including the UK, to routinely detect a range of IMDs within the early days of life.[1, 3, 17] Currently, the national NBS screening programme in the UK does not include galactosaemia, owing to ongoing uncertainty around the benefits there of.[1, 14, 17, 18] In the absence of formal national NBS screening, galactosaemia cases in the UK are mainly detected and diagnosed following clinical presentation.[1, 3, 17, 18]

Dietary management

The primary treatment for CG is a therapeutic diet involving instant removal and lifelong restriction of dietary sources of galactose and lactose (a disaccharide comprised of glucose and galactose), including breastmilk.[1, 2, 9] Lactose-free products are unsuitable due to the residual high galactose content following enzymatic degradation of lactose.[1, 2, 16, 19] Despite the robust evidence that dietary intervention following diagnosis of CG in infancy is life-saving,[1-3, 9, 12, 19] there remain discrepancies worldwide in dietary prescribing practices for galactosaemia.[1, 12, 19] International management guidelines were developed in 2016 by the Galactosemia Network (GalNet).[1, 19] These guidelines comprise forty evidence-based recommendations that have been widely accepted in UK practice and are referenced throughout.[1, 19, 20]

Galactosaemia study

Although some studies have investigated quality of life (QoL) of children and adults living with CG,[21-23] none have explored the impact of the therapeutic diet on caregivers of infants/children with the disease.[1, 22, 24] During infancy and early childhood the therapeutic diet is managed primarily by the caregiver.[1] Evidence suggests that living with galactosaemia can be burdensome, not only for patients but for their families too.[1, 11, 19, 21-24] This survey aimed to investigate the nutrition-related knowledge, perceptions, practices and barriers of caregivers related to the galactosaemia diet for their child with CG in the UK.[1]

Methods

Between April-July 2022, a cross-sectional survey was conducted, focusing on primary caregivers of children (<18 years) with CG following a galactose-restricted diet in the UK. The study used a novel online questionnaire developed with reference to the United Nations (UN) Food and Agriculture Organization (FAO) guidelines,[25] for assessing knowledge, attitudes and practices.[1] The survey, consisting of 48 mainly multiple-choice items, underwent face and content validation through a pilot study and expert review, respectively. Caregivers from the Galactosaemia Support Group (GSG) and Metabolic Support UK (MSUK) charities were recruited via volunteer sampling, totalling 98 eligible participants.[1] The survey was promoted through email advertisements and social media platforms, with regular reminders to enhance participation and response rates. The final sample consisted of 43 participants and the response rate was 44%.[1]

Results & discussion

Participant characteristics

Most caregivers were mothers (84%, *n* = 36) and resided in England (79%, *n* = 34). All participants were members of the GSG, while few (19%, *n* = 8) were members of other galactosaemia patient associations. Furthermore, almost all caregivers (93%, *n* = 40) reported that these memberships were beneficial to managing the galactosaemia diet for their child. Reassuringly, caregivers primarily obtained information about the galactosaemia diet from credible sources, such as local or international galactosaemia associations (75%, *n* = 32) or their child's dietitian (21%, *n* = 9). These findings demonstrate the value of galactosaemia patient associations as a major source of dietary information and support for caregivers.[1]

Caregiver knowledge

The study revealed that almost all caregivers (98%, *n* = 42) demonstrated a 'high level of knowledge' about the galactosaemia diet, with minimal variability in knowledge scores. The overall average ($\bar{x}$) knowledge score was 17.9 out of 20 (standard deviation (SD) = 1.7; 95% confidence interval (CI): 17.4, 18.4) and fathers tended to score the lowest overall for the knowledge assessment ($\bar{x}$ = 16.9). A noteworthy 84% (*n* = 36) of participants had education beyond basic schooling, revealing a significant correlation (*r* = 0.383, *p* = 0.013) between caregivers' education level and knowledge scores. When rating their own knowledge about the diet, 54% (*n* = 23) considered themselves as having 'very good' knowledge and caregivers' self-rated knowledge aligned with their actual scores. Most caregivers (66%, *n* = 29) identified UK extra-mature cheddar as a suitable cheese for dietary inclusion, suggesting possible unawareness of other allowed cheese varieties. Notably, the recent cheese update from the GSG[26] in 2022 reports on additional safe cheeses, offering an opportunity for dietitians to educate caregivers on diverse calcium-rich options for the galactosaemia diet. The survey did not account for these new cheese additions as the GSG announcement occurred post-survey closure.[1]

Caregiver perceptions

Caregivers' perceptions of the galactosaemia diet varied, with 42% (*n* = 18) having a positive view of the galactosaemia diet, and 40% (*n* = 17) expressing concern about their child's adherence to the diet. Most caregivers (49%, *n* = 22) expressed concern about being unable to provide breastmilk to their infant following the galactosaemia diagnosis. This perception was found to be positively correlated with their pre-diagnosis intentions to provide breastmilk to their infant (*r* = 0.450, *p* = 0.003). This is an important finding as galactosaemia remains one of the only infant diseases that is a true/absolute contraindication to breastfeeding.[1, 27] Parents are therefore faced with not only coping with a challenging diagnosis for their child, but with managing a restrictive diet where their fundamental choice of how they wish to nourish their offspring has been removed. Furthermore, little evidence exists on the parental views of being unable to provide breastmilk to their child within the context of conflicting universal public health messages that promote breastfeeding practices.[1, 27, 28] The psychological impact this may have on caregivers, albeit not explored in this study, remains noteworthy given that reduced duration of breastfeeding has been associated with increased levels of maternal depression.[1, 29] Therefore, caregivers of children with galactosaemia comprise a unique group, requiring special attention to dietary education and counselling; management of realistic parental expectations around infant feeding practices; and mental health support.[2]

Most caregivers (65%, *n* = 28) were classified as having high attitudinal scores (31–45, out of 45) based on the perceptions assessed in this study, indicating that most had an overall positive attitude towards the galactosaemia diet. Akin to previous studies,[1, 19, 30] many caregivers (40%, *n* = 17) reported distress related to dietary restrictions. Most caregivers (47%, *n* = 20) felt their child was socially excluded due to the diet, emphasising the need for healthcare professionals to provide advice on managing social situations. Results indicated caregivers generally rated themselves as 'very confident' (56%, *n* = 24) and 'confident' (42%, *n* = 18) with managing the diet for their child, aligning with their overall positive attitudes described above. These findings highlight the importance of support networks and galactosaemia associations for shared experiences and practical dietary advice.[1]

Caregiver practices

All caregivers reported that their child followed a 'dairy-free' type of galactosaemia diet, allowing inclusion of non-dairy galactose sources, aligned with international guidelines.[1, 19] The knowledge assessment showed caregivers were well-informed about the importance of calcium, vitamin D and iodine in the context of dairy avoidance, with most children receiving daily micronutrient supplementation containing both calcium and vitamin D (49%, *n* = 21) or vitamin D only (28%, *n* = 12). There are conflicting findings about the vitamin D and calcium status in children following a galactosaemia diet, suggesting a need for vigilance, especially in regions with limited sunshine, like the UK. All participants included at least two or more sources of calcium-rich foods in their children's diet weekly, with the main source being fortified plant-based dairy alternatives (98%, *n* = 42), thereby minimising the risk of deficiency. Soya milk, with its favourable nutritional profile,[1, 31] was the primary dairy alternative consumed (93%, *n* = 40).

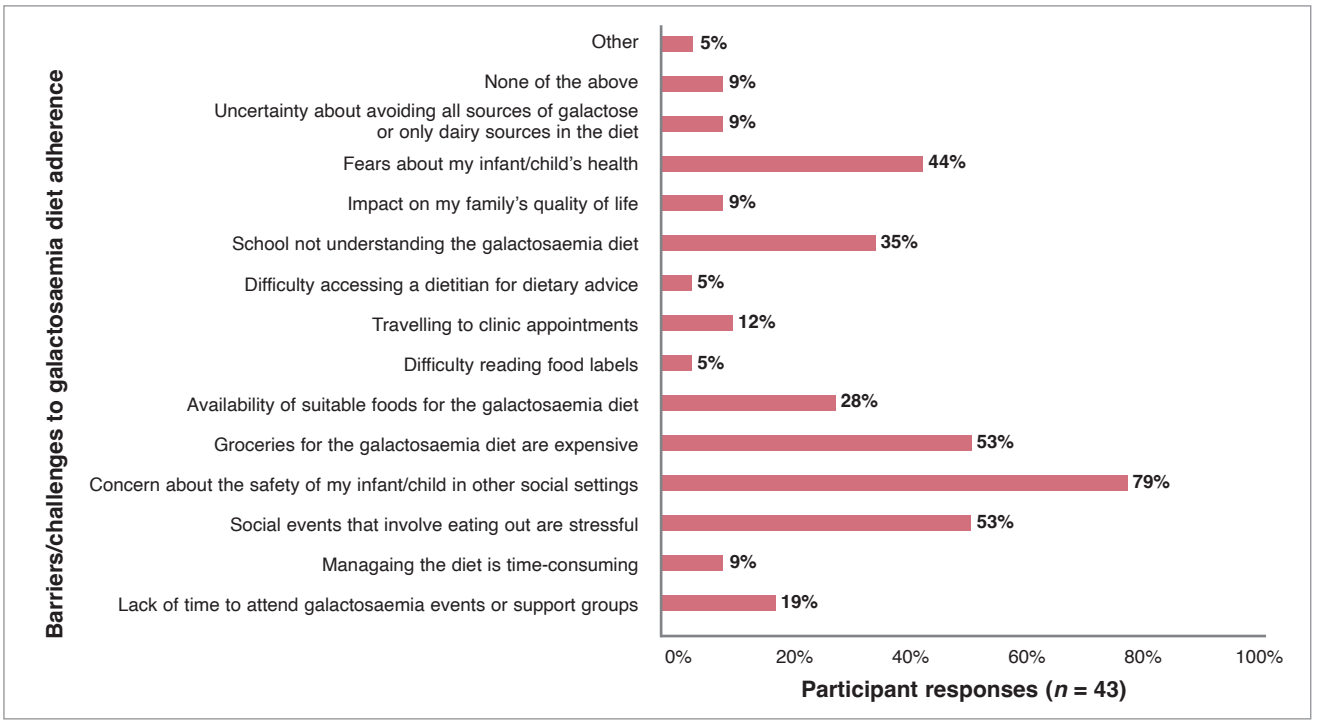
Caregiver barriers/challenges

This section addressed the barriers faced by caregivers managing the galactosaemia diet for their child, and the findings are displayed in **Figure 1**. The responsibility of managing the therapeutic diet that determines the clinical outcomes for their child can be onerous for caregivers.[1, 2] Main challenges included concerns for their child's safety in social settings (79%, *n* = 34), stress associated with eating out (53%, *n* = 23), cost of groceries (53%, *n* = 23), health concerns (44%, *n* = 19), and lack of school staff understanding (35%, *n* = 15). Most caregivers (54%, *n* = 23) encountered multiple barriers (≥ 4) to diet adherence, presenting valuable opportunities for healthcare interventions that address these. A significant association was found between the age of the child and the following barriers: 'managing the diet is time-consuming' ($p = 0.090$) and 'groceries for the galactosaemia diet are expensive' ($p = 0.048$), suggesting the need for tailored dietary counselling based on the child's age. Social settings, particularly safety and eating out, emerged as predominant barriers. Interestingly, unlike other metabolic disorders,[1, 32-35] the time-consuming nature and impact on family QoL were not barriers for most, aligning with normal health-related quality of life (HrQoL) reported in previous studies.[1, 22, 24]

Study limitations & conclusion

The study acknowledges methodological limitations, including potential bias from caregivers' GSG membership, impacting their knowledge and motivation levels. The small sample size and non-random sampling method may limit generalisability of results. Caregivers demonstrated high knowledge levels about the galactosaemia diet, therefore healthcare interventions should focus on addressing negative perceptions and unique barriers faced with dietary compliance, considering the child's life stage. Specialist multidisciplinary teams (MDT) should incorporate mental health/psychological support as standard care. Caregivers' negative perceptions, especially regarding the inability to provide breastmilk, should be routinely explored with referral to relevant support services, as required. Encouraging mutual support among caregivers through shared experiences and practical advice is required. Educating caregivers about suitable calcium-rich cheese varieties allowed in the galactosaemia diet is recommended following the updated advice from the GSG.[1, 26] Future research of this nature is vital to provide comparative data and insights to inform clinical practice and support for the galactosaemia community.[1]

Figure 1: Caregivers' perceived barriers/challenges to galactosaemia diet adherence (%) (*n* = 43)[1]



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