

Dietary management of homocystinuria (HCU) caused by cystathionine beta-synthase (CBS) deficiency: Perspectives from a global cohort of metabolic dietitians

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INTRODUCTION

- CBS-deficient HCU is an inherited, metabolic disorder associated with a wide range of progressive, debilitating, life-threatening clinical manifestations that may present and persist throughout the lifespan; characterized by elevated levels of total homocysteine (tHcy)
- Current interventions aim to lower plasma tHcy concentration, but metabolic control may be inconsistent, and patients are at risk of further complications, morbidity, and premature mortality from severe clinical manifestations of the disease
- HCU management guidelines (2017)¹ recommend a lifelong low-protein diet with methionine (met)-free L-amino acid (AA) supplements and/or betaine for pyridoxine nonresponsive patients
- An evaluation of current practice was last reported in 2013², but evidence on current management and practice for CBS-deficient HCU since publication of the 2017 guidelines is limited

STUDY OBJECTIVE

- To survey global metabolic dietitians, assess current management practices and patient adherence to dietary recommendations for CBS-deficient HCU

METHODS

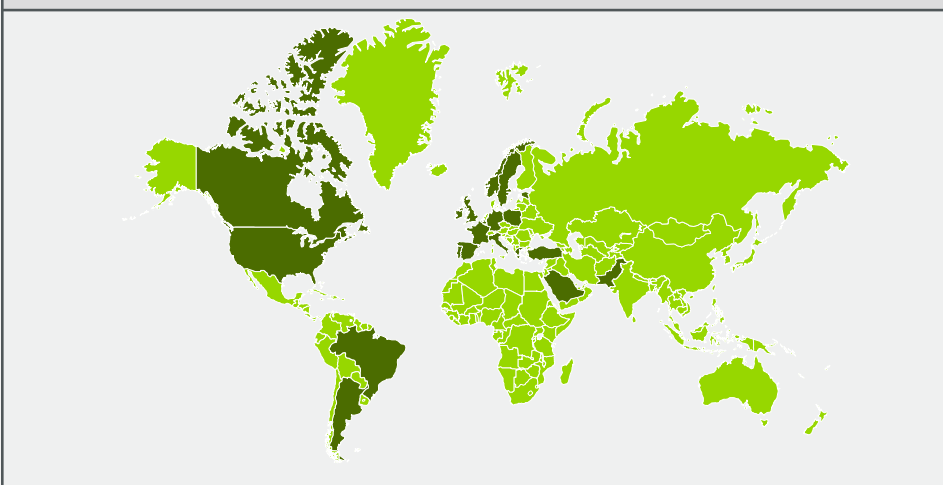
- An online survey was distributed via the Genetic Nutrition Online Metabolic Listserv for Genetic Metabolic Dietitian Nutritionists and faculty professional contacts
- The survey was conducted between September 20—November 10, 2021
- Respondents included metabolic dietitians involved in managing patients with CBS-deficient HCU
- Survey responses were categorized by the following patient age groups: ≤1 year, 2–10 years, 11–17 years, 18–49 years, and ≥50 years

RESULTS

Respondent demographics

- 59 responses, representing approximately 300 patients with CBS-deficient HCU, were received from 21 countries (Figure 1), with the greatest numbers from the United States (28%), United Kingdom (9%), Turkey (7%), Spain (7%), Sweden (6%), and Portugal (6%)

Figure 1 – Geographical distribution of survey responses

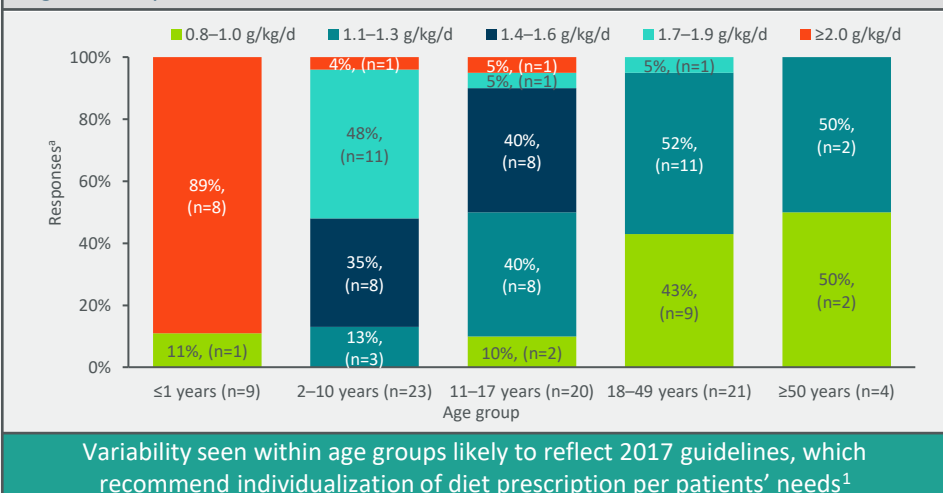


- Responses received per age group^a: 0–1 year n=10, 2–10 years n=24, 11–17 years n=22, 18–49 years n=23, and ≥50 years n=5

Management practices

- Most respondents prescribe a natural protein-restricted diet with a met-free L-AA supplement
 - For patients >1 year old: 91% prescribed a natural protein-restricted diet with a met-free L-AA supplement
 - 82% of ≤1-year-olds were prescribed a natural protein-unrestricted diet without a met-free L-AA supplement
- Prescribed total protein was inversely related to the age of the patient (Figure 2)
- Betaine was prescribed in 50% of ≤1-year-olds and 78–100% of patients ≥2 years old, and cysteine to approximately 33% of patients across age groups

Figure 2 – Amount of total protein prescribed was inversely related to the age of the patient



Variability seen within age groups likely to reflect 2017 guidelines, which recommend individualization of diet prescription per patients' needs¹

Need for additional non-dietary therapy to manage CBS-deficient HCU

- 71% of respondents agreed with the need for additional non-dietary therapy to manage CBS-deficient HCU for all age groups

CONCLUSIONS

- Adherence to a natural protein-restricted diet with a met-free L-AA supplement varied across age groups. Overall, 19% of patients almost never (0–24% of the time) adhered to met-free L-AA supplement compared to 13% to a natural protein-restricted diet
- Patients of all ages endure many challenges associated with adhering to current dietary management. This survey identified trends of decreased adherence to both diet and met-free L-AA supplement with increasing age
- Respondents' agreed and acknowledged that there is a significant need for an alternate non-dietary therapy to manage CBS-deficient HCU

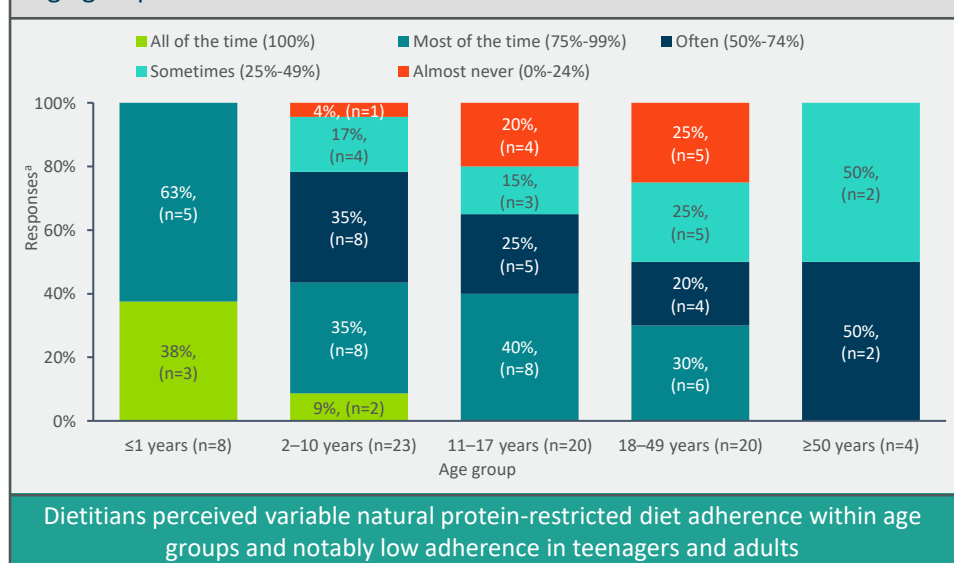
LIMITATIONS & FUTURE CONSIDERATIONS

- There may be selection bias for these data as respondents may be more knowledgeable of disease management guidelines compared with those who did not complete the survey
- Respondents may be skewed toward US and EU contacts due to the route of survey distribution; this could be addressed by the inclusion of more regions in future surveys, e.g., Asia and Australia
- There remains a need for an expanded understanding of tHcy control among patients and the prescription of additional vitamin, betaine and cysteine supplements

Patient adherence - Natural protein-restricted diet

- Natural protein-restricted diet adherence progressively decreased in patients aged 11–49 years, with 23% reporting that patients almost never (0–24% of the time) adhere to prescribed diet (Figure 3)
 - 33% consume approximately 101% to >200% more natural protein than prescribed
- Most commonly stated reasons for nonadherence to natural protein prescription by age were as follows:
 - 2–10-year-olds: limited knowledge of caregivers and inadequate family support
 - 11–17-year-olds: the social isolation associated with dietary restrictions
 - ≥18 years old: the difficulty and time to prepare a low protein diet

Figure 3 – Adherence to prescribed natural protein-restricted diet varied by age group

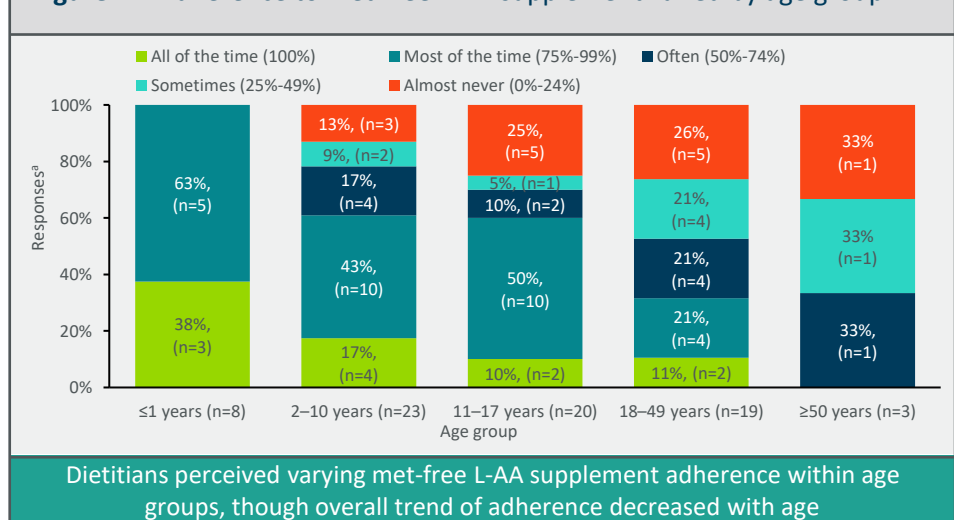


Dietitians perceived variable natural protein-restricted diet adherence within age groups and notably low adherence in teenagers and adults

Patient adherence - Met-free L-AA supplement

- Patients aged 0–17 years prescribed methionine-free protein/L-amino acid supplement/medical food were mostly adherent (Figure 4); nonadherence was mostly attributed to unpleasant taste
 - Across all age groups, 58% of respondents reported that their patients consume met-free L-AA supplements as prescribed or a little less (1–25%) than prescribed

Figure 4 – Adherence to met-free L-AA supplement varied by age group



Dietitians perceived varying met-free L-AA supplement adherence within age groups, though overall trend of adherence decreased with age

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^aThere were a total of 59 responses, however 4 did not feel comfortable completing the survey in English and were excluded. Of the remaining 55 dietitians who completed survey questions, a single dietitian may have treated patients from more than one age group and provided a single response for each age group. 1. Morris AA, et al. *J Inher Metab Dis.* 2017;40(1):49–74. 2. Adam S, et al. *Mol Genet Metab.* 2013;110(4):454–459.



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