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Research paper

Nutritional knowledge, attitudes and dietary behaviours amongst individuals with hypermobility syndromes and associations with co-morbid gastrointestinal symptoms and fatigue: an observational study

Nikki Paiba, Miranda Harris *

School of Allied Health and Community, University of Worcester, UK

A R T I C L E I N F O

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A B S T R A C T

Introduction: Hypermobile Ehlers–Danlos syndrome (hEDS) and hypermobility spectrum disorder (HSD) are hereditary connective tissue disorders involving joint hypermobility and coexisting multisystem symptoms, including gastrointestinal (GI) dysfunction and chronic fatigue. Research investigating nutritional knowledge, attitudes and behaviours (KAB) of individuals with hEDS/HSD does not exist, so this study aimed to objectively measure KAB and explore relationships between KAB, GI symptoms and fatigue.

Methods: Adults with hEDS/HSD were invited to complete an anonymous online survey. Utilising quantitative methodology, nutritional KAB, GI severity and fatigue scores were collected using validated questionnaires and statistically analysed using IBM SPSS. Multivariate regression explored relationships between KAB variables and GI scores, and Spearman-rho correlation analysis explored relationships between KAB and fatigue.

Results: 536 participants completed the questionnaire. Total scores for KAB were high, particularly for attitude and knowledge, although lower for behaviour. The total fatigue severity score was high, whilst upper and lower GI symptom scores were mid-range. Strong positive correlations were identified between knowledge and attitude, knowledge and behaviour, and attitude and behaviour. Behaviour contributed to predicting GI scores and small negative correlations were found between behaviour and GI symptom severity. There were no significant relationships between dietary KAB and fatigue.

Conclusion: A focus on improved dietary behaviour, utilising specific nutrition education and guidance based on dietary aspects with lower scores, would be beneficial and may contribute to GI symptom management. A generalised nutritional strategy has been proposed, involving an integrated approach to diet, lifestyle and behaviour change to improve dietary KAB in the hEDS/HSD population.

1. Introduction

Hypermobile Ehlers–Danlos syndrome (hEDS) and hypermobility spectrum disorder (HSD) are heritable disorders of connective tissue characterised by joint hypermobility, musculoskeletal symptoms and chronic pain [1]. Connective tissue is present throughout all body systems, so individuals may also present with coexisting multisystem symptoms, including GI disorders and chronic fatigue [2–5]; further comorbidities include dysautonomia, uro-gynaecological and pelvic conditions, headaches, neurological features and psychological manifestations [6–8].

The 2017 revised International Ehlers–Danlos Syndrome (EDS) classification [9] redefined hEDS based on clinical criteria and family history, whereas other EDS subtypes require causative genetic variants for diagnosis. Specific collagen gene variants for hEDS have not been isolated, although dysregulated expression of other connective tissue genes has been reported [10–13]. An HSD diagnosis is intended if more stringent hEDS criteria are unmet, reflecting a spectrum from asymptomatic hypermobility, through HSD, to hEDS [14]; however, both diagnoses are frequently considered together as hEDS/HSD [15,16]. Prior

Abbreviations: EDS, Ehlers–Danlos Syndrome; EDS-HT, Ehlers–Danlos Syndrome-Hypermobile Type; FSS, Fatigue Severity Score; GP, General Practitioner; hEDS, hypermobile Ehlers–Danlos Syndrome; HSD, Hypermobility Spectrum Disorder; IBS, Irritable Bowel Syndrome; JHS, Joint Hypermobility Syndrome; KAB, Knowledge-Attitudes-Behaviour; OI, Orthostatic Intolerance; PAGI-SYM, Patient Assessment of upper GastroIntestinal SYMptom severity index; POTS, Postural Orthostatic Tachycardia Syndrome; SSPS, Statistical Package for the Social Sciences.

* Corresponding author.
E-mail address: m.harris@worc.ac.uk (M. Harris).

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to the 2017 reclassification, individuals were diagnosed with EDS-hypermobile type (EDS-HT), EDS-type 3, joint hypermobility syndrome (JHS) or symptomatic hypermobility. The prevalence of hEDS/HSD is unclear [17], although estimates of 0.19–2% have been reported [18,19]; however, within musculoskeletal, rheumatology and pain clinics, symptomatic joint hypermobility has been identified in 30–49% of patients [20].

Symptoms vary with age, sex, lifestyle and epigenetic expression, but a progressive decline in quality of life is typically observed [21]. A sex bias has been identified, with an excess of affected females [22]; for example, in the large cohort study of Demmler et al. [18], 70% were female. Medication use is considerable due to chronic pain, multiple symptoms and coexisting conditions [23,24]. Individuals may receive separate diagnoses for simultaneous symptoms, despite joint hypermobility being the unifying feature [25], and multidisciplinary management is preferable for those presenting with complex symptomology.

There is a high burden of GI dysfunction; symptoms may arise from structural issues, such as prolapses and herniae, and from functional disorders, including dysphagia, gastro-oesophageal reflux, dyspepsia, dysbiosis, bloating, abdominal pain and irritable bowel syndrome (IBS) [26–29]. A large case-control study found that 98% of individuals diagnosed with hEDS/HSD satisfied Rome IV criteria for one or more functional GI disorders [23]. Constipation is often an early symptom and referrals for dysmotility are common [30]. Zweig et al. [31] found that in a group of individuals with IBS, the presence of joint hypermobility was significantly higher in those with constipation (57.8%), compared to diarrhoea (34.8%), and postulated that abnormal connective tissue biomechanics leads to a degree of colonic inertia. GI symptoms may be exacerbated by coexistent dysautonomia, such as postural orthostatic tachycardia syndrome (POTS) or orthostatic intolerance (OI) [32], in which abnormal gastric electrical activity has been reported [33]. POTS is over-represented in hypermobility disorders [34], with coexistent POTS reported in one-third [35] to 49% [36] of individuals with hEDS/HSD.

Chronic fatigue is another common symptom reported to coexist with hEDS/HSD [37–39], although the relationship with symptomatic hypermobility is poorly understood [40]. Possible underlying causes are multi-factorial and include chronic pain, physical deconditioning, bowel, bladder and autonomic dysfunctions, nutritional deficiencies, anxiety, depression, headaches and poor sleep quality [41,42]. Celletti et al. [43] additionally suggested a link with fear of movement and bodily disuse, due to pain-avoidance behaviour, although To et al. [20] reported fatigue to be centrally-mediated, rather than peripherally-mediated, due to poor proprioception and altered central nervous system sensory input. Fatigue may be considerable, and Krahe et al. [44] found that 79.5% of their study participants with JHS or EDS-HT demonstrated significant fatigue-related symptoms.

Patient education and dietary advice, including optimisation of the gut microbiota, have been promoted as effective management tools for hEDS/HSD symptom control [45,46]. However, there are no published studies relating to specific dietary interventions, although anecdotal evidence exists for lower carbohydrate diets and individualised exclusion diets [47]. Additionally, dietary manipulation may aid symptom control in coexisting IBS; Fragkos et al. [48] reported that individuals with JHS exhibited significant improvements in abdominal pain, bloating, constipation and diarrhoea following a low fermentable oligo-saccharide, di-saccharide, mono-saccharide and polyol (FODMAP) diet; however, concerns exist about longer term use [49]. Furthermore, a shift towards using food as medicine, rather than managing symptoms with medications, has been suggested for both prevention and treatment of common GI symptoms, particularly since dietary education is associated with improved clinical outcomes and quality of life [50].

Optimal nutrition is known to aid management of chronic disease, for example, by modulating epigenetic expression, regulating metabolic pathways and addressing nutritional deficiencies [51,52]. Importantly, improved nutritional knowledge, attitudes to healthy eating and dietary behaviours are major factors contributing to healthier dietary patterns and higher self-rated health [53]. The Knowledge-Attitudes-Behaviour (KAB) model assumes provision of nutritional information leads to gains in knowledge, thereby prompting beneficial changes in dietary attitudes and behaviours [54]. However, increased factual knowledge may not always result in healthier dietary practices [55] and an understanding of relationships between knowledge and dietary behaviour is important. Nutritional attitudes also correlate positively with nutritional knowledge [56], and Sims [57] suggested an attitudes-to-knowledge-to-behaviour model to be more relevant than knowledge-to-attitudes-to-behaviour. Noteworthily, attitude is the most recurrent positive predictor for intention and dietary behaviour change [58], which is important because sustained dietary modifications are required for beneficial longer-term health-related outcomes [59].

Knowledge of nutritional KAB is an important prerequisite for the development of dietary strategies. Whilst recognising the underlying and coexisting pathologies, it is hypothesised that a general improvement in nutritional KAB may contribute to the supportive management of individuals with hEDS/HSD and their comorbid conditions, particularly those directly impacted by diet, such as GI dysfunction and fatigue. Although beliefs and behaviours in relation to exercise have previously been studied [60], there has been no research to-date exploring nutritional KAB, or associations between KAB, GI symptoms and fatigue, in hEDS/HDS.

The overall aim of this study was, therefore, to explore relationships between nutritional KAB and to evaluate KAB associations with GI symptoms and fatigue in individuals with hEDS/HDS. Specific objectives involved exploration of characteristics of adults resident in the United Kingdom (UK), aged 18 and over, with hEDS/HSD, including age, sex, diagnosed comorbidities, medication and nutraceutical use, and previous nutrition advice; analysis of levels of dietary KAB, coexisting GI symptoms and coexisting fatigue; and critical evaluation of relationships between dietary KAB, KAB and GI symptoms, and KAB and fatigue.

2. Methodology

2.1. Study design

A quantitative study, utilising an online observational cross-sectional survey, was undertaken. Ethical permission was granted through the University of Worcester (2018) Research Ethics procedure; the need for a full ethics review was waived and ethical approval was confirmed by the University Research Ethics panel (reference number SAHC2021NP1).

Participant information included study purpose, inclusion criteria and details regarding consent, anonymity, confidentiality and data protection. A series of mandatory checkboxes enabled participants to confirm their understanding of the study, informed consent and eligibility to participate. A medical diagnosis of hEDS/HSD, or EDS-HT, EDS-type 3 or JHS prior to the 2017 reclassification, or symptomatic hypermobility was required, and participants were asked to confirm one of these diagnoses from a drop down menu; this precluded any individuals with a non-hEDS/HSD hypermobility-related diagnosis from taking part. Data was provided anonymously and in accordance with the University's Policy for the Effective Management of Research Data [61] and its Information Security Policy [62].

2.2. Population and sample

The population comprised all individuals in the UK, aged 18 or over, with a medical diagnosis of hEDS/HSD, EDS-HT, EDS-type 3, JHS or symptomatic hypermobility. The study sample was obtained *via* the two main UK hypermobility charities, the Hypermobility Syndromes Association (HMSA) and Ehlers–Danlos Support UK (EDS-UK), from members with the above diagnoses. Participants were asked to confirm the absence of coexistent long Covid, since related fatigue and GI issues overlap with the symptoms under study [63]. Recruitment was undertaken through the charity websites, newsletters and social media platforms, following written permission from a member of the HMSA Board of Trustees and the Managing Director of EDS-UK; individuals belonging to both charities were asked to participate once only.

Using the G*power calculator [64,65] for two-tailed bivariate correlations, based on 80% power and 95% confidence intervals for results generalising to the whole population, a minimum sample size of 82 was calculated to allow identification of medium (0.3) effect sizes.

2.3. Data collection instrument

Jisc online survey software [66] was used to construct the survey. Initial questions involved basic participant characteristics, with drop-down menus for age, sex and co-existing conditions; participants were asked to select from a list of common comorbidities, such as chronic fatigue, gastro-oesophageal reflux, gastroparesis, IBS, POTS and mast cell activation syndrome [67,68], whilst free text boxes were used to collect further information regarding additional diagnoses, medication and nutraceutical use. This was followed by the KAB, fatigue and GI questionnaires and, in order to minimise questionnaire bias, existing questionnaires already validated were selected. These included Harris's KAB questionnaire [69], the Fatigue Severity Score (FSS) [70], the Patient Assessment of Upper Gastrointestinal Symptom Severity Index (PAGI-SYM) [71,72] and the Birmingham IBS symptom questionnaire [73]; permission and licence agreements were obtained as appropriate. Each question was mandatory, avoiding incomplete survey responses. Consistent 5-point Likert [74] rating scales were used for the questionnaires: symmetric headings, ranging from 'Strongly disagree' to 'Strongly agree', were used for the KAB and FSS questions, whilst the PAGI-SYM and IBS statements utilised ascending headings to indicate increasing severity of symptoms.

The KAB questionnaire [69] required adaptation from a sport to a health focus, since it was originally used in a study of non-elite competitive cyclists based on research involving cross-country runners [75]. There were 17 questions for both knowledge and behaviour, each congruent with its counterpart; these focussed on intakes of fats, protein, carbohydrates, micronutrients and liquids, and were consistent with Scientific Advisory Committee on Nutrition (SACN) guidelines [76–78]. There were eight attitude questions based on general attitudes to nutrition and diet. Care was taken to ensure questions did not disadvantage participants who may have been following certain dietary approaches, such as gluten-free, dairy-free, low FODMAP and low histamine diets. Statements were presented in a mixed order and included ten reverse statements, whose scores were reversed prior to calculating the final scores, maintaining this feature from the original questionnaire. Each statement scored from 1 to 5 points, due to the 5-point Likert scale, and final scores were the summed scores of the statements within each KAB section. Maximum final scores, representing high levels of KAB, were 85 for knowledge (K) and behaviour (B), and 40 for attitude (A). Test-retest reliability for the modified KAB questionnaire was not possible due to time limitations, but Cronbach's alpha-coefficients showed good internal consistency for the knowledge (α=0.80) and behaviour (α=0.89) scales, although the value for attitude was lower (α=0.61); however, there were only eight scale items, with no negative values for corrected item-total correlation figures or in the inter-item correlation matrix, so, as detailed by Pallant [79], a value slightly below 0.7 was considered acceptable.

The FSS questionnaire [70] discerns the frequency and severity of fatigue between healthy subjects and those with chronic conditions, and has previously been used in JHS/EDS-HT studies [43,44,80]. It includes nine statements exploring the impacts of fatigue on physical functioning, motivation, exercise, duties and responsibilities. The final score was the mean of all nine items; the higher the score, the more severe the fatigue. A final score $\geq$ 4 (when using a 7-point Likert scale) has been interpreted as indicative of significant fatigue [81]; the equivalent cut-off score for this study's 5-point scale was 2.9, with a maximum final score of 5.

The PAGI-SYM [71,72] questionnaire contains 20 statements, with six subscales: heartburn/regurgitation, nausea/vomiting, post-prandial fullness/early satiety, bloating, upper abdominal pain and lower abdominal pain. The final score is represented by the sum of the means for each subscale; the higher the score, the more severe the upper GI symptoms. Using a 5-point Likert scale, the maximum final score was 30.

The Birmingham IBS symptom questionnaire [73] consists of 11 questions relating to frequencies of pain, diarrhoea and constipation. The final score is the sum of each question score; the higher the score, the more severe the lower GI symptoms. Using a 5-point Likert scale, the maximum final score was 55.

The whole survey was reviewed by an expert panel of three people, comprising two nutritional therapists with experience of managing clients with hEDS/HSD and a master's research student, following which a few minor amendments were made to questions relating to participant characteristics. The survey was piloted on a small group representative of the study population; all provided positive feedback, with no errors or suggested alterations, confirming feasibility [82]. The final survey was launched on 19 June 2021, with data collection continuing until 13 September 2021.

2.4. Statistical analysis

Data was exported from Jisc online surveys into Microsoft Excel for cleaning and editing; there was no missing data. Information from free text boxes was analysed, considering all possible variants of the same response, for example, 'vitamin D', 'vit D', 'vitD', 'and D', 'andD', '& D', '&D' and 'D3'.

Data was statistically evaluated using Statistical Package for the Social Sciences (SPSS) version 27 software [83]. Descriptive statistics described participant characteristics (sex, comorbidities, medication and nutraceutical use) as categorical variables; ages were collected as continuous variables and then collapsed into categorical 10-year age bands after an initial 18–29 age band. KAB, GI and fatigue scores were compiled as continuous variables and detailed using mean, median, mode, standard deviation, range, skewness and kurtosis values.

Knowledge scores were normally distributed, whilst behaviour, PAGI-SYM and IBS scores were close to normality, with small skewness and kurtosis values (between −0.5 and 0.4) and only a few outliers. Therefore, after preliminary analyses to ensure there was no violation of the assumptions of normality, linearity, multicollinearity and homoscedasticity, multivariate regression was undertaken to explore relationships between KAB variables and between KAB and GI scores; in addition, the effects of age, coexisting POTS or OI, and nutrition advice were considered. To explore relationships between KAB and fatigue, non-parametric inferential testing using Spearman-rho correlation analysis was performed, since FSS scores demonstrated obvious non-normality, with considerable positive kurtosis (1.96), negative skew (−1.18) and data outliers.

Mean scores were expressed as a percentage of the maximum participant score to create KAB, FSS, PAGI-SYM and IBS mean percentage scores; this enabled easier comparisons between the various scores. High mean percentage scores for KAB suggested good dietary knowledge, behaviour and attitude scores, whilst high FSS, PAGI-SYM and IBS mean percentage scores indicated higher symptom severity.

3. Results

3.1. Participant characteristics

A total of 536 participants completed the survey questionnaire. This allowed identification of 0.121 effect sizes for two-tailed bivariate correlations, based on 80% power and 95% confidence intervals for results generalising to the whole population.

Respondents were predominantly female (97.9%) and ages ranged from 18 to 75, with a mean age of 40.8 years (SD 12.8 years); the sample was slightly skewed (0.32) towards younger adults with proportionately fewer participants aged 60 and above. The most common diagnoses were hEDS (41.6%) and EDS-HT (26.5%), whilst HSD and JHS diagnoses were each reported by 14.7% of participants; of these, 57.7% were diagnosed using the 2017 criteria, whilst 42.3% received pre-2017 diagnoses. Although symptomatic, 2.4% did not meet any diagnostic criteria. Coexisting conditions were present in 488 (91%) participants, with 415 (85%) of these reporting more than one comorbidity. IBS was most common (51.5%), followed by chronic fatigue (36.8%), gastro-oesophageal reflux disease (36.5%) and POTS (33.4%). Participant characteristics are detailed further in Table 1.

Medication use was reported by 469 (87.5%) respondents, with 393 (83.8%) of these prescribed two or more. Analgesic and GI drugs were most commonly prescribed, followed by medications for depression, allergy, mast cell activation syndrome, hypothyroidism and POTS. Nutraceutical use was reported by 413 (77.1%) participants; vitamin D was most frequently used, followed by multi-vitamins and minerals, magnesium and vitamin C.

Nutritional advice had been received by 304 (56.7%) participants, predominantly involving NHS dietitians (29.5%), gastroenterology clinics (25.2%) and general practitioners (GPs) (22.9%). Approximately 6% of participants received nutrition advice from other doctors, including rheumatologists, allergy specialists, endocrinologists and gynaecologists, whilst nutritional therapy (NT) was sought by 9.9% of respondents and complementary modalities, such as naturopathy and medical herbalism, by 5%.

3.2. KAB, FSS, PAGI-SYM and IBS questionnaire scores

Questionnaire scores are detailed in Table 2, along with the mean and mean percentage scores. Comparison of mean percentage scores demonstrated high scores for attitude (86.8%) and knowledge (80.4%), although behaviour scores (72.0%) were slightly lower.

The mean percentage FSS score was high (86%); additionally, the mode was 5, such that the most common score was the maximum, and was scored by 84 (15.7%) participants. Application of the cut-off score for more severe fatigue [81] demonstrated that 519 of 536 participants (96.8%) fulfilled the criteria for significant fatigue.

PAGI-SYM (53.0%) and IBS (52.4%) scores were mid-range. Of the six PAGI-SYM subscales, bloating scored highest (70.0%), whilst of the IBS dimensions, pain and constipation were the highest (54.7% and 54.0%, respectively).

3.3. KAB responses

Analysis of the KAB responses identified some interesting observations. Attitudes towards nutrition were very high, with 92.3% of participants agreeing or strongly agreeing that the food they ate affected their wellbeing and quality of life, and 92.9% acknowledging the importance of learning about nutrition to achieve positive changes in food habits. Nonetheless, only 71.3% admitted that their knowledge influenced their diet. The full questionnaire and results are presented in Appendix 1, whilst Table 3 highlights areas where knowledge and/or behaviour scores were lower, providing areas of consideration for dietary recommendations.

Table 1
Participant characteristics.

Age and sex								
Age category	Female		Male		Unspecified		Total	
	Number	%	Number	%	Number	%	Number	%
18–29	106	*19.8%*	4	*0.7%*			110	*20.5%*
30–39	153	*28.5%*	4	*0.7%*	1	*0.2%*	158	*29.5%*
40–49	119	*22.2%*	1	*0.2%*			120	*22.4%*
50–59	105	*19.6%*	0				105	*19.6%*
60–69	34	*6.3%*	1	*0.2%*			35	*6.5%*
70 and over	8	*1.5%*	0				8	*1.5%*
Total	**525**	***97.9%***	**10**	***1.9%***	**1**	***0.2%***	**536**	***100%***
Hypermobility diagnoses								
Diagnosis	**Female**		**Male**		**Unspecified**		**Total**	
	Number	%	Number	%	Number	%	Number	%
hEDS	219	*40.9%*	4	*0.7%*	0		223	*41.6%*
EDS-HT or type 3	139	*25.9%*	3	*0.6%*	0		142	*26.5%*
HSD	77	*14.4%*	2	*0.4%*	0		79	*14.7%*
JHS	77	*14.4%*	1	*0.2%*	1	*0.2%*	79	*14.7%*
Symptomatic hypermobility	13	*2.4%*	0		0		13	*2.4%*
Total	**525**	***97.9%***	**10**	***1.9%***	**1**	***0.2%***	**536**	***100%***
Co-existing conditions and additional diagnoses								
Condition					**Number of reports**		*%*	
IBS					276		*51.5%*	
POTS or OI					257		*47.9%*	
POTS					179		*33.4%*	
Orthostatic Intolerance alone					78		*14.5%*	
Chronic fatigue					197		*36.8%*	
Gastro-oesophageal reflux disease					195		*36.5%*	
Fibromyalgia					170		*31.7%*	
Other					124		*23.1%*	
Mast cell activation syndrome/disorder					89		*16.6%*	
Other GI diagnosis					87		*16.2%*	
GI dysmotility					84		*15.7%*	
Autoimmune disease					81		*15.1%*	
Gastroparesis					58		*10.8%*	
SIBO					23		*4.3%*	

Abbreviations. EDS-HT, Ehlers–Danlos Syndrome-Hypermobile Type; hEDS, hypermobile Ehlers–Danlos Syndrome; HSD, Hypermobility Spectrum Disorder; JHS, Joint Hypermobility Syndrome; IBS, Irritable Bowel Syndrome; OI, Orthostatic Intolerance; POTS, Postural Orthostatic Tachycardia Syndrome; SIBO, Small Intestinal Bacterial Overgrowth.

Table 2
KAB, FSS, PAGI-SYM and IBS scores, with subscale and domain scores.

	Minimum participant score	Maximum participant score*	Mean participant score	Standard deviation	Mean% score**
KAB scores					
Knowledge total	46	85	68.3	7.0	80.4%
Behaviour total	23	85	61.2	12.8	72.0%
Attitude total	21	40	34.7	3.4	86.8%
FSS score					
FSS total	1	5	4.3	0.7	86.0%
PAGI-SYM total score and subscores					
PAGI-SYM total	6	30	15.9	5.0	53.0%
Heartburn/regurgitation	1	5	2.2	1.1	44.0%
Nausea/vomiting	1	5	1.9	0.9	38.0%
Post-prandial fullness	1	5	2.8	1.1	56.0%
Bloating	1	5	3.5	1.1	70.0%
Upper abdominal pain	1	5	2.7	1.3	54.0%
Lower abdominal pain	1	5	2.8	1.2	56.0%
IBS total score and domain scores					
IBS total	11	51	26.7	7.4	52.4%
Abdominal pain	3	15	8.2	3.0	54.7%
Diarrhoea	5	25	10.4	4.0	41.6%
Constipation	3	15	8.1	3.5	54.0%

Abbreviations. FSS, Fatigue Severity Score; IBS, Irritable Bowel Syndrome; KAB, Knowledge-Attitudes-Behaviour; PAGI-SYM, Patient Assessment of upper Gastro-Intestinal SYMptom severity index.

* Maximum scores for the questionnaires were reached for all but the IBS questionnaire, where the maximum score was 51 of a possible 55.

** Mean score expressed as a percentage of the maximum participant score.

Table 3
Knowledge and behaviour responses of interest.

Fats
Omega-3 fats were consumed at least twice weekly by only 47.6% of participants, despite 82.5% knowing that omega-3 fats lowered the risk of heart disease.
Unsaturated fats in general were consumed regularly by 72.2% of participants.
Saturated fat consumption in excess of 10% daily calories was reported by 26.3% of participants, and 22.7% regularly ate processed meats.
Proteins
Approximately 2/3 of participants (64.3%) knew about recommended daily protein intakes and 2/3 (66.8%) achieved these levels.
Only 39.9% included protein with each meal and snack, despite 69.8% agreeing that protein aids with satiety.
Carbohydrates
79.7% of participants agreed that the majority of carbohydrate intake should come from complex carbohydrates, although slightly fewer (71.9%) agreed to consuming mainly complex and unrefined carbohydrates.
33.6% reported consumption of sugary foods; however, 92.8% knew that sugar is associated with chronic disease.
Vegetables and fruit
Only 54.2% of participants reported eating five or more portions of vegetables and fruit daily, and only 69.4% ate three portions of vegetables daily.
Only 48.5% included dark green vegetables daily.
Micronutrients
Brightly coloured antioxidant-rich foods were consumed by 64.6% of participants, although 72.2% agreed that they are associated with reduced risk of some chronic diseases.
Despite good knowledge of nuts and seeds as sources of vitamins and minerals (85.1%), only 39.9% ate nuts and seeds daily.
Hydration
Only 64.9% drank 6–8 glasses of water or non-caffeinated drinks daily.
28.4% drank fizzy and sugary drinks, and 17.3% added sugar to hot drinks, despite 85.8% knowing that sweetened drinks affect blood sugar control and contribute to fatigue.

3.4. Relationships between KAB variables

Multiple linear regression was undertaken to assess the ability of KAB variables to predict each other. The regression models were statistically significant and are presented in Table 4. Each KAB variable made unique and statistically significant contributions to predicting the other two variables. For example, attitude and knowledge made unique contributions (5.8% and 6.6%, respectively) to predicting behaviour scores; however, the model as a whole explained 33% of the variance in behaviour, including the unique variance explained by each variable and the shared variance [79].

The analysis demonstrated large positive zero-order Pearson correlations between knowledge and attitude ($r=0.62$, $p<0.001$), knowledge and behaviour ($r=0.52$, $p<0.001$), and attitude and behaviour ($r=0.51$, $p<0.001$). Partial correlations, with each KAB variable controlled for individually, resulted in reduced strengths of each bivariate relationship; a medium-strength positive partial correlation was identified between attitude and knowledge ($r=0.49$, $p<0.001$), with partial correlations between knowledge and behaviour ($r=0.29$, $p<0.001$) and attitude and behaviour ($r=0.28$, $p<0.001$) being slightly smaller.

3.4.1. Controlling for age

Using behaviour as the dependant variable, hierarchical multiple regression assessed the ability of knowledge and attitude to predict behaviour whilst controlling for age. The regression model was statistically significant and is also presented in Table 4.

The analysis demonstrated positive zero-order Pearson correlations between KAB variables and age, with a medium-strength correlation between age and behaviour ($r=0.4$, $p<0.001$) and small correlations between age and knowledge ($r=0.21$, $p<0.001$) and age and attitude ($r=0.17$, $p<0.001$). The model as a whole explained 41% of the variance in behaviour scores; age contributed to 16%, whilst attitude and knowledge provided an additional 25% after controlling for age. Attitude and knowledge each made unique contributions to behaviour scores (5.1% and 4.7%, respectively), although slightly reduced in comparison to not controlling for age.

Controlling for age also demonstrated reduced strength bivariate KAB relationships. A medium-strength positive partial correlation was identified between knowledge and attitude ($r=0.49$, $p<0.001$), and small positive partial correlations between knowledge and behaviour ($r=0.27$, $p<0.001$) and attitude and behaviour ($r=0.28$, $p<0.001$).

3.5. Relationships between KAB and GI symptom severity

Multiple linear regression was undertaken to test if KAB variables significantly predicted GI scores. The regression models for both PAGI-SYM and IBS scores were statistically significant; the results are presented in Table 5.

Of the three KAB variables, only behaviour made a statistically significant unique contribution to predicting GI scores. For PAGI-SYM and IBS scores, 2% and 2.6%, respectively, of the total variance was uniquely

Table 4
Multiple regression for KAB relationships, and hierarchical multiple regression for behaviour relationships controlling for age.

KAB variables										
Predictor variable	B	SE B	Beta		sr	$(sr)^2$	R^2			
Model for knowledge and behaviour predicting attitude scores							0.44	p<0.001		
Constant	14.38	1.08								
Behaviour	0.07	0.01	0.26	p<0.001	0.22	0.049				
Knowledge	0.24	0.02	0.49	p<0.001	0.42	0.174				
Model for attitude and behaviour predicting knowledge scores							0.44	p<0.001		
Constant	24.55	2.33								
Attitude	1.00	0.08	0.48	p<0.001	0.42	0.122				
Behaviour	0.15	0.02	0.27	p<0.001	0.23	0.054				
Model for knowledge and attitude predicting behaviour scores							0.33	p<0.001		
Constant	−20.05	5.07								
Attitude	1.16	0.17	0.31	p<0.001	0.24	0.058				
Knowledge	0.60	0.08	0.33	p<0.001	0.26	0.066				
KAB variables controlling for age										
Step and predictor variable	**B**	**SE B**	**Beta**	**SIg**	**sr**	**$(sr)^2$**	**R^2**		**Change in R^2**	
Model for knowledge and attitude predicting behaviour scores, controlling for age										
Step 1							0.16	p<0.001		
Constant	44.96	1.69								
Age	0.40	0.04	0.40	p<0.001	0.32	0.101				
Step 2							0.41	p<0.001	0.25	p<0.001
Constant	−23.39	4.77								
Age	0.29	0.03	0.29	p<0.001	0.29	0.082				
Knowledge	0.51	0.08	0.28	p<0.001	0.22	0.047				
Attitude	1.09	0.16	0.29	p<0.001	0.23	0.051				

sr = semi-partial correlation coefficient (represents the unique contribution of each variable when overlapping effects of all other variables are statistically removed). $(sr)^2$ represents how much of the total variance in the dependant variable is uniquely explained by each independent variable; multiplication by 100 gives the percentage of the variance [79].

Table 5
Multiple linear regression for KAB variables predicting GI scores.

KAB variables predicting GI scores										
Predictor variable	B	SE B	Beta		sr	$(sr)^2$	R^2			
Model for KAB predicting PAGI-SYM scores							0.03	p=0.002		
Constant	18.87	2.45								
Behaviour	−0.07	0.02	−0.18	p<0.001	−0.14	0.020				
Knowledge	0.04	0.04	0.06	p=0.307	0.04					
Attitude	−0.05	0.09	−0.03	p=0.59	−0.02					
Model for KAB predicting IBS scores							0.04	p<0.001		
Constant	33.46	3.57								
Behaviour	−0.11	0.03	−0.19	p<0.001	−0.16	0.026				
Knowledge	0.07	0.06	0.06	p=0.263	0.05					
Attitude	−0.13	0.12	−0.06	p=0.285	−0.05					
KAB variables predicting GI scores, controlling for age										
Predictor variable	**B**	**SE B**	**Beta**		**sr**	**$(sr)^2$**	**R^2**		**Change in R^2**	
Model for KAB predicting PAGI-SYM scores, controlling for age										
Step 1							0.05	p<0.001	0.05	p<0.001
Constant	19.48	0.71								
Age	−0.09	0.02	0.22	p<0.001	−0.22	0.048				
Step 2							0.06	p<0.001	0.01	p<0.001
Constant	20.35	2.44								
Age	−0.07	0.02	−0.19	p<0.001	−0.17	0.029				
Behaviour	−0.04	0.02	−0.10	p=0.08	−0.07					
Knowledge	0.05	0.04	0.06	p=0.261	0.05					
Attitude	−0.06	0.06	−0.04	p=0.45	−0.03					
Model for KAB predicting IBS scores, controlling for age										
Step 1							0.03	p<0.001	0.03	p<0.001
Constant	31.03	1.05								
Age	−0.11	0.03	−0.19	p<0.001	−0.19	0.036				
Step 2							0.05	p<0.001	0.02	p<0.001
Constant	34.98	3.59								
Age	−0.08	0.03	−0.13	p=0.004	−0.12	0.014				
Behaviour	−0.08	0.03	−0.14	p=0.014	−0.10	0.010				
Knowledge	0.07	0.06	0.07	p=0.234	−0.05					
Attitude	−0.15	−0.12	−0.07	p=0.233	−0.05					

sr = semi-partial correlation coefficient (represents the unique contribution of each variable when overlapping effects of all other variables are statistically removed). $(sr)^2$ represents how much of the total variance in the dependant variable is uniquely explained by each independent variable; multiplication by 100 gives the percentage of the variance [79].

explained by behaviour; however, the KAB variables were all strongly correlated with each other (r=0.61, 0.52 and 0.51), so a lot of shared variance was controlled for within the model [79].

Small significant negative correlations were found between behaviour and PAGI-SYM scores (r=−0.16, p<0.001) and between behaviour and IBS scores (r=−0.19, p<0.001), suggesting improved dietary behaviour may have a small effect on reducing GI symptoms.

The regression analysis was repeated controlling for age (Table 5). Behaviour made a statistically significant unique contribution to predicting IBS scores but not PAGI-SYM scores.

3.5.1. Differences in mean GI scores between those with a POTS or OI diagnosis and those without

Linear regression, using the presence or absence of a POTS or OI (POTS/OI) diagnosis as a categorical independent variable, assessed for any difference in mean GI scores between those with a diagnosis and those without (Table 6). The regression models for both PAGI-SYM and IBS scores were statistically significant. An increase of 2.56 in the mean PAGI-SYM score, and of 2.43 in the mean IBS score, was found for the group with POTS/OI diagnoses, in comparison to the group without. This suggests that a coexisting POTS or OI diagnosis predicts a higher mean GI score with statistical significance.

3.5.2. Differences in mean GI and KAB scores between those who received nutrition advice and those who did not

Linear regression, using the presence or absence of nutrition advice as a categorical independent variable, assessed for any difference in mean scores (Table 6). The regression models for both PAGI-SYM and IBS scores were statistically significant. An increase of 1.71 in the mean PAGI-SYM score, and of 3.06 in the mean IBS score, was found for the group that received nutrition advice, in comparison to the group that did not. Although this suggests higher GI scores in those who received nutrition advice, it may not have been causative.

For KAB scores, the regression model for behaviour was statistically significant but those for knowledge and attitude were not. The model predicted an increase of 3.78 in the mean behaviour score for the group that received advice, in comparison to the group that did not.

Table 6
Linear regression for differences in mean GI scores between those with and without POTS/OI, and differences in mean GI and KAB scores for those who did and did not receive nutrition advice.

	B	SE B	Beta		R^2	
POTS/OI diagnoses or not						
Model for PAGI-SYM scores					0.06	p<0.001
Constant – No POTS/OI diagnosis	14.71	0.29		p<0.001		
POTS/OI diagnosis	2.55	0.42	0.25	p<0.001		
Model for IBS scores					0.03	p<0.001
Constant – No POTS/OI diagnosis	25.51	0.44		p<0.001		
POTS/OI diagnosis	2.43	0.63	0.16	p<0.001		
Nutrition advice or not						
Model for PAGI-SYM scores					0.03	p<0.001
Constant – No nutrition advice	14.96	0.29		p<0.001		
Nutrition advice	1.71	0.43	0.17	p<0.001		
Model for IBS scores					0.04	p<0.001
Constant – No nutrition advice	24.94	0.48		p<0.001		
Nutrition advice	3.06	0.63	0.21	p<0.001		
Model for behaviour scores					0.01	p=0.012
Constant – No nutrition advice	59.61	0.83		p<0.001		
Nutrition advice	2.78	1.11	0.11	p=0.012		
Model for knowledge scores					0.00	p=0.316
Model for attitude scores					0.01	p=0.074

3.6. Relationships between KAB and fatigue

Two-tailed Spearman-rho calculations identified a non-significant negative relationship between behaviour and fatigue severity (r=−0.056, p=0.194), and non-significant positive relationships between knowledge and fatigue (r=0.058, p=0.183) and attitude and fatigue (r=0.017, p=0.692).

4. Discussion

4.1. Participant characteristics

The 97.9% preponderance of female participants was surprising, exceeding the 70% female prevalence reported by Demmler et al. [18]; however, this may demonstrate a sex-related participation bias due to increased willingness of females to participate in surveys [84]. Comorbidities were common, particularly for fatigue, GI dysfunction and POTS/OI, consistent with existing literature [5,35,36]; 85% of participants revealed more than one comorbidity, further demonstrating the multi-system nature of hEDS/HSD. Medication use was high (87.5%), similar to the 84% reported by Lam et al. [23], as was utilisation of nutraceuticals (77.1%), illustrating application of strategies to manage symptomology.

4.2. KAB, fatigue and GI scores

The mean 80.4% score for knowledge was higher than the 74.7% equivalent score obtained in Harris's study [69]; however, dietary KAB studies in other health conditions used different data collection methods [85,86], so comparisons are not straightforward. The predominance of female participants may have led to higher scores since females tend to exhibit higher knowledge compared to males [87]; furthermore, chronic illness may have additionally contributed due to a positive association with knowledge [56].

The mean 86.8% score for attitude was greater than in Harris's study [69], demonstrating positive attitudes towards diet and nutrition in a large proportion of the study sample; this is encouraging because attitude is a positive predictor for behaviour change [58]. Whilst seven of the eight attitude statements were agreed or strongly agreed with by over 89% of the sample, the eighth related to knowledge of nutrition affecting food consumed and agreement was lower (71.3% of the sample). This suggests some difficulties putting nutritional knowledge into practice, as reported by Raji-Lahiji et al. [55].

The mean 72.0% score for behaviour was higher than in Harris's study [69] but lower than this study's mean knowledge score (80.4%), further illustrating that factual knowledge does not always reflect dietary behaviour. Whilst restrictive diets may have influenced some dietary choices, the high levels of significant fatigue could have adversely affected motivation for healthier dietary behaviour in general [88]. Additionally, disturbed eating behaviour may arise in individuals with hEDS/HSD secondary to issues such as temporomandibular joint dysfunction and smell and taste sensitivities [89].

Although only 36.8% of the sample had been formally diagnosed with chronic fatigue or chronic fatigue syndrome, the mean 86.0% fatigue score was high and 96.8% of participants exceeded the cut-off score for significant fatigue. This was considerably higher than expected when compared to the study of Krahe et al. [44], which, using the FSS, found significant fatigue in 79.5% of the 117 participants with JHS/EDS-HT. The high fatigue scores may reflect the large proportion of individuals with multiple comorbidities, as well as participation bias due to fatigue being a study focus; furthermore, consumption of sugary foods and drinks, which occurred in one-third of participants, is associated with increased fatigue [90].

The mean 53.0% PAGI-SYM and 52.4% IBS scores were lower than anticipated in view of existing literature demonstrating high GI morbidity [23], although the bloating mean subscale score was higher

(70%). However, medication and/or nutraceutical use may have confounded the true underlying scores; for example, laxative use could have lessened constipation scores. Additionally, the levels of dietary behaviour within the sample (72%) may have contributed to lower than expected GI symptom severity, although there were several areas identified where dietary behaviour could be further improved, as detailed in Table 3.

4.3. Correlations between KAB variables

This study found strong positive correlations between knowledge and attitude (0.62), knowledge and behaviour (0.52), and attitude and behaviour (0.51). Whilst a systematic review of 29 studies found positive, albeit weak, associations between knowledge and dietary intakes [91], this study suggests those with hEDS/HSD not only demonstrate good knowledge but also stronger interrelations between dietary knowledge and both behaviour and attitude. However, mediating effects of all three KAB variables were observed on the corresponding bivariate relationships, demonstrating contributory effects on the paths connecting the other two [92].

Age was found to be a confounding variable, introducing a source of bias; after controlling for age, the KAB correlations reduced in strength, although remained significant. The medium-strength (0.4) age-behaviour correlation and smaller age-knowledge (0.21) correlation suggest dietary behaviour and knowledge improve with increasing age, consistent with existing literature [56]. Low socio-economic status is another potential confounder and may result in lower KAB scores [87], although this was not studied; for example, some individuals with hEDS/HSD may be in receipt of disability allowances and benefits [93], which may lead to food insecurity, inability to afford healthier foods and lower behaviour scores [94,95].

The increase in mean behaviour scores for those who received nutritional advice, compared to those who did not, was encouraging and provides a rationale for appropriate nutritional education and guidance specific to those with hEDS/HSD. The types of healthcare professionals giving nutrition advice were quite diverse, so the advice was likely to have been varied; however, this could demonstrate motivation in those seeking further dietary support.

4.4. Correlations between KAB and GI symptoms and KAB and fatigue

Of the KAB variables, only behaviour made a statistically significant contribution to predicting GI scores. Small significant relationships were demonstrated between higher dietary behaviour scores and less severe GI symptoms, highlighting the importance of translating good nutritional knowledge and attitude into appropriate dietary behaviour. When controlling for age, which demonstrated a medium-strength correlation with behaviour, behaviour made a statistically significant contribution to predicting IBS scores, suggesting improved dietary behaviour may be more beneficial for IBS symptoms.

The increase in mean PAGI-SYM and IBS scores when there was a co-existing diagnosis of POTS/OI is consistent with existing literature [32, 34–36]. However, higher mean GI scores in those who received nutrition advice was surprising, although, rather than being causative, this could reflect those with more severe GI symptoms as being more likely to seek nutritional advice. Since the advice was likely to have been of varying quality, particularly if delivered by practitioners with little nutrition or dietary training, it would be necessary to undertake a prospective study to investigate the effect of consistent specialised dietary advice on GI scores.

There were no significant relationships between KAB variables and fatigue, although high levels of significant fatigue may have masked any underlying relationships; for example, fatigue has been shown to mediate poor levels of physical and social functioning, including sub-standard dietary patterns [96,97]. Studies to further explore these relationships following dietary intervention involving blood glucose regulation are required.

4.5. Nutritional strategies

Recommendations for dietary intakes identified by this study to have lower behaviour scores, such as those involving vegetables, antioxidant-rich foods, protein, omega-3 unsaturated fats, saturated fats and processed meats, alongside support for putting nutritional knowledge into practice, could contribute to a generalised nutritional strategy for individuals with hEDS/HSD. Additionally, high levels of sugar consumption and inadequate hydration were concerning and warrant consideration, due to their negative impacts on GI function, fatigue and POTS [98]. Whilst there is lack of high-level evidence for dietary interventions in hEDS/HSD, a generalised anti-inflammatory diet [99], due to the potential for pro-inflammatory states [12], with additional personalised aspects to account for specific comorbidities, such as IBS [31,48], underpinned with evidence where available, may form part of initial dietary management.

Integrative modalities, utilising a systems-biology whole-person approach and combining dietary and lifestyle methods to improve general health [100–102], may provide options for delivering personalised and evidence-based guidance to improve nutritional KAB in individuals with hEDS/HSD. Furthermore, dietary behaviour change could be supported by techniques such as motivational interviewing [103,104], which aims to increase motivation and compliance, thereby enabling individuals to maintain dietary changes longer term. Appropriate behaviour change support may additionally be beneficial for those with disordered eating patterns [89]. Patient-reported outcome measurements [105], such as 'Measure Yourself Medical Outcome Profiles' (MYMOP) [106,107], are well validated and may provide evidence for the impact of nutritional advice on the health and quality of life of individuals with hEDS/HSD. However, a sound understanding of hEDS/HSD complexities, alongside the need to refer where appropriate, is required; this provides additional scope for individualisation and can be applied to the target population beyond the study participants.

4.6. Limitations

This study used non-probability convenience sampling, which risked introducing sampling bias due to its self-selecting and non-random nature [108,109]. Additionally, charity members were trusted to complete the questionnaire once only if they belonged to both charities. Furthermore, not all individuals with hEDS/HSD are HMSA or EDS-UK members, so the sample could have had differing characteristics and attitudes [110]; for instance, charity members might have been better informed than non-members or experienced more severe symptoms, leading to selection bias and differing effects between the sample and the hEDS/HSD population. Moreover, only a proportion of people invited to take part in surveys do so, resulting in non-response bias, whilst both under and over-representation of participant characteristics may result in participation bias [111]. Additionally, besides age, additional confounding variables and effect masking, which are more likely in non-randomized studies, may have led to inaccurate findings due to interactions amongst variables, limiting separation of association from causation [112].

The self-reporting aspect of the survey instrument risked information error or misclassification bias [113] if participants provided inaccurate information, such as medically unconfirmed self-diagnoses or dietary intakes unreflective of actual behaviour [114]; furthermore, all self-reported dietary assessment tools involve inaccuracies and bias [115]. Additionally, use of a neutral 'Neither agree or disagree' midpoint in the symmetric Likert scale may have been disadvantageous if used as a 'Don't Know' option or because other factors affecting participant opinion could not be expressed [116].

5. Conclusion

This is the first study to explore nutritional KAB of individuals with hEDS/HSD; there were no significant associations between dietary KAB and fatigue, although very high levels of significant fatigue may have masked any underlying relationships, but the small negative correlation between dietary behaviour and GI symptom severity scores was a novel finding. This supports the hypothesis that improved KAB, especially behaviour, through nutritional education and guidance, may contribute to the supportive management of individuals with hEDS/HSD, specifically those with GI dysfunction. Finally, this study encourages collaborative working where possible, particularly if multi-disciplinary management is already in place, along with collection and sharing of outcome data to further the evidence-base for the role of dietary interventions in hEDS/HSD.

Author contributions

Nikki Paiba: Conceptualisation, Investigation, Methodology, Data curation, Formal analysis, Writing – original draft.

Miranda Harris: Project management, Supervision, Data curation, Writing – review & editing.

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Declaration of Competing Interests

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Data availability

Data and any supplementary material related to this article can be obtained from the corresponding author on request.

Supplementary materials

Supplementary material associated with this article can be found, in the online version, at doi:10.1016/j.eujim.2023.102231.

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