ORIGINAL ARTICLE

Relationship of Filipino MSUD Children's Nutrient Intake, Nutritional Status, and Leucine Level, and Caregiver's Nutrition Knowledge, Attitudes, and Practices

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ABSTRACT

Background and Objectives. Diet compliance is critical in managing Maple Syrup Urine Disease (MSUD) to prevent physiological and neurological damage. However, there is a lack of studies looking at factors critical to diet compliance. This study determined the caregivers' nutrition knowledge, attitudes, and feeding practices (KAP); and its relationship to Filipino MSUD children's leucine level, nutritional status, and nutrient intake.

Methods. A cross-sectional, sequential explanatory research approach using survey was utilized. Data tools were questionnaires and food records.

Results. The participants were 20 caregivers and 21 MSUD children (aged 6 to 83 months). Caregivers had moderately high feeding practices and knowledge scores and had positive attitudes towards providing adequate nutritional care; still, they were struggling with diet compliance.

Their nutrition knowledge was related to their attitude (p-value: 0.021), feeding practices (p-value: 0.037), and their children's weight-for-age (p-value: 0.036). Furthermore, knowledge and feeding practices were related to the children's natural-protein status (p-value: 0.043 and 0.006, respectively). The caregivers' sex was related to the children's leucine (p-value=0.010), those with female caregivers had lower leucine by 470 µmol/L on average. Moreover, children with good leucine control belonged to higher-income households (p-value=0.049).

Conclusion. With caregiver's nutrition knowledge having been possibly associated with the children's weight-for-age, and their knowledge and feeding practices with the children's natural protein status, as well as knowledge positively affecting both attitude and feeding practice, interventions for improving all caregivers' nutrition knowledge and feeding practices are recommended.

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Additionally, with caregivers' sex and income having been found to be related to metabolic control, it is suggested that strategies to better manage these barriers be carried out. These may include improving support for male caregivers, with children under their care having higher leucine than those cared for by their female counterparts. Added provisions may likewise be planned for further reducing the impact of income-related barriers.

Keywords: diet compliance, caregivers, nutrition knowledge, attitudes, feeding practices, Maple Syrup Urine Disease, children

INTRODUCTION

Maple Syrup Urine Disease (MSUD) is a rare inherited metabolic disorder characterized by a deficiency in branched-chain ketoacid dehydrogenase complex (BCKD), causing branched-chain amino acids (BCAA) to accumulate in the body.[1] In the Philippines, it is the most common inborn error of amino acid metabolism; and in 2021, it was estimated to affect one in 66,987 live births, almost three times more common compared to the global estimate of one per 185,000 live births.[2,3]

Clinical outcomes are good in MSUD children who are treated early.[4,5] However, if left undetected and unmanaged, metabolites build up causing irreversible physical and neurological damage to the child.[4,5] In the Philippines, the majority of children with MSUD suffer from developmental delay (80.6% from 1999 to 2016), with some having neurological damage. Furthermore, MSUD mortality rate is high—50.5% from 1999 to 2016.[6]

Proper diet is crucial in the management of MSUD as it has a direct impact on the child's chances of survival and achieving optimal growth and development. However, diet compliance remains one of the key problems in MSUD management.[7-10] Improper diet may result in protein deficiency, poor metabolic control, and anemia.[5]

The goals of MSUD diet management are giving sufficient amounts of macronutrients to avoid catabolism and keeping plasma BCAAs within the target range—with dietary adjustments being made depending on leucine level. It involves limiting the dietary intake of BCAAs, providing BCAA-free medical formulas, along with breastmilk or infant formula and later on, solid food with precautions on intact protein sources.[11] They may also be given isoleucine and valine supplements to help lower plasma leucine levels; and thiamine depending on the patient's case.[4,11,12] When sick, they are switched to a sick-day dietary regimen to prevent metabolic decompensation.[11] Small, frequent feedings are recommended to improve tolerance and prevent catabolism.[4,5]

In the Philippines, little is known regarding the actual nutrition knowledge, attitude, and feeding practices (KAP) of caregivers. As MSUD children are heavily reliant on their caregivers, particularly on nutrition, these factors are crucial for diet compliance.

This study had two general objectives. The first one was to determine the primary caregivers' nutrition knowledge, attitude, and feeding practice (KAP). The second was to determine the relationship of the caregiver's KAP to the leucine level, nutritional status, and nutrient intake of MSUD children consulting at the University of the Philippines - Philippine General Hospital (UP-PGH). The information and insights gained here could serve as a basis for strengthening the existing MSUD management program of Institute of Human Genetics - National Institutes of Health (IHG-NIH). Furthermore, since this is the first investigation into the said factors, its findings may serve as a foundation for succeeding scientific inquiries.

MATERIALS AND METHODS

This manuscript is part of a bigger research project on MSUD. This article focused on the relationship between MSUD children's nutrient intake, nutritional status, leucine levels, and their caregivers' nutrition knowledge, attitudes, and practices (KAP). The upcoming articles will explore differences in nutritional outcomes based on leucine control and examine the challenges and facilitators experienced by MSUD caregivers through a qualitative study.

This study employed a cross-sectional, sequential explanatory research design utilizing a survey. It was conducted at the UP-PGH. A total of 29 children with MSUD, aged 6 to 83 months, and their primary caregivers were included in the study (Figure 1). Purposive sampling was used to select participants. The study was reviewed and approved by the University of the Philippines Manila Research Ethics Board (Study Code: UPMREB 2022-0033-01).

Participant recruitment was conducted during routine clinical consultations. Informed consent was obtained from all participants, with consent forms available in both English and Filipino. The consent process and orientation were conducted individually and were witnessed by clinic nurses. The orientation included an explanation of the study's objectives, the participants' roles, the contents of the consent form, and other pertinent information. Caregivers received a copy of their signed informed consent form. In cases where the parent was not the study participant, they were also required to sign the consent form and were provided with a copy. For the caregiver of two children diagnosed with MSUD, a separate informed consent form was completed for each child.

Participants were informed that they could withdraw from the study at any time without affecting their relationship with their healthcare providers or the services and benefits they receive from the IHG-NIH, UP-PGH, and their continuity clinic. Participants received a mobile load allowance worth PhP 500 to cover internet-related expenses for the online interview and questionnaire. They also received a branded

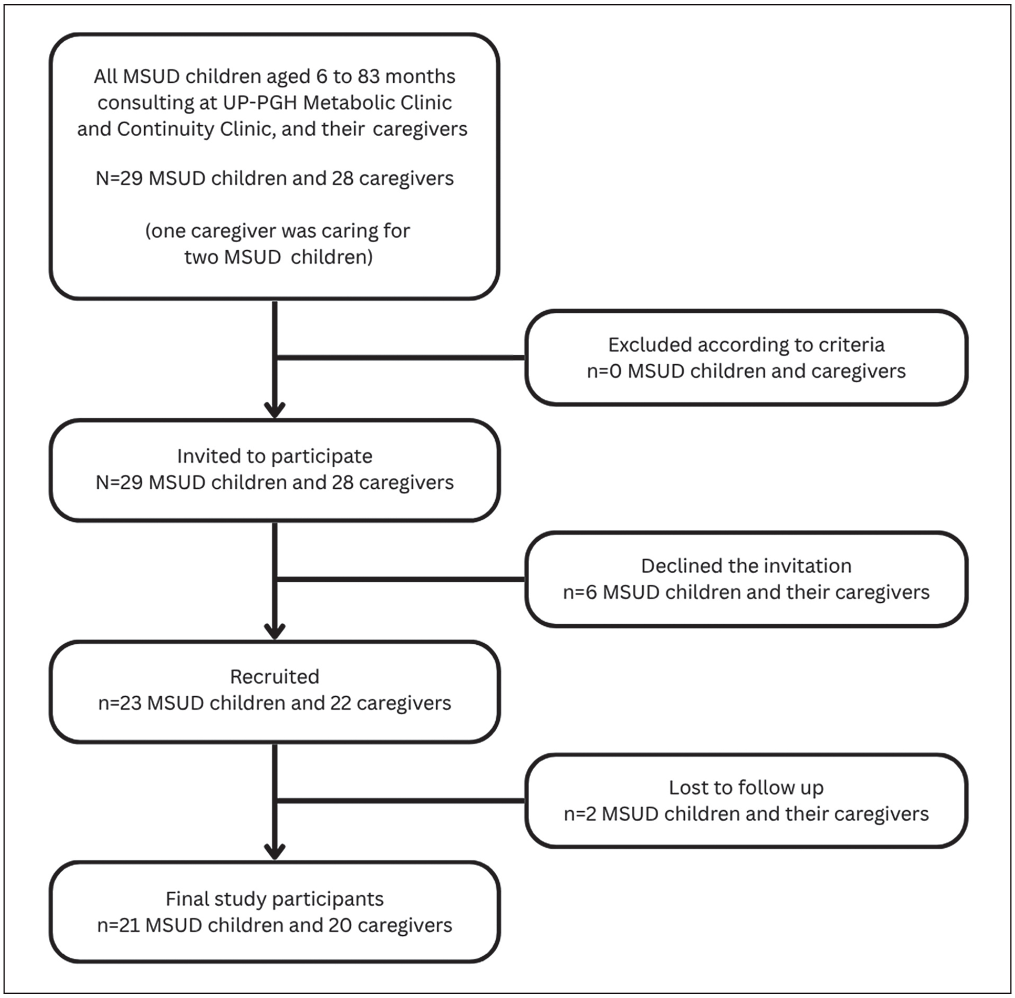

Figure 1. Recruitment flowchart for participants.

measuring cup and spoon. There were no risks associated with participating in the study beyond those encountered in an average conversation.

The study recruited MSUD children who fit the following criteria: Filipino and aged six months to less than seven years during the study, whether they belonged to one household or not, and consulting at the UP-PGH Metabolic Clinic or its continuity clinic; and have started complementary feeding. In recruiting primary caregivers, these criteria were followed: Filipino and able to speak either Filipino or English; either a relative or a non-relative of the patient, but must be responsible for the patient's meal preparations and healthcare at home, as well as belonging to the same household as the patient; able to read and write, so as to properly sign the informed consent form; able to use either a phone or a computer for the online survey and interview; and has internet access.

The following, on the other hand, were the exclusion criteria used in the study: MSUD children who are lost to follow-up or cannot be contacted by the UP-PGH Metabolic and continuity clinic for the past 12 months; have not started complementary feeding; living in residential institutions (e.g., orphanage); whose parents or guardians refused to give written consent; and those with caregivers without internet access or without an available device for answering the online questionnaire and doing the online interview.

Data collection began in November 2022 until February 2023. The data gathering phase was done online to limit the exposure of the participants and their caregivers to possible infection, as this study was conducted during the COVID-19 pandemic.

The study followed a cross-sectional design, using a quantitative (survey type) method. Data were collected using three instruments (details in the Appendix):

1. Self-administered socio-demographic questionnaire in Google Form
2. Knowledge, Attitude, and Feeding Practice (KAP) questionnaires which were administered through online interviews.
3. Three-day food record booklet

Average knowledge and practice scores from KAP questionnaires were considered low if they were ≤70%, moderate if between 71 and 89%, and high if ≥90%. These score categories are in accordance with Food and Agriculture Organization (FAO) guidelines, where "urgent nutrition intervention is recommended" for scores ≤70%, "should be considered" for scores ranging between 71 to 89%, and "not needed" if ≥90%.[13]

Questionnaire Pretesting, Validity, and Language Translation

The KAP questionnaire was developed in consultation with two practicing metabolic dietitians from UP-PGH and IHG-NIH, selected based on their extensive experience managing MSUD patients and their active involvement in metabolic clinics. The dietitians with the most years of relevant experience were chosen from these two reputable institutions. Consultation with a small expert panel is a well-established practice in the development and validation of KAP instruments to ensure their validity and cultural relevance.[13] Emphasis was given to topics on the needed knowledge for caregivers to provide appropriate MSUD nutrition at home, the barriers they commonly experience, and the required and correct nutrition practice at home. The questionnaires were initially developed using the English language and were then translated to Filipino by Sentro ng Wikang Filipino, University of the Philippines Manila; then pretested on a small group (five participants) for comprehension, clarity, and face validity. For the pre-testing phase, primary caregivers of MSUD children aged 8 to 12 years were selected because they shared similar characteristics with the target participants. They were knowledgeable about MSUD nutrition and feeding practices and had experienced, or were experiencing, similar challenges, concerns, and barriers. As such, they were well-positioned to provide meaningful insights during questionnaire pretesting. Pretesting with caregivers of children from a different age group was necessary to avoid reducing the already limited number of eligible target participants.

The questionnaire did not undergo reliability testing since the questionnaire's purpose was to provide clarity and ensure the subjects' understanding of all questions asked (not to measure statistical validity); and also, to avoid further erosion of the sample number.

Three-day Food Record Booklet

A self-reported, self-administered, open-ended three-day food record was used to assess the nutrient intake adequacy of the MSUD children. It also served to cross-check the primary caregivers' feeding practices at home, particularly with regard to the provision of low-protein table foods, appropriate amounts of table foods, breast milk or other milk, medical formula, and High Energy Drink, as well as adherence to the sick-day regimen. Caregivers were instructed to record all actual foods and fluids given to the child, over two weekdays and one weekend day. Upon completion, caregivers submitted photo scans of the food record via their preferred online method. Photos of unfamiliar food items, along with their corresponding nutrition labels, were also requested.

Caregivers were already familiar with completing food records, as they were routinely asked to submit them to their nutritionist-dietitians when necessary. However, they were still given a refresher during the study orientation on how to accurately complete the food record. In addition, the three-day food record booklet provided to them included a simple guide on recording food intake, along with reference images of food models and household measurements. Each caregiver also received a set of measuring cups and spoons to help quantify the food given and accurately record the corresponding details in the booklet. Participants who had food weighing scales at home were permitted to use them instead of the provided measuring tools.

Upon completion of the food record, caregivers submitted photo scans of the accomplished booklet through their preferred online method. They were also asked to send photos of unfamiliar food items along with their corresponding nutrition labels. Validation of the food record entries was conducted through Facebook Messenger, phone calls, and/or during the KAP interview.

Assessment of Nutrient Intake and Adequacy

The assessment focused only on calories, total protein, and natural protein because they are the only nutrient prescription consistently written in all the children's medical charts, which were used for computing nutrient adequacies. Analysis for carbohydrate and fat intake were not covered in this study.

For micronutrients, the study covered calcium, phosphorus, iron, vitamin A, thiamin, riboflavin, niacin, and vitamin C. To assess caloric and protein adequacies, the most recent doctor-prescribed diet indicated on the medical record was compared with the child's actual average intake from the submitted three-day food record. For micronutrient adequacy, the actual intake was compared to the recommendation of the 2015 Philippine Dietary Reference Intake (PDRI).

To translate the amount of food eaten from household measure to grams edible portion, the Food Exchange Lists (FEL) for Meal Planning, 4th edition of the Department of Science and Technology - Food and Nutrition Research Institute (DOST-FNRI) was used. Caloric and nutrient content of food consumed were computed using Menu Eval Plus, a software also developed by DOST-FNRI, with consideration of raw-to-cooked and conversion factors of the food items. For food items unavailable in Menu Eval Plus and for the formula milk, nutrient information from the package were used. Specifically, for the medical formulas, nutrient information from the manufacturer and those provided by IHG-NIH were used to compute the nutrient content.

The resulting data were encoded in Microsoft Excel 2019 and the average nutrient intakes were computed. Caloric and protein percent adequacies were considered "adequate" if 90-110%, "inadequate" if <90%, and "excess" if >110%.[14-16] For micronutrients, percent adequacies of calcium, phosphorus, iron, vitamin A, niacin (as NE), and vitamin C were considered “adequate” if, under the PDRI, they met 100% of the recommended nutrient intake per day, "inadequate" if <100%, and “excess” if above the UL values. For thiamin and riboflavin, there were no UL values in the PDRI and thus, only two categories were set for these nutrients: "inadequate" for <100% adequacy and “adequate” for 100% adequacy or higher. To determine whether the children were exceeding the UL values for calcium and niacin, intakes for the nutrients' synthetic forms were computed and assessed. For vitamin A's UL, only preformed vitamin A content was assessed.

Assessment of Leucine Control

Leucine control refers to the child's mean leucine level for the past six months from the date of recruitment, excluding results from when a non-nutrition-related illness (e.g., cold or infection, hospital admission) was present. Leucine control was defined as “good” if average concentration was ≤500 µmol/L, and “poor” if it was more than the aforementioned value.

Assessment of Nutritional Status

For the assessment of nutritional status, the child's most recent weight, height, and head circumference were collected from the medical record. BMI-for-age, height-for-age, and weight-for-age were determined for all MSUD children who participated in the study. The weight-for-height and head circumference were determined for those aged five years and below. The World Health Organization - Child Growth Standards (WHO-CGS) and WHO Growth Reference 2007 were used as reference for the assessment of the children's nutritional status.

In addition to doctor-prescribed diets, anthropometric data, and six-month leucine levels, information on developmental milestones and Global Developmental Delay diagnoses was gathered from medical charts to help validate caregiver responses on the attitudes questionnaire, as developmental delays can contribute to feeding difficulties.

The study variables and indicators are presented in Table 1.

Table 1. Variables and Indicators of the Study

Variables	Indicators
Dependent Variables	
MSUD children's leucine level	Average leucine level for the past six months
MSUD children's nutrient intake adequacy	Calories, total protein, natural protein, calcium, phosphorus, iron, vitamin A, thiamin, riboflavin, niacin, and vitamin C intake adequacy
MSUD children's nutritional status	BMI-for-age, weight-for-height, height-for-age, weight-for-age, and head circumference-for-age
Independent Variables	
Caregiver's nutrition knowledge	Mean nutrition knowledge score
Caregiver's attitude	Median attitude score
Caregiver's feeding practice	Mean feeding practice score
Caregiver's characteristics	Sex, age, relationship to child, marital status, occupation, breadwinner of the family, number of adults in the family, number of children with MSUD in the family, total number of children in the family, region, community, religion, education, income, years spent taking care of their MSUD children's need, frequency of nutrition counseling received, and completeness of nutrition counseling

Note: For the correlation between caregivers' KAP scores and their demographic characteristics (Table 13), the KAP scores served as the dependent variables, while the demographic characteristics were the independent variables.

Data Management and Statistical Test

Data were entered into Microsoft Excel 2019, which was password-protected and encrypted to ensure data privacy. All data were stored on encrypted hard drives and will be retained for as long as necessary for the purposes of the study, with a minimum retention period of five years. Participants' names and addresses, collected through the socio-demographic questionnaire for contact purposes only, were saved in a separate file accessible only to the primary researcher. The hard copy of this file is stored in a locked cabinet, while the digital copy is password-protected. For the KAP questionnaires and other procedures, respondent codes were used to identify participants.

Data were analyzed using Jamovi (https://www.jamovi.org), a free open-source statistical spreadsheet software. The results were presented using text and tables. Statistical significance was set at <0.05, or at 95% confidence interval. Summary statistics was applied to describe the demographic characteristics of the MSUD children and their primary caregivers. For variables analyzed using the Kruskal-Wallis test, descriptive statistics (mean/median ± SD/IQR) were not included, as the statistical software used (Jamovi) provides only rank-based outputs for non-parametric tests.

Data were subjected to normality testing through the Kolmogorov-Smirnov test. Variables found to depart from normality were treated using non-parametric statistical tests (e.g., Wilcoxon, Mann-Whitney). When no sufficient evidence of departure from normality was found, parametric statistical tests (e.g., T test) were applied.

For the two MSUD children from the same household, their caregiver provided separate data for each child, except for shared socio-demographic information. To ensure accurate statistical analysis, mean or median values were used appropriately for knowledge, practice, attitude scores, and leucine levels, while each child's data was analyzed separately for all other variables. Attitude and feeding practice responses were assessed separately due to differing caregiving experiences (e.g., one child was fed per orem, the other via nasogastric tube).

Figure 2 shows the study's methodology flowchart.

RESULTS

Socio-demographic Characteristics

A total of 20 primary caregivers and 21 MSUD children participated in the study. One caregiver was taking care of two MSUD children. The average age of MSUD children was 3.32 years (Table 2) and ranged between one year and zero months to six years and nine months. Most were male (61.9%, n=13) and the first child (38.1%, n=8). Among the 21 MSUD children, 57.1 % (n=12) had poor leucine control (>500 μmol/L) while 42.9 % (n=9) had good leucine control (≤500 μmol/L). The average leucine level of children with good control was 331 μmol/L, while the average for those with poor leucine control was 781 μmol/L. Global Developmental Delay (GDD), which is defined as having a delay in two or more developmental areas, was noted in 71.4% (n=15). The other 23.8% (n=5) of MSUD children were diagnosed to be developmentally at risk or that a substantial developmental delay may be experienced if early intervention is not provided. The average age of initiation of complementary feeding was 7.81 months and the median was six months.

The average age of caregivers was 32.5 years, and ranged from 22 to 45 years, and the median was 31 years. Out of the 20 caregivers, 90% (n=18) were female and 95% (n=19) were parents of their respective child or patient. Most of them had a marital status of either cohabitation (*live in*; 60%, n=12) or married (25%, n=5). The participants' families were on average composed of four adults and two children, while the average number of children with MSUD per household was one. Household income was either less than PhP 10,481 (85%, n=17) or anywhere from PhP 10,481 to PhP 20,961 (15%, n=3).

Caregiver's Demographic Factors and MSUD Children's Leucine Level

This study aimed to recognize how the primary caregiver's demographic factors contribute to leucine level of MSUD children. At 5% level of significance (Table 3), only sex had a

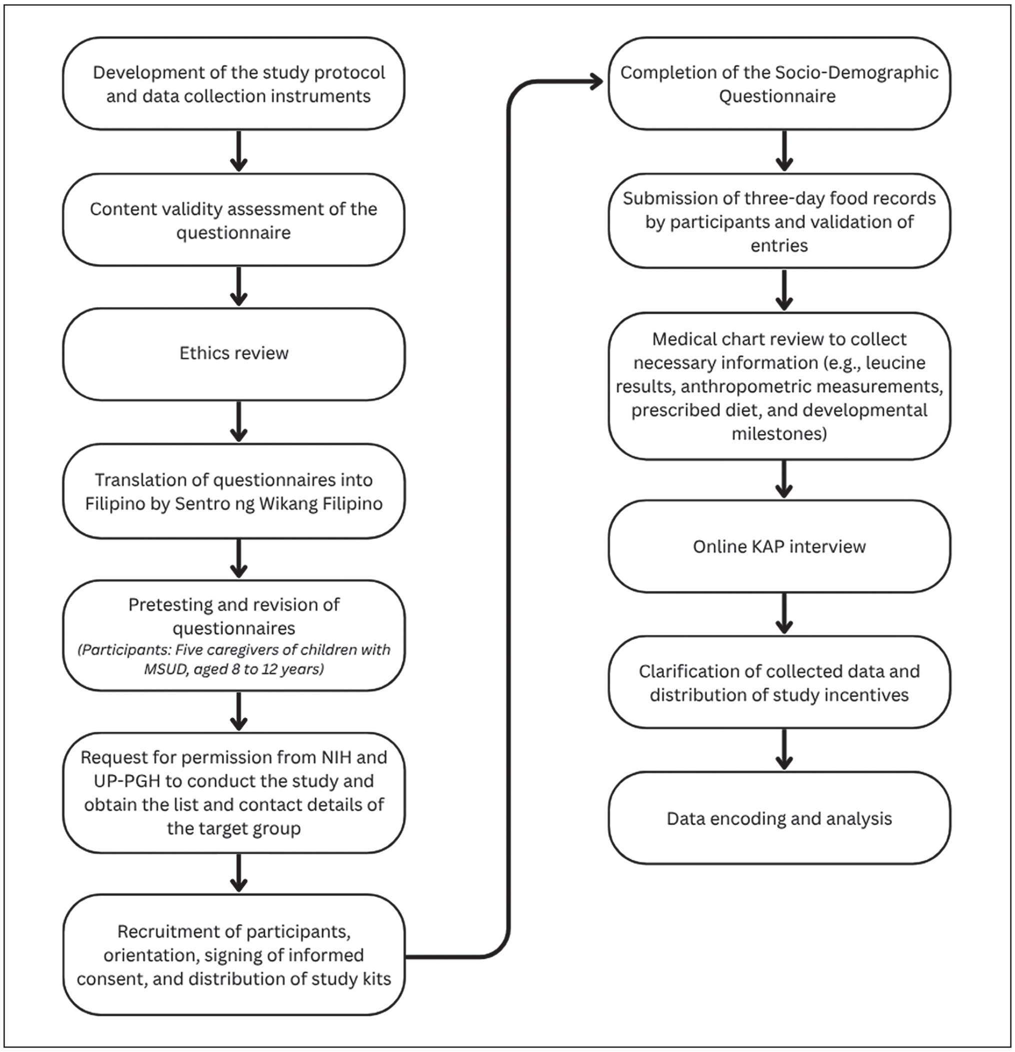

Figure 2. Methodology flowchart.

Table 2. Socio-demographic Characteristics of MSUD Children and their Caregivers

Variable	Item	Frequency	%	Mean	Median	Std Dev
MSUD Children (N=21)						
Age				3.32	3.25	1.548
Sex	Male	13	61.9			
	Female	8	38.1			
Birth order	1st	8	38.1			
	2nd	6	28.6			
	3rd	1	4.8			
	4th	2	9.5			
	5th	3	14.3			
	6th	1	4.8			
Leucine control	Good (≤500 µmol/L)	9	42.9	331		92.7
	Poor (>500 µmol/L)	12	57.1	781		139
Children's development	With Global Developmental Delay (GDD)	15	71.4			
	Developmentally at risk	5	23.8			
	For assessment	1	4.8			
Age when complementary feeding started (months)		21		7.81	6.00	3.234
Caregivers (N=20)						
Age				32.5	31	7.592
Sex	Male	2	10			
	Female	18	90			
Relation to child	Parent	19	95			
	Relative	1	5			
Marital status	Single	2	10			
	Married	5	25			
	Live-in	12	60			
	Separated	1	5			
Community	Urban	12	60			
	Rural	8	40			
Region	NCR	7	35			
	Region III	3	15			
	Region IVA	9	45			
	Region IVB	1	5			
Religion	Catholic	14	70			
	Christian	6	30			
Highest educational attainment	Elementary	2	10			
	High School	11	55			
	Vocational	4	20			
	Bachelor's Degree	3	15			
Occupation	Employed	3	15			
	Self-employed	2	10			
	Unemployed	15	75			
Breadwinner	Participant	5	25			
	Partner	13	65			
	Parent	1	5			
	Sibling	1	5			
Total no. of adults in the family				3.75	3.50	1.916
Total no. of children in the family				2.30	2.00	1.625
No. of children with MSUD in the family				1.05	1.00	0.224
Household's income (PhP)	Less than 10,481	17	85			
	10,481 to 20,961	3	15			

significant relationship to the MSUD children's leucine level (p value=0.010).

Welch's Test was used to compare mean leucine levels between children cared for by male and female caregivers due to unequal variances, though normality was satisfied. At a 5% significance level, it was found that children with female caregivers had lower average leucine levels than those with male caregivers. To check for the effect of the variable "sex" against the children's leucine level, it was put on a regression model. Results showed that compared to children with male caregivers, children with female caregivers had lower leucine levels— by as much as 470 µmol/L on average.

Comparison of Demographics between Caregivers of MSUD Children with Good Leucine Control and those with Poor Leucine Control

The demographics of caregivers of MSUD children with good leucine control and of those caring for children with poor leucine control were compared. Due to the small sample size, several demographic categories were pooled together for them to be tested statistically. As shown in Table 4, only the variable "income" had a significant p-value (0.049). Furthermore, among the 17 children from households with monthly incomes below PhP 10,481, which was the official poverty threshold in the Philippines at the time, the majority (70%, n = 12) had poor leucine control.[17] While all MSUD children (n=3) belonging to households with monthly incomes between PhP 10,481 to PhP 20,961, or households considered as low income but not poor at the time, had good leucine control.[17] This suggests that income is a possible contributing factor to better metabolic control.

Caregivers' Nutrition Knowledge

The source of caregivers' nutrition knowledge is mainly from the nutrition counseling provided by the nutritionist-dietitians and geneticists at UP-PGH. They were receiving regular nutritional counseling. Half of them were counseled on a monthly basis (50%, n=10), which is the usual nutrition counseling schedule set for young children. Some were even receiving counseling more than once a month (15%, n=3) with the help of online consultation. The rest received nutrition counseling once every three months (35%, n=7).

A majority of the caregivers (75%, n=15) reported that the nutrition counseling they received covered all of the following topics: foods the child may eat, how much table food the child may eat, what to limit or avoid; amount of medical formula to be taken daily; the child's sick-day regimen; how to prepare High Energy Drink; how to manage the child's feeding problem; and what symptoms to watch out for. However, some caregivers noted that topics on managing their children's feeding problem (15%, n=3) and the steps involved in preparing High Energy Drink for when medical formula is unavailable (15%, n=3) were not tackled during their counseling.

Table 3. Relationship of Caregivers' Demographics and the MSUD Children's Average Leucine Level

Demographics	Correlation	χ²	*p*
Age [1]	-0.032		0.895
Number of adults [1]	-2.232		0.324
Number of children with MSUD [1]	-0.179		0.450
Total number of children [1]	-0.063		0.791
Income [2]	-0.254		0.186
Years spent by caregiver taking care of patient [2]	0.336		0.067
Frequency of nutritional counseling [2]	-0.020		0.914
Sex [3]	-0.560		0.010*
Community type (urban or rural) [3]	-0.308		0.186
Completeness of nutritional counseling [3]	-0.221		0.350
Relation to patient [4]		0.0677	0.795
Marital status [4]		4.200	0.240
Occupation [4]		0.270	0.874
Breadwinner of the family [4]		0.078	0.994
Region (residency) [4]		2.56	0.465
Educational attainment [4]		3.590	0.309
Religion [4]		1.740	0.187

**Significant at 0.05; [1]Spearman Rank Correlation; [2]Kendall's Tau Correlation; [3]Point-Biserial Correlation; [4]Kruskal-Wallis Test*

Table 4. Test for Difference of Demographics of Caregivers Caring for MSUD Children with Good Leucine Control and of those Caring for Children with Poor Leucine Control

Demographics	*p*
Sex [1]	0.495
Relationship to the child [1]	1.000
Marital status [1]	0.242
Occupation [1]	0.347
Breadwinner [1]	0.347
Region [1]	0.642
Community [1]	0.167
Religion [1]	0.325
Education [1]	0.642
Income [1]	0.049*
Years spent taking care [1]	0.170
Frequency of counseling [1]	0.356
Completeness of nutrition counseling [1]	0.347
No. of adults in the family [2]	0.409
No. of children with MSUD in the family [2]	0.262
Total no. of children in the family [2]	0.656
Age of caregiver [2]	0.877

**Significant at 0.05; [1]Fisher's Exact Tests; [2]Mann-Whitney U-test*

All caregivers knew the table foods that MSUD children should limit and those they may eat more (Table 5). Most caregivers (85%) knew the reasons for limiting certain foods for MSUD children, food variety, ways of enriching porridge or rice, foods that may be given to a child who has chewing or swallowing difficulty, and age for starting complementary feeding.

The caregivers, however, had lower scores on questions asking about ways to encourage young children to eat (71.4%). For the question asking for High Energy Drink's ingredients, only 55% of caregivers answered correctly, especially those with children born in 2022. According to IHG-NIH, the High Energy Drink was last used in 2021 and was no longer being used by 2022 when the medical formula supply became stable.

Caregivers' Feeding Practice

Half of the caregivers of MSUD children (50%) had four to seven years of experience, while 35% of them (n=7) had one to three years of experience. The practice questionnaire's

Table 5. Percentage of Correct and Incorrect Answers Given by Caregivers for Knowledge Questions (N=20)

	Knowledge Questions	Correct, n (%)	Incorrect, n (%)	Total, n (%)
Q1	Table foods MSUD children should limit	20 (100.0)	0 (0.0)	20 (100.0)
Q2	Reasons for limiting certain foods for MSUD children	17 (85.0)	3 (15.0)	20 (100.0)
Q3	Table foods MSUD children may eat more	20 (100.0)	0 (0.0)	20 (100.0)
Q4	Age for starting complementary feeding	17 (85.0)	3 (15.0)	20 (100.0)
Q5	Food variety and ways of enriching porridge or rice	17 (85.0)	3 (15.0)	20 (100.0)
Q6	Foods that may be given to a child who has chewing or swallowing difficulty	17 (85.0)	3 (15.0)	20 (100.0)
Q7	Ingredients used in High Energy Drink preparation	11 (55.0)	9 (45.0)	20 (100.0)
Q8	Foods that may be given on the first day of sick-day regimen	16 (80.0)	4 (20.0)	20 (100.0)
Q9	Ways of encouraging young children to eat*	15 (71.4)	6 (28.6)	21 (100.0)

**Note: The base for Q9 is 21, while Q1–Q8 have a base of 20. This is due to one caregiver providing different responses to Q9 based on multiple children under their care.*

Table 6. Percentage of Correct Practices being Done and not Done by Caregivers Based on the Practice Questionnaire (N = 21)

	Practice Questions	Being Done, n (%)	Not Done, n (%)	Total (excluding "Not Applicable"), n (%)	"Not Applicable" to Respondent's Setting, n
Q1	Provides only low-protein table foods to MSUD child*	18 (85.71)	3 (14.29)	21 (100)	0
Q2	Provides the prescribed amount of table food*	6 (28.57)	15 (71.43)	21 (100)	0
Q3	Measures the amount of table food the child eats*	17 (80.95)	4 (19.05)	21 (100)	0
Q4	Monitors the amount of table food the child eats*	17 (80.95)	4 (19.05)	21 (100)	0
Q5	Provides the prescribed amount of breastmilk or formula milk*	4 (57.14)	3 (42.86)	7 (100)	14
Q6	Provides the prescribed amount of medical formula*	15 (71.43)	6 (28.57)	21 (100)	0
Q7	Provides food with consistency that the child tolerates*	13 (100)	0 (0)	13 (100)	8
Q8	Provides the prescribed amount of High Energy Drink*	NA	NA	0 (0)	21
Q9	Provides the sick-day regimen as prescribed*	NA	NA	0 (0)	21
Q10	Checks the nutrition label of a new food item before feeding it to the child	19 (90.48)	2 (9.52)	21 (100)	0
Q11	Enriches the rice or porridge by adding fruits, vegetables, or oil*	17 (89.47)	2 (10.52)	19 (100)	2
Q12	Does positive ways to encourage the child to eat	19 (100)	0 (0)	19 (100)	2
Q13	Reports feeding problems or challenges to doctor for proper intervention	17 (85.00)	3 (15.00)	20 (100)	1

**Notes:*

1. *Providing the prescribed amount of table food was considered "Done" if the average intake of the child in the three-day food record was 90% to 110% adequate when compared to the prescribed amount, and "Not Done" if it was inadequate (<90%) or in excess (>110%).*
2. *No participant was given High Energy Drink or was under a sick-day regimen during the study's data gathering; hence, responses for these were ticked as "Not Applicable" for all participants.*
3. *% Being Done and % Not Done were calculated as follows:*
   a. *% Being Done = (Number of Correct Feeding Practices "Being Done") ÷ (Total number of participants [21] − "Not Applicable") × 100*
   b. *% Not Done = (Number of Correct Feeding Practices "Not Done") ÷ (Total number of participants [21] − "Not Applicable") × 100*

results, as shown in Table 6 suggest that the caregivers were providing food with texture and consistency their child tolerates (100%) and checking the nutrition labels of new food items before feeding them to their child (90.48%). They were also doing positive ways to encourage their child to eat (100%), enriching rice or porridge by adding fruits, vegetables, or oil (89.47%), and reporting feeding problems or challenges to their doctor for proper intervention (85%). The majority of the respondents were exclusively providing low-protein table foods to their child (85.71%), and measuring (80.95%) as well as monitoring (80.95%) the amount of table food eaten.

However, the majority of caregivers (28.57%) were not able to provide the prescribed amount of table food. This was cross-checked with the patient's three-day food record and compared with the doctor's prescribed diet in the medical chart. Furthermore, the caregiver's compliance in providing the prescribed amount of formula milk (57.14%) and medical formula (71.43%) was also low.

Caregivers' Attitude

The results showed that the caregivers agreed that nutrition has a vital role in their child's health and development, and they believed that following the prescribed diet was very important (Table 7). In addition to this, they strongly agreed that it's good to have variety in their child's food.

The caregivers did not perceive the availability of medical formula and its ease of preparation as barriers. The cost of low-protein food items was thought of by the caregivers as affordable but finding them in their local market or grocery store was neither easy nor difficult. Preparation of low-protein meals was easy for caregivers of children with poor

Table 7. Caregivers' Median Attitude Score for each Question in the Attitude Questionnaire

Attitude Questions			Median	Interpretation
No.	Topic	Question		
Q1	Perceived benefit of nutrition to child's health and development	Nutrition has a vital role in my child's health and development.	1	Strongly agree
Q2	Belief on the importance of following the prescribed diet	Following the doctor's prescribed diet is:	1	Very important
Q3	Perceived benefit of food variety	It's good to give different types of food to the child each day.	1	Strongly agree
Q4	Perceived barrier: Availability of low-protein ingredients	Accessing low-protein ingredients at your local market or grocery store is:	3	Neutral
Q5	Perceived barrier: Availability of medical formula	Accessing your child's medical formula is:	2	Easy
Q6	Perceived barrier: Cost of low-protein food items	Low-protein food items are affordable.	2	Agree
Q7	Perceived barrier: Cost of formula milk	Formula milk is affordable.	4	Disagree
Q8	Perceived barrier: Difficulty in preparing low-protein meals	Preparing low-protein meals for the child is:	3	Neutral
Q9	Perceived barrier: Difficulty in preparing child's medical formula	Preparing the child's medical formula is:	2	Easy
Q10	Perceived barrier: Difficulty in preparing High Energy Drink	Making the High Energy Drink is:	3	Neutral
Q11	Perceived barrier: Difficulty in managing feeding challenges	Managing your child's feeding challenges (e.g., poor appetite, vomiting, or being picky) is:	4	Difficult
Q12	Perceived barrier: Difficulty in taking care of a child with MSUD	Overall, taking care of my child is:	3	Neutral
Q13	Perceived barrier: Difficulty accessing nutritional advice from nutritionist-dietitian or doctor	Accessing nutritional advice from a nutritionist-dietitian or a geneticist is:	2	Easy
Q14	Self-confidence in knowledge regarding the kinds of foods allowed/not-allowed	When it comes to your knowledge of foods allowed/not-allowed for the child, you're:	2	Confident
Q15	Self-confidence in knowledge regarding the child's sick-day regimen	In terms of your knowledge regarding the child's sick-day regimen, you're:	2	Confident
Q16	Self-confidence in taking care of the nutritional needs of a child with MSUD	How do you assess yourself in terms of your confidence in taking care of the nutritional needs of a child with MSUD?	2	Confident
Q17	Motivation in taking care of a child with MSUD	How do you assess yourself in terms of your motivation in taking care of a child with MSUD?	2	Motivated

Note: In the case of the caregiver with two MSUD children under her care, attitude questionnaire responses for the two children were counted separately as the caregiver's response was different for each child.

leucine control and neutral for caregivers of children with good leucine control.

The caregivers were confident in their knowledge of foods allowed and not allowed, and their knowledge of their child's sick-day regimen. They were also confident in ensuring that their child's nutritional needs were met and were motivated to take care of their child. Getting nutritional advice from a nutritionist-dietitian or a geneticist was likewise thought of as easy.

However, they think that providing care was, in a general sense, neither easy nor difficult. Managing feeding challenges (e.g., poor appetite, vomiting, or being picky) was deemed difficult for caregivers of children with poor leucine control and very difficult for caregivers with poor leucine control. Furthermore, the cost of formula milk was thought of as expensive by caregivers.

KAP Scores of Caregivers

Results showed that the caregivers had "moderate" knowledge and practice scores, 81.95% and 78.63%, respectively (Table 8), indicating the need to consider nutrition intervention, in accordance with FAO's (2014) guidelines. They also exhibited the proper attitude to provide adequate nutritional care (median=2).

As shown on Table 9, there was a significant relationship between caregiver nutrition knowledge and the attitude towards the child's nutrition (p-value: 0.021). This means that as the caregivers' MSUD nutrition knowledge score increased, their attitude score decreased or became more positive (note: 1=Very Positive; 5=Very Negative). Furthermore, there was also a significant relationship between knowledge and feeding practice (p-value: 0.037). As their MSUD nutrition knowledge increased, they managed to do a greater number of correct feeding practices at home.

Caregiver's KAP Scores and MSUD Children's Leucine

When compared, caregivers of children with poor leucine control had slightly higher knowledge (83.3% vs 79.9%) and practice (81.1% vs 74.9%) scores compared to caregivers of children with good leucine control (Table 8). Nonetheless, both groups' scores were still "moderate" or within the 71% to 89% cut-off. Caregivers across both groups also had a positive attitude (median=2), having exhibited proper attitude towards providing adequate nutritional care. As for their KAP scores, for which Mann-Whitney U-test was used, no significant difference between the two groups was observed (p values: 0.552, 0.445, 0.508).

For the relationship between caregiver's KAP scores and MSUD children's average leucine levels for the past six months, the results showed that there was no significant linear relationship or direct relationship (p values: 0.783, 0.715, 0.790) between the said variables (Table 10). It has to be noted that the KAP scores reflect caregiver responses at the time of data collection and not over the preceding six months, unlike the leucine level data.

Caregiver's KAP Scores and MSUD Children's Nutritional Status

This study also examined the relationship of caregiver KAP scores and the nutritional status of MSUD children. Mean KAP scores were compared across the nutritional status categories. Data on the children's nutritional status was not presented here.

There seems to be a difference (p-value: 0.036) in the knowledge scores across different categories of weight-for-age (i.e., underweight, normal, may have growth problem (>1 SD) (Table 11). This result indicates that caregiver MSUD nutrition knowledge might be related to the children's weight-for-age.

Table 8. KAP Scores of Caregivers Caring for Children with Good Leucine Control and those Caring for Children with Poor Leucine Control

	Good Leucine Control (n=8)		Poor Leucine Control (n=12)		All Caregivers (N=20)		*p*
	Mean	Std Dev	Mean	Std Dev	Mean	Std Dev	
Knowledge Score	79.90	15.684	83.30	19.244	81.95	17.552	0.552
Practice Score	74.90	20.823	81.10	17.537	78.63	18.639	0.508
Attitude Score*	2.13	0.641	1.92	0.515	2.00	0.562	0.445

**Median*

Table 9. Correlation between KAP Scores

	Correlation	*p*
Knowledge – Attitude	-0.513	0.021*
Knowledge – Practice	0.469	0.037*
Attitude – Practice	-0.256	0.277

**Significant at 0.05 level; Spearman Rank Correlation*

Table 10. Correlation of Caregivers' KAP Scores and MSUD Children's Average Leucine Level

	Correlation	*p*
Knowledge Score [1]	0.066	0.783
Attitude Score [2]	-0.068	0.715
Practice Score [1]	0.064	0.790

**Significant at 0.05; [1]Spearman Rank Correlation; [2]Kendall's Tau Correlation*

Caregiver's KAP Scores and MSUD Children's Nutrient Adequacy

The relationship between the caregivers' KAP scores and the MSUD children's nutritional adequacy was likewise determined. Mean KAP scores were compared across the nutrient adequacy categories (inadequate, adequate, excess).

The study was only able to determine the relationship of KAP scores to the nutrient adequacy categories of calories, total protein, natural protein, phosphorus, Vitamin A, and niacin. The tests cannot be performed on calcium, iron, thiamin, riboflavin, and Vitamin C, because the said nutrients' categories showed no variation (100% adequate for the whole population; values were zero for inadequate and excess categories, leading to invalid tests). Data on the children's nutrient adequacy was not presented here.

At 5% level of significance, knowledge and practice scores were different for at least one category of natural protein status (Table 12), indicating that the knowledge and practice of the caregivers may be related to the natural protein status of the children.

Caregiver's Demographics and KAP Scores

For the relationship between the caregivers' demographics and their KAP scores, the results showed that there was no significant linear relationship between the said variables (Table 13).

DISCUSSION

This study investigated the primary caregivers' KAP and determined the relationship of the said KAP to the leucine level, nutritional status, and nutrient intake of MSUD children, to identify the gaps in home MSUD nutritional management, and to help establish the impact of the caregivers'

Table 11. Difference of Caregivers' KAP Scores across MSUD Children's Nutritional Status Categories

Nutritional Status	Knowledge *p*-value	Attitude *p*-value	Practice *p*-value
Height-for-age	0.309	1.000	0.120
Weight-for-age	0.036*	0.287	0.138
Weight-for-height	0.225	0.070	0.551
BMI-for-age	0.136	0.393	0.226
Head circumference-for-age	0.723	0.068	0.705

**Significant at 0.05; Kruskal-Wallis Test*

Table 12. Difference of Caregivers' KAP Scores across MSUD Children's Nutrient Adequacy Categories

Nutrient Adequacy	Knowledge *p*-value	Attitude *p*-value	Practice *p*-value
Calories	0.862	1.000	0.551
Total Protein	0.464	0.411	0.067
Natural Protein	0.043*	0.211	0.006*
Phosphorus	0.734	1.000	0.505
Vitamin A	0.756	1.000	0.188
Niacin	0.734	1.000	1.000

**Significant at 0.05; Kruskal-Wallis Test*

Table 13. Correlation of Caregivers' KAP Scores and Demographic Characteristics (N=20)

Demographics	Knowledge		Attitude		Practice	
	Correlation	*p*-value	Correlation	*p*-value	Correlation	*p*-value
Age[a]	0.073	0.759	0.254	0.280	0.313	0.179
Number of adults[a]	-0.113	0.636	0.153	0.518	-0.048	0.841
Number of children with MSUD[a]	-0.184	0.437	0.000	1.000	-0.020	0.933
Total number of children[a]	-0.295	0.207	0.366	0.113	0.014	0.955
Income[a]	0.362	0.117	-0.256	0.277	0.135	0.571
Years spent by caregiver taking care of patient[a]	0.222	0.346	-0.382	0.096	-0.099	0.678
Frequency of nutritional counseling[a]	0.288	0.218	-0.148	0.535	-0.074	0.756
Sex[b]	0.190	0.422	0.000[c]	1.000	0.118	0.623
Community type (urban or rural)[b]	0.032	0.890	0.000[c]	1.000	0.145	0.540
Completeness of nutritional counseling[b]	0.105	0.665	0.178[c]	0.066	0.063	0.781
Relation to patient[b]	0.095	0.696	0.000[c]	1.000	0.145	0.546
Marital status[b]	0.370	0.488	0.047[c]	0.826	0.427	0.347
Occupation[b]	0.320	0.443	0.067[c]	0.531	0.253	0.571
Breadwinner of the family[b]	0.073	0.741	0.046[c]	0.831	0.402	0.404
Region (residency)[b]	0.221	0.652	0.045[c]	0.681	0.455	0.139
Educational attainment[b]	0.292	0.496	0.057[c]	0.782	0.195	0.889
Religion[b]	0.089	0.141	0.040[c]	0.385	0.000	0.946

**Significant at 0.05; [a] Spearman Correlation; [b] Eta Coefficient; [c] Rank Biserial Coefficient*

KAP on the growth, development, and overall health of the MSUD children.

It was identified that the caregivers had "moderate" knowledge scores and practice scores and exhibited the proper attitude to provide adequate nutritional care. Despite these, they were struggling with diet compliance, evidenced by the low percentages of caregivers who managed to follow the prescribed amount of table food, formula milk, and medical formula. Improvement in nutrition knowledge is needed in managing feeding problems (e.g., poor appetite, vomiting, or being picky), ways of encouraging young children to eat, and children's age to start complementary feeding, as the children's average age of initiation of complementary feeding was 7.81 months.

This study determined that there was a significant relationship between caregiver nutrition knowledge and the attitude towards the child's nutrition; as the caregivers' MSUD nutrition knowledge score increased, their attitude score decreased or became more positive. This supports some of the links in the study's conceptual framework, where it was theorized that a caregiver's knowledge or cognition shapes their attitude towards a behavior.[18] Furthermore, there was also a moderate positive correlation between knowledge and feeding practice (p-value: 0.037, r: 0.469), as their MSUD nutrition knowledge increased, they managed to do a greater number of correct feeding practices at home. These findings would likely be useful to IHG-NIH, especially when it comes to providing knowledge and skill enhancement training for caregivers, to improve their nutritional care at home. By enhancing the caregivers' MSUD nutrition knowledge, IHG-NIH could also positively affect the caregivers' attitude and feeding practices, which are both crucial factors when it comes to diet compliance.

Aside from managing feeding problems, the cost of formula and other supplies was perceived by the caregivers as a barrier to providing optimal nutritional care at home. In this study, the majority of the caregivers (85%) had a household income of less than PhP 10,481 and were dependent on their partner for income. They were unable to seek employment as they had to take care of their MSUD child, which took up most of their time and energy. The results of this study also found that there was a significant difference in the income of caregivers caring for children with good leucine control and those with poor leucine control. Furthermore, all children with poor leucine control had a household income of less than PhP 10,481, and the majority of children with good leucine control (62.5%) had a household income of anywhere between PhP 10,481 to PhP 20,961, which indicates that that income is a possible contributing factor to better metabolic control.

According to the Congressional Policy and Budget Research Department of House of Representatives (CPBRD), at a national level in 2021, a family of five required a minimum income of PhP 10,071 to purchase nutritionally adequate food items and ensure that they remain economically and socially productive.[19] In Region IVA and NCR, wherein most of the study's participants resided, it was PhP 10,750 and PhP 11,609, respectively. The participants' families had an average of four adults and two children, a total of six family members—larger than the number of family members in the CPBRD's estimate of five. Most of them had a household income below the per-capita food threshold in Region IVA and NCR. This means that most of the MSUD children's households do not meet the minimum income needed to cover their basic needs, including nutritionally adequate food. If the basics can't be met, providing for the children's special needs is less likely to be achieved.

Caring for a child with MSUD requires the capacity to consistently provide for their special needs for better metabolic control, such as low-protein foods, supplements, formula milk, and medical formula, in addition of course to their basic needs. Some of these needs, such as medical formula as well as isoleucine and leucine supplements, were being given for free at IHG-NIH but were dependent on supply availability and funding. Still, having a higher income does translate to being more capable of acquiring and meeting these needs, especially whenever IHG-NIH's supplies of medical formula and supplements run out.

MSUD children who belong to households in the lowest income bracket and those screened for having difficulty procuring food, supplements, medicine, and other supplies should be referred to UP-PGH's social workers for assessment and inclusion into relevant government-run subsidy programs such as Pantawid Pamilyang Pilipino Program (4Ps), Protective Services for Individuals and Families in Difficult Circumstances, and Tax Reform Cash Transfer Project, and other benefits as stated in the Rare Disease Act of the Philippines (Republic Act No. 10747) and Magna Carta for Disabled Persons (Republic Act No. 7277).

Aside from income, the sex of the caregivers also plays a role in the children's metabolic control. Results of this study showed that compared to children with male caregivers, children with female caregivers had lower leucine levels— by as much as 470 µmol/L on average. This is in stark contrast to findings in similar scientific inquiries. For example, in the study of Jackson et al., the gender of primary care providers (n=586) in primary care clinics and medical centers did not affect the quality of primary care provided.[20] Likewise, in Polanen et al.'s research, they found that male and female caregivers (n=42) showed the same levels of attention, sensitivity, and stimulation toward three-year-old children (n=42).[21] Both these findings suggest that the same quality of care can be achieved regardless of gender.

From a biological standpoint, however, females are better equipped to take on the parental sex role. In a study, it was explained that the hormone oxytocin, which is higher in females, plays a greater role in influencing women's social behavior than men's, especially when the individual is faced with stress.[22] Alternatively, it was explained in another study that male caregivers are less likely to seek help with their caregiving burden, be it emotionally, financially, or physically, and with their skill development.[23] This is despite the fact that having help in these areas could lead to significant improvements in caregiving quality. Thus, taking all these into account, IHG-NIH has to exert effort in knowing the challenges specific to male caregivers and, if needed, provide skill development interventions that may enhance the quality of care they provide.

The results of the study also showed that there was no significant linear relationship between the caregivers' KAP scores (p values: 0.783, 0.715, 0.790) and the MSUD children's average leucine levels. This result may be confirmed in future studies with a larger sample size. Certain limitations in this study may also be improved upon. The dietary assessment tool, namely the three-day food record, which was used as a validating tool for feeding practice, might not have captured the children's habitual intake. It also comes with limitations regarding the caregivers' recall capacity and the accuracy of their provided data. It is, thus, recommended to use direct observation in validating feeding practices in further studies and to use a dietary assessment tool that may capture longer durations of intake (habitual intake), as discussed earlier. Although the statistical data was not conclusive, this study was able to find the areas that need improvement in the caregiver's nutrition knowledge and feeding practice.

As for the relationship between KAP scores and nutrient adequacy, the results of this study indicate that the knowledge and practice of the caregivers may be related to the natural protein status of the children. This finding may be useful in further developing IHG-NIH's nutritional interventions, especially those aimed towards improving caregiver diet compliance. To be clear, however, natural protein is defined in this study as protein from table foods, breast milk, and milk formula.

Caregiver compliance with the doctor's prescribed amount of natural protein is crucial in limiting the BCAA intake of children, and keeping their plasma BCAAs within the target range.[11] According to this study's findings, the caregivers' MSUD nutrition knowledge is related to their feeding practices, and both knowledge and feeding practices are related to natural protein adequacy. Improving caregiver MSUD nutrition knowledge will also impact their feeding practices, and both variables may affect the natural protein adequacy of MSUD children.

For the KAP scores and children's nutritional status, this study determined that caregiver MSUD nutrition knowledge might be related to the children's weight-for-age. Other studies reported a direct relationship between the caregiver's knowledge and the child's nutrition status.[24] The relationship of the caregiver's nutrition knowledge to the MSUD children's nutritional status may be confirmed by the IHG-NIH in further studies with a larger sample size. Still, the result of this study may serve as a good lead, supporting the notion that what caregivers know about MSUD nutrition possibly impacts the physical growth of their children.

Strengths and Limitations

The study was able to investigate multiple variables affecting the nutrition knowledge, attitude, and feeding practice (KAP) of primary caregivers caring for MSUD children; and the relationship of the said KAP to the leucine level, nutritional status, and nutrient intake of the children. This is the first study in the Philippines that was able to investigate this objective and scope, and it may serve as a foundation for succeeding studies with the same goal.

This study also has its limitations. First, the small number of participants, given that this is a rare disease, may have weakened statistical power. Second limitation was the mode of data gathering, which was online due to the ongoing pandemic. In-person interviews were still noted to be better compared to video calls.[25] Third limitation is the dietary assessment tool used in the study, which is the three-day food record. The results indicate that the three-day food record might not have captured the children's habitual food intake. It is, therefore, recommended that future studies instead use a dietary assessment tool that allows for capturing longer nutrient intake durations and, by extension, habitual intake data. Multiple 24-hour food recalls may be used for this purpose. Alternatively, food records that caregivers submit every follow up may be utilized. Seven-day weighed FR has likewise been used as the standard for validating other methods, and is thus recommended for further studies.[26] Other validating measures may be done, such as sending pictures of the children's plates before and after feeding. If feasible, weighed food records may be accomplished by the investigators themselves. This will, however, require greater effort compared to the previously mentioned approaches but should offer higher accuracy than self-reported ones. Also, for a more thorough nutritional assessment, observed nutrition-related clinical signs and symptoms, as well as confirmatory biochemical tests, may be included.

Another limitation of this study was the absence of an explicit recall period (e.g., "in the past seven days") for the Attitude and Feeding Practice questions, which may have reduced the specificity of the responses. Additionally, the study setting, UP-PGH, may limit the generalizability of the findings, as participants could represent a subset of MSUD cases with potentially better access to specialized care, counseling, and metabolic formula. The last limitation of the study was the non-inclusion of some variables that may have had an effect on the MSUD children's leucine control including medications taken which may exacerbate feeding problems, and compliance to other aspects of care like sick-day regimen, and supplementation with isoleucine and valine.

CONCLUSION

This study found that as caregivers' MSUD nutrition knowledge increased, they exhibited more positive attitudes and better feeding practices. Despite having a generally positive attitude in addition to having moderate knowledge and practice scores, however, the study's participants still faced challenges in diet compliance, particularly in following prescribed diets and managing feeding problems. It was also identified that caregivers' sex and income could influence leucine control, although there was no significant link between caregivers' KAP scores and MSUD children's leucine levels. Caregivers' knowledge was possibly associated with children's weight-for-age, as was caregivers' knowledge and practices with children's natural protein status. It is, thus, recommended to improve support for male caregivers and address income-related barriers to better metabolic control, as well as provide interventions aimed at improving all caregivers' nutrition knowledge and feeding practices.

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Statement of Authorship

All authors certified fulfillment of ICMJE authorship criteria.

Author Disclosure

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REFERENCES

1. Nyhan W, Barshop B, Ozand P. Maple syrup urine disease (branched-chain oxoaciduria). In: Koster J, Edwards D, Wilkinson N, eds. Atlas of metabolic diseases, 2nd ed. London: Hodder Education; 2005. pp. 159-64.
2. Newborn Screening Reference Center. Newborn screening panel: cumulative prevalence from 1996 to December 2021 [Internet]. 2023 [cited 2023 Aug 21]. Available from: https://newbornscreening.ph/wp-content/uploads/2023/08/prevalence-2021rev.pdf.
3. Chapman KA, Gramer G, Viall S, Summar ML. Incidence of maple syrup urine disease, propionic acidemia, and methylmalonic aciduria from newborn screening data. Mol Genet Metab Rep. 2018 Apr 5;15:106-9. doi: 10.1016/j.ymgmr.2018.03.011. PMID: 30023298. PMCID: PMC6047110.
4. Blackburn P, Gass J, Pinto e Vairo F, Farnham K, Atwal H, Macklin S, et al. Maple syrup urine disease: mechanisms and management. Appl Clin Genet. 2017 Sep;10:57-66. doi: 10.2147/TACG.S125962. PMID: 28919799. PMCID: PMC5593394.
5. De Castro-Hamoy LG, Chiong MAD, Estrada SC, Cordero CP. Challenges in the management of patients with maple syrup urine disease diagnosed by newborn screening in a developing country. J Community Genet. 2017 Jan;8(1):9-15. doi: 10.1007/s12687-016-0281-5. PMID: 27714667. PMCID: PMC5222756.
6. Faner MR, Chiong MAD. Clinical profiles and outcomes of the most common inherited metabolic diseases in the Philippines: a review of the National Institutes of Health - Institute of Human Genetics Metabolic Registry. Acta Med Philipp. 2020 Jun 23;54(3):236-43. doi: 10.47895/amp.v54i3.1648.
7. Evans S, Alroqaiba N, Daly A, Neville C, Davies P, MacDonald A. Feeding difficulties in children with inherited metabolic disorders: a pilot study. J Hum Nutr Diet. 2012 Jun;25(3):209-16. doi: 10.1111/j.1365-277X.2012.01229.x. PMID: 22320889.
8. Kemper AR, Brewer CA, Singh RH. Perspectives on dietary adherence among women with inborn errors of metabolism. J Am Diet Assoc. 2010 Feb;110(2):247-52. doi: 10.1016/j.jada.2009.10.030. PMID: 20102852.
9. Lim JY, Rajikan R, Amit N, Ali NM, Hamid HA, Leong HY, et al. Exploring the barriers and motivators to dietary adherence among caregivers of children with disorders of amino acid metabolism (AAMDs): a qualitative study. Nutrients. 2022 Jun 18;14(12):2535. doi: 10.3390/nu14122535. PMID: 35745265. PMCID: PMC9228574.
10. Sulaiman RA, Al-Owain M. Inherited metabolic disorders in adults: a view from Saudi Arabia. Eur J Med Genet. 2019 Nov;62(11): 103562. doi: 10.1016/j.ejmg.2018.10.014. PMID: 31610876.
11. Frazier DM, Allgeier C, Homer C, Marriage BJ, Ogata B, Rohr F, et al. Nutrition management guideline for maple syrup urine disease: an evidence- and consensus-based approach. Mol Genet Metab. 2014 Jul;112(3):210-7. doi: 10.1016/j.ymgme.2014.05.006. PMID: 24881969.
12. Newborn Screening Reference Center. Fact sheets: information for doctors about the disorders included in the expanded newborn screening panel [Internet]. 2020 Oct 9 [cited 2023 Aug 21]. Available from: https://newbornscreening.ph/wp-content/uploads/2023/08/Expanded Screening Fact Sheets_Doctors_NSRC-INT-05_I1R1.pdf.
13. Food and Agriculture Organization of the United Nations. Guidelines for assessing nutrition-related knowledge, attitudes and practices [Internet]. 2014 [cited 2023 Aug 21]. Available from: https://www.fao.org/3/i3545e/i3545e00.htm.
14. Hulst JM, van Goudoever JB, Zimmermann LJ, Hop WC, Büller HA, Tibboel D, et al. Adequate feeding and the usefulness of the respiratory quotient in critically ill children. Nutrition. 2005 Feb; 21(2):192-8. doi: 10.1016/j.nut.2004.05.020. PMID: 15723748.
15. McClave SA, Lowen CC, Kleber MJ, McConnell JW, Jung LY, Goldsmith LJ. Clinical use of the respiratory quotient obtained from indirect calorimetry. JPEN J Parenter Enteral Nutr. 2003; 27(1):21-6. doi: 10.1177/014860710302700121. PMID: 12549594.
16. Maciel Barbosa J, Pedrosa F, Coelho Cabral P. Nutritional status and adequacy of enteral nutrition in pediatric cancer patients at a reference center in northeastern Brazil. Nutr Hosp. 2012 Jul-Aug;27(4):1099-105. doi: 10.3305/nh.2012.27.4.5869. PMID: 23165548.
17. Philippine Statistics Authority. Proportion of poor Filipinos registered at 21.0 percent in the first semester of 2018 [Internet]. 2019 [cited 2025 Feb 16]. Available from: https://psa.gov.ph/content/proportion-poor-filipinos-registered-210-percent-first-semester-2018.
18. Ajzen I. The theory of planned behavior. Organ Behav Hum Decis Process. 1991 Dec;50(2):179-211. doi: 10.1016/0749-5978(91)90020-T.

19. Congressional Policy and Budget Research Department, House of Representatives. Facts in figures on poverty statistics [Internet]. 2022 [cited 2023 Sep 30]. Available from: https://cpbrd.congress.gov.ph/2012-06-30-13-06-51/2012-06-30-13-36-50/1439-ff2022-07-poverty-statistics-update-first-semester-2021.
20. Jackson JL, Farkas A, Scholcoff C. Does provider gender affect the quality of primary care? J Gen Intern Med. 2020 Jul;35(7): 2094-8. doi: 10.1007/s11606-020-05796-0. PMID: 32291718. PMCID: PMC7352031.
21. Polanen M Van, Colonnesi C, Tavecchio L, Blokhuis S, Fukkink R. Men and women in childcare: a study of caregiver-child interactions. Eur Early Child Educ Res J. 2017 Mar 30;25(3):412-24. doi: 10.1080/1350293X.2017.1308165.
22. Taylor SE. Tend and befriend: biobehavioral bases of affiliation under stress. Curr Dir Psychol Sci. 2006 Dec;15(6):273-7. doi: 10.1111/j.1467-8721.2006.00451.x.
23. Lopez-Anuarbe M, Kohli P. Understanding male caregivers' emotional, financial, and physical burden in the United States. Healthc. 2019 May 22;7(2):72. doi: 10.3390/healthcare7020072. PMID: 31121905. PMCID: PMC6627587.
24. Prasetyo YB, Permatasari P, Susanti HD. The effect of mothers' nutritional education and knowledge on children's nutritional status: a systematic review. Int J Child Care Educ Policy. 2023 Apr 8;17. doi: 10.1186/s40723-023-00114-7.
25. Krouwel M, Jolly K, Greenfield S. Comparing Skype (video calling) and in-person qualitative interview modes in a study of people with irritable bowel syndrome – an exploratory comparative analysis. BMC Med Res Methodol. 2019 Nov 29;19. doi: 10.1186/s12874-019-0867-9. PMID: 31783797. PMCID: PMC6883529.
26. Baranowski T. 24-hour recall and diet record methods. In: Willett W. Nutritional epidemiology, 3rd ed. New York: Oxford University Press; 2012. pp. 55-62.

APPENDIX

Data Collection Instruments

1. Self-administered socio-demographic questionnaire in Google Form: The socio-demographic questionnaire asked for the caregiver's name, age (in years), sex, marital status, place of residence and type of community, religion, occupation, relationship to the MSUD child, highest educational attainment (completed), household's monthly income, whether the participant is the family's breadwinner (and if not, who), household size, total number of adults and children in the family, number of children with MSUD in the family, years spent taking care of the patient's nutritional needs, completeness of nutrition counseling received from a nutritionist-dietitian and/or geneticist, and contact details; and MSUD child's name, age in years and/or months, birth date, sex, and birth order; and age when complementary feeding started.

2. Knowledge, Attitude, and Feeding Practice (KAP) questionnaires, which were researcher-administered through online interviews. A PowerPoint Presentation containing the prepared questions was shown to the participants whenever possible for improved clarity.

   a. The Practice Questionnaire features thirteen questions to assess the primary caregivers' feeding practice to the MSUD children. The questions were focused on the following aspects of care provision: Caregivers' provision of allowed and within-the-prescribed-amounts of low-protein table foods; Measuring and monitoring what the patient eats to ensure that the right amount is maintained; Ensuring that the patient finishes the prescribed amount of medical formula, breastmilk, and other milk; Modification of food consistency to meet the patient's tolerance; Provision of High Energy Drink as prescribed (if applicable); Provision of the prescribed sick-day regimen; Checking nutrition labels before feeding new food items to the child; Whether they enrich rice or porridge to make it more nutritious; Whether they practice positive ways of encouraging the child to eat; and whether they seek the help of a doctor or nutritionist-dietitian for feeding problems they cannot manage.

      The options for the questions were "Yes," "No," and "Don't Know / No Answer." For those who answered "Yes," follow-up open-ended questions were asked (e.g., frequency per week of a given feeding practice, how many times per day were they providing a specific food item and how much, etc.). This was to gain understanding on how the respondents carry out certain feeding practices and to verify if they were indeed doing them.

      A preliminary analysis box was placed for each practice question. The said box had three options the researcher may tick, namely: "Done" if respondent's answer was true upon verification methods (e.g., food record) and follow up questions; "Not Done" if the respondent's answer to the question was "No" or "Don't Know/No Answer." "Not Done" was also ticked if the respondent answered "Yes" to the question but the answer was proven incorrect through the verification process; "Not Applicable" if the statement was not applicable to the respondent's setting.

   b. The Knowledge Questionnaire aimed to assess the primary caregivers' intellectual capacity to recall the needed nutrition for MSUD patients. The questionnaire contained nine questions focused on the following: What foods the patient should limit and the reason for such; Foods the patient may eat more; Age when to start feeding solid foods; Ways of enriching porridge; Foods the child may eat when faced with chewing or swallowing difficulties; High Energy Drink ingredients; Foods that may be given during the first day of the patient's sick-day regimen; and ways to encourage young children to eat.

The knowledge questionnaire required the respondents to answer in their own words. The Food and Agriculture Organization (FAO) in their 2014 KAP Manual, recommends this design to prevent respondents from guessing answers, such as in the case of multiple choice and true-or-false questions. From the researcher's end, there is a list of correct answers per question that can be ticked if provided by the respondent. There are also options for "Other" or "Don't Know" in cases when the participant gave an answer distinct from those in the existing list or simply does not know the answer. Similar to the practice questionnaire, the knowledge questionnaire also had a preliminary analysis box for each question. The researcher assessed whether a respondent knows the answer to a question during the interview. The option "Knows" was ticked if the respondent provided the correct answer; alternatively, "Does Not Know" was instead ticked if the correct answer was not given. One point was given for each question with "Knows," while a zero was given for those with "Does Not Know." The results were interpreted as the percentage of respondents who know the correct answer to a question.

c. The Attitude Questionnaire contains seventeen close-ended questions that measured the degree to which participants agree or disagree with statements regarding MSUD nutrition. These questions are focused on the primary caregivers': Perceived barriers (i.e., availability of low-protein ingredients; availability of medical formula; cost of low-protein food items and formula milk; difficulty in preparing low-protein meals, child's medical formula, and High Energy Drink; difficulty in managing feeding challenges; difficulty in taking care of a child with MSUD; difficulty accessing nutritional advice from nutritionist-dietitians or doctors); Belief regarding the importance of following the prescribed diet; Perceived benefits of proper nutrition for the patient's health and development; Perceived benefit of providing a variety of foods to the patient; Self-efficacy or confidence (i.e., self-confidence in knowledge of allowed/unallowed food; self-confidence in knowledge regarding the child's sick-day regimen; self-confidence in taking care of the nutritional needs of a child with MSUD); and level of motivation in taking care of a child with MSUD.

There were open-ended questions under each closed-ended question in the Attitude Questionnaire to explore the reasons behind the caregivers' perceived barriers, challenges, and concerns; and for gaining insights into the caregivers' perceptions on what could help resolve their challenges and concerns. This two-step approach was specifically done with the goal of achieving a better understanding of the respondents' answer for each question, allowing them to expound on their response as well as to provide further context where applicable.

The caregivers were asked to rate their responses using a five-point Likert scale. Statements were rated as follows: strongly agree (5), agree (4), neutral (3), disagree (2), and strongly disagree (1). Reversed statements were reversed back and then graded using the aforementioned rating scale. The modal answer of the caregivers was taken as the attitude score for each question. This score was then categorized as: 1 - Very Positive, 2 - Positive, 3 - Neutral, 4 - Negative, 5 - Very Negative.