

Effect of Bite-Sized Teaching Sessions on Mothers' Care of Their Children with Methylmalonic Acidemia

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Abstract

Background: Methylmalonic acidemia (MMA) is a metabolic disease in which proper dietary treatment may benefit pediatric patients' growth and development. **Aim:** Effect of Bite-Sized Teaching Sessions on Mothers' Care of Their Children with Methylmalonic Acidemia. **Design:** A quasi experimental design was used. **Setting:** This study was conducted at the Specialized Genetic Outpatient Clinic at Children's Hospital affiliated with Ain Shams University Hospitals. **Subjects:** A convenience sample consisting of 50 mothers accompanying their children with Methylmalonic acidemia. **Tools:** Tools of data collection included a structured interview questionnaire & Mothers reported practice checklist related to the care of their children with methylmalonic acidemia. **Results:** The results showed highly statistical significant improvement in the studied mothers' knowledge and reported practice regarding the care of their children with methylmalonic acidemia. **Conclusion:** Bite-Sized Teaching Sessions implementation had statistical significant positive effect on improving mothers' knowledge & reported practice regarding caring of children with methylmalonic acidemia. **Recommendation:** Continuous Bite-Sized Teaching Sessions should be provided for all mothers caring of children with methylmalonic acidemia

Keywords: Children, Knowledge, Practice, Methylmalonic Academia & Mothers

Introduction:

Methylmalonic Acidemia (MMA) is a genetic condition in which the body is unable to properly metabolise certain proteins and lipids. Excessive vomiting, dehydration, muscle weakness (hypotonia), delays in child development, lethargy, liver enlargement, and failure to thrive are the most common indications and symptoms of MMA. In the affected child, these symptoms might range from moderate to life-threatening. If left untreated, MMA can cause intellectual issues, eating disorders, kidney damage, coma, and death in the affected child (**Genetic Home Reference, 2019**).

Newborn screening is a public health initiative aiming at improving outcomes for children who have curable illnesses that go unnoticed in standard care. Inborn errors of metabolism (IEM) account for many of the illnesses eligible for newborn screening, including MMA (**McCrorry, et al., 2017**). Early diagnosis has been made possible thanks to the inclusion of MMA in newborn screening panels. The impact of newborn screening on the long-term outcomes of MMA is unknown, but according to the European registry and network

for Intoxication type Metabolic Disorders, newborn screening is effective in reducing the time to diagnosis for late-onset patients and in reducing the likelihood of movement disorders in MMA patients who respond to cobalamin supplementation. (**Almasi, et al., 2019**).

Methylmalonic Acidemia is divided into many categories based on how someone responds to vitamin B12 treatment: vitamin B12 responsive and vitamin B12 non-responsive. Some types of MMA however are "partially B12 responsive" and require injections of B12 in addition to a special diet (**Suormala et al., 2018**). A high-calorie diet with limited protein intake is part of the MMA treatment strategy, as does the prescription of particular medicines and antibiotics. Organ transplantation is required in some complex instance (**Haijes, et al., 2019**). Inadequate phenylalanine consumption can lead to a drop in the amounts needed for growth and bodily processes. Also, the amino acid leucine, which is used as a sweetener in several medications, should be avoided (**Hyman et al., 2018**).

The parents of such children should be provided genetic testing. Methylmalonate levels

in the amniotic fluid, maternal urine and enzyme activity in fetal white blood cells and cultured fibroblasts can all be used to make a prenatal diagnosis. Attempts have been made to give mothers prenatal vitamin B12 injections. Consequently, routine laboratory testing is critical for child with MMA. An essential part of the treatment of MMA is to do blood samples to measure the methionine, threonine, valine and isoleucine levels. Urine samples also need to be taken to measure the level of urinary MMA (Chu, et al., 2019)

In order to develop an appropriate management plan for a child with MMA, collaboration between healthcare providers, nurses, and parents is essential. (Radmanesh, et al., 2018). Cobalamin (vitamin B12), antibiotics, and carnitine are all given intravenously. The amino acids isoleucine, threonine, methionine, and valine are all restricted in protein intake. In the affected child, these amino acids are converted to methylmalonic acid. Dietary intake for the affected pediatric patient should be modified to ensure that certain amino acids are not present while other important amino acids are present. Each pediatric patient has a unique nutritional intake and treatment strategy (Dobson et al., 2019)

A proper education program will encourage open communication, provide compassionate and supportive treatment, encourage collaboration between parents and the health care professionals with whom they work, and realize that, while medical specialists are experts, parents know their children best (Young & Van Merriënboer 2014). Bite-Sized Teaching (BST) is an instructional strategy that breaks down difficult subject into small, manageable parts, focusing on important knowledge schemas and using multiple, focused 8 to 10 micro sessions, each lasting 10 minutes. Rather than reviewing all relevant knowledge, it focuses on a specific construct and provides a framework for learners to organize and recognize related facts and ideas in order to simplify learning by reducing superfluous load and facilitating working memory (Kimberly et al., 2021).

The needs of parents and caregivers must also be addressed as part of the therapy approach. Children's MMA is effectively controlled by their mothers. Mothers must make daily efforts to meet

their children's challenges and limitations, as well as ensure proper dietary intake and treatment plans. Mothers should be aware of the MMA disease, its diagnosis, and how to manage it so that their children receive appropriate care. (Zwickler et al., 2018).

Significance of the study:

The first children with MMA were reported by Oberholzer et al., (1967) and Stoke et al., (1973). In most cases, MMA is discovered in the first year of life. This disease affects approximately 1 in every 25,000 to 48,000 newborns born. However, because an infant may die before the disease is discovered, the true rate may be greater. Methylmalonic Acidemia has an equal impact on both boys and girls (Rezvani, 2007). Infants may appear normal at birth, but symptoms develop once they are weaned on a protein diet, which can exacerbate the problem. Lethargy (84%) is the most common symptom, followed by failure to thrive (73%), recurrent vomiting (73%), dehydration (71%), respiratory distress (67%), hypotonia (63%), developmental delay (47%), hepatomegaly (41%), and coma (40%). When a child exhibits these symptoms, it is referred to be a metabolic crisis, which if not managed promptly can lead to the illness worsening (Marquard et al., 2011). So that, the current study emphasized the importance of mothers in caring for their children who have MMA to avoid more issues and major health problems for their children, mothers must completely change their lifestyle.

Operational definitions:

- **Bite-sized Teaching Sessions (BSTS):** meant a short, concentrated learning unit built around a single purpose and delivered in 10 minutes of teaching micro-sessions.
- **Mother care:** meant mothers had knowledge & practice about caring of their children with MMA.

Aim of the Study

This study aimed to investigate the effect of Bite-Sized Teaching Sessions on mothers caring for their children suffering from Methylmalonic Acidemia. This aim was achieved through:

- Assessing mothers' knowledge and reported practice level regarding caring of children with Methylmalonic Acidemia.

- Designing and implementing the Bite-Sized Teaching Sessions about Methylmalonic Acidemia. Based on mothers need assessment.
- Evaluating the effect of the Bite-Sized Teaching Sessions on mother's knowledge, reported practice level regarding caring of children with Methylmalonic Acidemia.

Research Hypothesis:

H1: mothers' knowledge would improve post implemented Bite-Sized Teaching Sessions about caring for children with Methylmalonic Acidemia than pre its implementation.

H2: mothers' reported practice would improve post implemented Bite-Sized Teaching Sessions about caring for children with Methylmalonic Acidemia than pre its implementation.

Subjects and Method

Research design:

A quasi- experimental design was utilized to conduct the study.

Settings:

This study was done out in the Specialized Genetic Outpatient Clinic of the Pediatric Hospital partnered with Ain Shams University Hospitals, which is one of Cairo's largest hospitals and treats a great number of children with MMA and other genetic disorders. The specialized genetic outpatient clinic is located on the ground floor and has five rooms, each with two beds, for children with MMA and other genetic disorders.

Subjects:

A convenience sample of 50 mothers who were attending to the out-patient regardless their characteristics and having children with MMA within six months duration

Tools for data collection:

The following tools were used to collect data:

Tool 1. Interviewing questionnaire which consisted of two parts

It was developed by the researchers after reviewing the recent related literature (**Heringer**

et al., 2016 &Chapman et al ., 2018). It was written in Arabic language. This tool was divided into three parts:

Part I:

It included demographic characteristics of the studied mothers and their children. For mothers as age, level of education, marital status, and residence. For child it covered gender, age, birth order, and number of siblings and level of education.

Part II:

This part included the medical history of the child with MMA, such as the duration of the disease, how the disease was discovered, symptoms, time of manifestations appearance, previous hospitalization, and disease complications.

Part III:

It included mothers' knowledge about MMA and their care for children as a concept, causes, clinical manifestation, investigation, diagnosis of MMA, treatments, danger signs, complications, Dietary restriction, and Dietary management. This part was assessed by 35 closed-ended question items.

Scoring system: The researcher checked the studied mother's knowledge using a model answer; each question was given a score of zero if the answer was incorrect or if the mother didn't know, and a score of one if the answer was correct. The complete knowledge of mothers was categorized as the following:

- Satisfactory $\geq 60\%$
- Unsatisfactory $< 60\%$

Tool II. Mothers' Reported Practice checklist:

It was adopted from **Robinson & Drumm (2018)** To assess the studied mothers' reported practices regarding the care of their children with methylmalonic acidemia. In relation to; **Measuring of medical diet** (14 items), **General observation of children's** (16 items),

Measuring blood sugar in the home (9 items) and **Dental care** (8 items).

Scoring system: Each item was given a score of zero if the action was not done, one score if the action was reported incomplete or

incorrectly done, and two score if the action was reported complete or correctly done by the mothers. categorized as the following:

- Adequate reported practices $\geq 60\%$
- Inadequate reported practices $< 60\%$

Tools validity & reliability

Validity:

A group of five experts in pediatric nursing and pediatric medicine in Port Said university and Ain shams university evaluated the tools for content validity. The necessary changes were made in a timely manner.

Reliability

Cronbach alpha was used to test the study tools' reliability; the results were 0.76 for the mothers' knowledge questionnaire and 0.71 for mothers' reported practice checklist.

Pilot study:

A pilot study was done on 10% of the study subjects 5 mothers to assess the applicability and practicality of the study tools . Because no major changes were required, the mothers who participated in the pilot study were later enrolled in the full study sample. Then the final form of the tool was obtained as well as an estimate of how long each tool would take to complete.

Ethical Consideration

The researcher provided sufficient information on the consent form, and participants had the option to refuse or participate in the study at any time. The participants signed a consent form. The participants' and study data's confidentiality was preserved to an adequate level. The respondents were promised that their responses would only be used for research purposes.

Field Work

The actual field work was carried out over a period of 6 months from the beginning of August 2020 up to the end of January 2021. The researchers were available in the study settings 3 days/week by rotation and the actual field work was divided into four phases:

1- Assessment phase:

Throughout this phase, the researchers used the developed tools to collect data on mothers'

MMA knowledge and reported practices (pre-test). The researchers explained the study's purpose and expectations to the mothers before beginning the interviews and data gathering. The questionnaire was completed by the researchers. The mothers' own knowledge determined the length of time it took to complete the questionnaire. The duration was between 10 and 20 minutes on average. The mothers' reported practice checklists were completed by the researchers through asking the mothers to re-demonstrate their practices. The time needed to fill each procedure was ranged between 3- 5 minutes. The average time to complete all checklists was ranged between 15- 20 minutes.

2- Planning phase:

Mothers were interviewed regarding the contents, teaching techniques, and evaluation after the Bite-Sized Teaching Sessions goals were determined. In light of the literature review (**National Centre for Inherited Metabolic Disorders, 2019**). It was reviewed, arranged, and the materials were made to meet the educational needs of mothers in order to improve their knowledge and practice of MMA. Following the construction of the Bite-Sized Teaching Sessions contents, the relevant teaching methods and media for teaching these contents were chosen. Following an extensive review of related literature, the researchers created a booklet with illustrated graphics. It was utilized during the Bite-Sized Teaching Sessions and given to the mothers at the end.

3- Implementation phase:

The topic contents were sequenced through 8 sessions (4 sessions for theory and 4 sessions for practices) to implement the Bite-Sized Teaching Sessions, which took 12 weeks. Each session lasted 10 minutes. The mothers in the study were divided into 7 groups. Each group consisted of seven to eight mothers. An introduction to the Bite-Sized Teaching Sessions was presented at the outset of the first session, and each session began with a review of the previous session's feedback. Lectures, demonstrations, and re-demonstration were all used as instructional approaches. Real equipment, posters, and a booklet were used as appropriate media.

Evaluation phase:

The same tools were used as an indicator to determine the level of mothers' knowledge and practice regarding care of children with MMA after the Bite-Sized Teaching Sessions was implemented.

Statistical Design:

Using the number and percentage distribution, the acquired data was arranged, updated, scored, tallied, and evaluated. The Statistical Package for Social Sciences (SPSS) version 18 was used for statistical analysis. The Chi-square (X^2) test was used to compare qualitative variables, while the Pearson correlation coefficient was used to analyses quantitative variables (r). The following factors were considered while determining the importance of the findings: When $p > 0.05$, the difference was statistically insignificant; when $p \leq 0.05$ or $p \leq 0.001$, the difference was statistically significant.

Results:

Table (1) illustrates that the mean age of mothers was 25 ± 6.6 years and 84% of them were married. Also, 36% of mothers had high education and more than half of them 60% respectively were housewives and from urban areas.

Table (2) shows that, the mean children, age was 4.8 ± 2.49 years and 64% of them were males. This table also reveals that 64% of them ranked as the second child within their families.

Table (3) illustrates that 44% of studied children had the disease from 3<6 years and 50% discovered the disease through their manifestation. This table also reveals that respiratory distress, recurrent vomiting, Lethargy, dehydration and hepatomegaly were the main manifestations appeared in studied children as represented by 92%, 90%, 84%, 78%, & 70% respectively. Moreover, 76% & 66% respectively

of studied children had previous hospitalization and suffered from complications respectively.

Table (4) reveals that there are statistically significant differences ($p < 0.001$), in all items of mothers' knowledge regarding MMA between pre/post implementation of the Bite-Sized Teaching Sessions. Less than half (48.1%, 42.3% & 46.2%) respectively of studied mothers had satisfactory knowledge regarding causes, diagnosis and treatment of MMA pre-implementation compared with 92.3%, 90.4% and 86.5% of them respectively post implementation.

Figure (1) shows that statistical significant difference ($X^2 = 17.1$ at $p < 0.001$) between pre/post implementation of the Bite-Sized Teaching Sessions regarding total level of mothers' knowledge about a bout the care of their children with MMA, where 37.5% of studied mothers had satisfactory knowledge pre-implementation compared with 87.5% of them post implementation

Figure (2) illustrates that there was a statistically significant difference ($X^2 = 14.3$ at $p < 0.001$) between pre/post Bite-Sized Teaching Sessions implementation regarding mothers' total reported practices level toward MMA, where 46.9% of studied mothers had adequate level of practice pre-implementation of the program compared with 90.6% of them post implementation.

Table (5) reveals that there was statistically significant differences ($p < 0.001$), in all items of mothers' practices regarding caring children with MMA pre/post the Bite-Sized Teaching Session implementation.

Table (6) shows that there was a positive correlation between total scores of mothers' knowledge and their total score of reported practices regarding the care of their children with MMA. There was highly statistically significant difference.

Table (1): Distribution of the studied mothers according to their demographic characteristics (no=50).

Mothers' characteristics	No	%
Age (years)		
20 -	6	12
30 -	32	64
40+	12	24
$\bar{X} \pm SD$	25 ± 6.6	
Marital status		
Married	42	84
Divorced / widow	8	16
Educational level		
Illiterate	8	16
Read & write	6	12
Basic education (primary school)	6	12
Intermediate education (secondary school-Diploma)	12	24
High Education	18	36
Occupation		
Employee	20	40
Housewife	30	60
Residence		
Rural	20	40
Urban	30	60

Table (2): Distribution of the studied children according to their demographic characteristics (no=50).

Children' characteristics	No.	%
Age/ years		
Birth<3	15	30
3<6	15	30
6≤9	20	40
$\bar{X} \pm SD$	4.8± 2.49	
Gender		
Male	32	64
Female	18	36
order in family		
First	5	10
Second	32	64
Third and more	13	26

Table (3): Distribution of the studied children according to disease characteristics (no=50).

Items	No	%
Disease Duration / years		
<3	16	32
3 -	22	44
6+	12	24
$\bar{X} \pm SD$	4.26 ± 2.23	
Ways of disease discovered		
Accidentally	5	10
Through disease manifestations	25	50
Previous family case	18	36
Through periodic routine follow up	2	4
symptoms*		
Lethargy	42	84
recurrent vomiting	45	90
coma	27	54
dehydration	39	78
hepatomegaly	35	70
respiratory distress	46	92
Delayed growth and weak body structure	28	56
Time of manifestations appearance		
In the first week after birth	6	12
In the first month of the child's life	14	28
In the first year of the child's life and more	30	60
Previous hospitalization		
Yes	38	76
No	12	24
Complications of disease		
Yes	33	66
No	17	34

*Numbers are not mutually exclusive

Table (4): Distribution of the studied mothers Satisfactory Knowledge Regarding caring of children with methylmalonic academia Pre/Post Implementation of the Bite-Sized Teaching Sessions implementation (n=50).

Satisfactory mother' knowledge regarding methyl malonic academia	Pre		Post		X ²	p value
	No.	%	No.	%		
Concept of MMA	20	38.5	45	86.5	25.6	<0.001*
Causes of MMA	25	48.1	48	92.3	24.3	<0.001*
Manifestations of MMA	18	34.6	46	88.5	22.2	<0.001*
Investigation	15	28.8	42	80.8	28.3	<0.001*
Diagnosis of MMA	22	42.3	47	90.4	26.9	<0.001*
Treatment of MMA	24	46.2	45	86.5	18.9	<0.001*
Danger signs	14	26.9	40	76.9	26.1	<0.001*
Complications of MMA	20	38.5	43	82.7	21.3	<0.001*
Dietary restrictions	16	30.8	41	78.8	24.3	<0.001*
Nursing role	21	40.4	44	84.6	21.7	<0.001*

* Statistically significant at p < 0.001

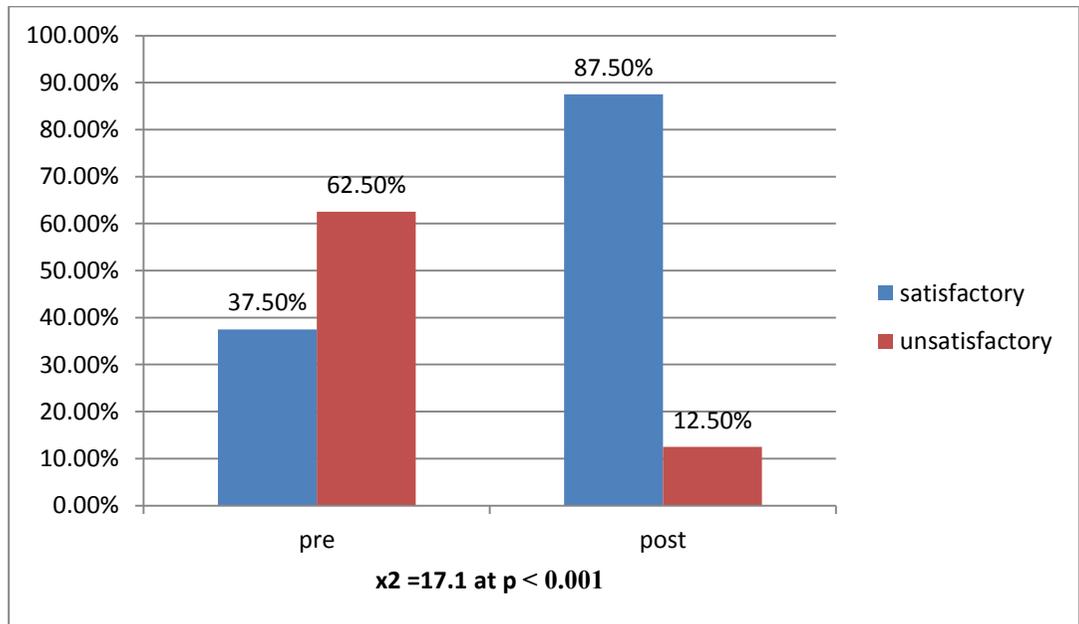


Figure (1): Percentage distribution of the studied mothers' total knowledge level regarding care of their children with methylmalonic academia pre & post Bite-Sized Teaching Sessions implementation.

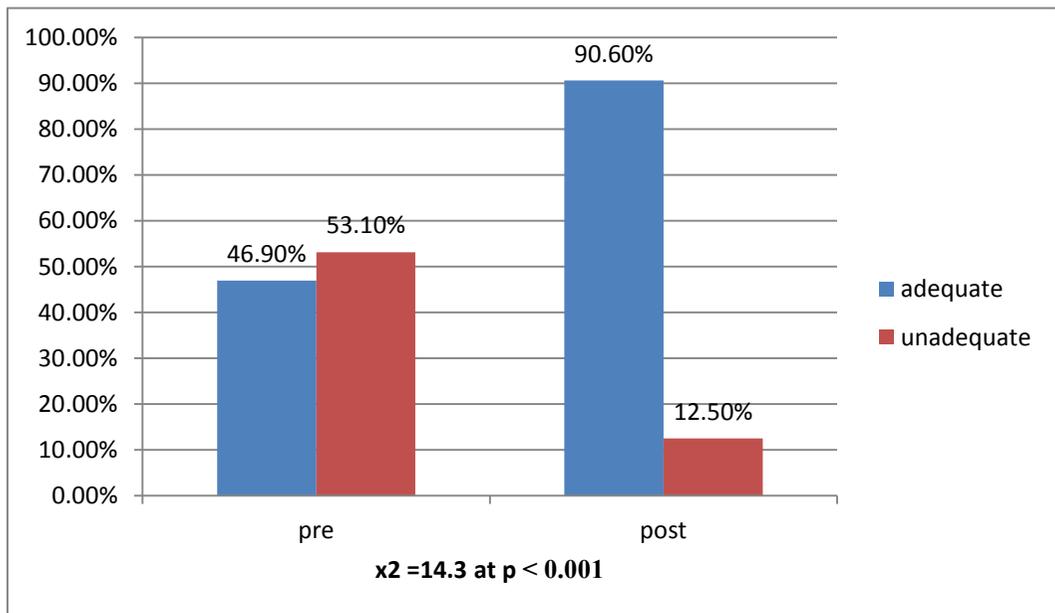


Figure (2): Percentage distribution of the studied mothers' total reported practice level regarding care of their children with methylmalonic academia pre & post Bite-Sized Teaching Sessions implementation.

Table (5): Distribution of the Studied mothers ' adequate reported Practices regarding care of their children with methylmalonic academia Pre/Post Bite-Sized Teaching Sessions Implementation (n=50).

Mothers' reported Practices Regarding MMA	Pre program		Post program		X ²	p-value
	No.	%	No.	%		
Measuring of medical diet	20	38.5	44	84.6	23.4	<0.001*
General observation of children's	23	44.2	46	88.5	22.8	<0.001*
Measuring blood sugar in the home	25	48.1	45	86.5	17.5	<0.001*
Dental care	22	42.3	48	92.3	29.5	<0.001*

*Statistically significant $p \leq 0.05$

Table (6): Correlation between total knowledge of the studied mothers and their total reported practices regarding the care of their children with Methylmalonic academia.

Item	Total score of mothers' reported practices	
	r	p-value
Total score of mothers' knowledge	0.47	0.001**

**Highly statistically significant $p \leq 0.01$

Discussion:

Methylmalonic academia (MMA) is a genetic disorder caused by a malfunctioning gene. Children with MMA have deficient in a protein that the body needs to break down lipids and cholesterol within cells. As a result, toxic chemicals accumulate in cells, causing damage to the brain, liver, kidneys, and other organs that worsens with time *Lerner-Ellis et al., (2020)*.

According to the findings of the current study, less than half of the studied children were diagnosed between the ages of 3<6 years and less than two-thirds of them noticed signs during their first year of life. These findings corroborated with *Morrow et al., (2020)* who found that approximately half of the patients were still not diagnosed MMA early. Meanwhile, these findings are contradicted by the findings of *Peters et al., (2019)*, who revealed that the majority of pediatric patients were diagnosed with MMA at the beginning of their lives. This could be because the disease is rare and its symptoms are fatal, and cannot be ignored. In a similarly, *McLaughlin et al., (2017)* discovered that the cases were diagnosed within the first ten months of life.

Various clinical symptoms of MMA including recurrent vomiting, metabolic acidosis, and even developmental delay (*Dobson et al., 2019*). Regarding the manifestations of MMA, the current study's findings revealed that the majority of the children had the following main manifestations: respiratory distress, recurrent

vomiting, Lethargy, dehydration and hepatomegaly were the main manifestations. This could be because these are the most common MMA manifestations. These findings contradicted those of *Brown et al., (2016)*, who concluded that the majority of the studied children had feeding difficulties, lethargy, seizures, vomiting, and coma.

According to previous hospitalization, the current study's findings revealed that more than one third of the studied children had been previously hospitalized. According to the researchers, this result could be attributed to mothers' lack of knowledge about caring for their children with MMA and irregular follow-up in a specialist outpatient genetics unit. This finding is consistent with the findings of a study conducted by *Gruenbaum et al., (2019)*, who discovered that the majority of children had been previously hospitalized, with some admitted to ICU.

In aspects of MMA complications, the findings of this study revealed that approximately two-thirds of the mothers reported that their children with MMA were experiencing complications. These findings were consistent with those of *Evans et al., (2019)*, who found out that majority of the studied children had complications

Regarding mothers' level of knowledge the current study found that, most of the studied mothers had unsatisfactory level of knowledge about caring of children MMA pre implementation while the majority of them had

satisfactory level of knowledge post Bite-Sized Teaching Sessions implementation. This might be attributable to the regular explanations, as well as the provision of posters to motivate those mothers. As a result, mothers need basic information in order to comprehend their children's disease and how to deal with it. This is in agreement with **Manoli et al., (2016)** who stated that the minority of mothers had satisfactory knowledge regarding their children with MMA and its care before program implementation.

The results of the present study revealed that most of the mothers had inadequate.

Practices toward the care of children with MMA pre- implementation and became adequate among the majority of the studied mothers after Bite-Sized Teaching Sessions implementation. This may be due to the fact that the researcher taught each mother individually about the way of measuring medical diet, General observation of children, Dental care and measuring blood sugar in the home, let them demonstrating most of care techniques in front of the researcher. This study result was similar to a study performed by **Tejada-Ortigosa, et al., (2019)** who observed that most of the studied mothers had inadequate practices before program implementation

Concerning the correlation between the studied mothers' total reported practices and their total knowledge, the present study revealed that there was a positive correlation. This emphasized that the Bite-Sized Teaching Sessions implementation can be effective in improving knowledge that led to improve practices. This result was supported by the study performed by **McGill et al., (2019)** who stated that there was a very high statistically significant correlation between mothers' knowledge and mothers' practices. Also, result was supported by **Brown et al., (2016)** who found that a statistical correlation between the total knowledge and practice scores of the family caregivers.

Conclusion:

Based on the findings of the present study, it could be concluded that:

Bite-Sized Teaching Sessions implementation had statistically significant positive in improving the studied mothers' knowledge & reported practice regarding caring

of their children with MMA. Moreover, there was a positive correlation between mothers' knowledge about the care of children with MMA and their reporting practices.

Recommendations:

The following recommendations can be suggested based on the results and conclusion of the present study:

- Continuous Bite-Sized Teaching Sessions should be provided for all mothers caring of children with methylmalonic acidemia .
- Nurses should play a key role in the health teaching and counseling mothers about the care of their children with
- An illustrated booklet about MMA should be available as reference to all mothers caring of children with methylmalonic acidemia

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References

- Almasi, T.; Guey, L.T.; Lukacs, C.; Csetneki, K.; Voko, Z.; Zelei, T. (2019):** Systematic literature review and meta-analysis on the epidemiology of methylmalonic acidemia (MMA) with a focus on MMA caused by methylmalonyl-CoA mutase (mut) deficiency. Orphanet. J. Rare Dis. 14, 84. [CrossRef]
- Bell, C.G., Ledley, F.D., Lumetta, M.R., Zoghbi, H.Y., VanTuinen, P., Ledbetter, S.A. and Ledbetter, D.H. (2018):** Mapping of human methylmalonyl CoA mutase (MUT) locus on chromosome 6. American journal of human genetics; 42(6):839-46.
- Brown, A., Crowe, L., Boneh, A. and Anderson, V. (2016):** Parent coping and the behavioral and social outcomes of children diagnosed with inherited metabolic disorders, In JIMD Reports, Volume 31 (pp. 29-36).Doi: 10. 1007/8904_2016_544 Springer, Berlin, and Heidelberg

- Chapman K., Gramer G., Viall S., & Summar M., (2018):** Incidence of maple syrup urine disease, propionic acidemia, and methylmalonic aciduria from newbornscreening data. *Mol Genet Metab Rep.*;15:106–9.
- Chu T., Chien Y.,& Lin H., (2019):** Methylmalonic acidemia/propionic acidemia - the biochemical presentation and comparing the outcome between liver transplantation versus non-liver transplantation groups. *Orphanet J Rare Dis.*;14(1):73.
- Dobson, C.M., Wai, T.,Leclerc, D., Wilson,A., Wu, X. and Dore, C. (2019):** Identificationof the gene responsible for the cblA complementation group of vitamin B12responsive MMA based on analysis of prokaryotic gene arrangements. *Proceedings of the National Academy of Sciences of the United States of America*; 99(24):15554-9.
- Evans, S., Preston, F., Daly, A., Ashmore, C., Holden, C.and MacDonald, A. (2019):** Home enteral tube feeding in children with inherited metabolic disorders: a review of long-term carer knowledge and technique. *J Hum Nutr Diet.*; 25:520–525. Doi: 10.1111/j.1365-277X.2012.01274.x.
- Genetics home Reference (2019):** Methylmalonic academia. Availableon: [http:// www. ghr. nlm. nih. gov/ condition/ methylmalonic-acidemia.](http://www.ghr.nlm.nih.gov/condition/methylmalonic-acidemia) Accessedon Oct1, 2019.
- Gruenbaum, S., Dhaher, R., Rapuano, A., Zaveri, H., Tang, A., de Lanerolle, N. and Eid, T. (2019):** Effects of Methylmalonic Acidemia Supplementation on Spontaneous Seizures and Neuronal Viability in a Model of Mesial Temporal Lobe Epilepsy. *Journal of neurosurgical anesthesiology*, 31(2): 247-256.
- Haijes H.A., van Hasselt P.M., Jans J.J., & Verhoeven-Duif N.M., (2019):** Pathophysiology of propionic and methylmalonic acidemias. Pt 2: Treatment strategies. *J Inherit Metab* 42(5):745-761.
- Heringer J, Valayannopoulos V, & Lund AM,(2016):** Impact of age at onset and newborn screening on outcome in organic acidurias. *J Inherit Metab Dis.* ;39:341–53.
- Hyman, D.B., Saunders, A.M.and Tanaka, K. (2018):** A rapid spot test for urinary methylmalonic acid collected on ion-exchange filter paper. *Clinica Chimica Acta*; 132(3):219-27.
- Kimberly, D., Jennifer, O., Golub, L., Akbashev, K & Klein, R. (2021):** The micro revolution: effect of Bite-Sized Teaching (BST) on learner engagement and learning in postgraduate medical education. *BMC Medical Education* (2021) 21:69.Retrieved from [https:// bmcmededuc.biomedcentral.com/](https://bmcmededuc.biomedcentral.com/)
- Lerner-Ellis, J.P., Tirone, J.C., Pawelek, P.D., Dore, C., Atkinson, J.L. and Watkins, D. (2020):** Identification of the gene responsible for methylmalonicaciduria and homocystinuria, cblC type. *Nature genetics*; 38(1):93-100.
- Manoli, I., Sloan, J. L. and Venditti, C. P. (2016):** Isolated methylmalonic acidemia. In *GeneReviews*® [Internet]. University of Washington, Seattle.
- Marquard J, El Scheich T, Klee D, Schmitt M, Meissner T,& Mayatepek E, (2011) :** Chronic pancreatitis in branched-chainorganic acidurias: a case of methylmalonic aciduria and anoverview of the literature. *Eur J Pediatr*; 170:241-5.
- McCrory, N., Edick, M., Ahmad, A., Lipinski, S.,Schwoerer, J., Zhai, S.,Justice, K., Cameron, C., Berry, S., Pena, L., (2017) :** Comparison of methods of initial ascertainment in 58 cases of propionic acidemia enrolled in the inborn errors of metabolism information system reveals significant differences in time to evaluation and symptoms at presentation. *J. Pediatr.* , 180, 200–205.
- McGill, B., Wakefield, C., Vetsch, J., Barlow-Stewart, K., Kasparian, N., Patenaude, A., and Tucker, K. (2019):** Children and young people's understanding of inherited conditions and their attitudes towards

- genetic testing: A systematic review, *Clinical genetics*; 95(1): 10-22.
- McLaughlin, P., Hinshaw, J., and Stringer, A. (2017):** Methylmalonic Acidemia (MMA): a case with long-term follow-up after liver transplantation. *The Clinical neuropsychologist*, 27(7), 1199-1217.
- Morrow, G., Barness, L.A., Cardinale, G.J., Abeles, R.H., & Flaks, J.G. (2020).** Congenital MMA: enzymatic evidence for two forms of the disease. *Proceedings of the National Academy of Sciences of the United States of America*. 1969; 63(1):191-7.
- National Centre for Inherited Metabolic Disorders, (2019):** Metabolic Diet Available at <http://metabolic.ie/patient-family-information/metabolic-conditions/methylmalonic-acidaemia/>
- Oberholzer V., Levin B., Burgess E., & Young W., (1967):** Methylmalonicaciduria. An inborn error of metabolism leading to chronic metabolic acidosis. *Arch Dis Child*; 42:492-504.
- Peters, H.L., Nefedov, M., Lee, L.W., Abdenur, J.E., Chamoles, N.A., and Kahler, S.G. (2019).** Molecular studies in mutase-deficient (MUT) methylmalonicaciduria: identification of five novel mutations. *Human mutation*; 20(5):406.
- Radmanesh, A., Zaman, T., Ghanaati, H., Molaei, S., Robertson, R., and Zamani, A. (2018):** "Methylmalonic Acidemia: Brain imaging findings in 52 children and a review of the literature". *Pediatric Radiology*; 38(10): 1054- 1061.
- Rezvani I., (2007):** Defects in metabolism of amino acids. In: Kliegman RM, Behrman RE, Jenson HB, Stanton BF, editors. *Nelson textbook of paediatrics*. 18th ed. Philadelphia; Elsevier.; p. 85.
- Robinson, D., and Drumm, L. A. (2018).** Methylmalonic Acidemia: A standard of nursing care. *Pediatric nursing*, 27(3), PP: 255-255.
- Stoke O, Jellum E, Eldjarn L, & Schnitler R. (1973):** The occurrence of beta-hydroxy-n-valeric acid in a patient with propionic and methylmalonic acidemia. *Clin Chim Acta*; 45:391-401.
- Suormala, T., Baumgartner, M.R., Coelho, D., Zavadakova, P., Kozich, V., and Koch, H.G. (2018).** The cblD defect causes either isolated or combined deficiency of methylcobalamin and adenosylcobalamin synthesis. *The Journal of biological chemistry*. 279(41):42742-9.
- Tejada-Ortigosa, E.M., Flores-Rojas, K., Moreno-Quintana, L., and Munoz-Villanueva, M. C. (2019).** Health and socio-educational needs of the families and children with rare metabolic diseases: Qualitative study in a tertiary hospital. *A Pediatr (Barc)*; 90(1):42-50.
- Young, J and Van Merriënboer, J. (2014):** Cognitive load theory: implications for medical education: AMEE guide no. 86. *Med Teach*. 2014; 36(5):371–84.
- Zwickler, T., Lindner, M., Aydin, H.I., Baumgartner, M.R., Bodamer, O.A., Burlina, A.B., Das, A.M., DeKlerk, J.B., Gokcay, G., Grunewald, S., Guffon, N., Maier, E.M., Morava, E., Geb, S., Schwahn, B., Walter, J.H., Wendel, U., Wijburg, F.A., Mueller, E., Kölker, S., and Hörster, F. (2018).** Diagnostic work-up and management of patients with isolated methylmalonic acidurias in European metabolic centres. *J Inherit Metab Dis*; 31:361–367. Doi: 10.1007/s10545-008-0804-2.