

Functional Assessment of Anorexia/Cachexia Therapy among Egyptian Children with Cancer Disease after Nutritional Management

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ABSTRACT

Background: Nutrition plays a deciding role and a key factor in children with cancer and can influence their outcome. It is essential for appropriate growth and development and a critical component in the optimization of clinical outcomes. **Objective:** This study aimed to improve the nutritional status of children and evaluate the impact of nutritional counseling and support for these children with cancer.

Patients and Methods: This interventional study was performed in the Oncology Pediatric Department, at the Zagazig University Children's Hospital for the period from February to August 2021. The study included 54 pediatric cancer patients who will start chemotherapy. **Results:** there were no statistically significant differences between the studied groups according to the Patient-Generated Subjective Global Assessment (PG-SGA) scale at a baseline or 45th day but there was a statistically significant increase in the frequency of type A among the interventional group and a statistically significant increase in C and D type among the control group at 90th day. The interventional group showed a statistically significant increase in type A at 90th day compared to baseline. There was a statistically significant increase in the mean physical, social, functional domain, anorexia/cachexia subscale (A/CS), and total FAACT scores among the interventional group compared to the control group.

Conclusion: nutritional intervention is mandatory for cancer patients to prevent cachexia and improve their physical and social state. Functional assessment of anorexia/cachexia therapy (FAACT) scale and anorexia/cachexia subscale (A/CS) have good content validity and can be used for characterizing the effect of nutritional intervention and treatment of anorexia symptoms and/or anorexia-related concerns in patients with cancer.

Keywords: Children Cancer, Nutritional Status, Impaired quality of life, PG-SGA scale, FAACT.

INTRODUCTION

Children's cancer is an illness related to severe morbidity and mortality. Diagnosed children with specific cancer types develop nutritional-related problems more often than others. Nutritional status in those children at diagnosis and during therapy is important to maintain the appropriate functioning of vital organ systems. Respiratory, cardiac, gastrointestinal, hepatic, pancreatic, renal, hematopoietic, and lymphoreticular dysfunction has been documented in malnutrition situations ⁽¹⁾.

Nutrition plays a deciding role and a key factor in children with cancer and can influence their outcome. It is essential for appropriate growth and development and a critical component in the optimization of clinical outcomes ⁽²⁾.

The importance of nutrition in children with cancer is indisputable. Nutrition influences most cancer control parameters in pediatric oncology, including prevention, epidemiology, biology, treatment, supportive care, recuperation, and survival. It is widely recognized that the nutritional status (NS) of children diagnosed with and treated for cancer will be probably affected during the disease ⁽³⁾.

The Subjective Global Assessment (SGA) is a validated screening tool for malnutrition in hospitalized patients and the PG-SGA has been adapted for cancer patients. The PG-SGA incorporates questions for patients regarding weight history, caloric intake, functional status and requires additional assessments by a healthcare professional including

comorbid conditions, fever, and medications such as steroids which impact nutrition as well as a detailed physical examination of seven muscle groups, three adipose depots, and evidence of edema at three sites ⁽⁴⁾.

Quality of life (QoL) for children diagnosed with cancer decreases due to chemotherapy, radiotherapy, surgical interventions, prolonged hospitalization, side effects of treatments, being isolated from the society, physical and emotional problems, changes in the child's position, and absence of role within the family and society, disruption of school life, lack of support systems and coping methods. Early and effective treatment is essential for successful cancer treatment and high QoL ⁽⁵⁾.

Assessing QoL is the critical endpoint in cancer patients with cachexia. The functional assessment of the anorexia/cachexia therapy (FAACT) scale consists of the functional assessment of cancer therapy general (FACT-G) scale and the anorexia/cachexia subscale (AC/S) and is a QoL scale specific for cancer patients with cachexia ⁽⁶⁾.

The current study aimed to improve the nutritional status of children and evaluate the impact of nutritional counseling and support for these children with cancer.

PATIENTS AND METHODS

This interventional study enrolled 54 pediatric oncology inpatients (age 2 to 18 years) in the Oncology Unit, at the Department of Pediatrics, Zagazig University Children's Hospital between

February 2021 and August 2021 and started chemotherapy treatment.

Inclusion criteria; Children aged 2 to 18 years of both sexes with newly diagnosed malignancy and undergoing treatment in the Pediatric Oncology Department.

Exclusion criteria; Patients who did not give consent. Presence of any other disease that may affect the child's nutritional status as diabetes mellitus or renal failure.

Ethical consent:

An informed written consent form was obtained from all patient's parents or their relatives. The purpose of the study was explained to them and the protocol of the study was approved by the Ethical Committee of Zagazig University Hospital. This work was carried out following The Code of Ethics of the World Medical Association (Declaration of Helsinki) for studies involving humans.

Patients were divided into two groups:

The interventional group included 27 cancer patients starting the chemotherapy and completing the nutritional intervention. They were 14 (51.9%) males and 13 (45.8%) females with a mean age of (7.97±3.32 years) ranging between 3.5 – 15 years old.

The control group included 27 cancer patients starting the chemotherapy and refused to complete the nutrition intervention. They were 19 (70.4%) males and 8 (29.6%) females with a mean age of (7.19±3.09 years) ranging between 2 – 13 years old.

Tools for data collection:

Subjective Global Assessment (SGA):

The subjective assessment consisted of an adapted version of the PG-SGA with some minor modifications to simplify the instrument, and the classification of mild malnutrition was added. It was completed with information provided by the patients and parents ⁽⁷⁾.

For the global assessment categories of the nutritional status, patients were assigned to well-nourished (PG-SGA A, at least three sections rated as normal), mildly malnourished (PG-SGA B, at least three sections rated as mild malnutrition), moderately malnourished (PG-SGA C, at least three sections rated as moderate malnutrition) and severely malnourished (PG-SGA D, at least three sections rated as severe malnutrition). It should be mentioned that the PG-SGA score and the subjective global rating are related, but are independent assessment and triage systems.

Questioner Instrument of Healthy Related-Quality of Life (HR-QoL) after and before Nutritional Intervention Treatment:

Parents of 54 patients were interviewed face to face; the latter interviews were conducted by the researcher trained in the management of pediatric cancer patients to complete the PedsQoL™ 3.0 booklet ⁽⁸⁾.

The PedsQoL™ 3.0 Cancer Module—designed to measure HR-QoL dimensions specifically tailored for pediatric cancer—was the instrument in use. It investigated 8 domains with a total of 27 items for the whole module; 2 items for pain and hurt, 3 for each procedural anxiety, treatment anxiety, worry, perceived physical appearance, and communication, whereas 5 items for each nausea and cognitive problems.

Functional Assessment of Anorexia/Cachexia Therapy (FAACT):

During the study period, and according to detection of anorexia, diagnostic instruments were performed by using the Anorexia/Cachexia Subscale (A/CS) of the Functional Assessment of Anorexia/Cachexia Therapy (FAACT) questionnaire.

To examine anorexia, patients were asked to fill out the FAACT– A/CS (4th version, Dutch) for appetite before starting chemotherapy. These instruments were presented to the patients on paper and assistance was offered if required. Both instruments were filled out based on the patients' experience regarding their appetite during the last 7 days.

The 12 items of the FAACT–A/CS (9) were scored on a five-point Likert scale (0 = not at all, 1 = a little bit, 2 = somewhat, 3 = quite a bit, and 4 = very much). The scores of negatively worded items were reversed. The sum score ranges from 0 to 48, whereby a lower score indicates less appetite. For scoring the FAACT–A/CS, the FACIT manual was applied ⁽¹⁰⁾.

Follow up: (1) By patients generated subjective global assay (PG-SGA) ⁽⁷⁾. (2) The follow-up was performed up to 3 months (every 2 weeks). (3) Quality of life at 0 and 3 months: using quality of life tools ⁽⁷⁾. (4) Anorexia questionnaire (FAACT/ACS) ⁽⁴⁾.

Statistical Analysis

The data were entered in SPSS (version 22.0, 2011; SPSS, Inc., Chicago, IL). Baseline variables were analyzed by descriptive statistics. A comparison of proportions was performed with chi-square and Fisher's exact tests. Comparison of medians between the two groups at baseline and 3 months were performed with the Mann-Whitney U test. We will impute the missing values using the "last observation carried forward" method and then carried out an intention-to-treat analysis. Data analysis was performed using the student t-test. Quantitative data were expressed as mean ± SD (Standard deviation). Independent samples t-test was used to compare the two independent groups of normally distributed variables (parametric data). P-value < 0.05 was considered significant.

RESULTS

Table (1) showed that there were no statistically significant differences between the studied groups regarding age, sex distribution or family size, and type of cancer.

Table (1): Demographic data of the studied groups

Variable	Interventional Group (n=27)		Control Group (n=27)		Sign. Test	P value
Age: (years) Mean ± SD Range	7.97±3.32 3.5-15		7.19±3.09 2-13		t = 0.90	0.37 NS
	No	%	No	%		
Sex: Female Male	13 14	48.1 51.9	8 19	29.6 70.4	$\chi^2 = 1.95$	0.16 NS
Family size: 4-5 6-7 >7	18 7 2	66.7 25.9 7.4	16 11 0	59.2 40.7 0	$\chi^2 = 3.01$	0.22 NS
Cancer type: Acute lymphocytic leukemia Burkitt's lymphoma Hodgkin lymphoma Neuroblastoma	19 2 3 3	70.4 7.4 11.1 11.1	15 7 0 5	55.6 25.9 0 18.5	$\chi^2 = 6.75$	0.08 NS
Type of treatment: Chemotherapy	27	100	27	100	----	----

Table (2) showed that there were no statistically significant differences between the studied groups on the PG-SGA scale at the baseline or 45th day but there was a statistically significant increase in the frequency of type A among the interventional group than the control group and a statistically significant increase in C and D type among the control group at 90th day. The interventional group showed a statistically significant increase in type A at 90th day compared to baseline.

Table (2): Frequencies of Patient-Generated Subjective global assessment (PG-SGA) scale among the studied groups

PG-SGA scale	Interventional Group (n=27)		Control Group (n=27)		χ^2	P value
	No	%	No	%		
Baseline: A B C D	10 8 6 3	37.1 29.6 22.2 11.1	9 9 5 4	33.3 33.3 18.5 14.8	0.35	0.59 NS
45th day: A B C D	12 9 4 2	44.4 33.3 14.8 7.4	6 9 7 5	22.2 33.3 25.9 18.5	4.10	0.25 NS
90th day: A B C D	15 9 3 0	55.6 33.3 11.1 0	8 7 8 4	29.6 25.9 29.6 14.8	8.56	0.03*
Fr	4.05		1.12			
P	0.04*		0.23 NS			

χ^2 : Chi-square test; Fr: Fridman test; NS: Non-significant (P>0.05); *: Significant (P<0.05)

A= Well-nourished; B= Mildly malnourished; C= Moderately Malnourished; D= Severely malnourished

Table (3) showed that there was a statistically significant increase in dietitian visits and administration of oral nutritional supplements among the interventional group compared to the control group.

Table (3): Nutritional intervention among the studied groups

Variable	Interventional Group (n=27)		Control Group (n=27)		Sign. Test	P-value
	No	%	No	%		
Dietitian visit:	20	74.1	6	22.2	$\chi^2=14.54$	<0.001**
Administration of oral nutritional supplements(ONS) :	20	74.1	5	18.5	$\chi^2=16.67$	<0.001**
Nasogastric tube insertion:	16	59.3	3	11.1	$\chi^2=13.72$	<0.001**
Time (days) to any nutritional intervention Median (IQR)	22 (3 – 90)		14 (2 – 85)		MW=2.03	0.04*
Time (days) to nasogastric tube insertion intervention Median (IQR)	16 (2 – 65)		8 (2 – 64)		MW=2.13	0.02*
Time (days) to initiating oral supplements intervention Median (IQR)	22 (3 – 70)		12 (1 – 52)		MW=2.20	0.02*

MW: Mann Whitney test χ^2 : Chai square test IQR: Interquartile range NS: Non-significant (P>0.05) *: Significant (P < 0.5)

Table (4) showed that there was no statistically significant difference between the interventional and control groups in QoL domain score before intervention.

Table (4): Scores of health related-quality of life (HR-QoL) before intervention and its subscales among the studied groups

Domain	Interventional Group (n=27)	Control Group (n=27)	MW/t	P-value
Pain and hurt: Mean ± SD Range	66.02±11.45 0.3-99.42	65.56±12.19 0.4-99.20	0.05	0.95 NS
Nausea: Mean ± SD Range	62.47±13.13 0.0-98	60.04±14.7 0.2-99	0.48	0.62 NS
Procedural anxiety: Mean ± SD Range	55.41±11.46 0.0-100	55.11±11.25 0.0-100	0.03	0.97 NS
Treatment anxiety: Mean ± SD Range	64.91±12.34 0.0-100	63.41±13.28 0.0-100	0.26	0.79 NS
Worry: Mean ± SD Range	40.07±9.58 0.0-100	38.41±8.28 0.0-100	0.58	0.56 NS
Cognitive problems: Mean ± SD Range	66.27±13.67 0.0-100	64.41±12.25 0.0-100	0.43	0.67 NS
Perceived physical appearance: Mean ± SD Range	45.78±11.04 0.0-100	43.41±9.23 0.0-100	0.47	0.64 NS
Communications: Mean ± SD Range	66.07±15.38 0.0-100	62.41±14.06 0.0-100	0.64	0.51 NS
Total QoL Mean ± SD Range	62.18±11.34 20.2-96.14	60.56±12.19 19.4-95.20	0.51	0.61 NS

SD: Standard deviation t: Independent t-test MW Mann Whitney test NS: Non-significant (P>0.05)

Table (5) showed that there was a statistically significant increase in the mean score of nausea, worry, cognitive problems, perceived physical appearance, communication domains score, and total QoL among the interventional group compared to controls.

Table (5): Scores of health related-quality of life (HR-QoL) after intervention and its subscales among the studied groups

Domain	Interventional Group (n=27)	Control Group (n=27)	MW/t	P- value
Pain and hurt: Mean ± SD Range	67.90±13.9 0.3-100	65.56±12.19 0.4-99.20	0.17	0.87 NS
Nausea: Mean ± SD Range	70.52±16.16 0.0-100	60.04±14.7 0.2-99	2.03	0.04*
Procedural anxiety: Mean ± SD Range	56.59±14.99 0.0-100	55.11±13.25 0.0-100	0.16	0.87 NS
Treatment anxiety: Mean ± SD Range	64.89±13.83 0.0-100	63.41±12.28 0.0-100	0.24	0.81 NS
Worry: Mean ± SD Range	45.89±12.83 0.0-100	38.41±9.28 0.0-100	2.36	0.02*
Cognitive problems: Mean ± SD Range	73.89±17.64 0.0-100	64.41±16.25 0.0-100	2.05	0.04*
Perceived physical appearance: Mean ± SD Range	55.89±12.71 0,0-100	43.41±8.23 0.0-100	2.41	0.01*
communications: Mean ± SD Range	75.89±17.39 0.0-100	62.41±14.06 0.0-100	2.28	0.03*
Total QoL Mean ± SD Range	69.30±13.9 26.3-98	60.56±12.19 19.4-95.20	2.46	0.02*

SD: Standard deviation t: Independent t-test MW Mann Whitney test

NS: Non-significant (P>0.05) *: Significant (P<0.05) **: Highly significant (P<0.001)

Table (6) showed that there was a statistically significant increase in the mean physical, social, functional domain, anorexia/cachexia subscale (A/CS), and total FAACT scores among the interventional group compared to the control one.

Table (6): Functional Assessment Anorexia/Cachexia Therapy (FAACT) scale among the studied groups

Weight	Interventional Group (n=21)	Control Group (n=20)	T	P-value
Physical well being:				
Mean ± SD	16.63±3.9	13.56±2.19	3.57	0.001*
Range	11-20	11-20		
Social well being:				
Mean ± SD	20.52±1.16	16.04±2.7	7.94	<0.001**
Range	18-22	12-18		
Emotional well being:				
Mean ± SD	11.59±3.99	11.11±2.15	0.55	0.58 NS
Range	8-18	9-16		
Functional well being:				
Mean ± SD	17.89±2.83	15.41±1.28	4.15	<0.001**
Range	14-22	14-18		
FAACT- G:				
Mean ± SD	66.63±11.88	56.12±8.32	3.77	<0.001**
Range	51-82	46-72		
Anorexia Cachexia subscale:				
Mean ± SD	29.48±3.13	25.41±2.53	5.26	<0.001**
Range	25-36	20-28		
FAACT score:				
Mean ± SD	62.52±7.8	55.48±5.08	3.90	<0.001**
Range	45-71	50-68		

SD: Standard deviation t: Independent t-test

NS: Non-significant (P>0.05) *: Significant (P<0.05) **: Highly significant (P<0.001)

DISCUSSION

Nutrition plays a deciding role and a key factor in children with cancer and can influence their outcome. It is essential for appropriate growth and development and a critical component in the optimization of clinical outcomes (2).

To our knowledge, the current study is the first to assess the nutritional intervention for children with cancer undergoing chemotherapy treatment in Oncology Pediatric Department, at Zagazig University Children's Hospital.

The patients in our study were 14 (51.9%) males and 13 (45.8%) females with a mean age of (7.97±3.32 years), The family size ranging between 4-5 persons was recorded in 18 (66.7%) patients. On the other hand, the control group included 27 cancer patients, 19 (70.4%) of them were males and 8 (29.6%) were females with a mean age of (7.19±3.09 years). The family size ranging from 4-5 people was found in 16 (59.2%) of patients. Regarding the clinical manifestation findings, the current study revealed that 19 (70.4%) patients in the interventional group had acute lymphocytic leukemia, followed by 3 (11.1%) had Hodgkin lymphoma; and 3 (11.1%) had neuroblastoma, while 2 (7.4%) cases had Burkitt's lymphoma. While in the control group the majority of cases 15 (55.6%) had acute lymphocytic leukemia, followed by 7 (25.9%) had non-Hodgkin Lymphoma (Burkitt Lymphoma); and 5 (18.5%) had

neuroblastoma. There were no statistically significant differences between the studied groups regarding age, sex distribution or family size, or type of cancer. These findings agreed with the study of Gallo *et al.* (1) Viani *et al.* (2) and Dos Maia Lemos *et al.* (11).

The study of Khalil *et al.* (12) demonstrated that the socio-demographic characteristics of the studied children with cancer show that their ages ranged between 3 and 12 years with a mean of 7.6±3.1 years. About two-thirds of them were males (64.8%). However, Totadri *et al.* (7) conducted and analyzed 50 patients—25 cancer patients in the study arm and 25 in the control arm. The median age of them was 4.5 years, and the male to female ratio was 2:1.

Moreover, Dos Maia-Lemos *et al.* (11) conducted 1154 pediatric cancer patients; 53.09% were males with a mean age of 10.24 years. The distribution of types of cancer to age and gender of the patients are described as the following: 256 (22.2) had central nervous tumor, followed 204 (17.6) had Leukemias, followed 119 (10.3) had lymphoma, followed 54 (4.7) had neuroblastoma, followed 47 (4.1) had Wilms tumor and others.

Regarding the frequencies of Patients Generated Subjective global assessment (PG-SGA) therapy scale at baseline and different time follow-up, the current study revealed that there were no statistical significance differences between the studied groups in PG-SGA scale at base line or 45th day; but there was a

statistical significance increase in frequency of type A among interventional group more than control group and a statistical significance increase in C and D type among control group at 90th day. Interventional group showed statistical significance increase in type A at 90th day compared to baseline. In accordance, the study of **Vazquez de la Torre et al.**⁽¹³⁾ confirmed our results.

The study of **Afonso et al.**⁽¹⁴⁾ conducted 579 pediatric cancer patients. According to Pediatric subjective global nutritional assessment (PSGNA) data at admission 66.3% were well nourished, 33.7% were malnourished (27.2%) or severely malnourished (6.5%). Considering the region, the southeast presented a higher percentage of severely malnourished children (8.5%), according to the PSGNA. They concluded that, PSGNA revealed a high percentage of children with poor nutritional conditions at the time of admission, which may contribute to unfavorable clinical outcomes. The PSGNA seems to be a good alternative for the nutritional evaluation of children with cancer.

Regarding the nutritional intervention treatment among the studied groups, the current study demonstrated a statistically significant increase in dietitian visit and administration of nutritional supplements among interventional group compared to control group. These findings were in accordance with **Arezzo di Trifiletti et al.**⁽¹⁵⁾.

The study of **Viani et al.**⁽²⁾ consisted of hospitalized patients who were intensively monitored by the nutrition team, or who were referred to the nutrition outpatient clinic at diagnosis. Thus, the patients included in this study received nutritional care from diagnosis and had their nutritional condition monitored closely and managed intensely, including a nutritional intervention, when required. This may partially explain the lack of impact of the nutritional status at diagnosis on the overall survival, since nutritional status has been shown to be a modifiable risk factor, although to date, only for patients with ALL^(16, 17). In 2012, a nutritional therapy algorithm and protocol was developed and implemented by the institution nutrition team, which improved care systematization and clinical support for patients and may well have impacted positively on overall survival. These points to the importance of an established nutrition program as part of the treatment of children with cancer⁽¹⁸⁾.

According to scores of health related-quality of life (HR-QoL) and its subscales before and after nutritional intervention treatment among the studied groups, the current study revealed that there was no statistical significance difference between among interventional group and control group in QoL score before intervention. However, after nutritional intervention treatment, there was a statistical significance increase in mean nausea, worry, cognitive problems, perceived physical appearance,

communication domains score and total QoL among interventional group compared to control group.

Abu-Saad Huijer et al.⁽¹⁹⁾ clarified that the total cancer scale score was 72.75 (SD=15.47) indicating acceptable HR-QoL. Five of the eight subscale scores were greater than 70. The highest scores among the five subscales were communication (score=86.56; SD=20.77) and cognitive problems (score=80.47; SD=21.43). The lowest scores denoting more problems as viewed by the parents were found in nausea (score=55.22; SD=25.37), treatment anxiety (score=67.74; SD=30.17) and worry (score=68.62; SD=28.27).

Our findings also were to great extent like a Chinese study, where parents reported their children who were receiving cancer treatments to have more problems in nausea, worry, treatment anxiety, and procedural anxiety⁽²⁰⁾.

According to the questionnaire of peds-FAACT scale and A/CS scores which performed in children and adolescents (age 7–17) among interventional group (n = 21) compared to control group (Refusal) (n = 20), the current study demonstrated a statistical significance increase in mean physical, social, functional domain, A/CA and total FAACT score among interventional group compared to control group. These findings were agreed with **Lai et al.**⁽²¹⁾.

In the current study, we have developed a scale that has good and stable psychometric properties across children between the ages of 7 and 17. The resultant six-item peds-FAACT scale had good internal consistency, met assumptions of unidimensional measurement, and demonstrated stable performance across gender, age, and cancer type.

The study of **Lai et al.**⁽²¹⁾ aimed to test the psychometric properties of a newly developed pediatric Functional Assessment of Anorexia and Cachexia Therapy (peds-FAACT) for children with cancer. Ninety-six patients (ages 7-17 years) receiving cancer treatment and their parents were asked to complete the 12-item peds-FAACT. The authors implemented both classical test theory and item response theory to evaluate the agreement between parents and patients, internal consistency and unidimensionality of the scale, and stability of items across subgroups. As a result, a patient-reported six-item scale was recommended as the core measure for all pediatric patients with cancer and four additional peripheral items were recommended for adolescent patients. The author concluded that, peds-FAACT demonstrated good psychometric properties, differentiated patients with different functional performance status, and were determined to be a useful tool for future clinical trials.

CONCLUSION

Nutritional intervention is mandatory for cancer patients to prevent cachexia and improve their

physical and social status and improve their quality of life. Functional assessment of anorexia/cachexia therapy (FAACT) scale and anorexia/cachexia subscale (A/CS) have good content validity and can be used for characterizing the effect of nutritional intervention and treatment on anorexia symptoms and/or anorexia-related concerns in patients with cancer.

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