The Effects of Nutritional Status on Treatment Outcomes of Pediatric Oncology Patients: A Systematic Review

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ABSTRACT

Learning Outcome: To review current research determining associations between nutritional status and treatment outcomes in pediatric cancer.

Background: In childhood cancer, malnutrition has been proposed to increase complications and reduce survival. Although research has been done to associate how treatment can cause malnutrition, understanding of the relationship between malnutrition and patient outcomes is limited.

Methods: A systematic review was conducted using five databases: CINAHL, Health Source, Academic Search Complete, Wiley Online Library, and SpringerLink. Key terms included were "childhood cancer," "nutrition," "outcomes," and related terms. In total, 584 articles were found. Inclusion criteria covered: 2011-2021 publications, peer-reviewed articles, English publications, and a focus on pediatric cancer and nutritional status. Data extraction was completed using the AND Evidence Analysis Manual.

Results: Eight articles were included in this review. Findings suggest that malnutrition is associated with lower survival, infections, and complications in childhood cancer patients. Some studies suggested that undernutrition was associated with decreased survival. Malnutrition may also affect relapse, hospital readmission, and length of stay.

Discussion: All eight studies were designed as observational cohort studies and two were prospective. Further research should be conducted to determine the association between nutritional status and treatment outcomes. Prospective longitudinal studies may be beneficial to improve research in this area.

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INTRODUCTION

- In healthcare, malnutrition among hospitalized children is associated with longer lengths of stay, higher infection rates, and adverse clinical outcomes (Carvalho-Salemi et al., 2017).

- Although it is well documented that pediatric oncology treatments may lead to malnutrition, research on the role of nutritional assessment to predict clinical outcomes is lacking (Carvalho Ventura et al., 2019).

- The aim was to find associations between nutritional status and survival rates, infections, and other health-related complications of pediatric oncology patients.

METHODS

Search Strategy: A systematic process was used to select relevant studies for the final review.

- The first step was choosing the five databases. Initial eligibility filters were 2011-2021 publication and peer-reviewed articles.

- Inclusion criteria was then expanded to include English publications and articles with a focus on pediatric cancer and nutritional status.

- The distillation phase included abstract and title exclusions and removal of duplicates (see Figure 1).

Data Extraction and Synthesis: The next phase independent review of the articles.

- Each was rated for relevance and validity using the checklist from the Academy of Nutrition and Dietetics Evidence Analysis Manual (AND, 2021).

- Data was extracted into a table to be used in the final analysis (see Table 1) .
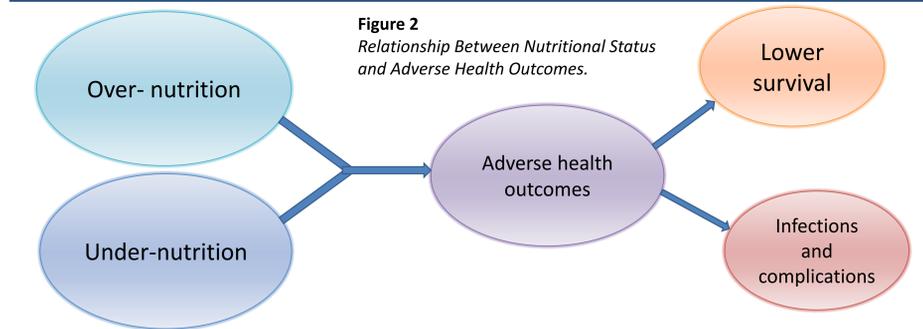
RESULTS

- A total of 584 articles were found meeting the initial filters, 29 full-text articles were reviewed, and 8 articles were included.
- All were cohort studies, two were prospective in design, six were retrospective, and all but one were longitudinal.
- Several different types of cancer were included in the data.
- The objective of all studies was to determine if nutrition status had any effects on health-related outcomes.
- The descriptive characteristics were used to analyze the data by systematically comparing the individual study results (see Table 1).
- Follow-up time period ranged from 12 hours- 5 years after initial nutrition status measurements were taken.
- All studies used either BMI alone, or a combination of BMI and other anthropometric measurements to determine nutritional status.
- Malnutrition was associated with lower survival rates in five of the studies and with infection or complications in seven of the studies.
- Only one study found no significant association between malnutrition and survival or complications.
- Studies that had a longer follow-up time, $\geq$ 3 months showed stronger associations between malnutrition and survival or complications.
- Retrospective components, including strict inclusion criteria and complete medical files were followed adequately.

Figure 1
PRISMA Diagram to Show Article Selection Process

Table 1
Summary of studies used in systematic analysis.

1st Author, Year	Population (n=2,509)	Independent Variable (Measurements)	Dependent Variable (Outcomes Observed)	Follow-up	Results/Outcomes (p-values)	Country
Loeffen et al., 2014	Child 0-18 y.o. (n=269)	Nutritional Status (BMI and % wt. loss)	Prognosis (infection and overall survival rates, FN episodes)	Dx, and 3, 6, and 12 months	Malnourished pts. showed worse survival than well-nourished (p=0.004). Weight loss more than 5% related to higher FN episodes (p=0.012).	The Netherlands
Pribnow et al., 2017	6 months- 18 y.o. (n=282)	Nutritional Status (wt., ht., BMI, MUAC, TSFT, serum albumin)	TRM, abandonment of therapy, relapse, mortality, and EFS	Dx and during first 90 days of tx	Malnutrition associated with severe infection (p=0.033), TRM on more days (p=0.023), inferior EFS (p= .049), and abandoned Tx more (p=0.015).	South Africa
Draper et al., 2018	1-12 y.o. (n=77)	Nutritional Status (WFA, HFA, WFH, BMI, MUAC, TSFT, albumin)	Prevalence, frequency, and duration of Tx-related neutropenia	Dx (monitored for episodes during Tx)	Higher rate of neutropenia in malnourished pts. (p=0.032).	Nicaragua
Feng et al., 2021	30 days-18 y.o. admitted to PICU (n=160)	Nutritional Status (WFA, WFH, HFA, MUAC)	Mechanical ventilation, PICU stay, hospital stay, mortality, readmission, infection rate	Within 12-48 hours of admission	No statistically significant associations found between nutritional status and infections, complications, or survival.	China
Burke et al., 2013	2-21 y.o. (n=468)	Nutritional Status (BMI)	Toxicity and survival	12, 24, and 42 weeks	Malnourished pts. trended toward toxicity and inc. LOS (p=0.0615 and p=0.0463). Underweight pts. trended toward inferior survival (p=0.0596).	United States
Altaf et al., 2013	2-20 y.o. (n=710)	Nutritional Status (BMI)	Survival and frequency of treatment-related toxicities	Dx, first 10 weeks of tx, 3 years, 5 years	Renal toxicity higher in high BMI group (p=0.01)Pts. with high BMI had worse survival at 5 years (p=0.005) and 3 years (p=0.05).	United States
Hingorani et al., 2011	0-30 y.o. (n=498)	Nutritional Status (BMI)	Wound complications (infections)	Before tx, 30 days post-tx	Wound infection seen in low BMI pts. (p=0.07). Arterial thrombosis more common in high BMI pts. (p=0.03).	United States
Gurlek-Gokcebay et al., 2015	0-18 y.o. (n=45)	Nutritional Status (BMI, WFA, WFH, MUAC, TSFT)	Biochemical parameters, infectious complications, health-outcomes	3 and 6 months	Infectious complications higher in malnourished pts. (p=.001). Survival was lower in this group (p=.003).	Turkey

DISCUSSION

Figure 2
Relationship Between Nutritional Status and Adverse Health Outcomes.
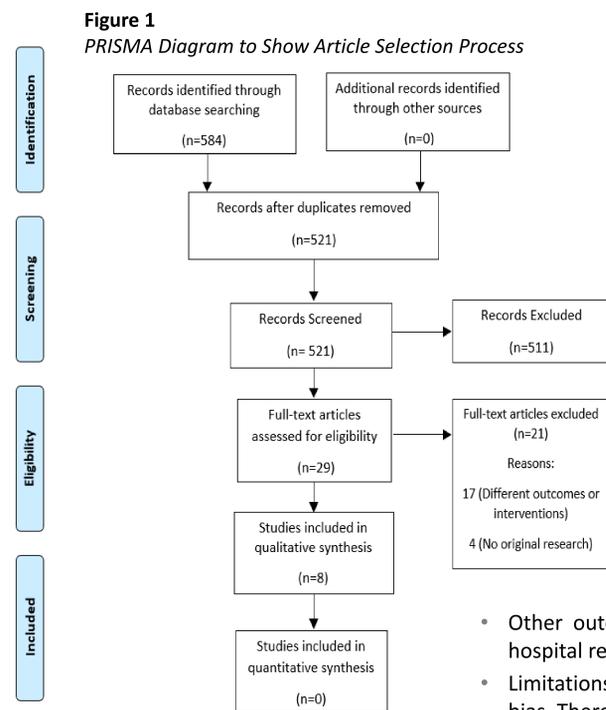
- Results indicate that malnutrition has a more significant association with inferior survival, infections, and complications than adequate nutrition status in childhood cancer, reflecting the findings of other recent research (Barr & Stevens, 2019).
- Longer follow-up periods in observational studies may be more effective when identifying health-outcomes within this population. The studies that had a follow-up time $\geq$ 3 months showed stronger associations with most outcomes.
- Adverse outcomes can be associated with over-nutrition (High BMI), under-nutrition (low BMI), and weight loss during treatment (see Figure 2). Although, most of the studies used did not directly differentiate between under-nutrition and over-nutrition.

- Other outcomes that may be associated with malnutrition include relapse, need for mechanical ventilation, hospital readmission, abandonment, and increased length of stay.
- Limitations of this study include that most of the studies were retrospective so there could have been selection bias. There was also insufficient time during the course to evaluate all possible connections that can be made.
- The data shows the need for more research to be done in this area, specifically prospective, longitudinal studies.
- Evidence supports early nutrition screening and interventions in pediatric cancer

CONCLUSION

- The nutritional status of pediatric cancer patients is and important variable for consideration, before starting treatment.
- Health care teams can learn a lot about the outlook of treatment and disease progression, from nutritional status.
- The effect of outcomes seem to become stronger over time, so early interventions could help in the care of these patients.
- Recruiting a Registered Dietitian as part of the interdisciplinary team would be a good step to address critically ill patients.

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