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Elucidating the Role of Malnutrition in Acute Leukemia Patients and How it Leads to Adverse Events During Hospitalization: An Interesting Study

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Abstract

Background: Malnutrition negatively impacts patients with hematologic malignancies and is considered a poor marker and indicator of prognosis. Our study explored the association between malnutrition and patients hospitalized with acute leukemia, including patients with both acute myeloid and acute lymphocytic leukemia.

Methods: The National Inpatient Sample (NIS) 2019-2020 was analyzed with the use of the International Classification of Diseases, Tenth Revision (ICD-10) codes to identify the patients admitted with the primary diagnosis of Acute Leukemia (that included patients with both Acute Myeloid and Acute Lymphocytic Leukemia). The cohort was further classified into patients who had concurrent malnutrition and those without malnutrition. The association between several outcomes was studied after adjusting for the confounding variables through multivariate regression analysis.

Results: A total of 24855 patients with the primary discharge diagnosis of acute leukemia were included in the study. Among these, 3425(13.7%) were found to have concomitant malnutrition. After adjusting for the confounding variables, patients with malnutrition were found to have significantly increased odds of mortality (OR 2.89, 95% CI: 2.11-3.94, P<0.001). Similarly, the length of stay was increased by 9.1 days, 95% CI: (7.01-11.19), P<0.001 and the total cost of hospitalization was also increased by 177994 USD, 95% CI: (122573-2334152), P<0.001 in patients who had concurrent malnutrition.

Conclusion: Malnutrition is associated with poor outcomes in patients hospitalized with acute leukemia.

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Introduction

Leukemia is a hematologic malignancy that poses a significant challenge due to its rapid proliferation of immature blood cells, affecting individuals of all ages. As of January 1, 2019, there were an estimated 166,412 people with leukemia in the United States, based on diagnoses made between 2014 and 2018. This statistic underscores the significance of leukemia as a public health concern [1]. Thus, it is important to examine deeper into the factors that shape prognosis and mortality among those diagnosed with this condition.

Research has indicated that malnutrition is prevalent in 30-85% of individuals diagnosed with cancer, thus corroborating it to be a critical factor that influences both disease progression and patient outcomes [2,3]. The roots of malnutrition in acute leukemia are multifaceted, stemming from the disease's metabolic demands, treatment-related side effects, and inadequate dietary intake. This nutritional deficit can exacerbate disease-related complications, compromising the immune system, impeding the healing process, and diminishing the body's capacity to tolerate and respond to treatment [4].

Previous studies have established a broad connection between poor nutritional status and undesirable outcomes, such as prolonged hospital stays, increased admission rates, and elevated cancer-related mortality [5,6]. Nutritional status is assessed by considering six potential indicators of malnutrition, with a diagnosis of malnutrition deemed appropriate if two or more criteria are met: insufficient energy intake, weight loss, loss of muscle mass, loss of subcutaneous fat, localized or generalized fluid retention, and diminished functional capacity measured through hand grip strength [7]. However, despite its undeniable significance, the precise impact of malnutrition on acute leukemia's progression and treatment outcomes remains an area in need of further exploration.

To bridge this knowledge gap, this retrospective study leveraged data from a large cohort of hospitalized acute leukemia patients in the United States. Our analysis included patients hospitalized with acute myeloid leukemia or acute lymphocytic leukemia. The aim was to comprehensively assess the impact of malnutrition on disease progression and clinical outcomes, ultimately shedding light on this critical aspect of leukemia care.

Materials and methods

Data source: Our study relied on the data provided by the NIS database, which was developed as an integral component of the Healthcare Cost and Utilization Project (HCUP), generously sponsored by the Agency for Healthcare Research and Quality (AHRQ). This massive all-payer inpatient healthcare database offers a wealth of public information to researchers and boasts an impressive sample size that approximates 20% of stratified discharges from community hospitals across America [8]. Employing a systematic sampling design, this comprehensive resource is crafted from state-initiated patient databases, generating distinctive discharge records that encompass vital medical information. These records include primary and secondary diagnoses, alongside procedures conducted during hospitalization. Additionally, each record incorporates demographic details, comorbidities, severity of illness, and mortality risk based on All Patient Refined Diagnosis-Related Groups (APR-DRG). Other incorporated elements consist of the Length of Hospital Stay (LOS), teaching status, hospital location, geographic region, and an estimated median household income quartile based on the patient's zip code. Furthermore, primary payer information, discharge disposition, and in-hospital mortality are meticulously documented in each record.

Study design and population: Since Leukemia is often diagnosed in childhood but can also affect individuals of all ages, our study encompassed patients both below and above 18 years old. The National Inpatient Sample for 2019-2020 was analyzed to specifically identify patients who had been admitted with a diagnosis of Acute Myeloid or Lymphocytic Leukemia. Subsequently, the patient cohort was segregated into two distinct groups based on their respective nutritional statuses: one group comprising individuals without malnutrition and the other including those with concurrent malnutrition.

Outcomes: The primary objective of the study was to evaluate and contrast mortality rates between two groups. In addition to this vital outcome measure, various secondary parameters, such as length of hospitalization and total hospital charges, were examined to gain a more comprehensive understanding of patient outcomes. These metrics provided insights into resource utilization patterns within each population. Furthermore, the study compared the Charlson comorbidity index, a tool capable of addressing numerous confounding factors, between patients with and without concomitant frailty.

Statistical analysis: The statistical analysis in this study prioritized ensuring the reliability and validity of results. We utilized Stata 17 software with weighted samples to align with Healthcare Cost and Utilization Project regulations when using the NIS database for national estimates. Continuous variables were represented by mean values and standard deviations, while categorical variables were expressed as percentages. For group comparisons, the «Student's t-test» on Stata was applied to continuous variables, and the «Chi-square test» was used for categorical variables. The multivariate analysis carefully considered variables that showed significant differences in outcomes from univariate analysis (p-value less than 0.2) and also included crucial determinants regardless of their statistical significance. It involved calculating odds ratios for all outcomes, adjusting for factors such as age, gender, ethnicity, insurance coverage status, hospital location, teaching status, bed size, and the Charlson comorbidity index to provide a comprehensive understanding of the data.

Results

A total of 24855 patients with the primary discharge diagnosis of acute Leukemia were included in the study. Among these, 3425(13.7%) had concomitant malnutrition, while the remaining 21430 had no malnutrition. The mean age of patients with Leukemia and malnutrition was 43.15 years (+/-25.80) compared to 35.26 years (+/-26.28) for those without malnutrition ($p<0.001$). Younger patients (<18 years) had fewer instances of malnutrition (22.04% vs. 35.49%, $p<0.001$), whereas older patients exhibited a higher prevalence of malnutrition (Aged 46-64: 23.8% vs 18.57%, Aged>65: 26.57% vs 18.88%, $p<0.001$). A more significant proportion of patients diagnosed with malnutrition were found to be covered by Medicare (28.75% vs 21.44%, $p<0.001$), whereas those without malnutrition exhibited a higher prevalence of Medicaid insurance (31.41% vs 24.11%, $p<0.001$). The representation of individuals with private insurance was nearly equivalent across both groups (43.12% vs 44.95%, p<0.001). Surprisingly, there was a higher prevalence of people without insurance in the group without malnutrition (4.04% vs 3.09%, p<0.001). Acute Leukemia with Malnutrition had a larger proportion of patients with fluid and electrolyte disorders (50.36% vs 31.68%, <0.001). A higher proportion of heart failure was noted in patients with malnutrition (8.03% vs 5.04%, p=0.001). Leukemia without malnutrition had fewer patients who underwent Hematopoietic stem cell transplant than patients with malnutrition (10.69% vs 20.15%, p<0.001). Conversely, a larger proportion of patients without malnutrition had undergone chemotherapy (2.66% vs 0.73%, p= 0.002). A larger percentage of patients with malnutrition were discharged to homes with home health services (23.43% vs. 13.61%, p<0.001), while patients without malnutrition had a large percentage that was discharged to homes and skilled nursing facilities (75.74% vs. 70.85% & 9.9% vs. 5.35%, p<0.001). Smaller hospitals had a higher proportion of patients without malnutrition (14.28% vs 9.78%, p<0.001), while larger hospitals had a greater percentage of patients with malnutrition (78.54% vs 64%, p<0.001). Additionally, non-teaching hospitals tended to have fewer patients with malnutrition and more patients without malnutrition (2.77% vs 5.76%, p=0.002) (Table 1).

Table 1: Comparison of baseline characteristics of acute leukemia patients with and without malnutrition.

	Acute Leukemia without Malnutrition (%)	Acute Leukemia with Malnutrition (%)	P-Value
No. of patients	21430 (%)	3425 (%)	
Patient characteristics			
Gender (%)			0.133
Male	11941 (55.72)	2005 (58.54)	
Female	9489 (44.28)	1420 (41.46)	
Age			
Mean age (SD)	35.26 (26.28)	43.15 (25.80)	<0.001
Age distribution (%)			<0.001
<18	7606 (35.49)	755 (22.04)	
18-35	3915 (18.27)	680 (19.85)	
36-45	1886 (8.8)	265 (7.74)	
46-64	3980 (18.57)	815 (23.8)	
>65	4046 (18.88)	910(26.57%)	
Race (%)			0.06
White	12166 (56.77)	2077 (60.65)	
Black	1875 (8.75)	376 (10.97)	
Hispanic	6187 (28.87)	801 (23.39)	
Other	1202 (5.61)	171 (5)	
Median household income national quartile for patient zip code (%)			0.343
$1-$49,999	5606 (26.16)	873 (25.48)	
$50,000-$64,999	5085 (23.73)	893 (26.08)	
$65,000-$85,999	5780 (26.97)	832 (24.29)	
>$86,000	4959 (23.14)	827 (24.14)	
Charlson comorbidity index (%)			<0.001
2	13516 (63.07)	1870 (54.6)	
3 or more	7914 (36.93)	1555 (45.4)	
Insurance provider (%)			<0.001
Medicare	4595 (21.44)	985 (28.75)	
Medicaid	6731 (31.41)	826 (24.11)	
Private	9241 (43.12)	1509 (44.05)	
Uninsured	866 (4.04)	106 (3.09)	
Comorbidities (%)			
Hypertension	6285 (29.33)	985 (28.76)	0.751
Diabetes mellitus	2959 (13.81)	465 (13.58)	0.87
Fluid and electrolyte disorders	6789 (31.68)	1725 (50.36)	<0.001
Chronic kidney disease			
CKD2	124 (0.58)	30 (0.88)	0.291
CKD3	446 (2.08)	65 (1.9)	0.758
CKD4	75 (0.35)	5 (0.15)	0.367
CKD5	25 (0.12)	4(0.11)	0.689
CKD Unspecified	371 (1.73)	80 (2.34)	0.201
ESRD	71 (0.33)	20 (0.58)	0.303
Hyperlipidemia (HLD)	3109 (14.51)	540 (15.77)	0.432
Obesity	2246 (10.48)	280 (8.18)	0.1
COPD	600 (2.8)	120 (3.5)	0.296
Heart Failure	1080 (5.04)	275 (8.03)	0.001
Coronary artery disease	1354 (6.32)	320 (9.34)	0.0213
History of CVA	56 (0.26)	20 (0.58)	0.147
Treatment			
HSCT	2291 (10.69)	690 (20.15)	<0.001
Chemotherapy	570 (2.66)	25 (0.73)	0.002
Discharge disposition (%)			<0.001
Home	16231 (75.74)	2427 (70.85)	
Home with home health	2917 (13.61)	802 (23.43)	
Skilled nursing facility	2122 (9.9)	183 (5.35)	
Against Medical Advice	163 (0.76)	13 (0.37)	
Hospital characteristics (%)			
Bed size of hospital (STRATA)			<0.001
Small	3060 (14.28)	335 (9.78)	
Medium	4655 (21.72)	400 (11.68)	
Large	13715 (64)	2690 (78.54)	
Hospital location			0.023
Rural	281 (1.31)	10 (0.29)	
Urban	21149 (98.69)	3415 (99.71)	
Hospital teaching status			0.002
Non-teaching hospital	1234 (5.76)	95 (2.77)	
Teaching hospital	20196 (94.24)	3330 (97.23)	
Region of hospital			0.309
Northeast	3521 (16.43)	675 (19.71)	
Midwest	3800 (17.73)	670 (19.56)	
South	8855 (41.32)	1420 (41.46)	
West	5255 (24.52)	660 (19.27)	

SD: Standard Deviation; CVA: Cardiovascular Accident; HSCT: Hematopoietic Stem Cell Transplant; COPD: Chronic Obstructive Pulmonary Disease; ESRD: End Stage Renal Disease.

Table 2: Univariate and multivariate regression analysis of odds of mortality in acute leukemia patients with and without malnutrition.

	Univariate regression			Multivariate regression		
Mortality	**Odds ratio**	**95% Conf. Interval**	**P-Value**	**Odds ratio**	**95% Conf. Interval**	**P- Value**
Malnutrition	3.33	(2.49-4.45)	<0.001	2.89	(2.11-3.94)	<0.001
Gender (%)						
Male	Reference					
Female	0.96	(0.73-1.24)	0.766	1.05	(0.78-1.41)	0.713
Age						
Mean age	1.17	(1.34-1.66)	0.001	1.03	(1.00-1.05)	0.012
Age distribution (%)						
<18	Reference					
18-35	2.22	(1.41-3.48)	0.001	1.84	(1.08-3.15)	0.025
36-45	2.04	(1.18-3.51)	0.01	1.59	(0.85-2.96)	0.142
46-64	2.68	(1.75-4.12)	<0.001	1.74	(1.01-2.97)	0.043
>65	5.4	(3.75-7.78)	<0.001	2.76	(1.43-5.31)	0.002
Race(%)						
White	Reference					
Black	1.62	(1.06-2.48)	0.025	1.74	(1.11-2.74)	0.015
Hispanic	0.69	(0.49-0.96)	0.031	0.84	(0.58-1.23)	0.39
Other	1.23	(0.70-2.14)	0.465	1.49	(0.82-2.72)	0.187
Median household income national quartile for patient zip code (%)						
$1-$49,999	Reference					
$50,000-$64,999	0.94	(0.65-1.37)	0.783	0.93	(0.60-1.42)	0.747
$65,000-$85,999	1.16	(0.81-1.67)	0.397	1.26	(0.83-1.91)	0.267
>$86,000	0.92	(0.63-1.36)	0.712	0.88	(0.56-1.37)	0.58
Charlson comorbidity index (%)						
2	Reference					
3 or more	4	(3.03-5.49)	<0.001	3.1	(2.20- 4.38)	<0.001
Insurance provider (%)						
Medicare	Reference					
Medicaid	0.35	(0.25-0.50)	<0.001	1.23	(0.68-2.20)	0.482
Private	0.4	(0.30-0.54)	<0.001	0.98	(0.60-1.62)	0.96
Uninsured	0.36	(0.15-0.85)	0.021	1.18	(0.45-3.06)	0.725
Comorbidities (%)						
Hypertension	1.04	(0.79-1.35)	0.767	1.04	(0.74-1.46)	0.819
Diabetes mellitus	1.31	(0.93-1.84)	0.116	0.54	(0.36-0.81)	0.003
Fluid and electrolyte disorders	3.18	(2.44-4.14)	<0.001	2.43	(1.81-3.27)	<0.001
Chronic kidney disease						
CKD2	Reference					
CKD3	3.21	(1.77-5.79)	<0.001	1.32	(0.63-2.76)	0.447
CKD4	4.16	(1.17-14.84)	0.028	0.87	(0.13-5.47)	0.883
CKD5	3.19	(1.32-6.84)	0.0325	1.52	(0.28-3.12)	0.325
CKD Unspecified	2.02	(0.94-4.33)	0.07	0.78	(0.30-2.03)	0.618
ESRD	7	(2.46-19.84)	<0.001	3.47	(1.18-10.12)	0.023
Hyperlipidemia (HLD)	1.39	(1.01-1.90)	0.039	0.66	(0.43-1.00)	0.05

Obesity	1.19	(0.80-1.77)	0.38	1.07	(0.69-1.65)	0.744
COPD	2.31	(1.31-4.08)	0.004	1.03	(0.55-1.94)	0.913
Heart Failure	4.09	(2.95-5.66)	<0.001	1.42	(0.91-2.23)	0.116
Coronary Artery Disease	2.33	(1.67-3.26)	<0.001	0.83	(0.52-1.32)	0.44
History of CVA	12.1	(4.28-34.65)	<0.001	8.45	(2.52-28.31)	0.001
Treatment						
HSCT	1.05	(0.72-1.53)	0.773	1.04	(0.67-1.61)	0.849
Chemotherapy	0.3	(0.07-1.23)	0.095	0.602	(0.16-2.22)	0.447
Hospital characteristics (%)						
Bed size of hospital (STRATA)						
Small	Reference					
Medium	1.58	(0.94-2.65)	0.08	1.95	(1.06-3.59)	0.03
Large	1.83	(1.17-2.87)	0.008	1.7	(0.99-2.93)	0.054
Hospital location						
Rural	Reference					
Urban	0.34	(0.16-.72)	0.005	0.41	(0.13-1.22)	0.111
Hospital teaching status						
Non-teaching hospital	Reference					
Teaching hospital	0.56	(0.36-.88)	0.013	0.81	(0.44-1.50)	0.516
Region of hospital						
Northeast	Reference					
Midwest	0.6	(0.39-0.93)	0.022	0.57	(0.35-0.93)	0.024
South	0.86	(0.61-1.23)	0.434	0.82	(0.57-1.18)	0.305
West	0.73	(0.50-1.08)	0.119	0.85	(0.56-1.29)	0.459

Univariate regression analysis revealed an association between increased mortality and concurrent malnutrition in patients with acute Leukemia (OR 3.33, 95% CI: 2.49-4.45, p<0.001). Upon conducting multivariate logistic regression analysis to adjust for confounding variables, it was determined that malnutrition independently contributes to higher mortality among hospitalized acute leukemia patients (OR 2.89, 95% CI: 2.11-3.94, p<0.001) (Table 2).

Likewise, Tables 3 and 4 present the results of univariate and multivariate analyses for length of stay and total hospitalization charges. Following adjustment for confounding factors, the multivariate regression analysis indicated a significant increase in both length of stay (+9.1 Days 95% CI: 7.01-11.19, p<0.001) and total hospitalization charges (+177994 USD, 95% CI: 122573-2334512, p<0.001) among acute leukemia patients with concurrent malnutrition.

Table 3: Univariate and multivariate regression analysis of length of hospitalization in acute leukemia patients with and without malnutrition.

	Univariate regression			Multivariate regression		
LOS (Days)	**Coefficient**	**95% Conf. Interval**	**P- Value**	**Coefficient**	**95% Conf. Interval**	**P- Value**
Malnutrition	12.22	(9.93-14.51)	<0.001	9.1	(7.01-11.19)	<0.001
Gender (%)						
Male	Reference					
Female	0.6	(-0.54-1.75)	0.303	1.1	(-0.17-2.38)	0.09
Age						
Mean age	-0.05	(-0.07-(-0.02))	<0.001	-0.16	(-0.25(-0.06))	0.001
Age distribution (%)						
<18	Reference					
18-35	2.97	(0.93-5.00)	0.004	0.81	(1.15-2.79)	0.417
36-45	1.53	(-0.65-3.72)	0.17	-1.28	(-3.47-0.91)	0.252
46-64	1.568	(-0.12-3.26)	0.07	-0.94	(-2.97-1.09)	0.365

>65	-4.29	(-6.21-(-2.37))	<0.001	-2.72	(-5.47-.01)	0.052
Race (%)						
White	Reference					
Black	1.07	(-0.80-2.94)	0.262	-0.95	(-2.69-0.78)	0.283
Hispanic	3.03	(1.30-4.76)	0.001	1.32	(0.01-2.63)	0.047
Other	3.84	(0.87-6.82)	0.011	2.3	(-0.31-4.97)	0.084
Median household income national quartile for patient zip code (%)						
$1-$49,999	Reference					
$50,000-$64,999	-0.53	(-2.50-1.43)	0.595	-0.56	(-2.45-1.31)	0.553
$65,000-$85,999	-1.27	(-3.03-.48)	0.154	-1.31	(-3.04-.41)	0.137
>$86,000	-0.55	(-2.38-1.27)	0.551	-0.96	(-2.73-0.79)	0.282
Charlson comorbidity index (%)						
2	Reference					
3 or more	1.89	(0.63-3.15)	0.003	3.68	(2.04-5.3)	<0.001
Insurance provider (%)						
Medicare	Reference					
Medicaid	6	(4.21-7.76)	<0.001	4.15	(2.05-6.26)	<0.001
Private	4.42	(3.10-5.73)	<0.001	2.47	(0.71-4.23)	0.006
Uninsured	1.93	(-1.38-5.26)	0.253	0.95	(-1.65-3.56)	0.474
Comorbidities (%)						
Hypertension	2.39	(1.15-3.64)	<0.001	2.49	(1.09-3.89)	<0.001
Diabetes mellitus	-0.64	(-2.31-1.02)	0.451	-2.02	(-3.96-(-0.08))	0.041
Fluid and electrolyte disorders	11.47	(10.10-12.85)	<0.001	8.94	(7.59-10.28)	<0.001
Chronic kidney disease						
CKD2	Reference					
CKD3	-4.77	(-7.41-2.13)	<0.001	0.57	(-2.31-3.47)	0.696
CKD4	-5.77	(-15.50-3.96)	0.245	-4.98	(-13.23-3.25)	0.236
CKD5	-15.31	(-16.10-(-14.53)	<0.001	-11.18	(-14.85-(-7.51)	<0.001
CKD Unspecified	-1.8	(-4.63-1.02)	0.212	-1.27	(-4.21-1.65)	0.393
ESRD	8.88	(-17.78- 35.55)	0.514	-2.56	(-12.02-6.90)	0.596
Hyperlipidemia (HLD)	-2.89	(-4.18-(-1.59)	<0.001	-1.28	(-2.59-.02)	0.055
Obesity	2.05	(0.33-3.76)	0.019	1.65	(-0.13-3.44)	0.071
COPD	-5.61	(-7.92-(-3.30)	<0.001	-3.42	(-5.95-(-0.88)	0.008
Heart failure	-1.14	(-3.76-1.48)	0.394	2.05	(-0.53-4.63)	0.12
Coronary artery disease	-4.3	(-5.95-(-2.64))	<0.001	-0.9	(-2.42-0.60)	0.239
History of CVA	17	(2.36-31.64)	0.023	15.24	(0.82-29.67)	0.038
Treatment						
HSCT	16.78	(14.66-18.91)	<0.001	13.25	(11.23-15.26)	<0.001
Chemotherapy	0.14	(-3.88-4.17)	0.944	1.47	(-2.47-5.42)	0.464
Discharge disposition (%)						
Home	Reference					
Home with home health	4.26	(2.75-5.78)	<0.001	3.26	(1.86-4.66)	<0.001
Skilled nursing facility	-10.1	(-12.28-(-7.92))	<0.001	-6.43	(-9.19-(-3.68))	<0.001
Against medical advice	-8.76	(-13.85-(-3.67))	0.001	-6.1	-11.07(-1.13)	0.016
Hospital characteristics (%)						
Bed size of hospital (STRATA)						

Small	Reference					
Medium	0.66	(-2.15-3.47)	0.646	2.2	(0.01-4.40)	0.048
Large	3.24	(1.41-5.07)	0.001	3.75	(2.11-5.39)	<0.001
Hospital location						
Rural	Reference					
Urban	12	(9.46-14.54)	<0.001	-0.22	(-3.54-3.09)	0.894
Hospital teaching status						
Non-teaching hospital	Reference					
Teaching hospital	11.67	(9.98-13.37)	<0.001	7.25	(5.57-8.94)	<0.001
Region of hospital						
Northeast	Reference					
Midwest	-3.48	(-6.38-0.57)	0.019	-3.52	(-6.05-(-0.99))	0.006
South	-4.27	(-6.41-(-2.13))	<0.001	-3.49	(-5.31-(-1.68))	<0.001
West	-2.79	(-5.30-0.29)	0.029	-3.27	(-5.37-(-1.16))	0.002

LOS: Length of Stay; CVA: Cardiovascular Accident; HSCT: Hematopoietic Stem Cell Transplant; COPD: Chronic Obstructive Pulmonary Disease; ESRD: End Stage Renal Disease.

Table 4: Univariate and multivariate regression analysis of the total cost of hospitalization in acute leukemia patients with and without malnutrition.

	Univariate regression			Multivariate regression		
Total charges (USD)	**Coefficient**	**95% Conf. Interval**	**P-Value**	**Coefficient**	**95% Conf. Interval**	**P-Value**
Malnutrition	241074	(172942-309206)	<0.001	177994	(122573-2334152)	<0.001
Gender (%)						
Male	Reference					
Female	-12146	(-39614.74-15320)	0.386	-984	(-28247-26278)	0.944
Age						
Mean Age	-2292	(-2868-(-1717))	<0.001	-705	(-3137-1726)	0.57
Age distribution (%)						
<18	Reference					
18-35	33434	(-16545-83413)	0.19	-34574	(-82629-13481)	0.158
36-45	-30085	(-94271-34099)	0.358	-116145	(-183158-(-49133))	0.001
46-64	-51340	(-95809-(-6872)	0.024	-128959	(-180341-(-77577)	<0.001
>65	-171022	(-213299-(-128744)	<0.001	-174717	(-234173-(-1152619))	<0.001
Race (%)						
White	Reference					
Black	9649	(-28568-47866)	0.621	-18239	(-55236-18756)	
Hispanic	108506	(-66686-150326)	<0.001	50159	(14314-86005)	
Other	138313	(40912-235715)	0.005	83790	(-2571-1701529)	
Median household income national quartile for patient zip code (%)						
$1-$49,999	Reference					
$50,000-$64,999	2.35	(-40057-40062)	1	-556	(-38264-371518)	0.977
$65,000-$85,999	-4180	(-42406-34045)	0.83	-9511	(-49152-30129)	0.638
>$86,000	39398	(-7187-85984)	0.097	17261	(-29118-636429)	0.466
Charlson comorbidity index (%)						
2	Reference					
3 or more	31681	(1815-61547)	0.038	103058	(64436-1416816)	<0.001
Insurance provider (%)						

Medicare	Reference					
Medicaid	176027	(136517-215538)	<0.001	56641	(11743-1015394)	0.013
Private	127732	(97269-158194)	<0.001	27973	(-8198-64145)	0.13
Uninsured	69214	(-11052-149482)	0.091	19842	(-45124-84810)	0.549
Comorbidities (%)						
Hypertension	24341	(-6155-54838)	0.118	47040	(14334-797454)	0.005
Diabetes mellitus	-41171	(-76190-(-6152))	0.021	-43588	(-84273-(-2903))	0.036
Fluid and electrolyte disorders	223743	(186465-261021)	<0.001	179347	(142487-2162072)	<0.001
Chronic kidney disease						
CKD2	4306	(-267427-276040)	0.975			
CKD3	-155663	(-200539-(-110786))	<0.001	-24337	(-74422-25748)	0.341
CKD4	8206	(-452915-469329)	0.972	61446	(-353672-4765649)	0.772
CKD5	-294682	(-319034-270329)	0.001	-237375	(-322733-(-1520168)	<0.001
CKD Unspecified	-75804	(-138780-12828)	0.018	-45690	(-98059-6678)	0.087
ESRD	310856	(-320893-942605)	0.335	63140	(-253520-3798008)	0.696
Hyperlipidemia (HLD)	-110815	(-139941-81689)	<0.001	-31877	(-62459-(-1295)	0.041
Obesity	25521	(-15341-66383)	0.221	23895	(-15904-63694)	0.239
COPD	-154875	(-198346-(-111404))	<0.001	-82430	(-131420-(-33441))	0.001
Heart Failure	-20405	(-78902-38092)	0.494	76610	(12026-141193)	0.02
Coronary artery disease	-133653	(-164490-(-102815))	<0.001	-31617	(-63167-(-68))	0.05
History of CVA	568867	(84078-1053655)	0.021	564339	(91306-103732)	0.019
Treatment						
HSCT	423121	(348684-497558)	<0.001	374343	(302562-4461248)	<0.001
Chemotherapy	-30098	(-123753-63557)	0.529	-20048	(-106566-66468)	0.65
Discharge disposition (%)						
Home	Reference					
Home with home health				39155	(5639-72670)	0.022
Skilled nursing facility				-68168	(-121801-(-14536))	0.013
Against medical advice				-80256	(-177628-17116)	0.106
Hospital characteristics (%)						
Bed size of hospital (STRATA)						
Small	Reference					
Medium	19066	(-60306-98438)	0.638	31708	(-35338-98755)	0.354
Large	54120	(-1989-106252)	0.042	55556	(4381-1067313)	0.033
Hospital location						
Rural	Reference					
Urban	268029	(237291-298767)	<0.001	3115	(-49891-56122)	0.908
Hospital teaching status						
Non-teaching hospital	Reference					
Teaching hospital	237696	(200644-274748)	<0.001	101844	(66207-1374813)	<0.001
Region of hospital						
Northeast	Reference					
Midwest	-112853	(-179928-(-45779))	0.001	-123239	(-185143-61335)	<0.001
South	-122192	(-184028-(-60357))	<0.001	-108294	(-165819-50768)	<0.001
West	10398	(-73145-93942)	0.807	-29572	(-103717-44571)	0.434

USD: United States Dollar; CVA: Cardiovascular Accident; HSCT: Hematopoietic Stem Cell Transplant; COPD: Chronic Obstructive Pulmonary Disease; ESRD: End Stage Renal Disease.

Discussion

Our comprehensive study revealed the alarming impact of malnutrition on hospitalized acute leukemia patients, with a staggering threefold increase in mortality. Additionally, our findings also highlighted its substantial influence on prolonged hospital stays and increased overall hospitalization costs. Research by Deenadayalan et al. shed light on the prevalence of malnutrition in Diffuse Large B Cell Lymphoma (DLBCL), revealing that 7% of chemotherapy-admitted patients suffered from concurrent malnutrition [9]. Another study conducted by Park et al. reported a higher range of 10-20% for the prevalence of malnutrition in DLBCL patients [10]. In alignment with these insights, our own research indicated a notable 13% prevalence rate of malnutrition among acute leukemia patients.

In our study, it was found that a higher percentage of Hematopoietic Stem Cell Transplants (HSCT) occurred in malnourished patients compared to those without malnutrition. According to Kim et al. HSCT failures are recognized as potential and devastating complications of malnutrition, and malnutrition is also considered a poor prognostic factor for outcomes in HSCT patients [11]. The increased occurrence of HSCT in our study's cohort of malnourished patients is likely due to the fact that HSCT failures necessitate multiple repeat interventions and procedures within this patient group. Previous studies have extensively elucidated the association between malnutrition and adverse outcomes in leukemia patients undergoing HSCT.

Amiri Khosroshahi et al. conducted a comprehensive single-center observational, longitudinal, and prospective study involving 98 adult leukemia patients who had undergone hematopoietic stem cell transplantation [12]. The study focused on evaluating outcomes such as mortality rates, the occurrence of oral mucositis, infection incidences, and readmission rates. Their findings suggested that malnutrition correlated with an increased risk of infections and readmissions; however, it did not show any significant difference in overall survival [12]. In contrast to their conclusions, our own research indicated a higher incidence of mortality among malnourished patients. It is important to note that while the aforementioned study had a relatively small cohort size, our study encompassed a larger group, including both transplant candidates and non-transplant candidates, for better representation.

Our study revealed a striking disparity in the rates of chemotherapy undergone by patients with malnutrition compared to those without. This discrepancy can be attributed to the formidable toxicity of induction and maintenance therapies, rendering them particularly challenging for individuals grappling with malnutrition. Not only does malnutrition compromise immune function, but it also undermines overall physical endurance and muscle capability, profoundly affecting quality of life. Additionally, it significantly attenuates the body's capacity to withstand chemotherapy, heightening susceptibility to treatment-related toxicity and complications while concurrently diminishing survival prospects.

Van Cutsem et al. conducted an extensive study highlighting the profound impact of chemotherapy on the immune system. They noted that when combined with malnutrition, these effects can drastically reduce a patient's ability to tolerate the adverse effects of chemotherapy, ultimately leading to decreased compliance rates and overall survival outcomes [13].

Similarly, Malihi et al. conducted a prospective study to comprehensively assess the alterations in the nutritional status of leukemia patients both prior to and following induction therapy [14]. Their cohort comprised 63 leukemia patients who were subjected to induction chemotherapy. The findings revealed that 19.4% of these patients experienced malnutrition before undergoing induction chemotherapy, while after the completion of therapy, this figure escalated significantly to 76.1% [14]. This data underscores the rationale behind our observation that individuals with pre-existing malnutrition were less inclined to undergo chemotherapy based on our results.

Several recent studies have delved into the profound impact of malnutrition on healthcare resource utilization and patient outcomes in various severe health conditions. A prospective study by Lim et al. meticulously utilized Subjective Global Assessment to identify malnourished patients, enrolling a substantial cohort of 818 individuals. The extensive analysis revealed compelling evidence linking malnutrition to prolonged hospital stays, escalated treatment expenses, and heightened readmission rates [15]. Furthermore, Inciong et al. conducted an expansive multi-country investigation across Asia due to the pervasive prevalence of malnutrition within the continent. Their findings underscored a significant upsurge in total hospitalization costs attributable to malnutrition-related factors, amounting to an estimated annual expenditure exceeding 30 billion dollars for additional treatments [16].

Malnourishment not only increases the likelihood of sickness and death among hospital patients, but it also contributes to a substantial increase in healthcare expenses. The prolonged duration of hospitalization and increased expenses could signify the intricate nature and seriousness of clinical intervention needed for malnourished patients. This underscores the need for a more thorough and holistic approach to their treatment, potentially involving extra resources such as specialized medical knowledge, personalized care plans, and continuous support services. By implementing a comprehensive screening tool, healthcare providers can effectively identify at-risk patients and provide them with the necessary care, ultimately leading to enhanced clinical outcomes and reduced healthcare costs.

Several constraints need to be recognized when interpreting the results of this study. Firstly, it's important to acknowledge that the analysis was based on retrospective data from the NIS 2019-2020 database, which relies on the accuracy and completeness of recorded data. Variations in coding practices across healthcare facilities could significantly impact these findings. It would be beneficial for future studies to explore utilizing prospective study designs to capture detailed clinical information directly, thereby minimizing variations and potential inaccuracies associated with databases' retrospective nature. Additionally, implementing a more comprehensive sampling approach that includes both hospitalized and outpatient cases should also be considered, as it may provide a more holistic view of the subject matter.

The absence of malnutrition severity in the NIS data could significantly impact the findings and their real-world relevance. By solely focusing on hospitalized patients, there is a potential for bias, as it excludes less severe cases treated on an outpatient basis. Moreover, the study overlooks consideration of various treatment methods that might have a substantial influence on the analysis of outcomes. Despite its limitations, this study provides valuable initial insights into the relationship between malnutrition and hospitalized acute leukemia patients. It suggests a need for additional prospective research to validate and build upon its findings with more depth and context into different aspects affecting these patients' nutritional status.

Conclusion

This retrospective study analyzed a compelling association between malnutrition and adverse outcomes in patients hospitalized with acute leukemia. The findings underscore the critical importance of addressing and mitigating malnutrition as an integral component of comprehensive care for this vulnerable patient population. Beyond serving as a prognostic marker, understanding the impact of malnutrition on clinical outcomes can inform tailored interventions and strategies aimed at improving the overall prognosis and quality of life for individuals with acute leukemia. Further research should delve into the underlying mechanisms linking malnutrition and poor outcomes, paving the way for targeted therapeutic interventions and enhanced supportive care strategies in the management of acute leukemia patients.

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