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Increasing BMI Z-Scores 3 Years after Diagnosis among a Multiethnic Cohort of Childhood Cancer Survivors Treated in South Los Angeles

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Abstract

Background: Due to successful treatment modalities, the majority of pediatric cancer patients will survive. Increased body mass index (BMI) is a complication among pediatric cancer survivors. Methods: This retrospective single-center study examined BMI changes among a cohort of predominantly Hispanic patients who were treated in South Los Angeles. Data were collected at diagnosis, 1, 2 and 3 years after. Analyses included z-scores derived from calculated BMIs compared over 3 years per gender, diagnosis, and treatment modality. The unhealthy BMI z-score was defined as >1.04. Results: Thirty-four percent of the predominantly Hispanic sample had unhealthy BMI z-scores of >1.04 correlating to at or greater than the 85th percentile for age and gender. The study cohort's BMI z-scores significantly increased from 0.15 to 1.29 at year 3 ($P < 0.0001$), putting 55% of this population in the unhealthy category. Median BMI z-score significantly increased to the unhealthy category at 3 years. Conclusions: Due to the predominance of Hispanic patients in this group, culturally sensitive interventions beginning at diagnosis should be considered.

Keywords

Pediatric Cancer Survivorship, Obesity, Health Disparities, Long-Term Side Effects, Hispanic Health

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1. Introduction

Around 15,000 children are diagnosed with cancer each year in the United States [1]. As a result of improved treatment modalities, more than 80% of pediatric cancer patients survive. There are currently over 500,000 pediatric cancer survivors in the United States [2]. However, survival can come with long-term sequelae. Two-thirds of childhood cancer survivors face health and psychological challenges as they age and 25% of those are severe, life-threatening and chronic health conditions. Obesity is the most commonly occurring morbidity amongst childhood cancer survivors [3].

Obesity is a significant health issue among the general population. The most recent prevalence of obesity was 18% in children 6 - 11 years and 20.6% in adolescents [4]. Hispanics (25.8%) and non-Hispanic blacks (22%) have been known to have a higher prevalence of obesity compared to non-Hispanic whites [4]. In South Los Angeles, the overall rate of obesity increased by 36% between 1997 and 2011, with a disproportionately higher increase (99%) seen among Hispanics [5].

Among pediatric oncology patients, obesity has been associated with increased risk of treatment toxicity [6]. Subsequently, individuals with higher body mass indexes (BMI) at time of diagnosis have worse outcomes [7] [8] [9] [10]. Orgel *et al.* report an association between obesity at diagnosis and persistent disease at end of induction as an important predictor of relapse [10]. Furthermore, there are studies that suggest that nutrients provided by adipocytes allow leukemic cells to thrive [11]. Adipose tissue can also alter the pharmacokinetics of chemotherapy medications [11]. Recent studies among survivors of Acute Lymphoblastic Leukemia (ALL) have reported the percentage of overweight and obese patients to be roughly 13% and 16%, respectively [12] [13].

The influence of chemotherapy and radiation on development of obesity has also been evaluated utilizing data from the Childhood Cancer Survivor Study; the largest national cohort of long-term survivors of childhood cancer. Hispanic race/ethnicity has been associated with an increased risk of obesity among male pediatric cancer survivors [14]. Because Non-Hispanic blacks and Hispanic children exhibit higher rates of obesity, understanding the impact of a cancer diagnosis and its treatment on BMI holds particular public health relevance. However, in the pediatric cancer survivorship literature [15], there is an underrepresentation of Hispanics.

This study took place at a safety net hospital located in South Los Angeles, that predominantly serves low income patients with state-sponsored health plans or no insurance. The objective was to identify patterns of change of weight status in a local cohort of childhood cancer survivors, most of whom are Hispanic. Our study objectives were to 1) compare BMI z-score changes over a three-year time period from diagnosis and 2) examine patient and treatment factors associated with weight gain over time.

2. Materials and Methods

2.1. Study Population

This study was approved by The Lundquist Institute of Biomedical Innovation at Harbor-UCLA Medical Center's Institutional Review Board. A retrospective chart review of pediatric oncology patients diagnosed and treated at Harbor-UCLA Medical Center between 1993 and 2009 was performed. A long-term childhood cancer survivor database of individuals at least two years post-treatment was used to identify forty-six potential patients to review. Subjects were excluded if they were either diagnosed at another institution or transferred to another institution prior to the third-year interval. Eligibility criteria included a diagnosis of cancer at the age of 18 years or younger and were diagnosed, treated, and received follow-up care for at least 3 years at our institution. Exclusion criteria included patients who relapsed (n = 2) and patients with Down Syndrome (n = 1), as these patients have different growth parameters, and patients not diagnosed at our institution (n = 4), for an analytical sample of 38 patients.

2.2. Procedures

Data was abstracted using a medical abstraction form by two trained research assistants from paper charts. Data was collected on age, gender, diagnosis, height, and weight, at the following time points: time of diagnosis, 1, 2 and 3 years post diagnosis +/− 2 months.

2.3. Outcome Measure

Body Mass Index Z-Score

Using a data abstraction form, patient's weights and heights were collected from medical records. BMI was then calculated using the BMI formula: weight (kg)/height (meters)^2. BMI z-scores were then determined for each patient using height, weight, sex and age data based on the Centers for Disease Control and Prevention National Center for Health statistics growth curves. Z-score data for age 20 years and older was used for individuals over the age of 20 years. A z-score > 0 represented a higher than average BMI [16].

Per BMI literature, BMI z-scores are considered more accurate than BMI percentiles as it accounts for adiposity in children across ages and gender [13] [17] [18] [19]. Z-scores are classified in the following manner: normal weight (z-score < 1.04), overweight (z-score > 1.04 - 1.64) and obesity (z-score > 1.64) [10] [13] [16] [19] [20] [21]. For our study BMI z-scores were dichotomized into weight status: 1) z-score < 1.04 classified as normal healthy, 2) z-score > 1.04 classified as "unhealthy" as it represented the BMI at 85th percentile and greater [21] [22].

2.4. Main Predictors

Patient's information abstracted from medical records included: age at diagnosis, cancer type, sex, ethnicity, and treatments received. Cancer types were dichotomized as solid tumors (Langerhan cell histiocytosis (LCH) n = 2, rhabdomyoscarcoma n = 1, pancreatoblastoma n = 1, Wilms tumor n = 5, hepatoblastoma n = 1, neuroblastoma n = 1 and osteosarcoma n = 1) and hematologic malignancies (acute lymphoblastic leukemia n = 18, Hodgkin lymphoma n = 4 and Non-Hodgkin lymphoma n = 1).

2.5. Data Analysis

Descriptive statistics (counts and proportions for categorical data) were generated to describe patient characteristics. Median BMI z-scores and weight statuses (normal versus unhealthy) were reported by patient and treatment characteristics per time period. We examined changes in weight status over a 3-year period and its association with patient and treatment characteristics using generalized linear models (population average) for longitudinal data. The generalized estimating equation (GEE) procedure with an autoregressive working correlation was used to estimate parameters. Generalized estimating equation (GEE) procedures with autoregressive correlation for linear and logistic regression were used to model BMI z-scores and unhealthy weight status, respectively, over time. We reported linear regression with beta coefficients, while logistic regression output is reported in odds ratios. Simple comparisons of BMI z-scores over time were analyzed with paired t-tests. All analyses were performed using SAS version 9.4 (SAS Institute, Cary, NC).

3. Results

3.1. Patient Characteristics

Thirty-eight patients met inclusion criteria and had follow up data 36-months from diagnosis. Table 1 shows the patient's characteristics. There was an equal distribution of males and females in the sample. The majority of patients were Hispanic white (89%) and the median age at diagnosis was 4.2 years. Twenty-six patients had a hematologic malignancy (62%), while twenty-two (64%) received chemotherapy alone and eleven received chemotherapy plus another treatment such as surgery and/or radiation. Of the nine patients that had radiation, three had cranial radiation.

3.1.1. Characteristics by Weight Status at Time of Diagnosis and Time Intervals

Thirty-four percent of the sample was at an unhealthy weight status at diagnosis and 55% at the 3rd year interval. Figure 1 shows the distribution of median BMI z-scores by time periods from diagnosis among varying patient characteristics. Overall, the total study population BMI z-scores increased from 0.15 at baseline to 1.29 at year 3, representing one standard deviation increase in BMI above the average, and putting the population in the unhealthy category (Figure 1(A)). Figure 1(A) shows that the greatest increase in median BMI z-scores occurred between baseline and year 1 (0.15 at baseline to 0.71 at year 1). The median BMI z-score became unhealthy for the total population starting at year 2 (1.07). At baseline, females and males had a similar distribution of normal weight status

Table 1. Characteristics of a cohort of 38 childhood cancer survivors.

Characteristics of study cohort (N = 38)		
	Total Population	
Characteristics	n	%
Sex		
Male	19	50.0
Female	19	50.0
Race/Ethnicity		
Hispanic	34	89.5
Non-Hispanic White	4	10.5
Cancer diagnosis		
Hematologic malignancies	26	68.4
Solid tumors	12	31.6
Treatment Type		
Chemotherapy only	22	57.9
Chemotherapy plus other therapy	16	42.1
Age at diagnosis	Median	(min - max)
Overall	4.25	(2 - 17)
Male	4.5	(2 - 17)
Female	4	(2 - 17)

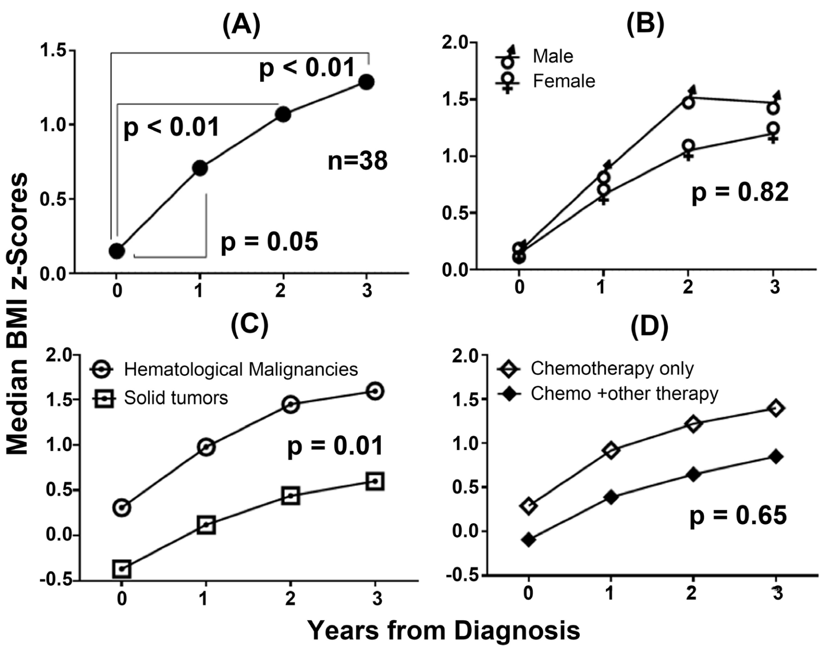

Figure 1. Comparison of median BMI z-scores for the overall cohort and among patient characteristics. Changes in Median BMI z-scores from time of diagnosis, 1, 2 and 3 years post diagnosis. (A) Overall changes in BMI z-scores changes among the cohort throughout the years. (B) Difference in BMI z-score changes among females versus males. (C) Difference in BMI z-score changes among hematological malignancies versus solid tumors. (D) Difference in BMI z-score changes among treatment regimens. **Figure 1** as a whole is identified by horizontal and vertical axes (Years from Diagnosis and Median BMI z-Scores, respectively).

(68% vs. 63%) and a similar median BMI z-score (**Figure 1(B)**). Individuals with hematologic malignancies at the third-year interval had 69% in the unhealthy weight category with a median z-score of 1.6, which is very close to obesity (correlated z-score of 1.64). Individuals with a hematologic malignancy started off with higher median BMI z-scores than individuals with a solid tumor diagnosis (**Figure 1(C)**). In regards to the treatment category, 64% of individuals that received chemotherapy only were at an unhealthy weight at the 3rd year interval (median z-score of 1.4, greater than the 90th percentile).

3.1.2. Association between Time from Diagnosis and Patient Characteristics with BMI Z-Score and Unhealthy Weight Status

There was a significant difference in BMI z-scores from baseline (0.26 ± 1.23, Mean ± SD) and year 3 (1 ± 1.01, Mean ± SD); $P < 0.0001$ in the paired t-test analysis. In the adjusted model, we found that the BMI Z-score increased over a 3-year period (B = 0.74; 95% CI: 0.42, 1.06; $P < 0.001$) indicating that these patients, who were on average at normal BMI-for-age at diagnosis, were at possible risk for being overweight (**Table 2**). Patients with hematologic malignancy had average BMI z-scores that were 0.83 points higher than patients with solid tumors (Beta = 0.83, P = 0.012). Sex and treatment type were not significant predictors.

Table 2. Multivariable regression model for BMI z-scores from time of diagnosis.

Associations between time from diagnosis and patient characteristics with BMI Z score (N = 38)					
		BMI Z score			
		Estimate	Standard Error	95% CI	P-value
Time					
	Baseline	Ref.			
	Year 1	0.33	0.17	0.00, 0.67	0.050
	Year 2	0.66	0.17	0.34, 0.99	**<0.0001**
	Year 3	0.74	0.16	0.42, 1.06	**<0.0001**
Sex					
	Male	Ref.			
	Female	−0.07	0.30	−0.65, 0.51	0.821
Cancer diagnosis					
	Hematologic malignancies	Ref.			
	Solid tumors	0.83	0.33	0.18, 1.48	**0.012**
Treatment Type					
	Chemotherapy only	Ref.			
	Chemotherapy plus other therapy	−0.13	0.28	0.68, 0.43	0.651

**adjusted for sex, hematological malignancy and treatment with chemotherapy only.

4. Discussion

Obesity is a known complication of treatment for pediatric cancer patients, especially those undergoing treatment for ALL [3] [6]. Obesity has also been known to increase morbidity and mortality among pediatric patients [7] [8]. Hispanic adolescents and children have been known to have a higher prevalence of obesity [23]. This study's data adds to the current literature that 1) our South Los Angeles cohort BMI z-score increased and changed weight status into the unhealthy category after childhood cancer treatment, 2) that it occurred within the first three years of diagnosis, and 3) that this observation was made in a predominantly Hispanic cohort.

In our study we observed a slightly higher percentage (34%) of individuals at an unhealthy weight status at time of diagnosis, as has been previously reported for a sample of Hispanic ALL pediatric cancer survivors [21]. The median BMI z-score became unhealthy for the total population starting at year 2, with a similar distribution being seen among patients with hematologic malignancies. This could be attributed to corticosteroids used in the treatment of pediatric leukemias, as our sample consisted of more individuals with hematologic malignancies. Also, patients at this point tend to be in the maintenance cycle with a less aggressive regimen and potentially with better appetite and less mucositis or gastrointestinal complications from chemotherapy. In our sample of patients, males had their greatest median BMI z-score at 2 years from diagnosis, and it decreased slightly to 1.47 at 3 years from diagnosis, while females had a 1.05 median BMI z-score that steadily increased to 1.20 at 3 years from diagnosis. As compared to prior reported data, our cohort of females showed a gradual increase in median BMI z-score throughout the intervals, as opposed to decreasing at the 3-year interval. Which at this point, most females would be off-therapy. This increase is also appreciated when comparing trends of overweight/obesity among Hispanic females in the United States during this time period [24]. Overweight/obesity trends overall fluctuated among the general population during this time period [24].

The relationship between obesity and outcomes in ALL has demonstrated inconsistent results. Some studies have linked obesity and poor outcomes among patients with ALL [6] [25]. Some investigators have noted an association between obesity and an increased risk of relapse, as well as increased adverse events throughout treatment [11]. Obese patients are more likely to require treatment for hypertension and hyperglycemia while undergoing therapy. Obesity has also been shown to be a risk factor for neutropenic fever [26], and other toxicities that may prolong treatment or result in standard treatment modifications. Thus, targeted interventions for this population are needed. Overall, our data suggests a need for a targeted intervention for all pediatric cancer patients presumably at the first year of therapy.

Our cohort consists of a majority of Hispanic patients treated at a publicly funded urban hospital. With this data we introduce a different population than has previously been studied [13] [27] [28] [29] [30]. Literature assessing overweight/obesity rates among predominantly Hispanic pediatric cancer patients is sparse. Prior studies assessing BMI changes in this population consisted of patients that were treated at children's hospitals and had minimal representation of Hispanic patients [13] [27] [28] [29]. Studies have demonstrated that nearly half of Hispanic pediatric cancer survivors are more likely to be overweight and obese at time of follow up [14] [30]. This is not surprising given that recent CDC National Center for Health Statistics (NCHS) data brief reports Hispanic and non-Hispanic blacks have the highest prevalence of obesity compared to the general population, 25.8% and 22.0% [4]. Furthermore, the early childhood longitudinal study demonstrated an inverse relationship between SES and an unhealthy weight among Hispanic children [31]. Socioeconomical conditions have been shown to affect lifestyle choices and access to appropriate health care [32]. These conditions can include living in neighborhood with poor accessibility to healthy food, dangerous neighborhood environments that affect walkability, low income and low education [33]. At baseline minorities have a higher incidence of diabetes and cardiovascular disease [32].

Data suggests that a family-centered, culturally tailored intervention can improve BMI among children [34]. Systematic reviews have shown that a multi-component, culturally appropriate intervention can help in reducing health disparities. This is not surprising given literature that has shown that "familism" is important among Hispanic families and thus family plays a significant role in the patient's life and decision making [35].

Limitations should be noted when considering the results of our study. Although there appears to be a significant association of BMI and time, the sample was relatively small and the study may benefit from a larger sample with more robust estimates. Furthermore, certain comparisons may be non-significant due to the underpowered sample. Other potential limitations include the retrospective study design in which a convenience sample was used. These and data from a single institution can affect the generalizability of our results. Our study also assesses individuals with solid tumors as well. A strength, however, is the availability of multiple data points over time per patient.

In addition to diet, exercise, and other lifestyle factors that may affect obesity, further studies should consider assessment of genetic risk factors. For example, neuronal function genes may alter the risk of obesity [36], and can be explored after radiotherapy in childhood cancer survivors.

5. Conclusion

Our sample of predominantly Hispanic pediatric oncology patients had overall healthy weight status at diagnosis but showed an increase in median BMI z-score 3 years from cancer diagnosis—change that resulted in a greater number of subjects in the overweight/obese category. Thus, more studies are needed to assess culturally sensitive interventions starting from the time of cancer diagnosis and its effect on BMI among this population.

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Conflicts of Interest

The author(s) indicated no conflict of interest.

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