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Obesity in pediatric patients with Acute Lymphoblastic Leukemia increases the risk of adverse events during pre-maintenance chemotherapy

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Abstract

Purpose—Obesity correlates with adverse events (AE) in children with acute myelogenous leukemia and during maintenance therapy for acute lymphoblastic leukemia (ALL). Less is known about AEs in obese ALL patients during pre-maintenance chemotherapy. We evaluated the relationship between obesity (BMI ≥ 95th %-ile) and AEs during pre-maintenance chemotherapy in pediatric patients with ALL.

Methods—155 pediatric ALL patients diagnosed at a single institution between 2006–12 were retrospectively evaluated for infections, treatment-requiring hypertension, insulin-requiring hyperglycemia, pancreatitis, PICU admissions, sepsis, febrile neutropenia admissions (FN), thrombosis, hepatotoxicity, and nephrotoxicity. Univariate and multivariable analysis compared proportions of obese versus non-obese patients experiencing AEs.

Results—AEs occurring significantly more frequently in obese patients by univariate analysis included treatment-requiring hypertension (17.5% vs. 6.1%, OR 3.27, 95% CI 1.1–10.0, p=0.0497) and insulin-requiring hyperglycemia (25.0% vs. 11.3%, OR 2.62, 95% CI 1.04–6.56, p=0.04). Obese patients had greater incidence rates for recurrent admission-requiring infections (Incidence Rate Ratio (IRR) 1.64, 95%CI 1.08–2.48, p=0.02) and recurrent FN admissions (IRR 1.53, 95%CI 1.10–2.12, p=0.01). Accounting for combined age and NCI risk status, obesity was a risk factor for treatment-requiring hypertension (OR 3.90, 95%CI 1.19–12.76, p=0.02), insulin-requiring hyperglycemia (OR 3.92, 95%CI 1.39–11.05, p=0.01), and FN admission (OR 2.92, 95%CI 1.27–6.73, p=0.01).

Conclusions—During pre-maintenance chemotherapy for ALL, obesity is a risk factor for the development of hypertension, hyperglycemia, and FN admissions. This research provides implications for augmented preventive and supportive care guidelines in obese ALL patients.

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CONFLICT OF INTEREST

The authors declare that there is no conflict of interest.

Keywords

Acute Lymphoblastic leukemia; obesity; pediatric; adverse events

INTRODUCTION

Acute Lymphoblastic Leukemia (ALL) accounts for 30% of all childhood malignancies[1]. Progress in clinical trials and advances in supportive care have dramatically improved outcomes in pediatric ALL in the last 50 years. Despite this, patients remain at risk for disease- and treatment-related morbidity and mortality. Reduction of these risks may improve outcomes[2].

The relationship between obesity and outcomes in ALL has yielded conflicting results. While some studies have identified a link between obesity and outcome in children with ALL[3–5], others have not[6–8]. Further conflict arises when accounting for age. Some investigators have noted an association between obesity and increased risk of relapse, as well as decreased event-free survival, in patients exclusively older than 10 years[8], while others have demonstrated the link in only those younger than 10 years[7].

While the relationship between obesity and disease-related outcomes in childhood ALL has been studied, less is known about how obesity affects adverse events (AEs) related to treatment. In Acute Myelogenous Leukemia, obesity has been correlated with lower survival and higher treatment-related mortality[9]. Further, obese children with ALL have demonstrated increased hepatic and pancreatic toxicity during maintenance therapy[3]. Given this, we hypothesize that treatment-related morbidity in the pre-maintenance period of treatment, when use of corticosteroid and myelosuppressive chemotherapy is most intense, will occur more frequently in children who are obese at the outset of treatment. This study seeks to evaluate the frequency of AEs in obese and non-obese children with ALL during the pre-maintenance phase of chemotherapy. Recognizing the significance of age and National Cancer Institute (NCI) risk status, we further sought to identify the independence of obesity as a risk factor for AEs.

METHODS

Study Population and Data Collection

We performed a retrospective study of children aged 2–22 years who completed pre-maintenance chemotherapy for pre-B and T-cell ALL at a single academic children's hospital between 2006–2012. Patients with BMI < 10th percentile (n=33), major pre-existing medical conditions (n=1), Down Syndrome (n=6), relapsed disease at presentation at treating hospital (n=17), age less than 2 years old (n=19) or missing data (n=1) were excluded. Patients with BMI <10th percentile were excluded in order to eliminate confounding factors such as poor growth or other disorders which may be associated with low weight prior to diagnosis.

Eligible patients were identified by obese/non-obese status at the start of therapy, NCI risk status, and age. Obesity was defined as a body mass index (BMI) ≥ 95th percentile for age

and sex[10]. BMI percentiles were obtained in the medical record or were calculated using the US Centers for Disease Control and Prevention Program BMI Percentile Calculator for children 2–19 years[11]. NCI Risk Status was defined as “standard”, “high”, or “standard to high” risk. “High risk” patients had any one or more of the following factors: WBC counts ≥50,000 at the time of diagnosis, age ≥10years, testicular disease, or overt central nervous system (CNS) disease at diagnosis. Based on the treatment protocols used at the institution, subjects classified as being high-risk did not undergo corticosteroid randomization during induction therapy. The majority of high-risk patients received prednisone as the induction corticosteroid. “Standard risk” patients did not have these criteria at diagnosis and maintained this status at their end of induction risk assessment[12]. “Standard to high risk” patients began therapy as “standard risk” but were reassigned to “high risk” therapy by protocol due to unfavorable disease status at the end of induction therapy as dictated by the Children’s Oncology Group Classification of Newly Diagnosed ALL protocol[12]. All children were treated either on protocol or as per standard therapy utilizing a modified BFM backbone.

AEs were recorded during the pre-maintenance phase of treatment: Day 1 of induction through Day 1 of maintenance therapy. Collected AEs included: hypertension requiring treatment, hyperglycemia necessitating insulin, pancreatitis, infections requiring admission, PICU admissions, sepsis, febrile neutropenia admissions (FN), Grade 3 nephrotoxicity necessitating delay or dose reduction in chemotherapy, Grade 3 hepatotoxicity necessitating delay or dose reduction in chemotherapy, and thrombosis. Nephrotoxicity was identified by creatinine greater than or equal to 1.5 times the patient’s baseline. Hepatotoxicity was classified as direct bilirubin greater than 1.2 mg/dL or ALT greater than ten times the upper limit of normal. Pancreatitis was acknowledged by increased lipase levels and documented diagnosis in electronic patient records. Sepsis events were recorded based on documentation in electronic patient records.

Quantitative Data Analysis

Continuous variables are summarized as mean±standard deviation; categorical variables are summarized as n(%). Univariate analysis on patient characteristics and AEs between non-obese and obese patients were performed using chi-squared or Fisher’s exact tests. Incidence rate ratios (IRR) were calculated for both recurrent events of infections requiring admission and FN admissions. Multivariable analysis with logistic regression was completed for AEs associated with obesity adjusting for age and NCI risk status. Since NCI risk status and age are highly correlated, we chose to create a new variable solely for the multivariable analysis model which melds both age and risk status (age <10 + NCI standard risk or NCI standard to high risk, age <10 + NCI high risk, age ≥10 + NCI high risk). P value <0.05 was considered as statistically significant. All statistical analyses were performed using IBM SPSS Statistics Version 22.0.

RESULTS

155 of 232 ALL patients were eligible. Of these 40 (25.8%) were obese and 115 (74.2%) were non-obese. The mean age at diagnosis was 7.64± 5.19 years, with the median age at

diagnosis of 6 years. The majority were Caucasian, male, and were diagnosed with Precursor B-Cell ALL (135, 87.1%). A smaller subset had T-Cell ALL (20, 12.9%). All patients remained in remission with no relapses during the allotted time of the study. Most were CNS Disease Group 1 (145, 93.5%) and Rapid Early Responders (134, 86.5%). CNS Disease Group 1 were defined as less than 5 WBCs per high power field and no leukemic blasts on cytospin. Rapid Early Responders were defined as less than 5% leukemic blasts in their bone marrow and negative minimal residual disease at day 29 of induction. An approximately equal number of patients were divided between the NCI Standard Risk Status Group (74, 47.7%) and High risk group (71, 45.8%), with 6.5% classified as Standard to High risk (Table 1).

Obesity was not significantly associated with ALL type (p=0.30), age (p=0.19), gender(p=1.0), and race (p=0.53). Clinical characteristics of NCI risk status (p=0.35) and early response to treatment (p=0.87) were similar between groups. Obese patients had a higher incidence of CNS status 2a disease at diagnosis (12.5% (5/40) vs. 2.6% (3/115), p=0.03) compared to CNS status 1 (Table 2).

On univariate analysis, obese patients were more likely to require treatment for hypertension (Obese vs Non-Obese 17.5% vs.6.1%, OR 3.27, 95% Confidence Interval 95%CI 1.07–10.0, p=0.049), insulin for hyperglycemia (25.0% vs.11.3%, OR 2.62, 95%CI 1.04–6.56, p=0.04), admission requiring infection (62.5% vs 42.6%, OR 2.25, 95% CI 1.07–4.70, p=0.03) and FN admissions (77.5% vs. 53.9%, OR 2.95 95% CI 1.29–6.74, p<0.01). Additionally, obese patients had a greater incidence rate for recurrent admission for infection (IRR 1.64, 95%CI 1.08–2.48, p=0.02) and recurrent admission for FN (IRR 1.53, 95%CI 1.10–2.12, p=0.01). While a greater percentage of obese patients had PICU admissions (20.0% vs. 14.0%, p=0.37), sepsis (12.5% vs. 5.2%, p=0.15), and thrombosis (10.0% vs. 7.0%, p=0.51) these were not statistically significant. Pancreatitis (2.5% vs. 9.6%, p=0.30), hepatotoxicity (5.0% vs. 7.8%, p=0.73), and nephrotoxicity (5.0% vs. 7.0%, p=1.0) were the only AEs occurring with a higher percentage of non-obese patients, but none were statistically significant (Table 3).

Multivariable analysis assessed obesity as a risk factor for hypertension requiring treatment, hyperglycemia requiring insulin, admission for infection and admission for FN (Table 4) adjusting for NCI risk status combined with age. Both obesity (OR 3.90, 95%CI 1.19–12.76, p=0.02) and NCI risk status combined with age (p=0.02) were associated with hypertension requiring treatment. Both obesity (obesity OR 3.921, 95%CI 1.39–11.05, p=0.01) and NCI risk status combined with age (p<0.01) were associated with hyperglycemia requiring insulin. Obesity's association with admission-requiring infections was no longer significant (OR 2.11, 95%CI 0.99–4.46, p=0.05) after adjusting for NCI risk status and age ≥10yo. The association between Obesity and FN admission remains significant after adjusting for NCI risk status combined with age (OR 2.92, 95%CI 1.27–6.73, p=0.01).

DISCUSSION

Obesity has doubled in children and quadrupled in adolescents in the past 30 years[10], and it equally affects children with ALL. Recognizing obesity's health risks, we sought to identify

if these risks occurred in children with ALL. The prevalence of obesity in our study population was slightly higher than nationally reported[10], but it is typical for the region in which the study took place.[13] Our study population was also similar to published frequencies of ALL type and NCI risk status[14]. In this sample of children with ALL, obesity was a risk factor during pre-maintenance chemotherapy for AEs including hyperglycemia requiring insulin and hypertension requiring treatment, and obese patients had a greater incidence rate of both infections requiring admission and FN admission. While age and NCI risk status contribute as additional risk factors for some AEs, obesity's effects remained independent of these factors for hypertension requiring treatment, hyperglycemia requiring insulin, and FN admission.

Infection related mortality is the most common cause of treatment related death in pediatric patients with ALL, and sepsis-related deaths in these patients occur more frequently in the induction phase of treatment[15]. Down Syndrome, NCI risk status and gender have been associated with an increased risk of infection in ALL[15]. Patients with FN are at an increased risk for infection. In our study, the IRR for infection is 1.64 (95%CI 1.08–2.48, p=0.019) indicating that the patients in the obese group have an 1.64 times greater incidence rate than the non-obese group. Additionally, the IRR for febrile neutropenia admission is 1.53 (95%CI 1.10–2.12, p=0.01) indicating that the patients in the obese group have a 1.53 times greater incidence rate than the non-obese group. While multivariable analysis confirmed obesity as an independent risk factor from NCI risk status combined with age for FN admissions (p=0.01), the same was not true regarding admission or infection (p=0.05). With an infectious source identified in approximately 20–25% of febrile neutropenic episodes[16], we expected to see a similar overlap in our documented infection admissions and febrile neutropenia admissions (17.2% overlap admissions for obese patients). Although we did not find increased risk of infection-related mortality, we did find a greater number of infections in obese patients. Our ability to detect infection-related mortality or identify a greater simultaneous occurrence between infection and FN in obese patients was limited by sample size and low rate of death during chemotherapy. A larger cohort may help us better understand infection-related outcomes in obese patients with ALL.

Hyperglycemia is a documented side effect of induction chemotherapy for patients with ALL due to the use of corticosteroids and asparaginase[17]. Indeed, 60.0% of hyperglycemia events occurred during the induction. Previous research has shown that being overweight (BMI ≥85th percentile) and age ≥10 years are significant predictors of transient hyperglycemia (≥2 random glucose values ≥200 mg/dl) for patients with ALL[17]. Our study parallels these conclusions, finding that the odds of hyperglycemia requiring insulin therapy among obese patients with ALL is 3.92 times the odds of non-obese ALL patients. We chose to include the requirement of insulin usage to underscore clinically significant events. Further, this eliminates limitations of previous studies including reliance on glucose levels for transient hyperglycemia and variable frequency of glucose checks after initial hospitalization. Hyperglycemia in pediatric patients with ALL is associated with increased risk of bacteremia/fungemia, cellulitis, and admission for febrile neutropenia[18]; therefore, it is a potentially serious complication of therapy. Our findings suggest the potential role for targeted glycemic monitoring which may include: random glucose checks at baseline and periodically throughout therapy, urine dipsticks during steroid therapy, and fasting glucose

levels at the time of procedures. Due to complications associated with uncontrolled hyperglycemia, the risk to this population may indicate a lower threshold for treatment with insulin.

We found that the odds of obese children with ALL requiring anti-hypertensive management are 3.9 times of the odds among non-obese children with ALL. This is consistent with the general pediatric population where obese children have an approximately 3-times higher risk for hypertension[19]. Focusing on clinically significant events, we only included hypertension-requiring treatment, which may explain why the relative risk of hypertension in our obese population is similar to that of the general pediatric population. This may have underestimated the number of hypertensive occurrences but avoided confounding the data with transient hypertension. Additionally, the similarities between the increased risk in hypertension amongst obese children with and without ALL, may indicate that pre-maintenance chemotherapy doesn't necessarily increase the risk of hypertension. However, none of the patients in our sample began therapy on anti-hypertensive medications which may indicate that ALL therapy may potentiate their baseline increased risk. The long-term consequences of hypertension, such as end organ damage rarely manifest in children, but previous studies have shown that hypertension during childhood is an independent risk factor for hypertension as an adult and may be associated with early markers of cardiovascular disease in childhood[20]. Additionally, pediatric patients with cancer have an increased risk of stroke that is perpetuated by atherosclerotic risk factors such as hypertension[21], and hypertension is the most significant risk factor for posterior reversible encephalopathy syndrome during pediatric cancer treatment[22]. Further, a large study with pediatric cancer survivors found that hypertension was a significant risk factor for the occurrence of potentially fatal cardiac events, independent of cancer therapy-related risk[23]. Given the impact of hypertension management, clinicians caring for obese children with ALL may consider screening for hypertension through home blood pressure checks, especially during steroid therapy, as this may reduce the risk of untreated hypertensive events.

While improved supportive care may mitigate obesity associated AEs, the management of these risks to patients can be burdensome. This would include increased laboratory monitoring and clinic visits, subspecialist involvement, and home monitoring. These significant health consequences and their associated burdens may be potentially limited by addressing obesity itself. Potential behavioral and nutritional interventions have been shown to be effective in adults[24] and children with ALL may present a good target for such interventions because of their frequent and prolonged interactivity with the oncology team. A structured program integrated into ALL therapy with close physician follow up and family involvement[25] provides the right ingredients for successful weight management. This could prevent additional weight gain during treatment[26] and the perpetuation of obesity into adulthood[27].

This study contains common limitations associated with retrospective chart reviews including the inability to determine causation. The limited sample size coupled with low prevalence prevented the analysis of mortality. Additionally, we appreciate that more information could be gleaned from identifying the exact phase of therapy in which the AE

occurred; however, given our sample size, identifying a particular time point as statistically significant would be challenging. Larger, perhaps cooperative, group studies may be able to better estimate the relationship between AE's and specific phases of therapy. Although one academic institution conducted the study, the sample population remained congruent with the general population in obesity rate and ALL type distribution[14,28]. Additionally, obese and non-obese groups were statistically similar in all demographics and clinical characteristics of NCI risk status group and early response group, assuring that these characteristics were not additional variables in the experimental versus control analysis. A minority of patients crossed BMI groups during the study period (7 from the obese group and 31 from the non-obese group), but re-analysis with these patients excluded did not result in any significant changes or affect the results of the study. Although we were unable to identify the concurrence of the duration of neutropenia with the timing of AEs, each patient received similar chemotherapy based on their NCI risk status, therefore attempting to control for this confounding variable on the comparison of obese versus non-obese patients. While the multivariable analysis accounted for major differences in therapy, such as NCI high risk versus standard risk status, it did not include more specific variables, such as timing of drug exposure or other subtleties in therapy between individual patients. Thus, our data suggests the possibility of this as an independent risk factor with these limitations in mind. Additionally, due to the amount of the number of events in the outcome of the multivariable analysis, the number of confounders we can adjust for in the multivariable model is limited. Chart reviews are limited to bias and deficient medical records, but all incomplete charts (n=1) were disqualified from the study. Abstractors were not blinded, but additional requirements to variables such as requiring hospitalization or necessitating medication ensured standardization to abstraction and avoided misclassification.

These data demonstrate that during pre-maintenance chemotherapy for ALL, obesity is a risk factor for FN admissions, the development of hyperglycemia requiring insulin, and hypertension requiring treatment. As such, obese children with ALL represent a group of patients at risk for poor outcomes due to treatment related morbidity. Early management of these AEs and surveillance initiated at diagnosis may mitigate risk in this distinct population of patients. Additionally, the creation of intensive weight management programs focused on improved nutrition and physical activity may also decrease the risk of treatment related complications and prevent long term sequelae related to ALL therapy and obesity itself.

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Abbreviation

ALL	Acute Lymphoblastic Leukemia
AE	Adverse Events
FN	Febrile Neutropenia admissions
PICU	Pediatric Intensive Care Unit

IRR	Incidence Rate Ratio
OR	Odds Ratio
NCI	National Cancer Institute
BMI	Body Mass Index
CNS	Central Nervous System

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TABLE 1

Demographics and clinical characteristics

# ALL Patients	155
ALL Type	
Precursor B-Cell	135 (87.1%)
Precursor T-Cell	20 (12.9%)
Demographics	
Age at Diagnosis (Years)	7.64 ± 5.19
Age Group	
< 10 years	99 (63.9%)
≥ 10 years	56 (36.1%)
Gender	
Male	93 (60.0%)
Female	62 (40.0%)
Race	
Caucasian	139 (89.7%)
Black-American	12 (7.7%)
Indian	1 (0.65%)
Asian	2 (1.3%)
Not Specified	1 (0.65%)
BMI Percentile	64.29 ± 28.00
BMI Percentile Group	
≥ 95	40 (25.8%)
85 ≤ x < 95	12 (7.7%)
10 ≤ x < 85	103 (66.5%)
Clinical Characteristics	
CNS Disease Group	
1	145 (93.5%)
2a	8 (5.2%)
2b	1 (0.65%)
2c	1 (0.65%)
NCI Risk Status Group	
Standard	74 (47.7%)
High	71 (45.8%)
Standard to High	10 (6.5%)
Early Response Group	
Rapid	133 (85.8%)
Slow	22(14.2%)

Categorical variables reported as n (%); continuous variables reported as mean ± Standard Deviation

TABLE 2

Obese and non-obese patients with ALL by demographics and clinical characteristics

	Group N	Obese Patients n (% of Obese Total)	Non-Obese Patients n (% of Non-Obese Total)	P-Value
# Patients	155	40	115	
ALL Type				0.31
Precursor B-Cell	135	33 (82.5%)	102(88.7%)	
Precursor T-Cell	20	7 (17.5%)	13(11.3%)	
Demographics				
Age Group				0.19
< 10	99	29 (72.5%)	70(60.9%)	
≥ 10	56	11 (27.5%)	45 (39.1%)	
Gender				1.00
Male	93	24 (60.0%)	69 (60.0%)	
Female	62	16 (40.0%)	46 (40.0%)	
Race				0.53[1]
Caucasian	139	34 (87.2%)	105 (91.3%)	
Black-American	12	4 (10.3%)	8 (7.0%)	
Indian	1	0	1 (0.9%)	
Asian	2	1 (2.6%)	1 (0.9%)	
Clinical Characteristics				
CNS Disease Group				0.13[2]
1	145	35 (87.5%)	110(95.7%)	
2a	8	5 (12.5%)	3 (2.6%)	0.03[3]
2b	1	0	1 (0.9%)	
2c	1	0	1 (0.9%)	
NCI Risk Status Group				0.35
Standard	74	21 (52.5%)	53 (46.1%)	
High	71	15 (37.5%)	56 (48.7%)	
Standard to High	10	4 (10.0%)	6 (5.2%)	
Early Response Group				0.87
Rapid	133	34 (85.0%)	99(86.1%)	
Slow	22	6 (15.0%)	16 (13.9%)	

[1] P-value reported for Caucasian vs. Non-Caucasian, excluded 1 patient race with not specified

[2] P-value reported for CNS Disease Group 1 vs. Combined CNS Group 2a, 2b, and 2c

[3] P-value reported for CNS Disease Group 1 vs. CNS group 2a between Obese vs. Non-Obese Groups

TABLE 3

Univariate Analysis: Incidence by obese and non-obese patients with ALL

	Total Pop	Obese Patients n (% of Obese Total)	Non-Obese Patients n (% of Non-Obese Total)	Odds Ratio	95% CI	P-Value
# Patients	155	40	115			
Hypertension, Requiring Treatment	15	7 (17.5%)	8 (6.9%)	3.27	1.07–10.0	**0.049**
Hyperglycemia, Requiring Insulin	23	10 (25.0%)	13 (11.3%)	2.62	1.04–6.56	**0.04**
Pancreatitis	12	1 (2.5%)	11 (9.6%)	0.24	0.03–1.96	**0.30**
PICU Admissions	23	8 (20.0%)	15 (13.0%)	1.53	0.60–3.91	**0.37**
Infection, Requiring Admission	74	25 (62.5%)	49 (42.6%)	2.25	1.07–4.70	**0.03**
Sepsis	11	5 (12.5%)	6 (5.2%)	2.60	0.75–9.03	**0.15**
Fever and Neutropenia Admissions	93	31 (77.5%)	62 (53.9%)	2.95	1.29–6.74	**<0.01**
Thrombosis	12	4 (10.0%)	8 (7.0%)	1.46	0.41–5.13	**0.51**
Hepatotoxicity	11	2 (5.0%)	9 (7.8%)	0.62	0.13–3.0	**0.73**
Nephrotoxicity	10	2 (5.0%)	8 (7.0%)	0.71	0.14–3.46	**1.00**

Statistics reported as n (%) of patients experiencing each event

TABLE 4

Multivariable effects on adverse events (hypertension, hyperglycemia, and infection)

Effects on Hypertension				
	Variable	**Odds Ratio**	**95% CI for Odds Ratio**	**P-Value**
	Obesity	3.901	1.193–12.763	0.024
	NCI Risk Status, Standard and Standard to High & Age <10	ref	ref	0.023
	NCI Risk Status, High & Age <10	9.541	1.802–50.505	0.008
	NCI Risk Status, High & Age ≥10	4.670	1.106–19.715	0.036
Effects on Hyperglycemia Requiring Insulin				
	Variable	**Odds Ratio**	**95% CI for Odds Ratio**	**P-Value**
	Obesity	3.921	1.391–11.053	0.010
	NCI Risk Status, Standard and Standard to High & Age <10	ref	ref	0.001
	NCI Risk Status, High & Age <10	0.820	0.089–7.564	0.861
	NCI Risk Status,High & Age ≥10	6.632	2.245–19.594	0.001
Effects on Infections Requiring Admission				
	Variable	**Odds Ratio**	**95% CI for Odds Ratio**	**P-Value**
	Obesity	2.106	0.994–4.464	0.052
	NCI Risk Status, Standard and Standard to High & Age <10	ref	ref	0.098
	NCI Risk Status, High & Age <10	1.467	0.482–4.472	0.500
	NCI Risk Status,High & Age ≥10	0.519	0.256–1.051	0.069
Effects on FN Admission				
	Variable	**Odds Ratio**	**95% CI for Odds Ratio**	**P-Value**
	Obesity	2.921	1.268–6.731	0.012
	NCI Risk Status, Standard and Standard to High & Age <10	ref	ref	0.486
	NCI Risk Status, High & Age <10	2.100	0.610–7.231	0.239
	NCI Risk Status,High & Age ≥10	1.014	0.501–2.051	0.969

*The grayed out p values are the p values comparing the NCI Risk status and Age group to the reference NCI Risk Status and Age group.