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Impact of pediatric obesity on acute asthma exacerbation in Japan

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Abstract

Background: Asthma and obesity are common health problems in children. This study investigated the impact of obesity on children hospitalized with acute asthma exacerbation.

Methods: We obtained the hospital discharge records of inpatients aged 3-8 years with a diagnosis of asthma using a national inpatient database in Japan. The patients were classified into underweight, normal weight, overweight, and obese groups using weight for height and body mass index for age provided by the World Health Organization. We compared 30-day re-admission, need for intensive care, mean total hospitalization costs, and length of hospital stay between the 4 groups using multivariable regression models.

Results: Overall, 38 679 patients were identified, including 3177 underweight, 28 904 normal weight, 3334 overweight, and 3264 obese patients. The obese group showed significantly higher 30-day re-admission (adjusted odds ratio, 1.26; 95% confidence interval, 1.03-1.54) and longer length of stay (adjusted difference, 0.12 days; 95% confidence interval, 0.10-0.20 days) than the normal weight group. The threshold was a 91st percentile of weight for length or body mass index for the relationship with 30-day re-admission. No significant difference was observed between the 4 groups regarding the need for intensive care and total hospitalization costs.

Conclusion: These findings demonstrated that obesity was a risk factor for repeated admissions caused by asthma in children, indicating the importance for the prevention of pediatric obesity.

KEYWORDS

asthma, children, Diagnosis Procedure Combination inpatient database, obesity

1 | INTRODUCTION

Asthma and obesity are common chronic illnesses and public health problems of children in developed countries. The prevalence of asthma and obesity is increasing, and several studies reported an association between obesity and asthma in children.[1-10]

Obesity is believed to be a complicating factor in the treatment and control of asthma. Obese children with asthma exhibited a poor control of asthma, were hospitalized more often, and had a lower quality of life compared with normal weight children.[11-14] In addition, obese children showed a decreased response to inhaled corticosteroids,

Abbreviations: ICD-10 code, The International Classification of Disease, Tenth Revision code; WFL, weight for length; BMI, body mass index for age; AR, allergic rhinitis; FA, food allergy; OR, odds ratio; CI, confidence interval.

which resulted in a greater need of beta-stimulants and corticosteroids during acute exacerbation.[11-14] Several studies conducted in a few hospital catchment areas reported the inconsistent results regarding the association between obesity, severity, and healthcare utilization of acute asthma exacerbation.[15-17]

Nationwide studies in the USA demonstrated obesity was associated with an increased risk for intensive care, prolonged length of hospital stay, and greater costs for pediatric inpatients with acute asthma exacerbation.[18-20] Thus, obesity seems to be a risk factor for severe asthma exacerbation and an economically complicating factor. Recently, a significant association between obesity and repeated admission was observed in adult women with asthma.[21,22] However, no study has investigated the impact of obesity on repeated admissions among children.

Therefore, this study aimed to investigate the relationship between obesity and repeated admissions in hospitalized children with acute asthma exacerbation, using a national inpatient database in Japan. In addition, we evaluated the impact of obesity on healthcare costs, length of hospital stay, and risk of intensive care, and compared the results with those in previous studies.[18-20]

2 | METHODS

2.1 | Study population and participation

We analyzed the hospital discharge records of hospitalized patients between 3 and 18 years of age with acute asthma exacerbation based on the Diagnosis Procedure Combination inpatient database between July 1, 2010, and March 31, 2015. The details of the database have been described elsewhere.[23] Briefly, the data were collected from more than 1000 hospitals that cover 50% of all inpatient admissions to acute-care hospitals in Japan. The database contains hospital discharge records and administrative claims data for approximately 7 million inpatients per year, including the information on the main diagnosis, preexisting comorbidities at admission, complications during hospitalization, the patient's age, sex, body weight and height, and the dates when the procedures were performed. We obtained study approval from the Institutional Review Board at The University of Tokyo. The requirement for informed consent was waived because of the anonymous nature of the data.

Hospitalizations with acute asthma exacerbation were identified from the main diagnosis at admission using *the International Classification of Disease*, *Tenth Revision code* (ICD-10 code, J45.x or J46). We used only data of index admission for patients who were hospitalized repeatedly. We excluded children with chronic medical conditions other than asthma and obesity (congenital heart, kidney, pulmonary, endocrine, hematologic, gastrointestinal, and neurologic diseases; cancer or leukemia; and autoimmune disease) using the pediatric complex chronic conditions classification system version 2.[24]

2.2 | Measurements of variables

The *z*-scores and percentiles of weight for length (WFL) or body mass index for age (BMI) were calculated based on the recommendations of the World Health Organizations. These recommendations are based on data from various international communities and are considered global standards for the growth of healthy children. Patients were categorized into 4 groups: underweight (<5 percentile), normal weight (5-85 percentile), overweight (85-95 percentile), and obese (>95 percentile). Patient characteristics included age, sex (male or female), and preexisting comorbidities of allergic disorders, such as allergic rhinitis (AR), atopic dermatitis or eczema (AD), and food allergy (FA). Hospital characteristics consisted of hospital type (academic or non-academic).

The outcomes of interests were 30-day re-admission, need for intensive care, the mean total length of hospital stay in days, and the mean total hospitalization costs in Japanese yen (¥). The currency exchange rate was approximately 100-120 Japanese yen per US dollar. The need for intensive care was defined as admission to an intensive care unit, use of non-invasive or invasive mechanical ventilations, or use of extra corporeal membrane oxygenation.

2.3 | Statistical analyses

Baseline characteristics (age, sex, preexisting allergic disorders, and hospital type) between the 4 groups of WFL/BMI were compared using Kruskal-Wallis tests and chi-square tests as appropriate. Multivariable logistic regression analyses were conducted to identify the associations of WFL/BMI categories with 30-day re-admission and the need for intensive care. Multivariable linear regression was used to assess the relationship between WFL/BMI categories, total hospitalization costs, and total length of hospital stay. Log transformations of total hospitalization costs and length of hospital stay were necessary to ensure the validity of error-term normality assumptions. For the adjustment of potential confounders, we added all the baseline characteristics listed above into the multivariable regression models.

We also investigated the dose-response relationship between the *z*-score of WFL/BMI and the odds of re-admission using a restricted cubic spline function fitted for logistic regression models. Restricted cubic spline functions can fit nonlinear associations. In restricted cubic spline functions, all data points are used to estimate the dose-response association between the continuous independent variable and the outcome.[25] Odds ratios and 95% confidence intervals were calculated for the *z*-scores of WFL/BMI with 4 knots corresponding to the 5th, 50th, 85th, and 95th percentiles of WFL/BMI. The reference level was set to the 50th percentile of WFL/BMI. The spline curve was constructed using the "mkspline" command in STATA.

The results were reported with 95% confidence intervals (95% CIs). Statistical significance was two-sided $P < .05$ for all analyses. All data were analyzed using STATA software version 14.1 (StataCorp LP, College Station, TX, USA).

3 | RESULTS

Overall, 38 679 patients hospitalized with acute asthma exacerbations were identified, including 3177 (8.2%) underweight, 28 904 (74.7%)

normal weight, 3334 (8.6%) overweight, and 3264 (8.4%) obese patients. The baseline characteristics between the 4 groups are summarized in the Table 1. Obese patients were older ($P < .001$), more likely to be male ($P < .001$), and more likely to have preexisting comorbidity of AR ($P < .001$) than children in other groups.

Table 2 shows the proportions of patients requiring 30-day re-admissions and need for intensive care between the 4 groups. Adjusted odds ratio (OR) of 30-day re-admission, comparing obese group with normal weight group, was statistically significant (adjusted OR, 1.26; 95% CI, 1.03-1.54). The need for intensive care was not different between the 4 groups in the adjusted analyses.

Multivariable linear regression analyses showed that the mean total costs for hospitalizations were similar between the 4 groups (Table 3). The mean total length of stay was 0.12 days longer in the obese group than in the normal weight group (95% CI, 0.10-0.20 day).

Figure 1 depicts the dose-response relationship between the *z*-score of WFL/BMI and re-admission within 30 days using a restricted cubic spline logistic regression model. The restricted cubic spline curve showed a U-shaped relationship between the *z*-score of WFL/BMI and the odds of re-admission. The OR of re-admission was lowest in patients with a *z*-score of −0.27 (39 percentile). The threshold for the relationship between the *z*-score and re-admission was a *z*-score of 1.34 (91st percentile).

4 | DISCUSSION

Our study demonstrated that obese children hospitalized with acute asthma exacerbation are associated with an increased risk of 30-day re-admission and longer length of hospital stay, compared with normal weight children. No significant differences in the need for intensive care and total costs for hospitalization were observed between underweight, normal weight, overweight, and obese groups.

Recently, obesity was reported to be associated with an increased risk of re-admission in adult inpatients with asthma.[21,22] Previous studies revealed potential risk factors associated with hospital re-admissions in pediatric asthma, including age, race/ethnicity, socioeconomic status, medication adherence, access to healthcare, and a history of sinusitis.[26-29] However, an association between pediatric obesity and re-admission because of asthma remains unclear. Our findings demonstrated that even in children, obesity was also associated with an elevated risk of re-admission. These results suggest that obese children require more attention and greater treatment to control their asthma after discharge from hospital.

Studies showed obesity led to greater illness severity in patients with asthma.[20,30] Nationwide studies in the USA revealed that obesity was associated with the use of non-invasive or invasive mechanical ventilation among hospitalized children with acute asthma exacerbation (odds ratio, 1.59; 95% CI, 1.28-1.99).[20] On the other hand, our study did not show a significant difference in the risk of intensive care, such as mechanical ventilation or intensive care unit admission, between obese and normal weight groups. We believe the reasons for these inconsistent results were multifactorial, including differences of access to health care, adherence of long-term treatment, and the severity of asthma and obesity between the USA and Japan.

Obesity is an economically complicating factor for children hospitalized with asthma in the USA. Nationwide studies in the USA from 2000 to 2012 revealed that obesity was associated with increased hospitalization costs and prolonged length of stay among children with asthma (Table S1).[18-20] The differences in cost and length of hospital stay between obese and normal weight pediatric inpatients with asthma were $1588-2145 and 0.24-0.59 days, respectively.[18-20] In contrast, our results demonstrated the difference

TABLE 1 Baseline characteristics between underweight, normal weight, overweight, and obese groups

	Underweight	Normal weight	Overweight	Obese	*P*-value
Total, n	3177	28 904	3334	3264	
Age (y), mean (SD)	6.69 (0.05)	6.37 (0.02)	6.76 (0.06)	7.57 (0.05)	<.001
Sex, n (%)					
Male	1955 (61.5)	16 645 (57.6)	2006 (60.2)	2191 (67.1)	
Female	1222 (38.5)	12 259 (42.4)	1328 (39.8)	1073 (32.9)	<.001
Preexisting comorbidity					
Food allergy, n (%)	37 (1.2)	428 (1.5)	41 (1.2)	34 (1.0)	.09
Atopic dermatitis, n (%)	67 (2.1)	636 (2.2)	79 (2.4)	66 (2.0)	.79
Allergic rhinitis, n (%)	161 (5.1)	1600 (5.5)	277 (6.8)	221 (6.8)	<.001
Hospital type					
Academic, n (%)	391 (12.3)	3622 (12.5)	388 (11.6)	367 (11.2)	.11

SD, standard deviation.

TABLE 2 Odds ratio (OR) of need for intensive care and 30-day re-admission, comparing underweight, overweight, and obese groups to normal weight group

	Underweight	Normal weight	Overweight	Obese
Re-admission, n (%)	102 (3.2)	841 (2.9)	104 (3.1)	117 (3.6)
Crude OR	1.11	–	1.07	1.24
Adjusted OR (95% CI)	1.13 (0.91, 1.39)	–	1.06 (0.87, 1.31)	1.26 (1.03, 1.54)
P-value	.26	–	.55	.02
Intensive care, n (%)	36 (1.1)	265 (0.9)	25 (0.7)	28 (0.9)
Crude OR	1.24	–	0.82	0.94
Adjusted OR (95% CI)	1.25 (0.88, 1.77)	–	0.82 (0.55, 1.25)	0.95 (0.77, 1.11)
P-value	.22	–	.36	.82

TABLE 3 Difference in total costs and length of hospital stay (LOS) comparing underweight, overweight, and obese groups to normal weight group

	Underweight	Normal weight	Overweight	Obese
Total cost in JPY, mean	29 679	29 320	29 751	30 121
Crude difference	359	–	431	802
Adjusted difference (95% CI)	454 (−5602, 1694)	–	371 (−667, 1576)	815 (−279, 2083)
P-value	.43	–	.51	.15
Total LOS (d), mean	5.22	5.21	5.13	5.30
Crude difference	0.01	–	−0.08	0.09
Adjusted difference (95% CI)	0.02 (−0.13, 0.12)	–	−0.06 (−0.13, 0.01)	0.12 (0.10, 0.20)
P-value	.65	–	.10	.003

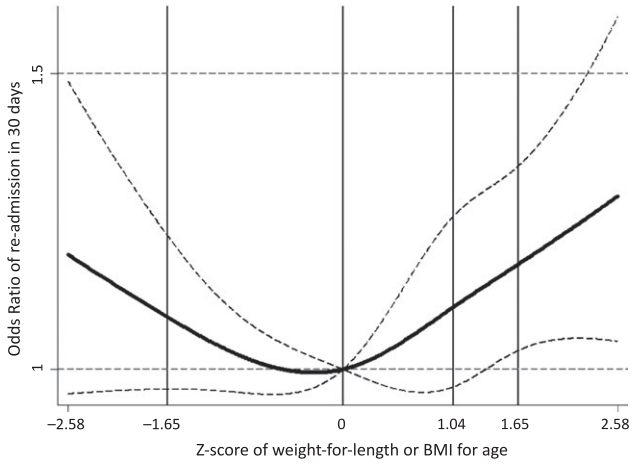

FIGURE 1 Adjusted dose-response relationship between the *z*-score of weight for length (WFL) or body mass index for age (BMI) and 30-day re-admission in acute asthma exacerbation. The dose-response curve was restricted to 4 knots represented by vertical lines (*z*-scores of −1.65 (5 percentile), 0 (50 percentile), 1.04 (85 percentile), and 1.65 (95 percentile)). *Y*-axis indicates the odds ratio (OR) of re-admission compared with the reference value of 0 on the *z*-score. Dashed black lines were the estimated 95% confidence intervals

in total costs between obesity and normal weight asthma patients was insignificant, which may have reflected the different payment and insurance systems between the USA and Japan. Furthermore, our study showed that the difference in length of hospital stay was 0.12 days between the 2 groups. These differences in length of hospital stay may reflect the difficulty and complexity of procedures such as airway management, complications, and greater severity of the illness.

There are several limitations in our study. The number of preexisting allergic disorders may have been under-estimated and led to the bias toward the null because of possible misclassifications. Several potential confounders could not be adjusted because detailed clinical information, patient socioeconomic factors, and laboratory data were unavailable in the Diagnosis Procedure Combination database. A unique feature and strength of this study was the use of a national inpatient database to examine the associations between WFL/BMI and the clinical outcomes of asthma among hospitalized children in Japan. The database contains information on patient weight and height, and the classifications of obesity were much more accurate than those in the Kids' Inpatient Database, where the classifications of obesity depend on ICD-9 codes.[18-20] Using the Japanese database,

we were able to calculate robust national estimates of the effects of obesity on asthma exacerbations among pediatric inpatients.

In summary, pediatric obesity was significantly associated with an increased risk of 30-day re-admission for Japanese children hospitalized with acute asthma exacerbation. Our investigations provide important information for the prevention of obesity in children with asthma.

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SUPPORTING INFORMATION

Additional Supporting Information may be found online in the supporting information tab for this article.

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