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Factors Associated With Pneumonia Among Overweight and Obese Under-Five Children in an Urban Hospital of a Developing Country

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Abstract

To our knowledge, there are no data on the role of overweight and obesity in childhood pneumonia. We sought to determine that impact of overweight and obesity in such children. In this retrospective chart analysis, we enrolled hospitalized children aged 6 to 59 months in the Dhaka Hospital of the icddr,b, Bangladesh (International Centre for Diarrhoeal Disease Research, Bangladesh), from January 2010 to June 2014. Children with pneumonia having overweight and obesity (body mass index *Z* score [BMIZ] >2.00) constituted cases (n = 25), and those who had pneumonia without overweight and obesity (BMIZ −2.00 to 2.00) constituted controls (n = 75). Controls were 3-fold of the cases and were randomly selected. Demographic, clinical, and laboratory data of the cases and the controls were compared. The cases more often had diarrhea and dehydration (36% vs 12%, $P = .013$), hypoxemia (SpO_2 < 90% in room air; 28% vs 7%, $P = .009$) on admission, and required to change antibiotics (32% vs 11%, $P = .023$) during hospitalization compared to the controls. However, in logistic regression analysis the cases were independently associated with diarrhea ($P < .001$) and hypoxemia ($P = .024$) on admission. Our data suggest that overweight and obesity in children with pneumonia is prone to be associated with hypoxemia on admission, which may guide clinicians in promptly managing pneumonia in order to evade its ramification in such children. However, future research with larger samples is imperative to consolidate or refute our observation.

Keywords

overweight and obesity, children, pneumonia, developing country

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Introduction

Pneumonia is a major concern for under-5 mortality and morbidity especially in developing countries.[1,2] It is estimated that about 0.9 million deaths happened due to pneumonia out of the total 6.3 million under-5 deaths in this population in 2013.[3,4] Malnutrition is also a global health burden for child health.[5] The spectrum of malnutrition is not limited to undernutrition but also includes over-nutrition. In 2013, the World Health Organization (WHO) estimated that more than 42 million under-5 children were overweight globally and close to 33 million were from Asia, Africa, Latin America, and Caribbean.[6] Moreover, the increasing incidence of childhood obesity has become a public health concern,

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and it not only deteriorates the quality of life but also has substantial role in morbidity.[7-9] Though obesity in children is an epidemic in developed countries, it is an emerging issue for children in low and middle income countries, especially those growing up in urban environments and able to afford a solvent lifestyle.[10,11] Although overweight and obesity in under-5 children is still not obvious in rural area in Bangladesh, it is about 10% among all the children in urban areas.[12] A systematic review also showed that overweight and obesity consisted of 10% to 25% among this age group in urban areas, though in rural areas it is insignificant.[13] Pneumonia is also a major health burden for under-5 children in Bangladesh. It has been estimated that every year there are 6 million new cases of pneumonia detected in this country.[14]

It has been evident that in case of adults, obesity shows some negative impacts on respiratory illnesses in terms of their susceptibility and prognosis.[15,16] Worse prognosis of respiratory infection can occur due to a significant alteration of pulmonary physiology leading to reduced lung volumes, decreased compliance, abnormal ventilation and perfusion relationships, and respiratory muscle inefficiency.[17] However, there were some contrasting results also. One publication showed that it has some protective effect up to 30 days postdischarge mortality from community-acquired bacterial pneumonia,[18] and another study did not find any difference in mortality between morbidly obese and non-obese patients admitted in the intensive care unit because of pneumonia.[19] These may create some paradox regarding the role of obesity in adult pneumonia. However, there is scarcity of data on child obesity and its impact on pneumonia. Thus, we ought to know whether overweight and obesity has any impact on children with pneumonia, especially those are under-5 years old, as the overall death rate is high in this age group.[20,21]

Materials and Methods

Study Site

The study was conducted at the Dhaka Hospital of icddr,b (International Centre for Diarrhoeal Disease Research, Bangladesh), the largest diarrheal disease hospital in the world that treats all diarrheal diseases with or without complication, acute respiratory infections, malnutrition and other enteric diseases free of cost. It has a fully electronic patients' database system, and all the patients' data are preserved for both clinical and research purposes. The detail description of the study site has been mentioned elsewhere.[1]

Design

In this retrospective chart analysis, we enrolled all hospitalized children aged 6 to 59 months with a diagnosis of pneumonia from January 2010 to June 2014. Cases were overweight and obese children. Controls were children having pneumonia with a normal body mass index *Z* score (BMIZ) and chosen in a ratio of 1:3; thus, there was 3-fold of cases from the rest of the children with pneumonia by computer-aided automatic random selection process for data collection and analysis. Chronic lung disease such as pulmonary tuberculosis or children with any congenital malformation were excluded from this study. Data were transcript from hospital electronic patients' database by using a predefined case record form.

Definition of Overweight and Obesity

According to the WHO, BMIZ score >2.00 is considered as overweight and BMIZ >3.00 as obesity among the children from birth to age 5.[22,23] BMIZ between −2.00 and 2.00 was considered as normal.[22,23]

Diagnosis and Management of Pneumonia

Pneumonia diagnosis was done following the WHO criteria for under-5 children;[24] the study children were managed in accordance with the protocolized guidelines of the hospital that is based on local and global evidence.[25-27] Explicit management of pneumonia is provided elsewhere.[1]

Diagnosis and Management of Diarrhea

Diarrhea was defined as having loose or watery stools at least 3 times per day, or more frequently than normal for an individual.[28] Management was done in accordance with the protocolized guidelines of the hospital that is based on local and global evidence.[26,27]

Ethical Statement

According to the organization's policy, no permission from the "Institutional Review Board (IRB)" is required for such retrospective chart analysis; however, permission from the 'Ethical Review Committee (ERC)' of icddr,b was obtained to collect data and for analysis. All data were analyzed anonymously, no information was disclosed with study participants and others.

Data Analysis

Pretested case record forms were used to collect patients' demographic, clinical, and laboratory data and

then transferred to a personal computer using standard statistical software (eg, Statistical Package for Social Sciences [SPSS], Windows Version 17.0; Chicago, IL) and Epi Info (Version 7.0, Stone Mountain, GA). Data were compared between the 2 groups to see differences. For continuous variables, Student's *t* test (for normally distributed data) or Mann-Whitney *U* test (for not-normally distributed data) was used to compare groups. For categorical variables, Fisher's exact test was used when a cell value of 2/2 table was <5; and for all other cases, χ^2 test with Yates correction was used. Finally, logistic regression was performed for comparison between the groups to determine the factors associated with pneumonia among overweight and obese children. Factors that were significantly associated in univariate analysis were included in the model and then it was further adjusted for age, gender, and other clinical variables. A probability of <.05 was considered as statistically significant.

Results

A total of 11 274 children aged 6 to 59 months were admitted with pneumonia during the study period, of whom 25 were overweight and obese (32% obese and 68% overweight) and 11 249 had normal BMI. In our observation, the median age of the children was 9 months (interquartile range [IQR] = 7.5, 14.5) in cases and 10 months (IQR = 6.0, 15.5) among controls, and the distribution is comparable among the groups (Table 1). Though male sex was predominant among the cases compared to the controls (68% vs 64%), the distribution was also comparable among the groups (Table 1). Similarly, the rate of breastfeeding at least up to 6 months of age was slightly higher among the cases than the controls, but there was no significant difference between these 2 groups (Table 1).

Overweight and obese children often had diarrhea, some or severe dehydration and hypoxemia on admission, and required to change antibiotics during hospitalization compared to those among normal weight children (Table 1). As per hospital guidelines, we used combination of parenteral ampicillin and gentamycin as first-line antibiotics for pneumonia, ceftriaxone and levofloxacin as second-line antibiotics, and ceftazidim and amikacin as third-line antibiotics. Antibiotics were changed when there was no clinical improvement within 48 hours from staring of antibiotics or if there was any deterioration within 24 hours. Moreover, in logistic regression analysis after adjusting the potential confounders, diarrhea and hypoxemia remained as independent associated factors of pneumonia among overweight and obese children (Table 2). Other variables shown in Table 1 were still comparable among the groups.

Due to 100% free of cost hospital and resource limited setting, we do not have the luxury to perform any test for viral isolation to know the causative organism for these infections (pneumonia, diarrhea). However, in some cases we perform bacterial culture if clinical conditions warrant for such tests for prognostic purposes. In this study population, we also did some bacteriological cultures of some patients as per requirements but the isolation rate was poor (Table 3).

Discussion

This study found some significant associated factors of pneumonia among children having overweight and obesity, and frequent observation of hypoxemia is the leading one. Inflammation in lung parenchyma in pneumonia may further deteriorate by the production of adipocytokines, leptin and adiponectin, cytokines, acute-phase proteins, and other mediators produced by the adipose tissue that trigger immune response of lung.[29,30] Children with obesity and overweight potentially have increased amount of adipose tissue, which subsequently produce more inflammatory mediators and may contribute in deteriorating the condition. Therefore, overweight and obese children often encounter rapidly deteriorating pneumonia, potentially resulting in profound ventilation perfusion mismatch and hypoxemia.[31] However, due to lack of proper logistic support in this resource-limited hospital we could not elicit the CO_2 level and other biochemical changes in their blood gases. This retrospective study also restricted us from knowing about how long oxygen was required for those patients to becoming non-hypoxemic on room air.

On the other hand, we may speculate that the obese children were late in hospitalization, which may have contributed to this worse scenario of pneumonia. However, the data suggest that the perception of caregivers regarding diarrhea is much better than the perception of pneumonia.[32] As 86% (6/7) of hypoxemic cases had diarrhea, we could anticipate that there might not have been any delay in hospitalizing these children by the caregivers.

The requirement of frequent changing of antibiotics in pneumonia among children with overweight and obesity is another important observation of this study. As we have already mentioned that this is a resource-limited setting, the antibiotics was changed on the basis of clinical deterioration, not on the basis of bacterial or viral isolates. In some cases we did bacterial culture but the rate of isolation was poor. A number of evidences linking adipose tissue and immune competent cells with clinical and epidemiological data support that the incidence and severity of infectious illnesses are higher in

Table 1. Demographic, Clinical and Laboratory Characteristics of Pneumonia Among Overweight and/or Obese and Normal Weight Children Aged 6 to 59 Months With Pneumonia on Hospital Admission[a].

Indicators	Overweight and/or Obese (n = 25) (%)	Normal BMI (n = 75) (%)	OR	95% CI/Mean Difference	*P*
Demographic and clinical characteristics					
Age in months (median, IQR)	9 (7.5, 14.5)	10 (6.0, 15.5)	1.01	0.96-1.07	.728
Male child	17 (68)	48 (64)	1.20	0.42-2.38	.716
Breastfed at least up to 6 months	10 (40)	22 (30)	1.61	0.72-2.80	.322
Diarrhea	18 (72)	22 (29)	6.19	2.06-19.25	**<.001**
Severe pneumonia	16 (64)	40 (53)	1.56	0.68-2.85	.352
Hypoxemia (SpO_2 < 90%)	7 (28)	5 (7)	5.44	1.34-22.94	**.009**
Dehydration (some/severe)	9 (36)	9 (12)	4.13	1.25-13.80	**.013**
Vomiting	9 (36)	18 (24)	1.78	0.60-5.23	.241
Fever (temperature >37.9°C)	16 (64)	36 (48)	1.93	0.69-5.44	.165
Laboratory characteristics					
Hypokalemia (K^+ < 3.5 mmol/L)	2/11 (18)	2/8 (25)	0.67	0.05-9.55	1.00
Hypernatremia (Na^+ > 150 mmol/L)	4/11 (36)	1/8 (12)	4	0.27-121.78	.337
Hypocalcemia (Ca^{2+} < 2.0 mmol/L)	4/6 (66)	0/5 (0)			.06
Admission hematocrit % (mean ± SD)	33.3 ± 4.3	32.6 ± 4.4	0.96	0.86-1.09	.552
Admission WBC count (median, IQR)	11 475 (9000, 18 100)	14 000 (10 560, 18 000)	1.0		.846
High creatinine level (>35 mmol/L in infants and >62 mmol/L in children)	4/11 (36)	1/7 (14)	3.43	0.22-106.3	.595
Antibiotics required for recovery					
Required to change antibiotics	8 (32)	8 (11)	3.94	1.13-13.84	**.023**

Abbreviations: BMI, body mass index; OR, odds ratio; CI, confidence interval; SD, standard deviation; IQR, interquartile range.
[a]Data represent n (%), unless specified.
Note: Statistically significant P values are expressed as bold

Table 2. Logistic Regression Analysis for Clinical Characteristics Among Overweight and Obese Versus No Overweight And Obese Among Under-5 (6-59 Months) Children.

Variables	OR	95% CI	*P*
Comorbidity: Diarrhea	5.89	2.08-16.65	**<.001**
Hypoxemia (SpO_2 < 90%)	4.91	1.24-19.45	**.024**
Severe pneumonia	0.537	0.16-1.75	.303
Dehydration (some/severe)	1.49	0.38-5.81	.566
Fever (temperature > 37.9°C)	1.51	0.49-4.65	.471
Required to change antibiotics	2.02	0.49-8.38	.333

Abbreviations: OR, odds ratio; CI, confidence interval.
Note: Statistically significant P values are expressed as bold

Table 3. Bacterial Isolates Among Cases and Controls During Hospital Stay.

Sample	Overweight and/or Obese	Normal BMI
Blood	1/11 (*Enterococcus faecalis*)	0/10
Urine	1/9 (*Campylobacter* species)	1/11 (*Shigella* species)
Stool	2/5 (*Candida* species X 02)	0/3

Abbreviation: BMI, body mass index.

obese persons as compared to normal individuals, together with poor antibody responses to antigens in overweight subjects.[33,34] Consequently, overweight and obesity may result in a severe form of pneumonia. Thus, these children either often do not improve in time or develop rapidly deteriorating pneumonia or often require frequent changes in antibiotics according to the WHO recommendation of deteriorating pneumonia.[24]

The observation of independent association of diarrhea among children with pneumonia who are overweight and obese is difficult to explain; however, we anticipate that these may have happened as the data were collected from a large diarrheal disease hospital where admission of children with pneumonia having diarrhea are dominant compared to those without diarrhea.

The ultimate observation of dehydration as insignificant in children with pneumonia who are overweight and obese after adjusting for potential confounders is consistent with observations of recent studies.[35]

We noted one important observation in our study participants, that is, lack of breastfeeding or practice of formula feeding had no association with overweight or obesity, and this might be due to the fact that 70% of our control children were non-breastfed or had received

formula milk. Although previous studies showed that lack of breast feeding had a significant impact in protecting childhood obesity,[36,37] most of the patients in our hospital come from low-income households and may have a chance of using diluted formula feeding for their children, and so the children did not develop overweight or obesity.

There are some limitations in this study. Although the national average of overweight children in an urban site is about 10%, it was found to be much less (<1%) in this study due to the hospital setting. The icddr,b hospital is a 100% free of cost hospital for people and the patients of this hospital usually come from very poor socioeconomic status. This may have contributed to this poor number of overweight children. The retrospective nature of our study instigated us to avoid many important variables such as socioeconomic status of the children and food habit in relatively older children. Another one is the small sample size, which might not reflect the scenario of the large population. Finally, Dhaka Hospital of icddr,b is well known as a diarrheal disease hospital, and most of the children with pneumonia had diarrhea that led to diarrhea predominance.

Conclusion

The results of our data suggest that overweight and obesity are independently associated with pneumonia-related ramifications such as hypoxemia and changing antibiotics aiming for better outcomes during hospital stay. However, we essentially need prospective research with a larger sample to consolidate our observation.

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Author Contributions

KMS: Contributed to conception and design; contributed to acquisition; drafted manuscript; gave final approval and agrees to be accountable for all aspects of the work in ensuring that questions relating to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

TA: Contributed to conception and design; critically revised manuscript; gave final approval.

MIH: Contributed to analysis and interpretation; critically revised manuscript; gave final approval.

SKD: Contributed to conception; critically revised manuscript; gave final approval.

ASGF: Contributed to analysis; critically revised manuscript; gave final approval.

MMI: Contributed to design; critically revised manuscript; gave final approval.

ASMSBS: Contributed to acquisition; critically revised manuscript; gave final approval.

JD: Contributed to acquisition and interpretation; critically revised manuscript; gave final approval.

MHRS: Contributed to acquisition; critically revised manuscript; gave final approval.

MJC: Contributed to conception and design; contributed to analysis; critically revised manuscript; gave final approval.

Declaration of Conflicting Interests

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