Title of the Project:

Association between weight gain during first years of life and early childhood respiratory and atopic diseases

Investigator List:

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Background and Significance:

Early childhood respiratory outcomes, including wheezing in the early years of life, have always been complex and perplexed clinicians for decades in differential diagnosis, short-term versus long-term treatment and prognosis with regards to subsequent development of recurrent wheezing and asthma.[1-3] A study conducted using a questionnaire-based survey reported that approximately 40% of children experienced wheezing at some of point of life during the first 6 years of life.[4] Similarly earlier studies reported that approximately 20-30% of children were diagnosed with bronchiolitis or early wheezing during the first year of life.[2,3,5] In addition, approximately 3% were hospitalized for early wheezing resulting in an estimated burden of 120,000 hospitalizations each year.[3,6,7] Because of its burden, associated morbidity and mortality, and subsequent development of recurrent wheezing and asthma, it is important to identify risk factors that might contribute to development of the disease. Several maternal and early life factors have been identified to be associated with early childhood wheezing,[8-12] including overweight and obesity in the first years of life.[13-26] While debate continues to understand the obesity-asthma association with respect to its causal relationship and/or existence of a distinct phenotype, several epidemiological studies have found overweight and/or obesity in children is associated with increased risk of asthma in adolescents and adults.[13,18,21,26-28] However, limited research has been conducted to understand the obesity-asthma relationship, with respect to weight changes during the early years of life. [29,30]

Abnormal weight gain during early years of life have adverse consequences for full term children including overweight, childhood obesity and high blood pressure.[31-35] But how or how much the weight gain influences childhood respiratory outcomes remains unclear. These concerns are highly relevant and demands attention with emergence of obesity-asthma phenotype[36-39] and increasing prevalence of childhood obesity and respiratory and atopic diseases outcomes in the world. Our long term objective is to understand role of several maternal and early life factors, in this case *weight gain during first years of life*, associated with risk of development of childhood respiratory and atopic disease outcomes in children. Findings from this work will provide crucial information for clinicians, parents, public health workforce and health policy regarding the importance of optimal rate of weight gain during infancy and its subsequent risk of childhood respiratory health. To conduct this study, we propose the following aim & hypothesis:

Study Aim and Hypotheses:

To determine the extent to which weight gain during the first two years of life is associated with early childhood respiratory and atopic disease outcomes.

Hypothesis:
In healthy term infants, rapid weight gain during the first two years of life is associated with wheezing and atopic dermatitis in children at 3 years age.

Approach:

Using a prospective cohort of mother-child dyads (from Conditions Affecting Neurocognitive Development and Learning in Early Childhood; CANDLE), we will determine the association between weight gain during the first two years of life and the risk and severity of respiratory outcomes among 3- year old children, specifically childhood wheezing and atopic dermatitis. This protocol is to support a request for CANDLE study cohort data for writing a journal manuscript, conference presentation and to conduct preliminary analyses for future grants.

Outcome:
The outcome variable is current wheeze, defined as ≥1 wheezing attacks during the past 12 months. We will categorize children as having wheezed in the past 12 months or not (yes/no). In addition, the secondary outcome variable include atopic dermatitis categorized into self-reported physician diagnosis of atopic dermatitis or not (yes/no).

Primary exposure variable:
We will utilize birth weight and length, weight and length at 12 months, and weight and height at 2 years age to determine the patterns of weight gain during the first two years of life. Using all recorded body weight and length/height data, Z scores will be generated by comparing them with the 2000 CDC growth charts. Changes in weight gain will be calculated as changes in weight Z scores during 0-24 months, and used as a continuous measure in the analyses. We will identify different patterns/trajectories of weight gain during the first two years of life and categorize them accordingly to fit in the regression models.

Covariates or confounding variables:
We included a number of maternal and child characteristics that potentially modify the relationship between weight gain during the first years of life and child respiratory and atopic diseases based on the existing literature.[3,40] The maternal characteristics include age, race, smoking during pregnancy, marital status, education, insurance status, prepregnancy weight, weight gain during pregnancy and history of asthma. The child characteristics include sex, gestational age and season of birth.

Proposed statistical analyses:
We will analyze the data obtained from the CANDLE study cohort for descriptive and inferential statistics. We will conduct univariate analyses of the outcome variables (current wheeze and atopic dermatitis), primary exposure variables (weight gain during first two years of life) and co-variates, and report them as proportions for categorical variables, and median and interquartile range (IQR) for continuous variables. Using $\chi 2$ statistics for categorical variables and Kruskal – Wallis test for continuous variables, we will compare the differences in weight gain trajectories

by selected maternal and child characteristics. Finally, we will conduct generalized linear models to assess the association of weight gain during first two years of life with relative odds of current wheeze and atopic dermatitis at 3 years age when adjusted for maternal age, race, education, insurance status, smoking during pregnancy, prepregnancy weight, weight gain during pregnancy, history of asthma, child sex, gestational age and season of birth. Point estimates along with associated 95% confidence intervals will be reported. A 2-sided statistical significance will be used for all statistical inferences. All data analyses will be conducted using SAS ver. 9.3 (SAS Institute Inc., Cary NC).

Variable List

Please reference "Variable List Template" on the CANDLE website for instructions on building proper variable list

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