Exploring the Relationship Between Childhood Obesity, Asthma, and Metabolic Disease

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Why Childhood Obesity, Asthma, and Metabolic Disease?

- Significant health issues for state and nation
  - National prevalence among children (7 million children under 18 years; 9%)
  - West Virginia prevalence among children (43,465 children; 14.7%)

- Parallel rise in childhood obesity and asthma rates
  - Asthma prevalence has doubled among children in the last two decades
  - Obesity prevalence has tripled among children in the last two decades

- Similar patterns
  - Both are more prevalent among younger boys but become greater among girls in adolescence
Associations

- **Obesity and asthma are related**
  - Asthmatics are more likely to become overweight/obese over time
  - Obese children are more likely to develop asthmatic symptoms
    - Obese children are less effected by select asthmatic treatments

- **Which comes first?**
  - Obesity is central but which comes first in most instances is unknown

- **How is obesity, asthma, and metabolic disease related?**
  - Obesity as central hub - these illness are related to dyslipidemia, cardiovascular risk factors
How are asthma, obesity, and metabolic function associated with one another across a spectrum of children?

Most studies are conducted using obese child samples or only asthmatics.

Is childhood obesity always the central support for the triad, if it exists?

Studies prior to our project did not control for obesity in analyses. It was always included as an independent variable of models.

Are there developmental differences associated with puberty and other physiological milestones that should be considered?

Most studies have used adolescent or young adult samples.
Phase I Project

- Examine the relationship between asthma and body mass in children in a wide spectrum sample
- Test whether early derangement in lipid and glucose metabolism is independently associated with increased risk for asthma

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**Initial Research Questions**

**Phase I Project**

- **Examine the relationship between asthma and body mass in children in a wide spectrum sample**
- **Test whether early derangement in lipid and glucose metabolism is independently associated with increased risk for asthma**

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**Metabolic Abnormalities in Children with Asthma**

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**Abstract**

In this phase I project, children with asthma and non-asthmatic controls were compared for differences in body mass index (BMI), body mass index (BMI)-z scores, and several metabolic markers, including fasting insulin, triglycerides, and high-density lipoprotein cholesterol. Children with asthma had significantly higher BMI and BMI-z scores compared to controls, indicating an association between asthma and increased body mass. In contrast, there were no significant differences in fasting insulin, triglycerides, or high-density lipoprotein cholesterol levels between the two groups. These findings suggest that childhood asthma is associated with increased body mass, but further research is needed to determine the underlying mechanisms.

**Keywords**

Childhood asthma, body mass index, metabolic markers, fasting insulin, triglycerides, high-density lipoprotein cholesterol

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**References**


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**Note**

This project was funded by the New York University School of Medicine, Department of Pediatrics Research Institute.
Phase I Participants

- CARDIAC Participants from 2007-2008 academic year (n = 17,944)
  - kindergarten (4-5 years) - n = 6,314
  - second grade (7-8 years) - n = 5,609
  - fifth grade (9-10 years) - n = 6,021

- 49.3% males
- 90.7% Caucasian

- Parental consent and child assent
Phase I Measures

- **Childhood Obesity**
  - Body mass index percentile (BMI%)
    - SECA Road Rod stadiometer
    - SECA 840 Digital Scale
  - Categorical Variable
    - < 5th% - underweight
    - 5th-84.9th% - healthy weight
    - 85.0-94.9th% - overweight
    - 95.0-98.9th% - obese
    - ≥ 99th% - morbidly obese
Phase I Measures

- **Metabolic Disease**
  - Acanthosis Nigricans (AN)
    - Neck and axilla hyperpigmented skin rash
    - Associated with insulin resistance and hyperinsulinemia in children (Hud, Cohen, Wagner, Cruz; 1992)

- **Dichotomous Variable**
  - Present/Absent
Phase I Measures

- **Childhood Asthma**
  - Single item for parent report
  - "Has your child been diagnosed with asthma"
  - Yes/no response

- **Lipids**
  - Fifth grade students only
  - Total cholesterol, LDL, HDL, Triglycerides
Asthma Prevalence Based on BMI

- 37.6% were overweight or above
- 1 in 5 children were obese or morbidly obese
- 14% had been diagnosed with asthma
- General trend: asthma prevalence rate increased as BMI% increased
- Significantly more obese/morbidly obese children were asthmatic than healthy weight children (p<.001) across grades
Metabolic Variables Based on BMI

- Obesity was associated with:
  - higher means of total cholesterol, LDL and log-transformed triglycerides
  - lower means of HDL

- Presence of AN was associated with:
  - higher means of triglycerides
Independence from Obesity

- Significant asthmatic effect (p<.01)
- Significant associations between asthma and:
  - triglycerides (p<.01)
  - AN (p<.001)
- regardless of weight status
- controlling for sex and smoke exposure
Hierarchical linear regressions illustrated that:

- asthma associated with hypertriglyceridemia after controls (p<.01)

- asthma associated with AN after controls (p<.001)
Phase I: Summary Points and Limitations

**Summary Points**
- Additional evidence of obesity and asthmatic burden in WV among children
- Provides initial evidence for an alternative model without obesity as the central hub but rather, diet as the initiator of asthma-obesity-diabetes triad

**Limitations**
- "Indirect" assessments/ variables
- Cross-sectional design
- Limited lipid analyses
What Does this Mean?

- Metabolic abnormalities induced by imbalanced diet in childhood may constitute central hub of asthma-obesity-diabetes triad
- Possibly different type of asthma and metabolic abnormalities that are linked directly to asthma without obesity as central structure
- What is the mechanism?
  - Inflammation?
Phase II: The Family Lifestyle Project

- Designed to...:
  - replicate Phase I analyses with direct, clinical assessments of model variables;
  - continue to assess obesity-asthma-metabolic abnormality triad across spectrum of children; and
  - explore potential mechanisms supporting asthma-metabolic abnormality association independent of obesity.
Phase II: Assessments

- **Blood Samples** (15 cc total)
  - Lipids, glucose, insulin, IgE, Vitamin D, Hemoglobin
  - Serum nitrate/nitrite
  - GWAS
  - Cytokines, NGF, BDNF
  - Store serum for future questions

- **Urine Sample**
  - Nicotine and cotinine

- **Clinical Assessments**
  - PFTs
  - Exhaled Breathe Condensate (EBC)
  - Anthropometrics & DEXA
  - History and Physical
  - Allergy Testing

- **Surveys**
  - Demographics
  - Child Health Questionnaire
  - Parental Stress Index
  - Sleep Questionnaire
  - Physical Activity & Diet
  - Executive Function
  - Asthma Control
Phase II: Procedures

- **Prior to Visit**
  - Discontinue medication and fast overnight (at least 12 hours before visit)
  - Complete series of surveys

- **During Visit**
  - Check-in, anthropometrics, fasting blood draw, urine collection
  - DEXA
  - History & Physical
  - PFTs, EBC
  - Allergy Testing

- **After Visit**
  - Health report mailed to family
  - Health literacy survey
Phase II Participants

- 178 children
  - 56.8% males
  - 85.4% Caucasian
  - Positive family hx for diabetes = 42.4%
  - Child diagnosed with diabetes = 1.1%

- Mean age = 9.4 years (SD = 1.7)
  - 7-13 years of age included
- Mean BMI% = 67.6 (SD= 30.2)
  - 2.9% underweight
  - 53.5% healthy weight
  - 16.9% overweight
  - 18.6% obese
  - 8.1% morbidly obese
Asthma Prevalence

Confirmation Method
- medications
- PFT
- prior history
- physical & history

Asthma Prevalence in Sample
- 102 (57.3%) non-asthmatic
- 76 (42.7%) asthmatic
- 36.8% of females; 45.4% of males
- 42.8% of 7-9 year-olds; 39.0% of 10-12 year-olds
Lipid and Metabolic Abnormalities

- % abnormal - fasting lipids
  - 4.5% Total cholesterol (cut off value = 200 mg/dL)
  - 2.1% LDL (cut off value = 190 mg/dL)
  - 10.1% HDL (cut off value = 39 mg/dL)
  - 2.9% Triglycerides (cut off value = 200 mg/dL)

- % abnormal - metabolic function
  - 1.2% HOMA IR (cut off value = 5.22 in boys; 3.82 in girls; Kurtoglu et al., 2010)
  - 0.6% HbA1C (cut off value = 6.5%; WHO report; 2011)
3.1% underweight
18.0% healthy weight
9.0% overweight
9.0% obese
3.9% morbidly obese

Significant association between variables (p<.01); non-linear
Greater BMI% was significantly associated with:

- higher triglycerides ($p<.01$)
- lower HDL ($p<.001$)
- higher LDL ($p<.001$)
- higher insulin ($p<.001$)
- higher HOMA-IR ($p<.001$)

Note: association with abnormal HbA1c but NS
Asthma, Lipids, and Metabolic Function

- Asthmatics were significantly more likely to have:
  - elevated triglycerides (p<.05)
  - hyperinsulinemia (p<.01)
  - abnormal HOMA-IR (p<.01)
Hierarchical linear regressions controlling for age, gender, and obesity significantly predicted:

- Triglycerides (p<.05)
- Insulin (p<.05)

- HOMA-IR, HbA1C - not significant
Phase II: Summary Points and Limitations

Summary Points

- Partial replication of the original question using clinical and direct assessments was supported
- Asthma may be directly related to metabolic abnormalities, perhaps through diet but this is not consistent across measures

Limitations

- Despite recruitment strategies, sample includes fewer obese/asthmatics
- Some cut offs are not confirmed for children in literature at this time
Next Steps

- Conduct ROC analyses using different cut offs for metabolic assessments
- Explore inflammatory markers and other variables to begin to detangle differences in metabolic measures
- Explore fatty acids and other nutritional indices from serum to look potential role of diet on triad
- Use DEXA (on subsample only) instead of BMI% to assess model
Lab Members

**WVU**
- Brian Ansell
- Rafka Chaiban
- Brad Foringer
- Michael McCawley
- William Neal
- Jan Rapp
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**Other Institutions**
- Greg Hawkins (Wake Forest)
- Adam Gower (Wake Forest)
- Srinivas Nagaraj (U of Florida)
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