

**Association between Cotonine Level
in Urine and Severity of Bronchial Asthma
in Children Aged from 2 to 12 Years**

Thesis

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Family Medicine

By:

Noha Zidan Mohamed

Under supervision of:

Prof. Mohsen Abdel Hamid Gad alaah

Professor at Community, Environmental and Occupational Medicine Department
Faculty of Medicine - Ain Shams University

Ass.Prof.Mona Abdel-Aal Abdel-Hamid

Assistant Prof.at Community, Environmental and Occupational Medicine Department
Faculty of Medicine - Ain Shams University

Dr. Lamyaa Saeed Elbagoury

Lecturer at Community, Environmental and Occupational Medicine Department
Faculty of Medicine - Ain Shams University

**Ain Shams University
Faculty of Medicine
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List of Contents

	Page
List of Abbreviations	i
List of Figures	ii
List of Tables	v
Abstract	vi
Protocol	--
1. Introduction	1
2. Aim of the Work	5
3. Review of Literature	6
Chapter 1: Bronchial asthma in childhood.....	6
Chapter 2: Environmental tobacco smoke.....	31
Chapter 3: Assessment of exposure to ETS	58
4. Subjects and Methods	67
5. Results	73
6. Discussion	88
7. Summary and Conclusion	103
8. Recommendations	107
9. References	108
10. Appendix	
11. الملخص العربي	--

List of Abbreviations

Abb.	Meaning
ANOVA	Analysis of variance
CCR	Cotinine creatinine ratio
CO	Carbon monoxide
DHEA	Dehydroepiandrosterone
DNA	Deoxyribonucleic acid
ECP	Eosinophil cationic protein
eGFR	Estimated glomerular filtration rate
EIA	Exercise induced asthma
EPA	Environmental Protection Agency
ETS	Environmental tobacco smoke
FEV ₁	Forced expiratory volume in first second
FVC	Forced vital capacity
GINA	Global initiative for asthma
GWAS	Genome –wide association studies
HC(n)	Hydrogen cyanide
IARC	International agency for research on cancer
IFN. γ	Interferon γ
IgE	Immunoglobulin E
IL-13	Interleukin 13
MENA	Middle East and North Africa region
MS	Main stream smoke
NICU	Neonatal intensive care unit
OR	Odds ratios
PA(HS)	Polycyclic aromatic hydrocarbons
PEFR	Peak expiratory flow rate
RAST	Radio allergosorbent testing
RSP	Respirable suspended particulates
RSV	Respiratory syncytial virus
SD	Standard deviation
SHS	Second hand smoke
SIDS	Sudden infant death syndrome
SS	Side stream smoke

THS	Third hand smoke
TSNAs	Tobacco specific nitrosamines
VOC	Volatile organic compounds
WHO	World health organization

List of Figures

Fig.	Title	Page
1	New genetic classification of asthma and atopy.	12
2	Hypothesized associations of genetic, intrauterine, and perinatal risk factors with asthma onset and severity in infancy.	21
3	Pediatric spirometry.	25
4	Pediatric peak flow meter.	26
5	Skin Prick Test.	29
6	Diagram of a cigarette.	35
7	Diagram of a filtered cigarette.	36
8	Air flux during smoking.	41
9	Effect of second hand smoke.	50
10	Correlation between urinary cotinine level and reporting of child exposure to ETS in the last 24 hours.	83

List of Tables

Table	Title	Page
	Review of literature	
3-1	Constituents in cigarette smoke & their effect on respiratory tract	38
3-2	Gas phase components generated by tobacco.	39
3-3	Particulate phase components generated by burning of tobacco.	40
3-4	Selected constituents of cigarette smoke: Ratio of constituents in SS smoke to MS smoke.	40
	Results	
5-1	Sociodemographic characteristics of the studied sample.	73
5-2	Home environmental conditions of the studied group.	74
5-3	History of bronchial asthma among studied sample.	75
5-4	Urinary cotinine level of the studied sample	76
5-5	Pulmonary function tests of the studied sample	76
5-6	Level of diagnosis of asthma among the studied group.	77
5-7	Sources of exposure to ETS among studied groups.	77
5-8	Comparison between mean cotinine level among different sources of exposure.	78
5-9	Correlation between cotinine level and home environmental condition among children exposed at home only.	78
5-10	Correlation between cotinine level and household smoking behavior among children exposed to smoking inside home only.	79

List of Tables (Cont.)

Table	Title	Page
5-11	Comparison between mean urinary cotinine level among levels of diagnosis of bronchial asthma in exposed group.	80
5-12	Correlation between cotinine level and no. of attacks of bronchial asthma during last month and last year in exposed group	80
5-13	Correlation between cotinine level and pulmonary function test in exposed group.	81
5-14	Comparison between exposure to ETS by self-reporting and by urinary cotinine.	82
5-15	Relation between socio-demographic factors and ETS exposure by reporting and by urinary cotinine level	84
5-16	Relation between child's medical condition and ETS by reporting and by urinary cotinine level	85
5-17	Relation between household smoking behavior and ETS exposure by reporting and by cotinine level	86

Abstract

Introduction: Exposure of children to environmental tobacco smoke has been linked to many complications including bronchial asthma. Cotinine is a nicotine biomarker measurable in the blood, urine or saliva. Household smoking is associated with higher cotinine levels among asthmatic children.

Aim of the work: this study aimed to identify the relation between urinary cotinine level and severity of bronchial asthma in asthmatic children exposed to environmental tobacco smoke aged from 2 to 12 years and to measure reliability of self-reporting of exposure to environmental tobacco smoke compared to urinary cotinine level.

Subjects and methods: 113 asthmatic children attending chest clinic in pediatric department in Ain Shams University were enrolled in this study. Their parents were interviewed to fill a questionnaire and urine sample were collected from the children. Children with diagnosis other than asthma were excluded from this study.

Results: for those children who were exposed to ETS (n=82), the mean urinary cotinine level differs significantly among different levels of diagnosis of bronchial asthma ($p=0.001$), being lowest for mild disease (24 ± 16.97) ng/mg creatinine, and highest for severe form (88.21 ± 60.11) ng/mg creatinine. children exposed to ETS (cot. ≥ 30) differed significantly from those not exposed as regard reporting of exposure; sensitivity of reporting to detect ETS exposure was (89.1%), and specificity to exclude ETS exposure was 49%. Reporting detected false exposure of 51% from those not exposed to ETS (cot. less than 30).

Conclusion: Severe asthma is associated with high urinary cotinine levels which indicate that, environmental tobacco smoke exposure increasing the asthma severity. Reporting for exposure to ETS is not reliable for quantitative assessment of ETS exposure, which means that there was misreporting by parents about the exposure of their children

Keywords: bronchial asthma, environmental tobacco smoke, cotinine.

Introduction

Involuntary (or passive) smoking is the exposure to second-hand tobacco smoke (SHS) which is a mixture of exhaled mainstream smoke and side stream smoke released from a smouldering cigarette or other smoking device (cigar, pipe, shisha etc.) and diluted with ambient air. Second-hand tobacco smoke is also referred to as "environmental" tobacco smoke (ETS). Involuntary smoking involves inhaling carcinogens and other toxic components that are present in second-hand tobacco smoke (*WHO, 2015*).

Third hand smoke (THS) consists of pollutants that accumulate and remain on indoor surfaces long after secondhand tobacco smoke dissipates. Toxins present in THS can persist for weeks to months and undergo chemical transformations and produce potent carcinogenic tobacco-specific nitrosamines (*Drehmer et al., 2012*).

Routes of exposure to THS include inhalation, ingestion, or dermal uptake, and young children are more likely exposed to THS dust than adults as they have mouthing behaviors, and spend more time at home and on the floor where dust is collected, disturbed, and re-suspended into the air (*Becquemin et al., 2010*).

Smoking is a public health problem in Egypt. The WHO report on the global tobacco epidemic 2009 reported that the adult daily smoking prevalence was 14% (*GATS, 2009*).

Egyptian Ministry of Health demographic health surveys were completed in 2005 and 2008. In 2005, 0.6% of

ever-married women aged 15–49 years currently smoked cigarettes or used other forms of tobacco. In 2008, among women and men aged 15–59 years, 0.7% of women currently used tobacco (0.4% cigarettes only, 0.2% other forms of tobacco only, and 0.1% both) compared with 43.9% of men (34.7% cigarettes only, 5.6% other forms of tobacco only, and 3.6% both (*GATS, 2009*).

Despite quantitative differences between secondhand smoke (SHS) and the mainstream smoke inhaled by the active smoker, sufficient qualitative similarity exists to deserve fear that the health of nonsmokers may be injured by SHS, just as active smokers are harmed by mainstream smoke (*Homa et al., 2015*).

There is now abundant scientific evidence to justify these concerns about adverse health effects in nonsmokers. Indeed, the Global Burden of Disease Study estimated that exposure to SHS is responsible for more than 601, 000 premature deaths worldwide in 2010 (1 percent of mortality) (*Lim et al., 2012*).

Children exposed to secondhand smoke are at an increased risk for sudden infant death syndrome, acute respiratory infections, ear problems, and more severe asthma. Smoking by parents causes respiratory symptoms and slows lung growth in their children; one of the most dangerous effects of passive smoking on children is bronchial asthma (*Kabir et al., 2011*).

Bronchial asthma is a heterogeneous disease, usually characterized by chronic airway inflammation. It is defined by the history of respiratory symptoms such as wheeze, shortness of breath, chest tightness and cough that vary over

time and in intensity, together with variable expiratory airflow limitation (*GINA, 2014*).

Secondhand smoke can trigger asthma episodes and increase the severity of attacks. Secondhand smoke is also a risk factor for new cases of asthma in preschool aged children who have not already exhibited asthma symptoms. It is linked to other health problems, including lung cancer, ear infections and other chronic respiratory illnesses, such as bronchitis and pneumonia (*American Lung Association, 2015*).

Many of the health effects of secondhand smoke, including asthma, are most clearly seen in children because children are most vulnerable to its effects. Most likely, children's developing bodies make them more susceptible to secondhand smoke's effects and, due to their small size, they breathe more rapidly than adults and taking in more secondhand smoke. The developing lungs of young children are severely affected by exposure to secondhand smoke for several reasons including that children are still developing physically, have higher breathing rates than adults, and have little control over their indoor environments. Children receiving high doses of secondhand smoke, such as those who have parents who smoke, are of the greatest risk of suffering from the damaging health effects (*American Lung Association, 2015*).

Active and passive smoking have been associated with a range of adverse effects on health. The development of valid and accurate scales of measurement for exposures associated with health risks constitutes an active area of research. Tobacco smoke exposure still lacks an ideal method

of measurement. Exposure to ETS can be measured by 3 means: (1) measuring tobacco smoke components in the air to which subjects are exposed (environmental measurements), (2) self-reported indicators of exposure through questionnaires or interviews, and (3) measuring concentrations of components of smoke in the body of exposed individuals (biomarkers) (*Avila-tang et al., 2013*).

The best way to identify ETS exposure is unclear. Classifying smoking status by self-report alone may be unreliable because children may have ETS exposure outside their own homes or because caregivers may under-report household smoking. Cotinine is a nicotine biomarker measurable in the blood, urine or saliva. Household smoking is associated with higher cotinine levels among asthmatic children. Many children considered non-exposed to tobacco smoke have elevated cotinine levels. Parental surveys about sources of ETS do not adequately predict children's cotinine levels (*Avila-tang et al., 2013*).

Rational of the study:

According to search on internet database (mainly pubmed), there are no research in Egypt reported the relation between urinary cotinine level and severity of bronchial asthma among children. Therefore, this study will estimate this association.

Research questions:

- 1- Is there a relation between level of urinary cotinine and severity of bronchial asthma in children exposed to ETS aged 2-12 years?

- 2- Is the level of urinary cotinine affected by home ventilation and family members' smoking behavior in children exposed to ETS at their homes?
- 3- Is self reporting of exposure to ETS is reliable in comparison to urinary cotinine level for assessment of exposure to ETS in children aged 2-12 years old?

Aim of the Work

- To estimate the relation between cotinine level in urine and the severity of bronchial asthma in children exposed to Environmental Tobacco Smoke aged from 2 to 12 years.
- To measure reliability of self reporting of exposure to environmental tobacco smoke compared to urine cotinine level.