Passive smoking and lower respiratory tract illnesses in children

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علاقة التدخين القسري (السلبي) بأمراض الجهاز التنفسي السفلي في الأطفال

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خلاصة : تم استقصاء العلاقة بين التعرض لدخان التبغ في المنزل وبين أمراض الجهاز التنفسي السفلي المصحوبة وغير المصحوبة بالأزيز في صغار الأطفال . واستعمل استبيان لهذا الغرض ، وقيست النسبة بين الكوتنين والكرياتنين في البول لتقدير مدى التدخين القسري . وأجريت دراسة على حالات وشواهد ، شملت ستين طفلا (في السنة الخامسة أو أقل من العمر) من المصابين بأمراض في الجهاز التنفسي السفلي ، وأربعين طفلا شاهداً . وأظهرت النتائج أن التدخين القسري في المنزل يمكن أن يكون من عوامل التأهب أو التفاقم لأمراض الجهاز التنفسي السفلي في صغار الأطفال ، سواء كانت الحالات مصحوبة أو غير مصحوبة بالأزيز ، وسواء كانت الأمراض معدية أو غير معدية . وتبين كذلك أن تقدير الآباء لمستوى تدخينهم يمكن أن لا يكون دقيقا ، وهكذا فلابد من إجراء قياسات كيميائية حيوية موضوعية للتدخين القسري من أجل التعرف على ما يسببه من أخطار .

ABSTRACT The relationship between household tobacco smoke exposure and wheezing and non-wheezing lower respiratory tract illnesses in young children was investigated using both a questionnaire and the urinary cotinine/creatinine ratio to assess passive smoking. A case–control study was conducted on 60 children (≤5 years) with lower respiratory tract illnesses and 40 control children. The results showed that household passive smoking may be a predisposing and/or aggravating factor for lower respiratory tract illnesses in young children whether wheezing or nonwheezing, infective or noninfective. Parents' assessment of their own level of smoking may be inaccurate and objective biochemical measures of passive smoking are needed to identify its risks.

Le tabagisme passif et les maladies des voies respiratoires inférieures chez les enfants
RESUME La relation entre l'exposition à la fumée de tabac dans le milieu familial et les maladies des voies respiratoires inférieures avec ou sans respiration sifflante chez les jeunes enfants a été étudiée au moyen d'un questionnaire et en utilisant le taux de créatine/cotinine urinaire pour évaluer le tabagisme passif. Une étude cas-témoins a été réalisée chez 60 enfants (≤ 5 ans) atteints de maladies des voies respiratoires inférieures et chez 40 enfants témoins. Les résultats ont montré que le tabagisme passif au foyer pouvait être un facteur prédisposant et/ou aggravant chez les jeunes enfants pour les maladies des voies respiratoires inférieures avec ou sans respiration sifflante, infectieuses ou non. L'évaluation faite par les parents de leur propre niveau de tabagisme peut être inexacte et des mesures biochimiques objectives du tabagisme passif sont nécessaires pour identifier les risques liés à celui-ci.

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Introduction

Tobacco smoke is probably the most important source of air pollution in the home. Many studies have reported that children exposed to parental cigarette smoking may develop a chronic cough, phlegm and persistent wheezing (asthma), and may have higher risks of attacks of pneumonia and other respiratory illnesses [*1–8*]. Additional evidence suggests that parental smoke may adversely affect the rate of lung growth during childhood [*9*] and children whose parents smoke have also been found to differ in lung function [*10,11*].

Many researchers have investigated the relationship between passive smoking and wheezing illnesses [*3,6,7,12,13*] but few have examined the relationship with other types of lower respiratory tract illnesses (LRTIs) [*14,15*]. Also many studies have identified illness outcomes solely on the basis of parental recall, which may bias such reports [*1,2,3,4,6,7,14*]. The current study was conducted therefore to investigate the relationship of household tobacco smoke exposure to wheezing and non-wheezing LRTIs in young children using both a questionnaire and the urinary cotinine/creatinine ratio (CCR) to assess passive smoking.

Subjects and methods

A case control study was conducted from September 1995 to October 1996 on 100 children (≤5 years) from low income families who were receiving health care at the Alexandria University children's hospital, Alexandria, Egypt. The study was approved by the Researches Committee of Alexandria Faculty of Medicine and informed consent to participate in the study was obtained from the caregivers of each child. The study population comprised 60 consecutive cases with LRTIs, whether wheezing or non-wheezing, and 40 children of matched age and sex with any presentation other than LRTIs and who also had no previous history of LRTIs. Children (cases and controls) who were reported by their caretakers to have been continuously exposed to household tobacco smoke since birth and those who were never exposed were included, while children who were intermittently exposed were excluded from the study population. Children with any hepatic or renal disorders were also excluded as the metabolism and excretion of cotinine could be affected by disturbed hepatic and renal functions.

Using a specially designed questionnaire, the accompanying parents/caregivers were interviewed in detail about smoking habits to identify smoking individuals at home (mother, father and/or others), duration of exposure, and the average daily cigarette consumption by all smokers at the place where the child was present (especially during the week before the interview). At the time of interview, the investigators completed a standardized form on the presence or absence of a list of symptoms and signs and made a diagnosis, which was confirmed by chest radiography. The severity of LRTIs was assessed by clinical and radiological findings, in addition to oxygen saturation using pulse oximetry [*16*].

Urinary cotinine/creatinine ratio

Urinary cotinine/creatinine ratio (CCR) was measured for all cases and control children to verify the reported smoking habits. A urine specimen was collected from each child at the time of interview, labelled with a code number and kept frozen at –20 °C until being analysed for urinary creatinine

and cotinine without knowledge of the exposure state or the diagnosis of the child. Creatinine reacts in alkaline solution with picrate to form an orange complex which is measured colorimetrically [*17*]. The urinary cotinine was measured by an ^{125}I-radioimmunoassay procedure [*18,19*]. It is a liquid phase radioimmunoassay in which ^{125}I-labelled cotinine competes for a fixed time with cotinine in the patient's urine sample for antibody sites. Patient sample concentrations were read from a calibration curve and the results expressed in ng/ml.To adjust for the effect of variable dilution on the spot concentration of cotinine, urinary CCR was calculated, expressed as nanograms of cotinine per milligram of creatinine (ng/mg). Henderson et al. reported that a cutoff CCR of 30 ng/mg identifies children exposed to smoking at home with a high degree of sensitivity (80%) and specificity (100%) [*20*]. This cutoff was therefore used to categorize our patients into exposed and not exposed.

Statistical analysis

The chi-squared test (χ^2), the *t*-test, the *F*-test, the least significant difference test (LSD), the *Z*-test and the correlation coefficient (*r*) were used as tests of significance. The odds ratio (OR) was used to estimate the risk of LRTIs associated with tobacco smoke exposure. The 95% confidence interval (95% CI) for the odds ratio was also used to conclude whether the association was statistically significant or not. The level of significance was considered at $P < 0.05$.

Results

The demographic features (age, sex and residency) which might affect the results were similar in children with LRTIs and those in the control group (Table 1). The different diagnoses of children with LRTIs and control children are also shown in Table 1.

Comparing the reported exposure variables, namely proportions having any smoker at home (reported exposure) and the mean daily cigarette consumption by all smokers, there was no significant difference between children with LRTIs and those in the control group (Table 2). However, the percentage of exposed children (measured exposure with CCR ≥ 30 ng/mg) was significantly higher in the LRTI group than the control group (85.0% versus 67.5% respectively, $P = 0.03$). It was also found that the exposed children (CCR ≥ 30 ng/mg) had a 2.7 times greater risk of developing LRTIs than unexposed children (CCR < 30 ng/mg). This risk was significant (OR = 2.7, 95% CI = 1.02–9.54). Moreover, the mean urinary CCR was higher in children with LRTIs than control children (138 ng/mg versus 46 ng/mg respectively); this difference was statistically highly significant ($P = 0.00005$). It was found that, in children with LRTIs, the percentage of exposed children (CCR ≥ 30 ng/mg) was significantly higher than the percentage of reported exposure (85.0% and 66.7% respectively, $P = 0.02$), while in the control group, no significant difference was found between measured and reported exposures (67.5% and 60.0% respectively, $P > 0.05$).

With regard to the reported degree of exposure (none, a little, some, a lot), the mean CCR level was significantly higher in children whose parents reported a greater degree of exposure whether in cases or controls ($P < 0.05$ for both). No smoking mothers were reported in the study population. According to the different smoking groups

(none, only father, father and others), CCR levels were significantly higher in cases than controls ($P < 0.05$ with respect to each group). There was no significant correlation between CCR values and the reported daily number of cigarettes smoked by households, whether in children with LRTIs ($r = 0.121$, $P > 0.05$) or in control children ($r = 0.050$, $P > 0.05$).

Comparing the reported exposure variables of children with wheezing LRTIs, those with nonwheezing LRTIs and the controls, there was no significant difference in the proportion having any smoker at home or in the mean daily cigarette consumption by all smokers ($P > 0.05$ for both variables) (Table 3). The mean CCR values were 144 ng/mg in the wheezing group, 128 ng/mg in the nonwheezing group and 46 ng/mg in the control group. The least significant difference (LSD) test showed an absence of significant difference between wheezing and nonwheezing groups, while both had significantly higher values than the control group.

No significant difference was found between children with severe LRTIs, those with mild LRTIs and the controls as regards the percentage having any smoker at home ($P > 0.05$) (Table 4). On the other hand, the LSD test showed that the reported mean daily cigarette consumption by all smokers and the CCR level were significantly higher in the group with severe LRTIs (8.6 cigarette/day and 154 ng/mg respectively) compared that with mild LRTIs (3.8 cigarette/

Table 1 **Characteristics and diagnosis of cases with lower respiratory tract illnesses and control group**

Characteristic	LRTI ($n = 60$)		Control ($n = 40$)		Test of significance
Age (years)					
Range	0.17 – 5		0.25 – 5		
Mean ± *s*	2.00 ± 1.8		2.7 ± 1.8		$t = 1.80$, NS
Sex, No. (ratio)					
Male/female	43/17 (2.5)		28/12 (2.3)		$\chi^2 = 0.93$, NS
Residence, No. (ratio)					
Urban/rural	43/17 (2.5)		27/13 (2.1)		$\chi^2 = 0.20$, NS
Diagnosis	**No.**	**%**	**Diagnosis**	**No.**	**%**
Wheezing LRTIs	33	55.0	Upper respiratory tract infections	14	35
Bronchial asthma	19	31.7	Skin and soft tissue diagnosis	6	15
Bronchiolitis	7	11.7	Intestinal parasitic infection	10	25
Wheezing bronchitis	7	11.7	Other medical diagnoses	10	15
Nonwheezing LRTIs	27	45.0			
Bronchopneumonia	14	23.3			
Lobar pneumonia	5	8.3			
Bronchitis	8	13.3			
Total	60	100		40	100

s = *standard deviation* NS = *not significant, P > 0.05*

Table 2 **Exposure variables and urinary cotinine/creatinine ratio (CCR) (LRTI versus control groups)**

Variable (n = 60)	LRTI (n = 40)	Control	
Reported exposure, No. (%)	40 (66.7)	24 (60.0)	χ^2 = 0.46, NS
Measured exposure,[a] No. (%) (CCR ≥ 30 ng/mg)	51 (85.0) Z = 2.34[b]	27 (67.5) Z = 0.69 NS	χ^2 = 4.28[b]
Daily cigarettes by all smokers, ± s	7.3 ± 8.7	4.8 ± 6.7	t = 1.56, NS
Mean urinary CCR ± s (ng/mg)	138 ± 119.9	46 ± 23.5	t = 4.76[c]
CCR (ng/mg) according to reported smoking habits	**No. Mean ± s**	**No. Mean ± s**	
Was child exposed?			
Yes	40 181 ± 123.6	24 61 ± 19.4	
No	20 48 ± 19.7	16 25 ± 7.0	
	t = 4.79[b]	t = 7.01[b]	
How much exposure? (cigarettes per day)			
None (0.0)	20 48 ± 19.7	16 25 ± 7.0	
A little (1–10)	21 126 ± 68.2	17 53 ± 15.7	
Some (11–20)	13 192 ± 76.0	5 73 ± 12.3	
A lot (≥ 21)	6 350 ± 197.9	2 105 ± 1.7	
	F = 24.26[b]	F = 8.97[b]	
Household smokers			
None	20 48 ± 19.7	16 25 ± 7.0	t = 4.06[b]
Only father	30 179 ± 119.6	18 57 ± 16.9	t = 4.30[b]
Father and others (except mothers)	10 196 ± 109.5	6 76 ± 23.7	t = 2.62[b]
Only mother	0.0 –	0.0 –	–

[a] *Odds ratio = 2.7 (significant): 95% confidence interval = 1.02–9.54*
[b] *Significant, P < 0.05*
[c] *Highly significant, P = 0.00005*
NS = not significant, P > 0.05 *s = standard deviation*

Table 3 **Exposure variables and cotinine/creatinine ratio (CCR) for wheezing LRTI, nonwheezing LRTI and control groups**

Variable	Wheezing LRTIs (n = 33)	Nonwheezing LRTIs (n = 27)	Control (n = 40)	Test of significance
Reported exposure, No. (%)	23 (69.7)	17 (63.0)	24 (60.0)	χ^2_2 = 0.75 NS
Daily cigarettes by all smokers, mean ± s	7.5 ± 7.42	7.1 ± 10.14	4.8 ± 6.68	F = 1.215 NS
Mean urinary CCR ± s (ng/mg)	144 ± 138.5	128 ± 92.6	46 ± 23.5	F = 11.23 [a]

[a] *Significant, P < 0.05*
NS = not significant, P > 0.05 *s = standard deviation*

Table 4 **Exposure variables and cotinine/creatinine ratio (CCR) for mild LRTI, severe LRTI and control groups**

Variable	Mild LRTIs[a] (n = 33)	Severe LRTIs[b] (n =27)	Control (n = 40)	Test of significance
Reported exposure, No. (%)	9 (56.3)	31 (70.5)	24 (60.0)	$\chi^2_2 = 5.44$ NS
Daily cigarettes by all smokers, mean ± s	3.8 ± 5.22	8.6 ± 9.35	4.8 ± 6.68	$F = 3.47^c$
Mean urinary CCR ± s (ng/mg)	88 ± 55.5	154 ± 131.5	46 ± 23.5	$F = 14.70^c$

[a] *Mild LRTIs (no or mild respiratory distress and oxygen saturation > 90%)*
[b] *Severe LRTIs (marked respiratory distress and oxygen saturation ≤ 90%)*
[c] *Significant, P < 0.05*
NS = not significant, P > 0.05 *s = standard deviation*

Table 5 **Urinary cotinine/creatinine ratio (CCR) in various diagnostic subgroups of cases with LRTIs and control children**

Urinary CCR (ng/mg)	Wheezing LRTIs			Nonwheezing LRTIs			Control
	Asthma (n = 19)	Bronchiolitis (n = 7)	Wheezing bronchitis (n = 7)	Lobar pneumonia (n = 5)	Broncho-pneumonia (n = 14)	Bronchitis (n = 8)	(n = 40)
Mean	145	148	127	153	140	119	46
± s	± 140.5	± 183.6	± 102.1	± 103.5	± 79.9	± 60.9	± 23.5

F = 9.45 significant, P < 0.05
s = standard deviation

day and 88 ng/mg) and the control group (4.8 cigarette/day and 46 ng/mg). Comparing the same variables between the last two groups showed no significant difference.

The LSD test showed a significant difference in CCR between each of the diagnostic subgroups of LRTIs (being higher) in comparison with the control group (Table 5). On the other hand, no significant difference was found when each of the diagnostic subgroups was compared with the others.

There was no significant difference in the mean urinary CCR between children with LRTIs in the age group ≤ 2 years and those > 2 years (mean = 153 ± 131.1 ng/mg and 135 ± 112.6 ng/mg respectively, $P > 0.05$). There was also no significant difference in the mean urinary CCR between the same age groups of control children (mean = 51 ± 25.5 ng/mg and 45 ± 21.3 ng/mg respectively, $P > 0.05$). The mean age at first LRTI was lower in exposed children compared with unexposed ones (mean = 6.4 ± 5.3 months and 9.8 ± 9.3 months respectively, $P < 0.05$).

Discussion

Accurate biochemical measures of passive smoking are needed to identify its risks and

to quantify the benefits of antismoking interventions. Cotinine, the major metabolite of nicotine found in saliva, blood and urine, is a stable and accurate indicator of cigarette smoke exposure *[20–22]*. Measurement of cotinine in biological fluids has been found to be the most reliable method of estimating individual levels of exposure to tobacco *[18,20,21]*. As the half-life of cotinine in the blood is about 19–40 hours, urinary cotinine levels might therefore reflect exposure to tobacco smoke during the preceding few days *[21,23,24]*. Also the probability of contamination during sampling is low because cotinine is specific to tobacco and exclusively a product of *in vivo* metabolism *[21,23]*. For these reasons, this study was undertaken using urinary CCR as an objective measure of passive smoking to investigate the relationship between household tobacco smoke exposure and wheezing and nonwheezing LRTIs in preschool children.

As to whether cotinine is found in the urine of all people or only in those known to have been exposed to cigarette smoke, Henderson et al. *[20]* studied children who were known to be either exposed or not exposed to cigarette smoke at home (verified by home air sampling for nicotine). Small amounts of cotinine were detected in some unexposed children's urine samples, but a urinary CCR of less than 30 ng/mg could be used as a threshold level to accurately classify children as not exposed. Considering this cutoff, 78% of our study population were exposed to tobacco smoke; this rate of household cigarette smoke exposure is disturbingly high. A higher measured exposure rate was found in the group with LRTIs but not in the control group. CCR levels in children with LRTIs whose caregivers reported absence of household tobacco exposure ranged from 0 to 100 ng/mg with a mean of 48 ± 19.7 ng/mg, which exceeded the cutoff level of home exposure. This inaccurate reporting of exposure may have been due to the parents becoming more sensitized to the issue of passive smoke exposure by the study questionnaire itself and perhaps wanting to minimize the reported exposure. Outdoor accidental exposure (which was not included in the questionnaire) may be another explanation for this discrepancy. Our results are consistent with other studies which have shown that cotinine is measurable, sometimes at high levels, in children with no reported exposure at home *[19,25]*.

Measurement of urinary CCR showed that children with LRTIs (wheezing or nonwheezing) were definitely more exposed to cigarette smoke than control children. On the other hand, analysis of reported exposure variables (percentage having any smoker at home and daily cigarette consumption by all smokers) showed an absence of significant differences between those with LRTIs (wheezing or nonwheezing) and those in the control group. Moreover, there was no correlation between CCR values of children and the number of cigarettes smoked in their households. Therefore, depending only on the parents' subjective assessment of their own level of smoking to quantify their children's exposure to tobacco smoke is potentially inaccurate as factors, such as room ventilation, proximity to the smokers and the presence of other smokers, are likely to cause a wide variation in exposure. These factors, in addition to parents' recall (which may be biased), indicate the importance of using an objective measure of exposure to evaluate more critically a causal relationship between passive smoking and childhood ill-health.

In the present study, exposed children (CCR ≥ 30 ng/mg) were found to have a 2.7 times greater risk of developing LRTIs than unexposed children (CCR < 30 ng/mg).

Also the significantly higher mean CCR of children with LRTIs persisted when each of the diagnostic subgroups of LRTI patients was compared with control children. However, there was no significant difference in CCR values when each of diagnostic subgroups was compared with the others. These findings prove that passive smoking is a risk factor for many types of LRTIs whether wheezing or nonwheezing, infective or noninfective. Our results are consistent with those of many investigators who have found that environmental tobacco smoke produces an increased risk of the development of acute lower respiratory tract irritation, asthma and acute lower respiratory tract infections in children exposed in the home [*1–8,14,15*]. Unlike our study, most of these studies were based only on parents' subjective assessment of their own level of smoking [*1–4,7,14,15*], while other studies using an objective measure of tobacco smoke exposure investigated mainly wheezy children with asthma and bronchiolitis [*12,19,25,26*].

Heavy exposure to tobacco smoke might be an aggravating factor for LRTIs in young children as indicated by the significantly higher level of CCR in patients with severe episodes of LRTIs compared with mild LRTI cases or control children. Our findings are consistent with those of Chen et al. who suggested that exposure to household cigarette smoke in early life increases the risk of severe respiratory illness [*27*]. In addition, Willers et al. [*12*] and Reese et al. [*26*] found that passive smoking might be an aggravating factor for childhood asthma and bronchiolitis respectively.

It should be noted that most North American and European literature [*13,14*] has linked LRTIs and passive smoking to maternal rather than paternal smoking, and the correlation has appeared to be most marked for the first two years of life and has shown a steady decline with increasing age. The authors have attributed these findings to the fact that mothers usually spend more time with their infants than do fathers, especially in early life. Also, the children in these studies attended day care centres when they reached the age of two years so they spent some time outdoors away from parental smoking. However, in the present study, maternal smoking was not reported in any family in the study population. This might be real or explained by cultural factors and the stigma regarding women smoking in the Egyptian community, which may have led to false answers. Therefore, in the present study the relation between household smokers and LRTIs was restricted to fathers or fathers and others. In addition, we demonstrated an absence of significant difference in the degree of exposure between children below or above two years of age. This could be explained by the fact that children in our study did not attend day care centres and spent most of the time indoors with their smoking fathers and/or others.

Regarding the age at which the first LRTI occurred, we found that exposed children had their first attack at a younger age than unexposed children. This is consistent with the findings of Wright et al., who reported that when the amount smoked was considered, children whose mothers were heavy smokers were younger at first LRTI and at both first wheezing and first nonwheezing LRTI than other children [*14*]. This relationship was also found by other investigators [*28,29*], who reported that younger children may be more susceptible to smoke exposure and its hazards because of their proximity to their parents and also because of the presence of a number of anatomical and physiological peculiarities of their airways or their immunological status.

Conclusion and recommendations

Household cigarette smoke exposure of preschool children may be a predisposing and/or aggravating factor for LRTIs whether wheezing or nonwheezing, infective or noninfective. A questionnaire for measurement of passive smoking may inadequately reflect the child's dose of environmental tobacco smoke and the use of an objective measure (e.g. CCR) is more accurate to evaluate critically a causal relationship between tobacco smoke exposure and childhood ill-health.

The findings of this study should prompt renewed efforts to discourage smoking in families, especially during the first five years of children's lives. It is extremely unlikely that we will ever be willing or able to regulate the smoking of adults in their own homes; therefore, we must employ strategies other than coercion to help parents reduce their smoking, both for their own health as well as for their children's well-being. It is suggested that paediatricians should increase their efforts to inform parents about the hazards of passive smoking to their children, especially the association between parental cigarette smoking and the increased risk of a child developing lower respiratory tract illnesses. This strategy may help parents stop smoking in the interest of their children's health.

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