

## Is There any Association Between Passive Smoking and Esophagitis in Pediatrics?

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Received: Sep 02, 2012; Accepted: Nov 11, 2012; First Online Available: Feb 13, 2013

**Abstract**

**Objective:** Exposure to environmental tobacco smoke (ETS) is one of the major factors of predisposing children to develop several hazardous health problems. We decided to investigate the association between nicotine, one of the nicotine metabolites and esophagitis in children with gastroesophageal reflux disease (GERD).

**Methods:** In a case control study 46 children suffering from esophagitis referred to endoscopy ward were recruited. The control group consisted of 45 healthy children. Urine samples were collected and urinary cotinine level (UCL) measured.

**Findings:** The mean age of esophagitis and control groups were  $5.11 \pm 2.93$  and  $6.72 \pm 2.8$  respectively. Sixty children were passive smokers; 31 of them had non-smoker parents. In control group, 32 (71.1%) children and in esophagitis group 29 (63%) children had non-smoker parents. The mean value of UCL in patients suffering from esophagitis was significantly higher than those in normal group ( $P=0.04$ ,  $24.98 \pm 6.4$  ng/ml vs.  $15.16 \pm 3.9$  ng/ml). Considering 50ng/ml as a cutoff point for UCL, it was significantly higher in passive smoker group than in non smoker group ( $P=0.02$ ). The mean cotinine level differed significantly in esophagitis and control group.

**Conclusion:** Our results indicate the increased risk of developing esophagitis in children with ETS exposure.

Iranian Journal of Pediatrics, Volume 23 (Number 2), Apr 2013, Pages: 194-198

**Key Words:** Cotinine; Children; Esophagitis; Passive Smoking

**Introduction**

Exposure to environmental tobacco smoke (ETS) is one of the major factors of predisposing children to premature death and several hazardous health problems<sup>[1]</sup>. It has been estimated that children who are exposed to cigarette smoke by their parents inhale nicotine equivalent to smoking 150 cigarettes actively per year which can have undoubted long-term adverse effect on their body<sup>[2]</sup>.

The major metabolite of nicotine in our body is cotinine which is regarded as most important determiner of passive smoking<sup>[3,4]</sup>. Cotinine excretes in urine, semen, hair, blood, and saliva and has a half-life of 17 hours in comparison to nicotine with a half life of approximately 2 hours<sup>[5]</sup>. Since it is difficult and unnecessary to draw blood from children, urine sample is commonly used to measure the extent of second-hand tobacco exposure in pediatrics<sup>[6]</sup>.

Tobacco smoke contains numerous amounts of

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free radicals and carcinogenic substances that can cause tissue damage resulting in a number of gastrointestinal disorders. It has been shown that ETS not only reduces mucosal blood flow, immunity, and functional mucosal barrier integrity of the gastrointestinal tract cells, but also lowers the closure pressure of esophageal and pyloric sphincter that can result in an increased risk of developing gastroesophageal reflux disease (GERD)[7]. GERD, considered as the most common gastrointestinal disease in children, can cause several complications like erosive esophagitis or Barret's esophagus. Esophagitis may present with several symptoms in children including heartburn, acid regurgitation, vomiting, and nausea. Esophagoscopy with biopsy is one of the most reliable ways of evaluating esophagitis in pediatric patients[8]. Therefore, we decided to investigate the association between smoking and esophagitis in patients with above-mentioned symptoms whose diagnosis was confirmed accordingly.

To our knowledge, the correlation between ETS exposure concerning crowding index in pediatric patients with esophagitis has not been yet investigated thoroughly. Therefore, in this study, we aimed at investigating the correlation between urinary cotinine level (UCL), as a determiner of passive smoking, and esophagitis in children.

## **Subjects and Methods**

### **Patient characteristics:**

In this case-control prospective study, a total of 46 consecutive children suffering from esophagitis aged 2 to 10 years referred to endoscopy ward of Children's Medical hospital, Tehran, were recruited. Only patients who had no other gastrointestinal anomalies were included in the study.

Another criterion of inclusion in the study was having confirmed diagnosis of esophagitis by biopsy and endoscopy. The control group consisted of 45 healthy kindergarten or school children aged 2 to 10 years who were enrolled in the study randomly. The children in the control group had no history of previous gastrointestinal anomalies. Moreover, volunteers who had esophagitis or GERD symptoms such as dyspepsia,

heartburn, nausea, and vomiting were excluded. Children's families in both groups were asked to answer a self-administered questionnaire providing information on smoking habits in the family, demographic information (including age, sex), home surface as well as some information about family members. The parents agreed to collect urine to measure cotinine. Additionally information was gathered to measure crowding index in both groups of children. The children were divided into two groups according to age: 2-4 years old and 5-10 years old.

### **Histopathological studies:**

Esophagus biopsies were taken in gastroenterology ward of Children's Medical Center. Specimens were fixed in 10% buffered formalin, embedded in paraffin and cut into sections of 3  $\mu$ m to be stained with hematoxylin and eosin. The specimens were reviewed and investigated for presence of esophagitis changes carefully. Only patients with histopathological confirmation of esophagitis changes were included in the study group.

### **Determination of urinary cotinine:**

Urine samples were collected in the morning, and samples were kept frozen at -70 °C until measurement. Cotinine was measured in the samples according to DRG German Institute using Competitive Enzyme Immunoassay. To date, different cut-off points for determining urinary cotinine in passive smokers and non-smokers have been proposed, we considered 50ng/ml of UCL as cut-off point to distinguish between passive smokers and non-smokers[9,10].

### **Crowding index:**

Crowding index defined as living area ( $m^2$ ) divided by number of people living in a dwelling was calculated for each individual.

### **Statistical analysis:**

Statistical analysis was performed using SPSS version 16.0.1 (SPSS Inc., Chicago, IL, U.S.A.). Normality of data was evaluated with the Kolmogorov-Smirnov test. The results were expressed as mean $\pm$ SD for parametric and mean $\pm$ SEM for nonparametric data. The statistical differences between proportions were determined by  $\chi^2$  analysis. Numerical data were evaluated

**Table 1:** Cotinine level, esophagitis and history of passive smoking in each group

Group	Cases with low cotinine level [n(%)]	Cases with high cotinine level [n(%)]	Total of cases [n(%)]
Controls	41 (91.1)	4 (8.9)	45 (100)
Esophagitis	43 (93.5)	3 (6.5)	46 (100)
Total	84 (92.3)	7 (7.7)	91 (100.0)

using analysis of variance, followed by Turkey's post hoc test. *P*-value <0.05 was considered as significant.

The ethic committee of Tehran University of Medical Sciences approved the study and the study was in accordance with the Helsinki Declaration of 1975.

### Findings

The mean age of subjects in esophagitis and control group were  $5.11 \pm 2.93$  and  $6.72 \pm 2.8$  years respectively ( $P > 0.05$ ). Of the total study population, 51 children (56% of the individuals) were males while 40 (44%) children were females. Additionally, 60 children were passive smokers and 31 of them had non-smoker parents. In control group 32 (71.1%) children and in esophagitis group 29 (63%) children had non-smoker parents. Patients with esophagitis mostly were presented with cough (23%), vomiting (16%) or poor weight gain (14%). Thirty one (34.1%) cases were passive smokers totally, of whom 25 (27.5%) cases had low and 6 (6.6%) high urinary cotinine level.

Prevalence of esophagitis was higher in children older than 5yr than younger children ( $P = 0.001$ ). Table 1 and 2 show the status of cotinine level, esophagitis and history of passive smoking in both groups.

Considering 50ng/ml as a cutoff point for UCL, the presence of UCL in smoker group was significantly higher than in non-smoker group ( $P = 0.02$ ). The mean value of UCL in patients suffering from esophagitis was significantly higher than in normal group ( $P = 0.04$ ,  $24.98 \pm 6.4$  ng/ml vs  $15.16 \pm 3.9$  ng/ml and odds ratio=0.7).

No association was found between gender and UCL within and between groups and also no correlation was found between patients' age and UCL.

The least and the most crowding index was 6 and 58.33 in total. The mean crowding index in each group is indicated in Table 3. No significant relation between crowding and esophagitis was seen ( $P > 0.05$ ). Odds ratio (=1.01) could not show any association as well.

In this study, cotinine to creatinine ratio was higher than 30ng/ml in 45% of the esophagitis group and 36% of the control group. Our result was not significant although it revealed higher rate in esophagitis group.

### Discussion

Several investigations have been conducted regarding adverse effects of ETS exposure in adults, while in pediatrics most studies have focused on correlation between ETS exposure and respiratory diseases<sup>[11,12]</sup>. In this case-control

**Table 2:** Cotinine level, esophagitis and history of passive smoking in both groups

Group	Cases with low cotinine level n (%)	Cases with high cotinine level n (%)	Total of cases n (%)
No history of smoking	59 (64.8)	1 (1.1)	60 (65.9)
history of smoking (passive smokers)	25 (27.5)	6 (6.6)	31 (34.1)
2-4 years old	31 (34.1)	6 (6.6)	37 (40.7)
5-10 years old	53 (58.2)	1 (1.1)	54 (59.3)

**Table 3:** Mean (SD) crowding index in each group

	Total	Control group	Esophagitis group	P value
<b>Mean Crowding index(m<sup>2</sup>/n)</b>	21.58 (SD=10.98)	21.3 (SD=9.23)	22.13 (SD=12.43)	0.06

SD: standard Deviation; m<sup>2</sup>/n : Home surface divided by family number

study we intended to investigate the relationship between esophagitis and UCL in children. Our results revealed that the mean UCL was higher in patients group than in the control group. Moreover, the odds ratio indicated that exposure to ETS increases the risk of developing esophagitis. The higher median UCL in esophagitis group also confirmed the same results. Our results are in line with the study of Wielkoszynski et al that proposed nicotine metabolites are higher in esophagitis patients than healthy children<sup>[13]</sup>. Shabib et al has also found that passive smoking is a risk factor for esophagitis in children<sup>[14]</sup>.

In our study, we measured UCL instead of using questionnaires, this makes our study more reliable than studies that are only based on history of self-administered questionnaires. Self-reported history of ETS exposure has a low validity and reliability, it may mainly result from reluctance of parents on providing data on their smoking habits<sup>[15]</sup>.

Additionally, air ventilation, smoking patterns, nicotine yield in different cigarette brands, and the time of exposure to ETS varies widely that can affect validity of questionnaires. However, by measuring biomarkers for recent ETS exposure the bias created by above-mentioned factors may be reduced.

According to our findings, the mean UCL in children whose parents were cigarette smokers was higher than in children with non-smoker parents, this suggests correlation between passive smoking and UCL. The odds ratio also confirmed this issue as well. On the other hand, UCL was found to be higher in younger children that can be caused by the longer time younger children spend in close proximity to their parents.

Crowding index did not differ in the two groups which may be due to unequal air conditioning, number of windows and smoking pattern in each condition. However, it is expected that the adverse effects of ETS be raised in high-density populations exposed to tobacco smoke.

Our study had its own limitations. The major limitation of our study was lack of a specific cutoff point for urinary cotinine in pediatrics. There are several studies in adults regarding urinary cotinine cutoffs for passive smokers, non-smokers and active smokers, while in children few studies have investigated the cotinine levels and more research is needed to assess the values<sup>[9]</sup>. On the other hand, uptake, distribution, metabolism, and excretion of nicotine vary widely in each individual that can affect the results accordingly. Another limitation of our study was due to the short half-life of cotinine that cannot determine the time, frequency and pattern of tobacco exposure. Therefore, long-term cotinine levels must be measured to evaluate the exact ETS exposure in children because the pattern of smoking may be different shortly before sampling. Other issue to be in mind is that although we tried to homogenize our cases and also controls, socioeconomic status and living areas may differ and it was unenvitable.

We chose controls from outpatient healthy consecutive cases who visited the hospital for general health care or vaccination. We could not perform endoscopy or biopsy and the possibility exists that controls had esophagitis but the physicians examined children and found clinically no signs and symptoms of gastrointestinal disease.

## Conclusion

We show that the mean cotinine level differed significantly in esophagitis and control group; and it indicates the increased risk of developing esophagitis in children with ETS exposure. More investigations in larger series are needed in this issue to prevent the long-term consequences of ETS on children's health.

### Acknowledgment

The work was financially supported by Tehran University of Medical Sciences and was the postgraduate thesis of Dr Roohallah Soleymani. The authors thank Mrs. Heshmat Irani and Leila Kashi for their kind technical support.

**Conflict of Interest:** The Authors declare that there is no conflict of interest.

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