Cigarette smoking and second-hand smoking exposure in adolescents with chronic kidney disease: a study from the Midwest Pediatric Nephrology Consortium

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Abstract

Background. Smoking and second-hand smoking [SHS] cause significant cardiovascular mortality and morbidity. In healthy individuals and adults with chronic kidney disease [CKD], cigarette smoking is associated with albuminuria, increased risk for CKD, increased graft loss and progression of renal insufficiency. In children, SHS has been associated with higher blood pressure variability, blood pressure load, elevated C-reactive protein and decreased cognitive function. Using a survey document and urine cotinine, we sought to investigate prevalence of cigarette use and SHS in adolescents with CKD.

Methods. A cross-sectional study was conducted in which adolescents aged 13 to 18 years with CKD were asked to complete a single anonymous self-administered survey. In addition, a single freshly voided urine sample for cotinine measurement was obtained from eligible subjects.

Results. Of 182 subjects, 60 (34%), 25 (14%) and 93 (52%) were transplant recipients, were dialysis dependent and had a glomerulopathy, respectively. Renal status was lacking in four. Twenty-four per cent (24%) had smoked at some point in their lives, and 13% had smoked within the last 30 days of taking the survey. Fifty-two per cent (52%) of all respondents reported living with an adult who smoked, and 54% reported having friends that smoked. Forty-seven per cent (47%) and 44% of those who had never smoked lived with an adult and had friends that smoked, respectively. There was a discrepancy rate of 7% between self-reported non-smokers and urine cotinine, suggesting smoking rates were higher. The highest cotinine/creatinine levels among the non-smokers were observed in those who lived with a smoker and had friends that smoked.

Conclusion. Among adolescents with CKD, cigarette smoking and SHS exposure are prevalent and may be important variables to consider when evaluating renal and cardiovascular risk factors and outcomes in children with CKD.

Keywords: adolescents; cigarettes; CKD; second-hand smoking

Introduction

Tobacco use is the leading preventable cause of cardiovascular morbidity and mortality worldwide, and at least 35 000 deaths occur annually in the USA due to second-hand smoking (SHS), which increases the risk of cardiovascular disease [CVD] by as much as 30% [1]. Although the
prevalence of smoking in the USA has decreased, ~15–20% of adolescents use tobacco, with cigarette smoking being the most common form. Cigars, chewing and smokeless tobacco are other popular modes of tobacco consumption within this age group [2].

CVD is common in children with chronic kidney disease (CKD) due to multiple traditional and CKD-related risk factors [3]. In healthy adults, tobacco use is a well-known risk factor for CKD. In adults with CKD, cigarette smoking is associated with the development of end-stage renal disease (ESRD), kidney allograft loss, chronic allograft nephropathy, recipient death and increased incidence of cardiovascular events post kidney transplant [4–8]. In a recent review, Orth and Hallan concluded that smoking is an important renal risk factor and that nephrologists have to invest more efforts to motivate patients to stop smoking [9].

Unfortunately, there are no studies that have investigated the prevalence of smoking and SHS exposure in the paediatric CKD population. In addition to the survey instrument, the use of an objective parameter to measure tobacco exposure is important due to discrepancy between self-reported tobacco use and tobacco metabolites in body fluids [10]. Urine cotinine is a stable metabolite of nicotine that is not affected by the presence of other substances or renal function and has a half-life of ~20 h [11]. Urine cotinine levels are highly correlated with plasma cotinine concentrations [12], and contribution from non-tobacco sources is minimal [13]. Hence, we conducted a multi-centre study to determine the prevalence of cigarette use and SHS exposure in adolescents with CKD using both a survey and urine cotinine measurement.

Materials and methods

Subjects were recruited from paediatric nephrology outpatient clinics at seven centres from the Midwest Pediatric Nephrology Consortium (MWPNC) (http://mwpnc.org/). We included patients from 13 to 18 years from the following three groups: (i) documented primary or secondary glomerulopathy; (ii) receiving chronic dialysis; and (iii) functioning renal transplant. The Institutional Review Board of each participating centre approved the study. Written informed consent and assent were obtained from parents and subjects where applicable.

Subjects anonymously answered 12 self-administered questions during a routine clinic visit. The survey (Figure 1) was modified and used, with permission, from the Dayton area drug survey. Subjects answered the questionnaire in private without parent/guardian participation or assistance, placed the completed survey in an envelope and sealed the envelope. Current and lifetime smokers were defined as having smoked within the last 30 days of taking the survey and having ever smoked before, respectively.

A single freshly voided 2–5 mL sample of urine was collected at the time of the clinic visit from those with glomerulopathy or functioning renal transplant only. Dialysis-dependent subjects were excluded from urine collection to prevent selection bias because some were anuric. Samples were immediately frozen at −20°C until analysis. Cotinine assay was performed by the Tobacco Exposure Biomarkers Section, Division of Laboratory Sciences, Centers for Disease Control and Prevention, Atlanta, GA via the liquid chromatography-atmospheric-pressure ionization tandem mass spectrometry [LC API MS/MS] method. Limit of quantification was 0.036 ng/mL. Urine creatinine was measured on the Roche Hitachi Mod.
Since correction of urine cotinine for creatinine concentration improved correlation between urine and plasma cotinine [12], cotinine/creatinine ratios were compared between smokers and non-smokers and within non-smokers, between those exposed versus not exposed to SHS through living with a smoker and/or having friends who smoke. Because of the skewed nature of the variables, comparisons were made with Wilcoxon rank sum tests or Kruskal–Wallis one-way analysis of variance on ranks. Chi-square or Fisher’s exact tests were used to determine associations between demographic and other variables with current and lifetime smoking. Data were analysed with SAS version 9.2 for Windows (SAS Institute, Cary, NC).

Cotinine/creatinine ratios (ng/mg) are presented as medians with interquartile ranges (IQR). A urine cotinine level >200 ng/mL was used as a cut-off for defining discrepancies between self-identified non-smokers and urine cotinine. All response frequencies reported represent non-missing data.

Results

Survey results

A total of 182 (n = 182) adolescents were enrolled; demographics are shown in Table 1. Twenty-three (13%) and 43 (24%) subjects were current and lifetime cigarette smokers, respectively. Twenty (11%) had smoked within the past 24 h of participating in the study.

There was no association between the categories of smoking, gender and category of CKD (Table 2). Fifteen per cent of transplant recipients and 14% of those with a primary or secondary glomerulopathy were current smokers. There was one current smoker among the 25 dialysis subjects. Adolescents in the 16–18-year age group were significantly more likely to be lifetime smokers or current smokers than patients in the 13–15-year age group. White patients were significantly more likely to be lifetime smokers than the non-white patients. Having at least one friend who smoked and living with a smoker were significantly associated with being a current smoker or a lifetime smoker. Forty-nine per cent of the lifetime smokers began smoking in the eighth grade or earlier, with 23% beginning in the sixth grade or earlier. For the current smokers, 52% began smoking in the eighth grade or earlier, with 22% beginning in the sixth grade or earlier. Of the 23 current smokers, 17 (74%) had tried to stop smoking.

Fifty-two per cent of all respondents reported living with an adult who smoked, and 54% reported having friends that smoked. Among the 139 who never smoked, 65 (47%) were exposed to SHS by living with a smoker, and 61 (44%) had friends that smoked. Exposure to SHS at home occurred in 30 (32%) transplant recipients, 12 (13%) dialysis patients and 51 (55%) with a glomerulopathy. There were no significant differences in gender, race or type of CKD among those exposed versus not exposed to SHS. Age was not associated with living with a smoker, but a higher percentage of non-smokers in the 16–18-year age group have friends that smoked (61% of 76) compared with non-smokers in the 13–15-year group (33% of 77, P = 0.001).

There were 174 responses to question 10 about whether the patient believes people hurt themselves and their kidneys when they smoke cigarettes. Forty-five (26%) indicated ‘none/little/don’t know’, 19 (11%) indicated ‘some’
and 110 (63%) indicated ‘a lot’. There were no differences in type of CKD among those who answered ‘none/little/don’t know’. The subjects in the younger age group were more likely to state that smoking was harmful than the patients in the older age group (Table 3).

### Cotinine results

Of the 182 subjects enrolled, 157 were eligible for urine collection; cotinine levels were available for 130 (83%), and creatinine levels were obtained from 121 (77.1%). Nine subjects who indicated that they had not smoked in the previous 24 h had urine cotinine levels >200 ng/mL, giving a discrepancy rate of 6.9%. The results of all statistical analyses of cotinine and cotinine/creatinine ratios were similar, so only cotinine/creatinine data are presented. The median (IQR) values for these subjects was 971.5 (1613.8) for cotinine/creatinine ratio. These subjects were excluded from the comparisons between those who smoked in the previous 24 h versus those who did not. Urine cotinine/creatinine ratios were significantly higher in those who indicated they smoked in the past 24 h compared with those who had not (Table 4). Similar findings were observed among current smokers versus non-smokers, and lifetime smokers versus never smokers (Table 4).

Within the self-reported non-smoking subjects with cotinine levels <200 ng/mL, cotinine/creatinine levels were significantly higher in those who had friends who smoke versus those who did not and those who lived with a smoker versus those who did not. The highest cotinine/creatinine levels among the non-smokers occurred in those who lived with a smoker and had friends who smoked (Table 5).

### Discussion

While there is extensive literature about tobacco use in healthy children and adolescents, there are few data about tobacco use in adolescents with CKD and other chronic illnesses. To the best of our knowledge, this is the first study investigating tobacco use and exposure in the paediatric CKD population.

We observed that smoking and SHS exposure are common in adolescents with CKD. Smoking was more common in the older adolescents, and white adolescents were more likely to have smoked at some point than non-white adolescents. Adolescents with CKD who live with a smoker or who have friends that smoke are more likely to be smokers. Interestingly, older adolescents were less likely than their younger peers to view smoking as harmful. Urine cotinine levels were significantly higher in non-smokers who reside with a smoker compared with non-smokers who do not reside with smokers. We also observed a significant incremental increase in urine cotinine directly related to SHS exposure. The discrepancy rate between self-reported smoking and urine cotinine levels was ~7%.

In adults with CKD, tobacco use is a well-known risk factor for cardiac disease, albuminuria, hypertension and kidney allograft dysfunction and loss [4–8]. In healthy children, SHS exposure evaluated with a bio marker is associated with endothelial dysfunction, altered lipid profiles and elevated mediators of inflammation such as C-reactive protein (CRP) and homocysteine [14–19]. Other associated effects of SHS include higher blood pressure variability and increased blood pressure load and decreased bone mineral density [20,21].

A national study in teenagers reported that 22% were current smokers and 51% were lifetime smokers [22]. This is higher than the rate of current (13%) and lifetime smokers (24%) that we observed in our study. Reasons for the differences could be differences in methodology, patient population and different demographics, so exact comparisons are not valid. Nevertheless, it suggests that teenagers with CKD may be less likely to smoke compared with their peers in the general population. Speculated rea-

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**Table 3.** Comparison between ‘How much do people hurt themselves/their kidneys when they smoke?’ versus age groups  

<table>
<thead>
<tr>
<th>Group</th>
<th>13–15-year olds</th>
<th>16–18-year olds</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>No. (%)</td>
<td>No. (%)</td>
<td></td>
</tr>
<tr>
<td>None/little/don't know</td>
<td>18 (22)</td>
<td>27 (29)</td>
<td>0.004</td>
</tr>
<tr>
<td>Some</td>
<td>3 (4)</td>
<td>16 (17)</td>
<td></td>
</tr>
<tr>
<td>A lot</td>
<td>60 (74)</td>
<td>50 (54)</td>
<td></td>
</tr>
</tbody>
</table>

The median and IQR (in parentheses) values are reported.

**Table 5.** Urine cotinine/creatinine ratios for non-smokers grouped by SHS exposure  

<table>
<thead>
<tr>
<th>Group</th>
<th>Cotinine/creatinine ratio (ng/mg)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Have friend(s) who smoke = No</td>
</tr>
<tr>
<td></td>
<td>Have friend(s) who smoke = Yes</td>
</tr>
<tr>
<td></td>
<td>P-value</td>
</tr>
<tr>
<td></td>
<td>Live with smoker(s) = No</td>
</tr>
<tr>
<td></td>
<td>Live with smoker(s) = Yes</td>
</tr>
<tr>
<td></td>
<td>P-value</td>
</tr>
<tr>
<td></td>
<td>Friend(s) = No; Live with = No</td>
</tr>
<tr>
<td></td>
<td>Friend(s) = Yes; Live with = No</td>
</tr>
<tr>
<td></td>
<td>Friend(s) = No; Live with = Yes</td>
</tr>
<tr>
<td></td>
<td>Friend(s) = Yes; Live with = Yes</td>
</tr>
<tr>
<td></td>
<td>P-value</td>
</tr>
</tbody>
</table>

The median and IQR (in parentheses) values are reported.
sons for our observations could be that adolescents with CKD may have more frequent medical evaluations with the nephrology team, may have more direct parental supervision or may be more concerned about the deleterious consequences of smoking compared with their healthy peers. On the other hand, if the discrepancy rate we observed is taken into consideration, our study suggests current smoking rate in our patient population is comparable with national figures, a disturbing finding considering the extent of cardiac morbidity and mortality in the paediatric CKD population. Compared with Caraballo et al. [23], who described a discrepancy rate of 2.1% between self-reported adolescent non-smokers and serum cotinine, our rate was higher despite the anonymous nature of the study, thus leading to a relatively low but false rate of self-reported tobacco use. Stigma attached to smoking and fear of care providers or medical personnel discovering smoking habits are potential reasons for this discrepancy. Similar studies in children and adolescents with sickle cell disease, juvenile rheumatoid arthritis and cystic fibrosis did not evaluate for nicotine metabolite, so rates of discrepancy could not be ascertained to determine if higher discrepancy rates are unique to children with chronic illness [24].

SHS exposure rate at home among patients who never smoked was 47% in our study. This is comparable with the 55% rate reported in a national study [25]. We were surprised by the high rate (44%) of teenagers who never smoked who had friends that smoked, suggesting that these self-reported non-smokers may be at risk for smoking in the future. More important is the significant and gradual increase in cotinine levels directly related to increasing SHS exposure we demonstrated. Based on available literature, our finding raises the possibility that children with CKD exposed to SHS may have an increased risk for CVD. It stands to reason that chronic exposure to SHS independently or together with hypertension and dyslipidaemia, traditional risk factors for CVD, may accelerate not only the progression of CKD but also increase adverse long-term cardiovascular outcome in these adolescents. Indeed, it was recently reported that non-smoking adolescents with CKD demonstrated a significantly higher urine protein to creatinine ratio and higher prevalence of systolic hypertension in those exposed to SHS compared with those not exposed to SHS [26].

Of 23 subjects who acknowledged being regular smokers, 17 (74%) had tried to stop smoking, thus raising the issue of nicotine dependency. If appropriate intervention is not offered, it is possible that these adolescents may become chronic adult smokers with CKD. The importance of early and aggressive tobacco avoidance counselling is demonstrated by the high percentage of smokers who started smoking in the sixth grade or earlier; this especially raises some concern because of studies that have demonstrated that the earlier in life children or adolescents use tobacco, the more likely they are to become regular smokers [27].

The limited/poor knowledge of the ill effects of tobacco in over a quarter of subjects across the spectrum of smokers and non-smokers was unexpected. Even more surprising was that the younger age group was more likely to state that smoking was harmful than the older age group. This could be due to genuine lack of knowledge or impaired judgment associated with risky behaviour in older adolescents. Regardless of the explanation, it underscores the importance that clinicians not assume that older adolescents understand or accept the harmful effects of smoking.

As in the general population, we observed a strong association between residing with a smoker and smoking in our cohort, confirming that this strong association is present in families with a child with a chronic illness. The higher rate of smoking in the white adolescents was an unexpected finding also, and we are unsure of its significance but suspect it may be a reflection of a national trend showing that fewer black teens smoke cigarettes [22]. In adults, medication non-adherence has been associated with tobacco use [28,29], and similar findings have been noted in adolescents with chronic illness [24]. Although it is unknown if a similar association exists in adolescents with CKD, considering the consequences of medication non-adherence especially in the adolescent transplant population, it may be deserving of study as another way to evaluate the potential non-adherent patient.

A limitation of the study was the blinded fashion of the study design, which did not permit correlation of tobacco use and SHS exposure with degree of CKD, body mass index, blood pressure and other cardiovascular risk factors. Other limitations include the small sample size, lack of data on refusal rate by potential subjects and its regional nature. Despite these limitations, we have provided the first data on smoking behaviour, SHS exposure and knowledge about smoking in adolescents with CKD. We have also confirmed objectively that in adolescents with CKD, SHS may be an important unrecognized variable that may influence CKD progression and cardiovascular outcomes. Larger studies investigating this public health issue among the paediatric CKD population are essential to improve outcomes.

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Conflict of interest statement. None declared.

References
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