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Household air pollution and lung cancer risk among never-smokers in Nepal

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ABSTRACT

More than half of the global population relies on biomass fuels (wood, charcoal, crop residue, dung) for cooking and/or heating purposes. Household air pollution (HAP) resulting from the use of these solid fuels is of particular concern, given the overall prevalence as well as the intensity of exposure and the range of potential adverse health outcomes. Long term exposure to HAP is a major public health concern, particularly among women and children in low and middle income countries. In this study, we investigated the association between exposure to HAP resulting from combustion of biomass and lung cancer risk among Nepalese population. Using a hospital-based case-control study (2009–2012), we recruited 606 lung cancer cases and 606 healthy controls matched on age (±5 years), gender, and geographical residence. We used unconditional logistic regression to compute odds ratios (ORs) and 95% Confidence Intervals (95% CI) for lung cancer risk associated with HAP exposures, adjusting for potential confounders (tobacco use, TB status, SES, age, gender, ethnicity, and exposure to second hand smoke. In our overall analysis, we observed increased risk of lung cancer among those who were exposed to HAPs (OR: 1.77, 95% CI: 1.00–3.14). A more detailed analysis stratified by smoking status showed considerably higher risk of lung cancer associated with increasing duration of exposure to HAP from biomass combustion, with evidence of a borderline exposure–response relationship ($P_{trend}=0.05$) that was more pronounced among never-smokers ($P_{trend}=0.01$). Our results suggest that chronic exposure to HAP resulting from biomass combustion is associated with increased lung cancer risk, particularly among never-smokers in Nepal.

1. Introduction

Household air pollution (HAP) resulting from incomplete combustion of solid fuels (wood, coal, agricultural waste, charcoal, and animal dung) for cooking and/or heating is a major global public health concern (Lim et al., 2012). Recent estimates suggest that 3.5 million deaths are attributable to HAP, while additional 500,000 deaths are attributed to outdoor air pollution originating from indoor source annually (Lim et al., 2012). The vast majority of these deaths occur in low and middle income countries (LMIC) where a significant proportion of the population relies on solid fuels for cooking and/or heating (Gordon et al., 2014; IOM, 2007; Perez-Padilla et al., 2010; WHO, 2014). HAP is a complex mixture of pollutants including particulate matter, sulfur oxides, nitrogen oxides, carbon monoxide, polycyclic aromatic hydrocarbons, formaldehyde, and dioxins, to name few (Ding et al., 2012; EPA, 2007; Naeher et al., 2007; Pruneda-Álvarez et al., 2012; Ward et al., 2008). An increasing body of literature has illustrated the role of HAP in disease etiology of both acute and chronic health outcomes with women and children in LMIC bearing disproportionate disease burden (Adetona et al., 2013; Guarnieri et al., 2014; Lim et al., 2012; Naeher et al., 2007; Pokhrel et al., 2013; Pradhananga et al., 2009; Romieu et al., 2009; Smith et al., 2010, 2000; Smith-Sivertsen et al., 2009; WHO, 2014, 2013).

The carcinogenicity of HAP exposure was extensively evaluated by an expert panel convened by the International Agency for Research on Cancer in 2006 (IARC, 2010). The panel classified HAP from coal as a known human carcinogen (IARC Group 1), while HAP from biomass was classified as a possible human carcinogen (IARC Group 2A), citing lack of epidemiologic evidence (IARC, 2010). Since then few new studies have investigated the

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carcinogenicity of HAP particularly from biomass combustion (Sapkota et al., 2013, 2008) while others have conducted systematic review and meta-analysis of the literature (Bruce et al., 2015; Josyula et al., 2015; Martin et al., 2013). However, few studies have comprehensively investigated the risk of HAP related to biomass on lung cancer risk in high risk areas such as Nepal, where 75% of the population heavily relies on biomass for cooking (Ghimire et al., 2011).

Nepal is one of the poorest countries in the world with an estimated 24% of the nearly 30 million people living under $1 a day (WHO, 2009). Lung cancer is the most common cancer in men and third most common in women in Nepal (IARC, 2012). Compared with all cancers in Nepal, lung cancer accounts for 13% of new cancer incidence and 15% of cancer related mortality (IARC, 2012). Although, tobacco use is decreasing in Nepal, lung cancer incidence continues to rise and is projected to double by the year 2035 (Ferlay et al., 2010; Ghimire et al., 2011; IARC, 2012; WHO, 2009). In this study, we evaluate the role of HAP in lung cancer etiology in Nepal, one of the highest exposed areas globally.

2. Methods

A hospital-based case-control study was conducted at B.P. Koirala Memorial Cancer Hospital (BPKMCH), Chitwan District, Nepal, from November 2009 through December 2012. Located 150 km southwest of Kathmandu, BPKMCH is the major cancer hospital in Nepal. The details regarding participant recruitment and biological sample collections have been described previously (Hashibe et al., 2011; Raspanti et al., 2015). In brief, 606 incident lung cancer cases and 606 age ($\pm$5 years) and gender matched controls were recruited from the hospital. The inclusion criteria for a lung cancer case were: 1) 18 years of age or older 2) resident of Nepal for at least five years and 3) were admitted to BPKMCH. The eligible cases were recruited as soon as possible following lung cancer diagnosis with a target interval of one day and a maximum interval of 4 weeks. A trained medical staff member reviewed medical records to extract relevant diagnostic information, including the date and method of diagnosis, histological type, tumor location, stage, and grade. Final diagnosis of lung cancer was confirmed with histological, cytological, or X-ray based evidence.

The controls were visitors at BPKMCH excluding friends and family members of participating lung cancer cases, and were frequency matched by age, gender, and geographic residence. Prior to field implementation, standardized lifestyle and food frequency questionnaires were translated into Nepali language by native speakers and pilot tested in the field (Hashibe et al., 2011). Locally trained interviewers collected information on demographic characteristics, education, residential mobility throughout lifetime, type of cooking and heating fuel used at each residence, occupational history, and family history of cancer. The study was approved by the Institutional Review Board at the University of Utah, University of Maryland as well as the Government of Nepal (Nepal Health Research Council).

We computed a lifetime profile of exposure to HAP based on duration and type of solid fuel used at each reported residence across the lifespan. We defined solid fuel as wood, charcoal, agricultural waste and dung while modern fuel is defined as electricity and natural gas. For this analysis, individuals that predominantly used kerosene ($>$50% of their lifetime) were excluded (n=7) because while kerosene is a modern fuel, recent studies show that it has considerable adverse health impact (Bates et al., 2013; Epstein et al., 2013; Lam et al., 2012; Pokhrel et al., 2010). A variable reflecting duration of HAP exposure was created for each fuel type. These product specific variables (wood, agricultural waste, dung) were summed to generate total years of HAP exposures resulting from biomass combustion.

Tobacco user was defined as someone who smoked greater than 100 cigarettes or similar tobacco product in their lifetime. Furthermore, we calculated tobacco pack years based on the duration as well as frequency of each tobacco product smoked as described previously (Raspanti et al., 2015). Exposure to second-hand smoke (SHS) was captured by participant's indication of living or working with someone who actively smoked tobacco. We computed socioeconomic status (SES) index based on level of education, household monthly average income, and crowdedness in the home (number of individuals per room) (Ghosh and Ghosh, 2009; Sapkota et al., 2008). This SES index reflects the contributions of multiple indicators and a high value on this index can be interpreted as high SES. We categorized the SES index into quartiles which reflect low, mid-low, mid-high, and high categories.

Odds ratios (OR) and 95% Confidence Intervals (95% CI) were calculated using multivariate logistic regression models to investigate the relationship between HAP exposure and lung cancer risk. Tests for linear trends were performed by treating the categorical variables as continuous predictors in the logistic regression models. We included age, gender, ethnicity, tobacco use status, SHS exposure, and SES index (in quartiles) as confounders in the model as these are known contributors to lung cancer (Di Cesare et al., 2013; Hashibe et al., 2011; Raspanti et al., 2015), and were significant in the univariate analysis. We also investigated the influence of residential characteristics such as ventilation (window, chimney, or none) and self reported level of smokiness during cooking (none, some smokiness but not enough cause teary eyes, enough smokiness to cause teary eyes) by including them in the statistical model because physical characteristics of homes are known to contribute to the concentration and dispersion of HAP related pollutants (Batterman et al., 2006; Pokhrel et al., 2005; Seow et al., 2015; Zuraimi and Tham, 2008). Furthermore, we included physician diagnosed tuberculosis (TB) as a confounder in the model as prior studies have highlight the link between TB and lung cancer risk as well as solid cooking fuels potential contribution to TB (Huang et al., 2015; Lin et al., 2014; Pokhrel et al., 2010; Skowroński et al., 2015). We included interaction terms for HAP exposure and gender, as well as HAP exposure and ventilation; however, these terms were not statistically significant and were removed from the final model.

3. Results

The demographic characteristics of the study population are presented in Table 1. In general, cases and controls were similar in terms of ethnicity and family income. Lung cancer cases tended to be slightly older, male, and less educated. The prevalence of smoking, as expected, was considerably higher among cases (Table 1).

As shown in Table 2, the association between HAP exposure and lung cancer risk was statistically significant based on the overall analysis (OR 1.77; 95% CI 1.00–3.14). Furthermore, we observed significant increased lung cancer risk among tobacco users (OR 5.61; 95% CI 3.97–7.91), older age (OR 1.03; 95% CI: 1.01–1.04), and females (OR 2.03; 95% CI 1.55–2.67). Participants who had prior physician diagnosed TB had a considerably higher lung cancer risk compared to those who did not (OR 2.30; 95% CI 1.50–3.51). We also observed significant decreased lung cancer risk among those with higher SES status. We did not observe a significant association between lung cancer and presence of a separate kitchen, ventilation, or self-reported smokiness level during cooking and these variables were not included in the final model. Lastly, participants who reported living or working with a smoker